A Blueprint for Defining Health:
Making Medical Genetics in Canada, c. 1935-1975

Fiona Alice Miller

A thesis submitted to the Faculty of Graduate Studies in partial fulfilment of the requirements for the degree of
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Abstract

This project explores the making of medical genetics through analysis of two research communities in Ontario, Canada – Toronto and London. I examine the research of Toronto workers from the mid-1930s through the 1960s, and of London workers in the 1950s and 1960s. I also examine the efforts of these workers to consolidate institutional structures locally and nationally, and generate genetic services through the 1970s.

Medical genetics developed at the intersection of the research university and the research hospital. It drew financial support, collaborators, diseased and anomalous bodies, and distinct traditions of knowledge from these two domains – the biological, and the medical. While medical genetics was initiated in the inter-war and war-time years, it remained marginal until after the Second World War when the field participated in the expansion of biomedicine. Growth was further aided by disciplinary consolidation in North America, beginning in the late 1940s, which merged Canadian and US workers.

In the inter-war and war-time years, human and medical genetics was a minor undertaking in North America. The marginality of the Toronto community was symbolized and sustained by the social relations and symbolism of gender: the preponderance of women workers, the 'backwardness' of Canadian science, and the reliance upon a relatively neglected research tool – dermatoglyphics, or the study of skin patterns on the hands and feet. Toronto workers nonetheless built a robust indigenous tradition of research, concerned with the influences of both environment and heredity in disease causation.

After the war, workers in Toronto and London were integrated into the wider community of human and medical geneticists. Yet extant traditions of workplace organization, technical skill and disease management were still relevant. The making of the sex chromosome anomalies drew on the London community's expertise with the sex chromatin and the intersex, and Toronto workers drew on their expertise with the 'Mongol' (as the condition was called) and dermatoglyphics in making sense of the autosome anomalies. Finally, the coordination and reorganization of medical genetics locally, provincially and nationally in the 1960s and 1970s was informed by both local and generic approaches to genetic science and genetic disease.

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When I completed my Master's Thesis and it was time to finalize the forms I briefly considered the question of an acknowledgements page and then put the question aside. I have since regretted that refusal of ritual. There are too many people who deserve my thanks.

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Since I neglected to do so before, I want to take this opportunity to thank faculty members at the University of Victoria where I did my Master's degree. My sincere thanks go to Angus McLaren, my supervisor at the time, who taught me much, guided me through that hurdle and has been unfailingly supportive since. I also want to thank Peter Baskerville, whose kind and firm words helped me to believe that a Department of History was a good place for me to be.

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Lisa Chilton, James Moran, Peter Ives, Steven Penfold, Adele Perry and Sharon Wall, have been friends, advisers, allies and combatants, and I thank them for this. I owe thanks also to Jack Saywell, for welcoming me to the Department in his wonderfully caustic way, and to Bettina Bradbury, for supporting me through my comprehensive exams.

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Introduction

Overview of Dissertation

In the Spring of 1999, Toronto's Hospital for Sick Children became the new home for the "Genome Database" – the "official central repository for genomic mapping data resulting from the Human Genome Initiative." As an internationally important facility for research in medical genetics, Sick Kids was a logical institution to assume management of this "worldwide research effort to analyze the structure of human DNA."[1]

More than sixty years earlier, beginning in the mid-1930s, scientific studies of the Dionne quintuplets initiated a young zoologist into the study of human heredity. That scientist, Norma Ford Walker (née Norma Ford),[2] would come to lead a research school that would forge the human and medical genetics tradition at the university and at the Hospital for Sick Children in Toronto – a research tradition that I call the 'Ford Walker school.'[3]

Between these two events lies a complex history of the emergence and expansion of medical genetics in Toronto and, indeed, around the world. This project seeks to explore the first four decades of that history through a close analysis of developments in two research communities in Ontario, Canada – Toronto and London. These case studies detail local and particular approaches to the social and technical organization of medical

genetics research and applied practices, but also illuminate the role of broader structures of knowledge, institution and disease identity in the making of medical genetics.

The Toronto community stands at the center of my study serving as the basis for a continuous narrative of growth and change. I examine the research of Toronto workers during the period of Ford Walker's tenure, from the mid-1930s through the early 1960s, and for the remainder of that decade. I also examine the leadership of Toronto-trained and Toronto-based workers in consolidating institutional structures locally and nationally and generating genetic services in the 1970s. During this latter period, from the early 1960s through the 1970s, the Toronto community was led first by an ex-student of Ford Walker's, Margaret Thompson, and then by a representative of the "new biology," Louis Siminovitch.[4]

The London research community assumes a somewhat peripheral position in relation to the total story told here. Murray Barr, its head, was one of Canada's more famous medical researchers. In 1949, he announced the identification of a biological marker of sex visible in the cell nucleus of a female mammal. This discovery had theoretical implications for mammalian and thus human cytogenetics, yet it was a decade before Murray Barr and his students and colleagues engaged in research relevant to that emerging community. Barr's primary discipline was Microscopic Anatomy and he had an enduring interest in neuroanatomy. He never fully assumed the identity of a human geneticist. Indeed, he has been christened by one of his collaborators as the "reluctant geneticist."[5] Not until the 1960s did the research of members of the London community demonstrate clear intellectual and professional links to medical genetics. Thereafter,

London workers were integrated into provincial and national efforts to co-ordinate the profession and consolidate the emerging domain of clinical genetics in the 1970s.

In Toronto and London, Ontario, medical genetics was forged through local traditions of workplace organization, technical skill and disease management which were permeated by the social relations and symbolism of gender. The Toronto community was female dominated in an era when leading-edge science was definitely not 'women's work.' In the inter-war and war-time years, when human and medical genetics was a minor undertaking in North America, the marginality of the Toronto community was symbolized and sustained by the preponderance of women workers, the 'backwardness' of Canadian science, and the reliance upon a relatively neglected research tool: dermatoglyphics, or the study of skin patterns on the hands and feet. As the Toronto community grew, in the era of post-World War Two largesse, and was integrated into the rapidly institutionalizing discipline of human genetics in North America, local traditions were not entirely lost. While responding to the growth opportunities offered by the study of genetic-metabolic disease and cytogenetic anomaly, and the practical work of heredity counseling, genetic screening and prenatal diagnosis, workers in Toronto and London drew on extant traditions of disease metaphor and research technique. Toronto-trained workers re-tooled dermatoglyphics to help make sense of cytogenetic anomalies, drawing on metaphors of the 'Mongol' – as persons with Down's syndrome were then termed. And in London, Ontario, where 1950s sex chromatin research had led Murray Barr to the study of the intersex, 1960s studies preserved the sex chromatin technique, and the associated metaphors of sexual anomaly, in studies of sex chromosomes. Finally, the

coordination and reorganization of medical genetics locally, provincially and nationally in the 1970s was informed by long-standing traditions of contingency in the meaning of genetic disease, and a corollary willingness to re-interpret the meaning of medical genetics.

These local peculiarities were operative within broader structures of knowledge, institutional infrastructure and disease identity which are generalizable to the discipline as a whole. Medical genetics developed at the intersection of the research university and the research hospital, and allied clinical facilities. The nascent discipline drew financial support, collaborators, diseased and anomalous bodies and a facilitative research ethos from these two environments.[6] Indeed, medical genetics was constituted through the merging of the distinct traditions of knowledge housed within these two domains – the biological on the one hand, and the medical and clinical on the other. Medical genetics was informed by the biological disciplines of genetic science, and the changing emphases placed on the eugenic ideal therein. But it was also informed by independent, rather than simply derivative, medical sciences, by the clinical imperative to make sense of illness, and by the historically contingent meanings of genetic disease. Finally, while medical genetics was initiated in the inter-war and war-time years, it was consolidated within the context of the expansion of biomedicine in the post-World War Two era. Growing financial, institutional and political enthusiasm for biomedicine spurred the growth of individual communities engaged in medical genetics research and applied practices and fostered their integration into a coherent discipline that was North American in its scope and identity, merging Canadian and US workers.

The Best-Laid Plans ...

My study of the evolution of medical genetics in Canada differs in instructive respects from my original intentions. When I set out upon this project my primary interest was the science of medical genetics and my goal was to bring the tools of the "constructivist" tradition in science studies to bear in understanding the knowledge-producing practices and products of research in this highly significant field.[7] Relying heavily on the historical work of practitioners, notably the collection edited and in part written by Hubert Soltan, I turned my attention to two research communities where work of relevance to medical genetics had been pursued, and where pioneering Canadian efforts had been housed.[8] Since Hubert Soltan was trained by Norma Ford Walker in Toronto, and spent his professional working life in London – initially with Murray Barr – it is perhaps no surprise that these two communities, and these two individuals, became the focus of my study.

As an historian, my interest was with the period after the Second World War when medical research expanded under the aegis of growing state support and popular enthusiasm. This interest corresponded well with the study of medical genetics, which seemed to be a primarily post-war phenomenon. I fixed the starting date for my study at 1949. In that year, Ford Walker's title at the University of Toronto was changed from Associate Professor of Human Biology to Associate Professor of Human Genetics. In that

year also, Murray Barr and his graduate student, Ewart Bertram, published their discovery of sex chromatin – an event that seemed to initiate the London group's involvement in cytogenetic research. I fixed the end-date for my study at 1976. At that time, an Ontario Task Force on Genetic Services submitted its report declaring the intention of rendering genetics widely available to Ontarians as a medical service. Within the parameters of my proposed study, I believed I would capture the making of medical genetics in Canada, and the place of scientific research in that making.

Predictably, the carefully constructed logic of my study's parameters soon unraveled. The first major blow came as I analyzed the work of Murray Barr and his students and colleagues in London after the discovery of the sex chromatin. Rather than cytogenetic or genetic research, Barr's 1950s work was oriented toward the clinical management of physical and psychic hermaphrodites, and involved Barr's research school with the endocrinological and surgical communities. If Murray Barr had indeed been "one of the pioneers of medical cytogenetics," there was little evidence of this in the first decade of his internationally significant work.[9]

The second major blow came as I tried to make sense of the research of Norma Ford Walker and her students and colleagues in the period after 1949. In the first instance, much of Ford Walker's post-1949 research was continuous with her earlier work, which had begun in the latter half of the 1930s. Moreover, while I was prepared to find pedigree studies and mathematical estimations of Mendelian gene patterns, or even explicitly eugenic diatribes in her work, I was not prepared to find studies of the constitutional predisposition to polio, or analyses of the developmental peculiarities of

conjoined twins. Once again I had to ask myself, if Ford Walker was indeed one of the "early pioneers" of medical genetics in Canada, how did this early work relate to such an outcome?[10]

In some ways, these disruptions to my well-laid plans were welcome. Barr's 1950s work was far from uninteresting to me. Indeed, it provided new insight into the fascinating histories of hermaphroditism, hetero- and homosexualities and even transsexuality. Moreover, the manifest importance of following Ford Walker's research back to her earliest involvement with human heredity meant that my study would start in the inter-war years – admittedly, late in that period. Such a time-frame would better enable my use of existing historical scholarship on genetics, eugenics, human genetics and agricultural genetics – scholarship which has concentrated on the first half of the twentieth-century.

Yet, these disruptions also highlighted a persistent doubt: Did the subject that I wished to address actually exist? Was there anything tangible about the category, 'medical genetics'? True, Madge Thurlow Macklin, Canada's premier inter-war human geneticist and scientific defender of eugenics, had coined the term "medical genetics" in 1932. Yet her advocacy of medical genetics as a "necessity in the up-to-date medical curriculum," testified to its non-existence as a distinct science or practice at that time.[11] Moreover, while a discipline, profession and set of medical practices going under the rubric of medical genetics could be seen to exist by the 1970s, it was not clear that there was anything more than rhetoric and institutional formation to define its existence, nor anything more than teleology to guide a history of its emergence. It was certainly not

clear that there was a distinct 'science' of medical genetics, whose research practices and knowledge production could be analyzed. What was the relationship between medical genetics and human genetics, or indeed, between medical or human genetics and 'basic' genetics? What, in short, was medical genetics?

Obvious answers to these questions were not provided by the available secondary literature. While a rich scholarship has developed to explore the history of genetics, and there is a veritable "eugenics industry" to contemplate the history of eugenics, the history of *human* and *medical* genetics has suffered from a strange neglect.[12] What work has been published focuses on the troubled relations with eugenics, and takes as relatively unproblematic the relations with the genetic sciences generally. And the relations *between* medical and human genetics seem to have entirely escaped analysis. Making sense of the history of medical genetics requires that the histories of genetics, eugenics, and the medical sciences be placed in conversation with each other.

Recent studies in the history of genetics provide important insight into the heterogeneity of the genetic sciences in the first half of the twentieth century – making space for thinking about variant genetic traditions. While the Columbia Fly room produced a powerful community of workers and a hegemonic scientific tradition in classical genetics alternate traditions, some of which were profoundly iconoclastic, were concurrently operative in North America. Part of the heterogeneity of genetic science derived from attention to differing research organisms, organisms which implied varying degrees of association with institutions beyond the laboratory, and the capacity to answer

different kinds of questions. To study the flatworm planaria, As Charles Manning Child did, was to contest the Mendelian-Weismannism faith in the sequestered germ plasm.[13] To work with agricultural research organisms was to sustain a service relationship towards practical commercial needs in opposition to the laboratory-bias of academic biology.[14] To work with mammals, such as the mouse, was to attend to complex patterns of inheritance, in part, in the hopes of elucidating details relevant to the human animal.[15]

Human genetics can be understood, then, as one of the several genetic sciences. According to Daniel Kevles and Pauline Mazumdar, human genetics was initially pursued most effectively in Britain where a generation of brilliant polymaths gained financial and institutional support to pursue pioneering studies with mental retardation and blood groups, and developed and used sophisticated mathematical and statistical techniques to overcome the limitations of the human animal as a research organism.[16] It was not until the 1950s and 1960s, Kevles argues, that the US achieved the prowess in the field of human genetics that it had long held with respect to the non-human variety. In the interim, human genetics was an under-exploited field in America, retarded by the enthusiasm for laboratory-based experimental work and the absence of medical knowledge among genetics enthusiasts. It was tarred also by the association of human genetics with the politicking of eugenics.[17]

The status of human genetics as a sub-discipline of the genetic sciences is thrown into question by this association, Kevles suggests. The thrust of Kevles' work is thus to demonstrate both the significance of the original connection, and its attenuation over time as human genetics was constituted as an independent science. Kevles' analytic distinction

between 'mainline' and 'reform' eugenics points to the reduction in the negative connotations attached to eugenics, beginning in the 1930s, as the "patent social prejudice" of mainline eugenics was subjected to critique and some of the key institutional supports for old-style eugenic activism, such as the Eugenics Record Office at Cold Spring Harbor, were closed.[18] The growing scientific sophistication of human genetics implied a detachment from abhorrent forms of eugenics. And for Kevles, the fact that contemporary, scientifically advanced forms of medical genetics can be seen to represent a 'new eugenics,' which still pursues genetic improvement, is not itself negative, so long as individual choice is protected and explicit coercion is avoided.

Diane Paul is less sanguine about the eugenic dimensions of contemporary medical genetics, suggesting that voluntarism and individual choice do not protect against more subtle forms of coercion or abuse. Moreover, much of Paul's work is devoted to drawing out the continuing connections between eugenics and human and medical genetics, and to challenging the presumed tie between scientific sophistication and criticism of eugenics. In the first instance, Paul argues that the mainline-reform distinction can be over-drawn: not all who supported coercive interventions were scientific simpletons. Indeed, support for eugenics did not "rest on an elementary mistake." The scientific flaws of the old order eugenics, which optimistically presumed that a radical change in the biological status of the population could be quickly achieved through eugenic measures, could be corrected while sustaining eugenic arguments. "It is often said that support for eugenics declined in the 1930s as its scientific errors were exposed," Paul writes. "But the eugenics movement grew stronger during the

Depression."[19] Angus McLaren makes a similar point in his study of eugenics in Canada: eugenics was defended throughout the 1930s by Canada's premier human geneticist, Madge Thurlow Macklin.[20]

After World War Two, when conventional wisdom has it that eugenics was disgraced by Nazi atrocities, Paul suggests that the eugenic ties to human genetics were paradoxically reinforced. The founding of the American Society of Human Genetics in 1948 illustrates the closeness of the ties. Paul notes that "Four of the first five presidents ... were members of the Board of the American Eugenics Society."[21] The exception to this pattern was H.J Muller, a fierce critic of mainline eugenics who was nonetheless a lifelong supporter of reform eugenics and whose refusal to join the Eugenics Society was, Paul argues, largely tactical.[22]

The influence of eugenics on human genetics was not solely institutional, however. For Paul, human genetics constitutes a science whose knowledge-producing practices were also affected by the ties to eugenics.[23] Under the influence of eugenics, human genetics emphasized intellect over disease and a hereditarian rather than environmentalist behavioral genetics.[24] Moreover, the rhetoric of genetic "load," coined by Muller in what is termed the classical-balance controversy, imported eugenic assumptions into debates over mutations – debates which were heightened in the 1950s with Cold War rhetoric and anxieties over above-ground nuclear testing.[25]

Human genetics stands in an awkward relation to the other genetic sciences. One reason for this, the literature suggests, is its association with eugenics which either de-legitimated the knowledge, or constituted a compelling influence in that knowledge's

construction. Another reason for this awkwardness is the uncertain status of human genetics as a sub-discipline. On the one hand, human genetics exists as an independent form of scientific knowledge contributing to the broader field of genetics. This is especially true for population genetics research and for the celebrated statistical work of the British school in the inter-war and war-time periods. Yet, on the other hand, many who sought to gain knowledge about human heredity pursued research with non-human organisms, either partially or exclusively.[26] Indeed, in the 1940s, Diane Paul points out, "some of the chief contributors to the field of 'human genetics' worked with non-human organisms." Paul notes that, in this period, "there was no consensus that humans make the best subjects for human genetics, even the genetics of mental traits."[27]

Discussions of post-World War Two developments in human genetics conceive of knowledge developments in this sub-discipline as derivative of more 'basic' sciences. Kevles suggests that human genetics developed by drawing on two distinct sciences: biochemistry and cytogenetics. Human biochemical genetics advanced as practitioners "drew upon the results of work then underway in the biochemical branch of plant, animal, and, increasingly, bacterial genetics and upon the rapid growth of knowledge concerning the biochemistry of the human body."[28] Meanwhile, developments in human cytogenetics, occurring in the mid-1950s, awaited the application and development of technical capacities in tissue culture, cell management and staining.[29]

The status of human genetics as a science is even more uncertain when its practical, sister activity – medical genetics – is considered. Medical genetics is discussed in the historiography principally in relation to applied work, such as genetic counseling.

In these activities the historical links to eugenic institutions and agendas are compelling.[30] The first heredity counseling clinics opened in North America in the 1940s, under eugenic auspices, and by the 1950s and 1960s, Paul argues, "genetic counseling was characterized by most of its practitioners as an extension of eugenics."[31] Indeed, "Throughout the 1960s," Paul notes, "most of the leading figures in medical genetics ... bluntly described their work as a form of 'eugenics'."[32] As an applied field, medical genetics appears to be a solely derivative science, as Barton Childs, one of the American pioneers of medical genetics, argues.

> The history of medical genetics is conditioned by the history of the gene. When the gene was defined as a statistical entity medicine took little notice. Medical interest increased when the physical basis of heredity was established, but mainly among those who were interested in rare anomalies. It was in the 1950s that medical genetics began in earnest, following the one gene-one enzyme, functional definition.[33]

Childs' interpretation of the history of medical genetics assumes that practical sciences are responsible solely for the application rather than the production of knowledge. Yet this perspective is perhaps more a function of historiography than history.[34] Historians of science, together with the historical protagonists they study, tend to focus on 'basic' developments of knowledge. Within this framework humans are merely a particular research organism, generally not a very useful one. Thus, histories of the production of basic scientific knowledge in genetics tend to focus on work with 'better' research organisms: *Drosophila*, mice, and bacteriophage, for example. This tendency to see the human sciences as applied biological sciences is compounded for the medical sciences by

the presumed ascendancy of 'scientific medicine' in the twentieth century. Yet, as Daniel Kevles and Gerald Geison point out, the assumption that experimental biology forms the basis for the development of scientific medicine is more ideology than fact.[35]

Recent research in the history of the medical sciences suggests the importance of taking seriously the differences between biological and medical forms of knowledge, not as simple periodization differences, where the practical sciences lag behind the 'basic' sciences, but as substantively different ways of constituting knowledge.[36] This literature would suggest that, in assuming a service role towards medicine, human geneticists interacted with more than the biological sciences. They were in contact with independent, rather than simply derivative, medical sciences. If we take medical genetics seriously as a science, then we should investigate how its biological presumptions were made to fit into clinical systems of thought and practice – to 'make sense of illness,' to 'frame disease.' Such efforts at collaboration and integration would have responded to historically-specific negotiations between practitioners, patients and investigators – what Robert Aronowitz terms the "continual negotiation and shifting balance in medical research, clinical practice and social thought between ontological [i.e. specific causation] and holistic orientations" in disease interpretation.[37]

Overview of Dissertation Chapters

This dissertation is conceived in three sections with two chapters each. In the first section I focus on the Toronto community and examine the early research of the Ford Walker school from the mid-1930s through the 1950s. The second section brings the London community into focus. I examine research in medical cytogenetics in both communities and investigate how disease conditions were understood. Finally, part three returns to the Toronto community. I examine the institutional changes in Toronto, and nationally, as workers consolidated their institutional and professional identities and sought to demonstrate the utility of genetics for medicine.

My study begins, in Chapter 1, with the early work of Norma Ford Walker, a woman scientist who pioneered in the field of human genetics at a time when few women achieved security or responsibility in the research university.[38] The early history of human and medical genetics in Toronto was thus conditioned by the social relations of gender.[39] The career of Madge Thurlow Macklin, a more senior and, already by the 1930s, well respected human geneticist at the University of Western Ontario, exemplifies the challenges women faced in the research university. Macklin was treated as an auxiliary worker at Western and, in 1945, after being denied the right to teach, she moved to Ohio State University where she helped educate a new generation of American human geneticists.[40]

Ford Walker's career was also constrained by her gender. If women in the inter-war period were, as AB McKillop suggests, a "beleaguered minority on campus," the post-World War II cult of domesticity in many ways intensified the difficulties and there was a decline in the percentage of women who sought higher education.[41] Ford Walker

was better treated at the University of Toronto than Macklin had been at Western. Indeed, in 1943, when Norma Ford married Edmund Walker, then head of the Department of Zoology, the president of the university is said to have specifically urged her *not* to retire.[42] Yet though director of a Department of Genetics at the Hospital for Sick Children from 1947 through 1962 and a Fellow of the Royal Society of Canada Ford Walker was not promoted to the rank of full professor until 1958, four years before she retired.

Still, by the time of her death, in 1968, Ford Walker had achieved significant success. Moreover, her presence and success in human and medical genetics had a profound effect on the presence of women in the field, encouraging women to enter a field where a female mentor was available, and where women's scientific success seemed possible.[43] Ford Walker facilitated the higher education of a disproportionately large number of women: of her seven Ph.D. students, four were women; of her eight Master's students, six were women; finally, of the large number of graduate students who never appear to have completed their degrees, the vast majority were women.[44]

It is clear from available newspaper commentary on Ford Walker's public activities that she was actively interested in the scientific education of women – beginning in their earliest years.[45] "Miss Ford," a newspaper reporter noted in 1927, "combines with her intense love of nature a deep affection for girls and is making one of her hobbies the promotion of nature study in girls' camps. For several summers she has given part of her time to the visiting of such camps throughout the country, and during the academic year at the University of Toronto she constantly watches her classes in

biology and zoology for the appearance of students who might adapt themselves to the rather difficult task of teaching natural history to these holiday groups."[46] As a high profile and anomalous woman scientist in the inter-war decades,[47] she was called on to give many talks to women's groups, and she served as acting dean of women at the University of Toronto from 1931 through 1934.[48]

Ford Walker was trained as an invertebrate zoologist. Her 1923 Ph.D. dissertation, under the supervision of the man who in 1943 would become her husband was entitled "A Comparative Study of the Abdominal Musculature of Orthopteroid Insects," and her work in the 1920s and through the mid-1930s concentrated on two insects: *Grylloblatta* and *Wohlfahrtia vigil*.[49] Yet she came to the study of human biology in a manner typical of women academics.[50] By the late nineteen-teens, before she had completed her Doctorate, she was teaching a biology course for women, for "the teacher, social worker, nurse and mother."[51] And by the late 1920s, she had added to her repertoire of public talks on nature, for women's clubs and girl guide outings, the topic of human heredity.[52]

Ford Walker's formal indoctrination into the academic science of human heredity was fostered through her involvement in the collaborative research project on the Dionne quintuplets, beginning in the latter-half of the 1930s.[53] Her early research in human heredity was thus deeply influenced by her colleagues in this project, who preferred a heterodox approach to the dominant traditions of classical genetics, and tilted towards a critique of mainline eugenics. Hamilton Cravens has argued that, between the 1920s and the 1950s, the life sciences were attuned to an inter-disciplinary gestalt. In this period,

older visions of heredity in which "heredity was entirely antagonistic to environment" gave way to a perspective where "heredity and environment were understood as mutually interactive."[54] Cravens' description captures the intellectual milieu in which Ford Walker functioned in this period: a milieu which took the forces of nature and nurture seriously, indeed, a milieu in which workers seemed inspired by the heredity-environment controversies to pursue a broad etiological mandate of investigation. While not strictly environmentalist, unlike some disciplines that emerged in the 1940s, work by members of the Ford Walker school manifested a respect for environmental causation into the 1950s that, in retrospect, seems foreign to genetic inquiry.[55] I call the early work of this research school the 'indigenous tradition.'

The indigenous tradition developed in the late 1930s and through the 1940s, and continued in service into the 1950s. Workers within this tradition adopted the insights of classical genetics, but not the priorities of that experimental, laboratory science, and not that science's focus on non-human research organisms. As an explanatory system, the indigenous tradition was defined by its broad etiological framework – concerned more frequently with complex systems of causation than single mechanisms, and as interested in developmental and environmental as genetical influences. In essence, it was a school of human biology, as some geneticists suggested that any school of human genetics *should* be.

Ford Walker's research school developed both a human and medical genetics orientation concurrently. Norma Ford Walker collaborated with a range of disciplines in developing human genetics capacity in Toronto, from physical anthropology through

dentistry. But of principal significance for this project is the medical genetics tradition that she developed through her adoption of a service role towards medicine, establishing links with the Hospital for Sick Children and other clinical facilities, beginning in the late 1930s.

In forging its medical orientation, the indigenous tradition added the influence of distinct medical sciences to the existing biological orientation. In particular, in the 1940s, Ford Walker conducted and participated in research projects that drew on the resources of some of the chief architects of American constitutional medicine. Emerging against the backdrop of the seeming dominance of the infectious disease paradigm, from the 1920s through the 1950s, the attention to the human "constitution" explored "that aggregate of hereditarial characters, influenced more or less by environment, which determines the individual's reaction, successful or unsuccessful, to the stress of the environment."[56] Sarah Tracy suggests that this approach was both a version of holism and a home for researchers interested in heredity. For some scientists, Tracy argues, "constitutional medicine offered a more legitimate scientific framework for the study of human genetics than did the increasingly politicized eugenics movement."[57]

For Ford Walker, constitutional medicine supplied an interpretative medical framework that was congruent with her broad etiological interests. Rather than specific genes causing specific disease, the indigenous tradition emphasized hereditary factors and developmental processes. Applied to medical systems, with the aid of constitutional medicine, this etiological approach produced pre-dispositions, and constitutional types.

Yet the medical influence on the indigenous tradition operated in more ways than solely through formal systems of thought. Medical institutions and clinical traditions produced the diseased and anomalous bodies which might be subject to investigation, and they did so in particular ways. In Toronto and elsewhere, it was the pediatric hospital which helped to structure investigative opportunities, making infants and children available for review whose afflictions were principally congenital. The pediatric hospital enabled medical genetics workers in Toronto to benefit from a highly productive blurring of the distinctions between congenital and genetical disease. This blurring was intellectually consonant with Toronto's indigenous tradition, with its commitment to etiological breadth and disinterest in the identification of formal genetic mechanisms. In organizing research around these blurred categories, the range of investigative opportunities were greatly increased, since virtually all childhood disorders were, by definition, congenital, even where genetical influences were uncertain or unknowable. What constituted 'genetic disease' in the era of the indigenous tradition, then, was a broad range of congenital conditions for which genetical influences could be inferred but not necessarily formally delineated.

The technical resources utilized by members of the Ford Walker school were attuned to this broad etiological framework and the productive blurring of disease distinctions. The Toronto research school was built around a relatively marginal technology: dermatoglyphics, or the study of the skin patterns. Dermatoglyphic analysis provided little insight about simple genetic mechanisms. On the contrary, it was informative about complex mechanisms of causation, where both environmental and

hereditary forces might be implicated. Members of the Ford Walker school applied dermatoglyphic techniques in the development of two methods – one general and one more unique: the twin and Mongol methods.[58] The twin method moved beyond twin diagnosis to use mono- and di-zygotic twins as natural experiments for demonstrating the workings of genes, environment and development – without the requirement for, or the relevance of, simple models of genetic action. The Mongol method used the anomalous dermal patterns of the highly stigmatized phenomenon of 'Mongolism' as an analogy for developmental anomaly which might be the resultant of hereditary and/or environmental influences. The Mongol method served as a resource to make the twin method more robust – to provide evidence of developmental insult which could help to explain discordant phenotypes in genetically 'identical' twins. The Mongol method was also a stand-alone resource – providing evidence, by analogy, of constitutional types which were predisposed to disease, ranging from polio to cleft palate.

The etiological and technical components of Ford Walker's research program produced a coherent school. But this research tradition was marginal to what is known of early human genetics in the US and Britain. In part, this is a function of historiography. Historians may have discovered a lack of commitment to human genetics work in America into the 1940s because their definitions of 'genetics' have been too narrowly construed. Work such as that pursued by members of the Ford Walker school in the inter-war and war-time years is as likely to have been ignored in historical accounts as to have actually been absent. My use of the phrase 'indigenous tradition' is thus provisional.

Additional research will be necessary to ascertain how prevalent such a program was in North America.

Still, the marginality of the indigenous tradition was not solely epiphenomenal. It was also a function of the production of this research tradition in a country that was marginal to the broader currents of research,[59] to the use of a research tool that was marginal to the main instruments of human genetics research, and to the preponderance of women workers in the Toronto community.

That the social relations of gender have affected the structure of genetics as a science has been documented by several historians. Greg Mitman and Anne Fausto-Sterling suggest that gender contributed to the failure of Charles Manning Child, one of the more vocal critics of Morganian genetics, to build a school of devoted followers who continued to use his organism, the flatworm *Planaria*, and to investigate his hypotheses. Mitman and Fausto-Sterling point out that producing female Doctorates was not "an effective means for reproducing future generations of *Planaria* researchers with high academic visibility, when women were by and large excluded from professional science careers in top-ranking research universities."[60] Evelyn Fox Keller's *A Feeling For the Organism*, concerning the life and work of corn geneticist Barbara McClintock, provides a critical but more optimistic look at the structuring of science by gender.[61] McClintock's gender meant marginality – being a woman in science, with all the restraints on academic opportunity that implied, served to exacerbate her growing divorce from the community of scientists. Yet gender was more than a liability. McClintock's personal resilience in continuing her work, until its eventual acceptance by the scientific community, also

derived from her gender: she had become used to social isolation from long training, Fox Keller suggests.[62]

Karen Rader and Scott Gilbert have turned their attention to the history of one of the sister disciplines of genetics, embryology, in which the gender of workers has operated forcefully in the historical processes of disciplinary development.[63] Women played a significant role in the development of embryology in the first half of the twentieth century, and they are leaders and major players today in that field's successor – developmental biology.[64] Seeking to explain the historical phenomenon of women's past and present 'excellence' in this field, Rader and Gilbert suggest that gender operated through women's cultural identities and social roles to encourage their presence as workers in the field. In America, women played a prominent role as teachers in the life sciences from the late 19th century, and the proximity of embryology to questions of human reproduction might have served to encourage women's attention to this field.[65] In addition to the cultural norms which guided women towards embryology, women were encouraged in the field by their status as lesser scientific workers. As Rader and Gilbert put it "genetics research was at the cutting edge of the life sciences both intellectually and professionally, and this is where the men went." This reduced status also encouraged the active delegation to women students of some of the 'messier' research questions – ones that took longer to investigate and resulted in fewer publications. Attention to such research problems was a reasonable sacrifice for women workers, given the near impossibility of their finding employment at a 'good' university.[66] Finally, for women, the difficulty of researching and publishing in embryology – with the messy questions,

the long breeding seasons, the need for field research away from the laboratory, the requirement of fine motor skills – might have constituted an attraction. This "low prestige science" involved women in less competition and even relied on some of the fine technical skills educated women were apt to possess at this time.

Rader and Gilbert conclude that all of these pressures encouraged the production of a concentration of women in embryology by mid-century. These women served as examples for other women to imitate, and all stood ready to take advantage of their comparative success as the field gained prestige, and as opportunities for women in the academy expanded, after the war.[67] Embryology was 'women's work' because of the *historical* convergence between the lesser status of women as scientific workers, and the lesser status of embryology as a science.[68] This story has striking parallels with the history of human and medical genetics.

In North America, Daniel Kevles has argued, human genetics had the status of a *lesser* science. It was a science that bright young, and I would add male, researchers, were warned away from. In Toronto, the field was dominated in the early decades by women, at a time when women were indisputably *lesser* scientific workers. The convergence of these forces was perhaps not coincidental. Women dominated this field in Toronto because it was available for their exploitation, and because they were prepared – precisely because they could not anticipate great scientific careers – to embark on work that was of dubious merit. In the age of the 'scientist as hero,' human and medical genetics was insufficiently experimental – it was messy, and not conducive of sufficient publications.[69] Paraphrasing Rader and Gilbert, I would argue that '*basic* genetics is

where the men went.' Gender was, thus, a contingent yet consequential force in making medical genetics in Toronto.

The indigenous tradition was structured by gender, by etiological biases, and by technical resources. My investigation of the indigenous tradition frames this study in several ways. In particular, the peculiarities of the indigenous tradition suggest questions which are of sustained importance throughout the dissertation. First, what are the relations between the medical and biological sciences in making medical genetics? Second, what is the significance of method and metaphor in producing disease constitutions? Third, what is the meaning of 'genetic' and what is the scope of genetical investigation and practice? Fourth, what is the significance of gender – both the social relations of gendered persons and the metaphoric work of gender – in producing marginality, producing capacity, and generating disease conditions?

The indigenous tradition offers four initial answers. First, the making of the indigenous tradition illuminates the cross-cutting traffic between biology and medicine, as a biological community of researchers with a broad etiological framework drew on a similarly oriented medical science – specifically, constitutional medicine – to make sense of human infirmity. Second, the indigenous tradition advanced the tool of dermatoglyphics in support of its broad etiological mandate, and produced a method for discerning constitutional states that drew on the metaphor of the Mongol. Third, the indigenous tradition blurred the boundary between congenital and genetical conditions – not through any confusion about the reality of a distinction, but through the irrelevance of

that boundary for an etiological system which was primarily concerned with congenital disease. This blurring would prove to be of enduring importance even as this broad etiological system passed in favor of one more mechanical and genetical. Fourth, the indigenous tradition was marked by the social relations of gender. Its marginality from broader currents in classical human genetics was produced and sustained by its status as women's work. Its practitioners embraced a service role toward medicine that more academic biologists avoided, and produced a research tradition better suited to the needs of its clients in the hospital than to its colleagues among the brilliant group of British human geneticists whose work is seen to constitute the foundation of the field.

Yet the indigenous tradition, whose development I discuss in Chapter 1, did not endure. In the post-war era, under the influence of disciplinary consolidation, and the infrastructure of booming biomedicine, the Ford Walker school came to resemble a more generic and 'classical' human genetics enterprise and in Chapter 2 I examine the growth and ultimate transformation of the indigenous tradition. Broader North American changes in the organization of biomedical research and practice were manifested locally through developments at the Hospital for Sick Children and the University of Toronto. Ford Walker claimed that the new Sick Kids was the first hospital in North America to formally incorporate a Department of Genetics in its plans when it rebuilt in the early 1950s.[70] Whatever the truth of that statement it is certain that, in the 1950s, the renewed resources of the enlarged hospital, and the financial supports of the equally new Research Institute, enhanced the medical orientation of the Ford Walker school. Moreover, the Research Institute's commitment to full-time research and interdisciplinary collaboration

facilitated the adoption of techniques and ideas by the geneticists from other disciplines and a broader community of researchers.

In the 1950s, as workers in America and Britain were "drawn to biochemical subjects,"[71] as Daniel Kevles puts it, Ford Walker drew on biochemical-inclined workers in Toronto to develop what was widely termed 'biochemical genetics.' In this decade, Ford Walker aided in the application of a new biochemical technique to human genetics, starch gel electrophoresis. This technology allowed new components to be detected in human blood serum and Ford Walker helped to interpret these newly christened 'haptoglobins' in terms of classical human genetics. These local changes point to the importance of medical sciences in making human genetics, for the 'biochemical genetics' pursued by medical geneticists was rather different than the basic version developed by George Beadle and Edward Tatum in the 1940s for which they, with Joshua Lederberg, received a Nobel Prize in the late 1950s. Beadle and Tatum developed the one gene-one enzyme hypothesis which Barton Childs sees as so instrumental in the development of medical genetics. This hypothesis was central to the production of an interpretation of what genes 'actually do' and thus in moving beyond the exclusive classical concern with transmission in 'basic' genetics. Yet the Toronto workers, and their international human geneticist colleagues, were decidedly uninterested in what genes 'actually do.' Their interest was less with genes than with metabolic processes that could be seen, through the tools of classical genetics, to be hereditary. And rather than look to Beadle and Tatum for the authority of this model, they looked to Archibald Garrod, whom Beadle had elevated to the status of the long-neglected but true 'father' of biochemical genetics. It was a

distinctive form of medical biochemical genetics, then, and not the 'basic' genetics variety, that propelled a classical genetics model of simple gene effects to the forefront of human genetic inquiry in Toronto in the 1950s.[72]

Yet even as the indigenous tradition began to fade in the 1950s, under the influence of medical biochemical genetics, it retained explanatory relevance. The continuing salience of this research tradition was exemplified by the work Irene Uchida, a student and then colleague of Norma Ford Walker in Toronto. Uchida was a Japanese Canadian whose residence in Ontario was a consequence of Canada's internment policies during the Second World War. After receiving her Ph.D. in 1951, Uchida remained at Sick Kids through the decade of the 1950s and continued to use and develop the tools of the indigenous tradition. Yet though a representative of the older technical and epistemological model, Uchida's career was also illustrative of change. In 1960 she moved to Manitoba, to chair the Department of Medical Genetics at the University of Manitoba. Seemingly unleashed from the constraints of the Ford Walker school, and with the support of Rockefeller Foundation money, Uchida retooled herself as a cytogeneticist and was to make important contributions to that field. In 1969, Uchida was recruited to direct the cytogenetics program at McMaster's Health Science Centre.[73]

In the 1960s, then, a new technical development took center stage – cytogenetics – and these developments serve as the subject of the second section of this dissertation. By comparison with biochemical genetics, the distinctiveness of the medical and human science of cytogenetics is less certain. Human cytogenetics developed in the mid-1950s when basic techniques in tissue culture were adapted to the reading of the small and

tightly interwoven human chromosome complex. Kevles argues that "The exploration of the new regions – not only human cytogenetics but human biochemical genetics – surged ahead with remarkable force, drawing people in steadily increasing numbers, enlarging what was by now, a flourishing international community in the discipline."[74] Yet even here, where the human and medical science of cytogenetics seemed so clearly to follow from the technical capacity of the basic variety, there were permutations which drew on distinctive traditions of medical and human knowledge and practice. Indeed the contingent, socially constructed nature of disease, and thus the relevance of distinct medical sciences, was especially evident in the production of new forms of cytogenetic disease in the 1960s.[75]

The opportunities for cytogenetic research brought the London school into the community of human genetics workers. Thus, in the second section of my dissertation, the London workers come into focus. Murray Barr, the leader of the London research school, was trained as a physician and though he completed an MSc he was never able to take the time to complete a Doctorate.[76] Barr had tried out the life of the general practitioner during the harsh years of the depression, but he spent his career as a medical researcher within the University of Western Ontario's Faculty of Medicine. After the war, Barr was enthused by the pro-research agenda of the new Dean of Medicine at Western, and he set out to develop a research program in neuro-anatomy.[77] It was while performing experiments designed to assess the morphological changes in neurones under stress that Barr, and his graduate student Ewart Bertram, made the 1948 discovery that altered the course of his career.[78] Through the 1950s, Barr's research school was oriented

to the study of the sex chromatin, with the bulk of work devoted to the interpretation of sexually anomalous bodies and lives, notably, the intersex. By the late 1950s, after the mid-decade developments in human cytogenetics, sex chromatin work was beginning to have more cytogenetic overtones, as Barr and other sex chromatin researchers determined to directly investigate the chromosome complex in these medically compelling cases.

Medical cytogenetics was invented, then, with the discovery of chromosomal anomalies which appeared to map directly onto existing clinical syndromes. Drawing on what Evelyn Fox Keller has christened 'discourses of gene action,' these associations were immediately read as causal, and new forms of genetic disease were birthed.[79] By 1959, three distinct clinical syndromes – Mongolism, Turner's and Klinefelter's – could be attributed to major morphological changes in the human chromosome complex. Mongolism, as it was called into the 1970s, but which we now call Downs or Trisomy 21, was due to an extra chromosome, dubbed '21.' Turner's syndrome, which describes a complex in a woman involving short stature, primary infertility, and some distinct physical signs such as a webbed neck and broad chest, was due to the absence of one X chromosome: instead of XX, a woman with Turner's syndrome had a single X complex. Finally, Klinefelter's syndrome, a complex in a man involving atrophied testes, and in the late 1950s, several other sexual anomalies that were later seen not to be definitional, was due to the addition of one X chromosome: instead of XY, a man with Klinefelter's syndrome had an XXY complex.

These three syndrome complexes were iconographic in the production of two consequential categories of chromosome anomaly: sex chromosome anomalies and

autosome (non sex chromosome) anomalies. Chapters 3 and 4 examine the involvement of Toronto and London workers in making sense of these new forms of disease using extant technical and metaphorical traditions. The autosome anomalies drew on a tradition of research on the 'Mongol' in several ways. The Mongol served as a stigmatized – indeed racialized – phenomenon of severe defect which seemed analogous to the new autosomal diseases being discovered through cytogenetic surveys. Moreover, the Mongol was drawn into association with conditions like D and E syndrome through the ever-resilient tool of dermatoglyphics – shorn of its indigenous interpretative framework but still diagnostic of disease. The autosome anomalies drew, then, on traditions of interpretation and management of the Mongol by Toronto geneticists which had been in force long before this condition was understood as a strictly *genetic* disease.

The sex chromosome anomalies, by contrast, drew on a tradition of research which had used the sex chromatin, and which drew on the population to which the sex chromatin had been applied in the 1950s – the intersex. The transfer of the sex chromatin as a tool, and of the tool's research community, from the study of intersex bodies to the study of bodies with anomalies of sex chromosomes, suggested the coherence of the category of sex chromosome anomaly, and the relevance of gendered narratives of sexual pathology in their interpretation. By comparison with the autosome anomalies, and despite the contrary evidence suggested by Turner's syndrome, these anomalies were read as less severe. Indeed, expectations of sexual pathology and benignity drove investigations.

Research by workers in Toronto and London soon unearthed both new kinds of chromosomal anomaly and new kinds of clinical sequelae – upsetting, in some cases, the presumed direct association between chromosomal cause and clinical outcome.[80] More complex still, especially among conditions defined through their association with the sex chromosomes, were chromosomal anomalies which appeared to produce no coherent or consistent symptom complexes but had instead a range of potential risk effects. Medical cytogenetics worked to produce disease – drawing or consolidating links between chromosome morphology and clinical outcome. But some of these diseases were defined, to a greater or lesser extent, solely through the *risk* of pathological outcomes. Some of these diseases were risk-based.

The willingness of researchers to produce diseases that were risk-based was a function of the rising status of risk as a cultural category, and in making sense of disease.[81] Robert Aronowitz has pointed to the emergence of the "risk factor approach" to chronic disease in the late 1950s and 1960s. This approach assumed the existence of "specific, discrete, risks that individuals possess or experience to different degrees." It provided a credible scientific, and narrowly individualistic, way of accommodating the larger explanatory logics demanded by patient and practitioner – what Aronowitz terms the "'why me?' and 'why now?'" questions that have been sidelined with the rise of scientific medicine's reductionist focus on specific, causal agents in disease.[82]

These new risk-based diseases can be seen to be continuous, to some extent, with earlier forms of disease predisposition which members of Toronto's indigenous tradition had worked to produce in the 1940s and 1950s.[83] Yet there were also important

differences. The investigations pursued in this earlier age were undertaken, and patterns of predisposition discovered, only once a disease manifested itself. For example, Ford Walker investigated dermatoglyphic patterns that were suggestive of developmental disturbance, and which might retrospectively explain the course of disease in the affected individual. The risk factors which are the focus of Aronowitz's analysis are rather different – though clearly continuous. Focusing on such chronic conditions as coronary heart disease, Aronowitz's risk factors are identifiable behaviors and physiological signs that exist *prior* to disease manifestation.[84]

Aronowitz's risk factors also constitute disease.[85] They are what Charles Rosenberg terms "protodisease states" which "are artifacts of medicine's reductionist and laboratory-oriented style of practice."[86] The risk-based diseases produced through cytogenetic investigation parallel these protodisease states in being defined primarily by laboratory evidence rather than clinical or patient experience, and in having only a statistical association with a pathological outcome. Yet there are also important differences. Protodiseases are reifications of diagnostic signs. They emerge, for example, from the designation of a certain blood pressure reading as a disease in itself, one that is prognostic and can be treated. But chromosomal risk-based diseases are not diagnostic signs. They indicate present, rather that future, pathology – they constitute definitive evidence of genetic disease. Chromosome disorders have been seen to produce diagnosed disease states, some of which are manifested solely by the risk of a variable array of pathological outcomes. Medical genetic and clinical research to make sense of these

disease states – to assess the degree and extent of risk – has often been inconclusive. But the risk-based diseases, producing risk effects, persist.

The final section of this dissertation – Chapters 5 and 6 – returns the focus to Toronto. In it, I examine institutional and practical work, rather than research, and focus on developments in the 1960s and 1970s. By the 1960s, Toronto workers had shifted their research focus away from their previous concern with both environmental and hereditary forces to attend more narrowly to cytological and genetic modes of causation. Many of these changes in the technical and epistemological commitments of Toronto workers had occurred under Ford Walker's leadership, but her presence retarded the opportunity for formal change in the structure of human and medical genetics in Toronto. Such change awaited her retirement in the early 1960s at which time Toronto's generic – and in terms of international science, still marginal – research school was institutionally reorganized to reflect the ascendancy of the 'new biology,' and to consolidate a range of applied medical genetics practices as the new domain of genetic services.

After Ford Walker's retirement in 1962, and for the remainder of the decade, the university and the hospital, independently and then together, struggled to define their needs and appoint her replacement. In the interim, acting leadership was assumed by a human population geneticist, T Edward Reed, and most importantly, by a past student of Ford Walker, Margaret Thompson. Thompson had received her Ph.D., under Ford Walker's supervision in 1947. Married to another scientist, Thompson's career was interrupted by the birth of two children and by moves which were precipitated by her

husband's career. She spent a brief period in London, Ontario and then worked in Alberta for over a decade, where she served as geneticist to the province's Eugenics Board, before returning to Toronto in the early 1960s. Thompson was an extraordinarily flexible researcher. Over the course of her long career, she re-tooled herself repeatedly to participate in a vigorously changing field. When she took over the position of acting Director of Genetics at Sick Kids in the mid-1960s, she served capably to facilitate the transition towards a new, more experimental orientation in medical genetics. In this, she was assisted by the individual who would emerge, in the 1970s, as the Chief Geneticist at Sick Kids and the head of a Department of Medical Genetics that spanned the hospital and the university – Louis Siminovitch.

Louis Siminovitch was one of a new breed of research scientists. Trained as a chemist, he pursued biophysical experiments at the research facility of Canada's Atomic Energy Commission during World War Two. He then spent four years in France at the famed Pasteur Institute, working with André Lwoff. There, he helped to perform the experiments which demonstrated the phenomenon of lysogeny and brought a Nobel Prize to Lwoff.[87] These years also confirmed Siminovitch as a geneticist. Yet, unlike the members of the Ford Walker school, Siminovitch was committed to the new physicochemical biology in which, as Lily Kay has argued, "organisms became mere probes" to address "basic questions regarding vital processes common to all organisms."[88]

In the mid-1960s, as Head of the Division of Biological Research at the Ontario Cancer Institute, affiliated with the University of Toronto, Siminovitch worked to support

the re-direction toward basic science at the university's Faculty of Medicine. Though a researcher himself, with a particular interest in phage and somatic cell genetics, Siminovitch emerges in this story as an administrator – a central protagonist in the re-organization of medical genetics in Toronto, and a key protagonist at the provincial and national levels in coordinating research and consolidating the new clinical domain of medical genetics. Under his auspices, medical genetics in Toronto moved within the university's Faculty of Medicine, and the historic connection with Sick Kids was consolidated through university leadership and reorganization.

The institutional reorganization in Toronto was premised on epistemological and technical change. From the late 1930s through the 1960s, distinct human and medical sciences, and associated clinical logics, had joined with knowledge derived from the basic sciences in making medical genetics in Toronto and London. Throughout this period, workers in these communities defined themselves principally as researchers, detached for the most part from clinical concerns and patient management. But by the late 1960s, the authority of the basic approach in biomedicine was growing. And in the 1970s in Toronto the basic approach became institutionally dominant. With Siminovitch at the helm, medical genetics was transformed from a narrowly human science to a broader biological science.

These local changes in the organization of medical genetics in Toronto reflected broader shifts in the definition of medical genetics in North America. Medical genetics was re-defined from an applied sub-field of the autonomous human science of human genetics to a broad meta-field, encompassing and subordinating human genetics to basic

genetics in the investigation of health and disease. The American human geneticist, AG Motulsky, in his Presidential speech to the American Society of Human Genetics in 1977, articulated the earlier vision of medical genetics as a sub-field of human genetics. In doing so, he cautioned his colleagues about changes then underway. Human genetics, he warned, has been "medicalized." "The vast majority of work and subject matter under study," he noted, "is of medical interest." He also cautioned that this "medicalization" was responsible for the narrow concentration of human geneticists on only "1% to 2% of the total content of human genetics."[89] Motulsky's colleague, Victor McKusick, was later to articulate the newer model. "Medical genetics is more broadly encompassing than human genetics," McKusick wrote in 1993, "because all aspects of human genetics are relevant to the genetics of health and disease, but the converse is not necessarily true. Indeed, we are becoming powerfully aware of the relevance of all genetics to medical genetics. The mouse," he continued, "...is highly instructive to the understanding of human disease, for example, and even unicellular organisms, such as yeast, are teaching us much."[90]

In Chapter 5, I investigate the institutional reorganization of medical genetics in Toronto in the 1960s and 1970s to consolidate conceptual and technical changes which had been ongoing since the 1950s. If the turn to medical biochemical genetics and then medical cytogenetics represented a turn to a more classical genetics orientation, then the late 1960s and 1970s represented a shift to the 'new' biology. The medical geneticists who had been building their identities since World War II – the old-order geneticists, I call them – were participants in this transformation, ceding a space for 'fundamental'

inquiry in genetic mechanisms using non-human organisms, but also preserving their identity as researchers who were capable of producing fundamental knowledge using the human animal.

In the 1970s, as the departmental infrastructure of medical genetics in Toronto was reorganized to reflect changing emphases in research, medical geneticists were also working at the national and provincial levels to reorganize the practical work of genetic medicine. Through these parallel and complementary efforts, medical geneticists preserved a position which straddled a research world of increasing complexity, and a clinical domain of apparently expanding relevance.

The expanding relevance of genetics for medicine was a function, in the first instance, of increasing numbers of practical interventions that medical geneticists could bring to bear in the lives of individual patients. By the 1960s, the standby of heredity counseling had been complemented by the addition of treatment protocols for certain genetic metabolic diseases. And by the 1970s, prenatal diagnosis and genetic screening had further expanded the reach of genetic medicine. But this expanding relevance was also a more rhetorical and contingent process, relying on the triumphalism of biomedicine in its claims about the defeat of infectious disease and the shifting burden from acute to chronic conditions, and relying on Cold War rhetoric about the potential increase in mutations from exposure to ionizing radiation. Finally, the rhetoric of expanding relevance was constituted through blurred distinctions between congenital and genetical disease. This blurring had made sense of the early association between human genetics and the pediatric hospital – encouraging medical geneticists in Toronto to assert

an expansive relevance for their etiological systems. But even as workers in Toronto ceased to lay claim to a broad explanatory framework, they continued to exercise authority over a range of congenital diseases. Indeed, by the 1960s, the blurring had become a systemic slippage. In terms of practical work, the blurred categories of disease made sense of the fact that what medical geneticists actually did through genetic counseling and prenatal diagnosis was to seek to minimize the birth of children with congenital anomalies – anomalies that might simultaneously be genetical. In articulating a narrative of necessity for genetic medicine, then – that the 'burden' of genetic disease was growing – medical geneticists consistently inferred that chronic and congenital conditions were within their purview.

Such a blurring, or slippage, was tactical rather than epistemological. By the 1960s, at the latest, the fact of a distinction was clearly and consistently acknowledged. Yet the slippage was made nonetheless. Victor McKusick, in introducing his much reprinted 1970s textbook, *Medical Genetics*, listed "fourteen genetic misconceptions frequently encountered among physicians." Misconception number one was the assumption that "Congenital is synonymous with genetic." Against this obvious untruth McKusick noted that "Congenital merely means present at birth. It has no necessary etiological connotations. Some genetic disorders are not congenital in the usual sense of the word, and many congenital malformations do not have a predominantly genetic cause."[91] Yet McKusick had begun the introduction that he ended with his list of 14 Misconceptions with the statement that: "It is a commonplace that as infectious and nutritional diseases are better understood, controlled and managed, congenital and genetic

disorders assume greater relative significance....To this the increased importance of medical genetics in the last two decades can in large part be attributed."[92]

In Chapter 6, I look at changes in the shifting meaning and organization of practical work by medical geneticists. These developments took place against narratives about an expansive and growing burden of genetic disease, and an increasing capacity for practical intervention. Medical geneticists built on these narratives, and drew on and developed professional organizations, to coordinate themselves as the leaders of a new and expansive domain of clinical practice – genetic services.

Endnotes: Introduction

[1] "Mission Statement," The Genome Database, http://gdbwww.gdb.org/
[2] To avoid confusion, I will refer to Norma Ford as Norma Ford Walker, even prior to her marriage, and name change, in 1943.
[3] The community of workers around Ford Walker approximates a "research school" as defined by historian of Science Gerald Geison – "small groups of mature scientists pursuing a reasonably coherent program of research side-by-side with advanced students in the same institutional context and engaging in direct, continuous social and intellectual interaction.": Gerald Geison, "Scientific Change, Emerging Specialties, and Research Schools," *History of Science*, 19 (1981), 23. See also: Gerald Geison, "Research Schools, Historical Reappraisals," in Gerald Geison & Frederic Holmes, eds., *Osiris*, 8 (1993).
[4] On the "new biology" see: Lily Kay, *The Molecular Vision of Life: Caltech, the Rockefeller Foundation, and the rise of the new biology* (New York: Oxford University Press, 1993).
[5] G. Howard Valentine, Interview with Judith Friedman, on behalf of the author, Victoria, B.C., March 22, 1999. David Carr agreed with this characterization, he noted that in the late 1960s Barr returned to neuro-anatomy work: David Carr, Interview with the author, Hamilton, On., July 20, 1999.
[6] On the research university as the "true home of basic research" see: Roger Geiger, *To Advance Knowledge: The Growth of American Research Universities, 1900-1940*, (New York, Oxford: Oxford University Press, 1986), 172.
[7] With respect to this tradition, Donna Haraway notes that: "To be 'made' is not to be 'made up.' ... constructivism is about contingency and specificity but not epistemological relativism.": Donna Haraway, *Modest_Witness@Second_Millenium.FemaleMan©_Meets_Oncomouse™*, (New York, London: Routledge, 1997), 99.
[8] HC Soltan, ed., *Medical Genetics in Canada: Evolution of a Hybrid Discipline, Essays on the Early History*, (London, Ontario: The University of Western Ontario Regional Medical Genetics Centre, 1992).
[9] HC Soltan, "Regional Development: London and Southwestern Ontario," in Soltan, ed., *Medical Genetics in Canada*, 61. Daniel Kevles also discusses Murray Barr's significance in the development of the field: Daniel Kevles, *In the Name of Eugenics: Genetics and the Uses of Human Heredity*, revised edition, (Cambridge, Mass., London: Harvard University Press, 1985, 1995, 1997), 242.
[10] Margaret Thompson, Nancy Simpson and Michael Partington, "Early Pioneers – Norma Ford Walker," in Soltan, ed., *Medical Genetics in Canada*, 27-35.
[11] M.T. Macklin, ""Medical Genetics": A Necessity in the Up-To-Date Medical Curriculum," *Journal of Heredity*, 23, (1932), 485-486. This article is cited by Hubert Soltan, who argues that Macklin was the individual to coin the phrase: Hubert Soltan, "Early Pioneers – Madge Macklin," in Soltan, ed., *Medical Genetics in Canada*, 11-26. On Macklin's role in the eugenics movement see: Angus McLaren, *Our Own Master Race: Eugenics in Canada, 1885-1945*, (Toronto: McClelland & Stewart, 1990), Chapter 7.
[12] Jan Sapp argues that "Genetics, more than any other aspect of the life sciences in the twentieth century, has become the object of intensive historical investigation over the past twenty years.": *Beyond the Gene: Cytoplasmic Inheritance and the Struggle for Authority in Genetics*, (New York, Oxford: Oxford University Press, 1987), xi. On the "eugenics industry," see: Philip Pauly, "Essay Review: The Eugenics Industry – Growth or Restructuring?" *Journal of the History of Biology*, 26:1 (Spring 1993), 131-45.
[13] Greg Mitman and Anne Fausto-Sterling, "Whatever Happened to *Planaria*? C.M. Child and the Physiology of Inheritance," in Adele Clarke and Joan Fujimura eds., *The Right Tools for the Job: At Work in the Twentieth-Century Life Sciences*, (Princeton: Princeton University Press, 1992).
[14] Barbara Kimmelman, "Organisms and Interests in Scientific Research: RA Emerson's Claims for the Unique Contributions of Agricultural Genetics," in Adele Clarke and Joan Fujimura eds., *The Right Tools for the Job*. On the disunification of American biology in the decades around the turn of the twentieth-century see: Ronald Rainger, Keith Benson and Jane Maienschein, "Introduction," in R. Rainger, K. Benson and J. Maienschein, eds., *The American Development of Biology* (Philadelphia: University of Pennsylvania Press, 1988), 9; Toby Appel, "Organizing Biology: The American Society of Naturalists and its "Affiliated Societies," 1883-1923," in Rainger, Benson and Maienschein, eds., *The American*

Development of Biology. On the project of unification see: Vassiliki Betty Smocovitis, *Unifying Biology: The Evolutionary Synthesis and Evolutionary Biology* (Princeton, NJ: Princeton University Press, 1996). On producing an academic biology independent of its service role to medicine see: Philip Pauly, "The Appearance of Academic Biology," *Journal of the History of Biology*, 17 (1984), 369-97

[15] Karen Rader, "'The Mouse People': Murine Genetics Work at the Bussey Institution, 1909-1936," *Journal of the History of Biology*, 31 (1998).

[16] Kevles, *In the Name of Eugenics*, 163, 200, 202. Pauline Mazumdar, *Eugenics, Human Genetics and Human Failings: The Eugenics Society, its Sources and its Critics in Britain* (London and New York: Routledge, 1992), especially Chapter 4.

[17] James Neel, though trained in *Drosophila* genetics, was committed to taking up human genetics work in the early 1940s. "Neel's commitment to human genetics was unusual," Susan Lindee notes, "considering the status of the field in 1941. Academic jobs for human geneticists were rare to non-existent, the field was tainted by the excesses of the American eugenics movement, and the methodological problems posed by the study of human populations appeared to many geneticists as nearly insurmountable.": M. Susan Lindee, *Suffering Made Real: American Science and the Survivors at Hiroshima* (Chicago and London: University of Chicago Press, 1994), 68, 78.

[18] Kevles, *In the Name of Eugenics*, 176, 104, 199. See also: Garland Allen, "The Eugenics Record Office at Cold Spring Harbor, 1910-1940: An Essay in Institutional History," *Osiris*, 2nd series, 2 (1986), 225-64.

[19] Diane Paul, "Did Eugenics Rest on an Elementary Mistake?" in Diane Paul, *The Politics of Heredity: Essays on Eugenics, Biomedicine and the Nature-Nurture Debate*, (Albany, NY: State University of New York Press, 1998), 128. Paul points to Ronald Fisher, a brilliant, but socially conservative and in many ways mainline British eugenicist, in warning about the mainline-reform distinction in eugenics. Diane Paul, *Controlling Human Heredity: 1865 to the Present*, (New Jersey: Humanities Press, 1995), 119-120.

[20] Angus McLaren, *Our Own Master Race*, Chapter 7.

[21] Diane Paul, "Eugenic Origins of Medical Genetics," in Paul, *The Politics of Heredity*, 137-8.

[22] Diane Paul, *Controlling Human Heredity*, 121; Diane Paul, "Eugenic Origins of Medical Genetics," in Paul, *The Politics of Heredity*, 138. See also: Diane Paul, ""Our Load of Mutations" Revisited," *Journal of the History of Biology*, 20:3 (Fall 1987); Elof Axel Carlson, "Eugenics and Basic Genetics in H.J. Muller's Approach to Human Genetics," *History and Philosophy of the Life Sciences*, 9 (1987).

[23] Several scholars have discussed the historical ties between eugenics and various sciences, see: Barbara Kimmelman, "The American Breeders' Association: Genetics and Eugenics in an Agricultural Context, 1903-1913," *Social Studies of Science*, 13 (1983), 163-204; Kay, *The Molecular Vision of Life*.

[24] Diane Paul, "The Rockefeller Foundation and the Origins of Behavior Genetics," in Paul, *The Politics of Heredity*.

[25] Paul, ""Our Load of Mutations" Revisited,"; John Beatty, "Genetics in the Atomic Age: The Atomic Bomb Casualty Commission, 1947-1956," in K Benson, J Maienschein and R Rainger, eds., *The Expansion of American Biology* (Rutgers University Press, 1991).

[26] Kevles notes, for example, that many workers interested in human heredity, like Ronald Fisher, thought it "essential to test hypotheses of human heredity via controlled breeding in man's mammalian counterparts." Kevles, *In the Name of Eugenics*, 201. Many 'basic' geneticists were interested in human genetics questions. A clear example is Muller. Early in his career, Muller conducted some research using the human organism - his first contribution was published in 1925 and involved a study of a pair of identical twins raised apart, to assess the influence of environment and heredity in trait formation. Yet, as Elof Axel Carlson has argued, Muller was drawn to laboratory genetics and sought to make contributions to human genetics primarily through his experimental work on *Drosophila*: "Eugenics and Basic Genetics in H.J. Muller's Approach to Human Genetics," *History and Philosophy of the Life Sciences*, 9 (1987), 62, 65. After the war, tensions over the appropriateness of the human animal in human genetics research erupted in the Atomic Bomb Casualty Commission study. Muller was unimpressed, from the start, with the prospect of meaningful findings from this epidemiological study. In his debates with researchers, and his prolific public commentary, Muller prioritized the results from *Drosophila* and mammalian genetics over the inconclusive results of the human population study. He insisted on the *reality* of genetic effects in human bodies as a consequence of the bombs, whatever the human data might suggest. James Neel and William

Schull were less willing to deny the utility of the uncertain human data. Indeed, Neel defended to Muller and others the importance of a specifically *human* genetics. John Beatty, "Genetics in the Atomic Age: The Atomic Bomb Casualty Commission, 1947-1956," 312. Karen Rader, in her analysis of William Castle's mammalian genetics work, suggests that murine genetics supported insights about human heredity: "'The Mouse People'."

[27] Diane Paul, "The Rockefeller Foundation and the Origins of Behavior Genetics," 66, 63.

[28] Kevles, *In the Name of Eugenics*, 234.

[29] Jérôme Lejeune, the individual who first identified the extra chromosome in Down's syndrome, is said to have been inspired by the haplo-four fruit fly to investigate the cytogenetics of Down's syndrome. Kevles, *In the Name of Eugenics*, 246.

[30] Daniel Kevles, *In the Name of Eugenics*, 253.

[31] Diane Paul, "Eugenic Origins of Medical Genetics," in Paul, *The Politics of Heredity*, 133, 134.

[32] *Ibid.*, 137-8.

[33] Barton Childs, "Personal Reflections on the History of Medical Genetics in the U.S., " Abstract of talk presented at the New York Academy of Medicine, April 21, 1999. AG Motulsky, in his 1977 presidential address to the American Society of Human Genetics also articulated this enduring narrative. "It is noteworthy," he writes, "that the methodology which allowed the flowering of human genetics was usually introduced from other fields." AG Motulsky, "Medical and Human Genetics 1977: Trends and Directions," *American Journal of Human Genetics*, 30 (1978), 123.

[34] Daniel Kevles and Gerald Geison argue that "it is a mistake to think of medical or agricultural practices as 'applied' experimental biology; in fact, the interplay has gone both ways, and medical or agricultural interests have often been essential to shaping developments in so-called basic research.": "The Experimental Life Sciences in the Twentieth Century," *Osiris*, 10 (1995), 121.

[35] Kevles and Geison write that it is an "ideology [that] is widely accepted by the medical profession, private philanthropies, government agencies, and the public in general. The question of how fully this ideology of scientific medicine was or is justified by the actual results of basic research in various branches of the biomedical sciences [is] – a crucial issue woefully neglected by historians and other analysts.": "The Experimental Life Sciences in the Twentieth Century," 103. "The modernity of twentieth-century medicine consists of its reliance on the physical and biological sciences," Harry Marks notes. "Yet the association is deceptive....What does it mean, what should it mean, to call medicine a science?": *The Progress of Experiment: Science and Therapeutic Reform in the United States, 1900-1990*, (Cambridge: Cambridge University Press, 1997), 1. See also: Steven Epstein, "History and Diagnosis of 'Scientific' Medicine," *Social Studies of Science*, 28:3 (June 1998), 489-95.

[36] Illana Löwy, argues that "Biomedical research constantly oscillates between the temptation to escape the constraints imposed by medical practice by fleeing into the realm of pure research, and the need to maintain close contact with the clinics in order to benefit from the rewards recompensing the solution of medical problems.": "Biomedical research and the constraints of medical practice: James Bumgardner Murphy and the early discovery of the role of lymphocytes in immune reactions," *Bulletin of the History of Medicine* 63, 3 (Fall 1989), 391; Keith Wailoo, *Drawing Blood: Technology and Disease Identity in Twentieth Century Medicine* (Baltimore: Johns Hopkins University Press, 1997); Harry Marks, *The Progress of Experiment*.

[37] Robert Aronowitz, *Making Sense of Illness: Science, Society and Disease* (Cambridge University Press, 1998, 8-9. See also: Charles Rosenberg and Janet Golden, eds., *Framing Disease: Studies in Cultural History* (New Brunswick and New Jersey: Rutgers University Press, 1992).

[38] In her review of women's early employment at the University of Toronto, Alison Prentice identifies Norma Henrietta Carswell Ford as one of only two successful "pioneer career women in science" out of the generation of women who served at the rank of lecturer or above in the period of expanding opportunities for women after the Great War. Indeed, Ford Walker benefited from the comparatively better treatment of women in the natural and medical sciences at the University of Toronto. Alison Prentice, "Bluestockings, Feminists, or Women Workers? A Preliminary Look at Women's Early Employment at the University of Toronto," *Journal of the Canadian Historical Association*, New Series 2 (1991), 249, 253.

[39] As Evelyn Fox Keller argues, "gender matters to this story ... because of ... situatedness." Evelyn Fox Keller, "Developmental Biology as a Feminist Cause?" in Sally Gregory Kohlstedt and Helen Longino,

eds., Women, Gender and Science: New Directions, *Osiris*, 12 (1997), 28. See also: Evelyn Fox Keller, "Gender and Science: Origin, History, and Politics," *Osiris*, 10 (1995), 27-38.

[40] On Madge Macklin see: McLaren, *Our Own Master Race*, especially Chapter 7.

[41] "At the University of Toronto," McKillop notes, "the proportion of women had risen to 44.4 per cent in 1944-5, but by the 1950-1 academic year it had fallen to 27.2 per cent, a figure identical to that of 1913-4. At no point for more than twenty years after 1950 would the number of women at the University of Toronto reach the forty per cent level." AB McKillop, Matters of Mind: The University in Ontario, 1791-1951, (Toronto: University of Toronto Press, 1994), 421, 556.

[42] Margaret Thompson, Nancy Simpson and Michael Partington, "Norma Ford Walker," in Soltan ed., *Medical Genetics in Canada*, 29.

[43] Fox Keller has termed this 'founder' phenomenon the "Jewish violinist from Odessa effect." Fox Keller is specifically referring to the particular role of a current leader in developmental biology, Christiane Nüsslein-Volhard, whose highly visible presence and pre-eminence has encouraged many women to move into the field. Evelyn Fox Keller, "Developmental Biology as a Feminist Cause?", 23.

[44] The records for students who never appear to have completed are spotty, but until the mid-1950s the annual President's reports list students that are currently being supervised, so some information is available. Of those students identified as being supervised by Ford Walker with identifiable thesis projects, nine are clearly women and only one may be a man, being listed only by initials. See: University of Toronto *President's Reports*, various years.

[45] Ford Walker preserved no papers, so her intentions can only be gauged from such secondary sources.

[46] "Girls' Camp Feature to be nature Talks: Miss Norma Ford to Attend western Gathering at Victoria," *Globe*, April 7, 1927 (UT, A73-0026, 105, 61).

[47] In 1930, apparently on the occasion of her formal appointment as Assistant Professor at the university, the *Globe* provided Ford Walker's photograph with the caption "Brilliant scientist." Ford Walker and "Mrs. MM Kirkwood are the only women assistant professors in the Faculty of Arts." *Globe*, July 3, 1930 (UT, A73-0026, 105, 61).

[48] "Dr Norma Ford takes Annesley Hall Post: Appointed acting head of Women's Residence at Victoria." *Mail*, July 4, 1931; "Dr N Ford Honored at Annual Meeting," *Globe*, April 26, 1934 (UT, A73-0026, 105, 61).

[49] Ford Walker continued to be identified in the annual University of Toronto *President's Reports*, as engaged in work in invertebrate zoology through 1936-1937. Her publications in the field include: N Ford, "On the Behaviour of Grylloblata," *Canadian Entomologist*, LVIII (1925-6), 66-70; N Ford, "Observations on the Behaviour of the Sarcophagid fly, *Wohlfahrtia vigil*," *Journal of Parasitology*, (Dec 1932) XIX:2; N Ford, "Further observations of the Behaviour of *Wohlfahrtia vigil* (Walk.) with notes on the collecting and rearing of the flies," *Journal of Parasitology*, (August 1936) 22, 309-28.

[50] Margaret Rossiter, *Women Scientists in America: Struggles and Strategies to 1940* (Baltimore and London: Johns Hopkins University Press, 1984), especially Chapter 3 "'Women's Work' in Science."

[51] Norma Ford, "A Comparative Study of the Abdominal Musculature of Orthopteroid Insects," University of Toronto, Ph.D. Dissertation, 1923. Ford Walker wrote later that "Out of the selection of topics, human genetics loomed larger and larger." Norma Ford Walker, "The Development of Human Genetics at the University of Toronto," *Proceedings of the Genetics Society of Canada*, 3 (1958), 65. (NA, MG 28 I456, Vol. 1, File: Proceedings of the Genetics Society of Canada).

[52] Ford Walker appears to have been a fairly popular speaker. She specialized, in the 1920s, in nature talks and outings. In 1929 she was reported to have lectured on the topic of human heredity for a series of lectures on health sponsored by the Victoria Women's Association, at Victoria College, University of Toronto: "Heredity Topic Initial Victoria Health Lecture: Dr Normal Ford Compares Topic to Fortune Telling as a Matter of Chance," *Varsity*, December 10, 1929 (UT, A73 0026, 105, 61).

[53] Ford Walker's involvement with the study of multiple births is first mentioned in the University of Toronto *President's Reports* for the 1935-36 academic year. The Dionne quints are first mentioned by name in the report for 1937-38.

[54] This characterization of earlier visions of heredity as inherently in conflict with environmental interpretations has recently been challenged. The "heredity environment debate" may have been more

continuous than Cravens' periodization suggests. See: Kathy J Cooke, "The Limits of Heredity: Nature and Nurture in American Eugenics Before 1915," *Journal of the History of Biology*, 31 (1998), 263-78.

[55] One example of an emerging environmentalist science was the psychodynamic school of psychiatry which prevailed from the Second World War through the 1960s. Gerald Grob, "Psychiatry's Holy Grail: The search for mechanisms of mental diseases," *Bulletin for the History of Medicine*, 72:2 (Summer 1998), 210-214.

[56] Sarah Tracy, "An Evolving Science of Man: The Transformation and Demise of American Constitutional Medicine, 1920-1950," in Christopher Lawrence and George Weisz eds., *Greater than the Parts: Holism in Biomedicine, 1920-1950* (New York, Oxford: Oxford University Press, 1998), 161. Tracy is here citing George Draper's definition of constitution.

[57] Tracy, "An Evolving Science of Man," 165.

[58] Throughout this dissertation I use the highly problematic language of "Mongol," and "Mongolism." I do so for two reasons: to reflect more accurately the language of the time – a language that I think was highly influential – and to avoid a too-ready association between the "Mongolism" of the 1930s through the 1960s, and the "Down's syndrome," or "Trisomy 21" of today.

[59] According to one policy document, Canada "remained colonial and parasitic in relation to scientific accomplishment, and to the fruits of science and technology up to 1940." Louis-Philippe Bonneau, JA Corry, *Quest for the Optimum: Research Policy in the Universities of Canada*, The Report of a Commission to Study the Rationalisation of University Research, Vol. 1, (Association of Universities and Colleges of Canada, 1972), 7. See also: McKillop, *Matters of Mind*, 345.

[60] Of Child's twenty-three Ph.D. students, seven were women and one of these, Libbie Hyman, was "perhaps the most famous. A research associate of Child's for sixteen years, she ended her career working at the American Museum of Natural History in New York City in an unpaid position, supporting herself on royalties from books she had written while teaching at Chicago." Mitman and Fausto-Sterling, "Whatever Happened to *Planaria*?" 190.

[61] McClintock was active across the generations of classical genetics and molecular genetics. While achieving recognition during the early years, her retention of corn as her research organism, and of traditional breeding routines and observation, made her and her work marginal to the new developments. By the 1950s, with the ascendance of biochemical genetics, the language of maize genetics that she spoke was understood by fewer and fewer workers, and the insights she gained into the complex, indeed, according to dominant genetic theory, inconceivable processes, of 'jumping genes' through her intimacy (her 'feeling') for her organism made her work simply un-believable for decades.

[62] Fox Keller also suggests that gender ideologies were operative in the rejection of Barbara McClintock's work. Her science was confusing to her peers, in part, because her vision of the organism de-emphasized hierarchy and the dominant authority of "master" molecules – a gendered model of genetics which was then ascendant. In a recent article, Nathaniel Comfort disputes this gendered interpretation. McClintock's vision was not non-hierarchical, he argues, rather: "The real point [of McClintock's work] is control.": "'The Real Point is Control': The Reception of Barbara McClintock's Controlling Elements," Journal of the History of Biology, 32 (1999), 133. Fox Keller does not, to my mind, argue that McClintock was pre-disposed to the stance of intimacy and holism that she appears to have adopted towards her research organism, or that she produced a "feminine" and less hierarchical science because of her gender, though many readers and critics have taken this to be her point, and she does not explicitly deny the possibility. In more recent work Fox Keller explicitly argues against naturalistic arguments of affinity, preferring to emphasize situatedness: "For the record, let me say clearly that I don't believe that women do have a *natural* affinity for embryology, *qua* women, any more than I believe that women have a *natural* affinity for nature.": "Developmental Biology as a Feminist Cause?", 23 On questions of gender in genetics see also: Bonnie Spanier, *Im/Partial Science: Gender Ideology in Molecular Biology* (Bloomington and Indianapolis: Indiana University Press, 1995).

[63] Embryology emerged alongside genetics out of what had previously been the single subject of heredity-development-reproduction. Adele Clarke argues that a third field also developed out of the same constellation of concerns, the reproductive sciences, see: Adele Clarke, "Embryology and the Rise of American Reproductive Sciences, circa 1910-1940," In. Benson, Maienschein and Rainger, eds., *The Expansion of American Biology* 107-132. "Throughout the 1930s," Fox Keller argues, "the two disciplines

ran neck-in-neck, but by the advent of World War II embryology began a decline from which it did not recover.": "Developmental Biology as a Feminist Cause?", 19.

[64] Embryology attracts feminist attention, Fox Keller argues, for three reasons: first, it is a field in which women have been numerous and are currently among the leaders; second, it is a field which, in its association with reproduction, harbors "traces of implicit and explicit gender coding" which illustrate "the symbolic work of gender"; finally, this field conceives of the biological processes under review in ways which resist "resolution in terms of 'master molecules' and seems to require, instead, conceptual models of just the kind that contemporary feminists have shown partiality to – that is, models of complex interactivity.": "Developmental Biology as a Feminist Cause?", 18.

[65] Karen Rader and Scott Gilbert, "How does gender matter? Revisiting women, feminism and developmental biology," paper presented for the workshop, Science, Medicine and technology in the Twentieth Century: What Difference has Feminism Made? (October 2, 3, 1998, Princeton University). Also in: *Science, Medicine, Technology: The Difference Feminism Has Made*, Angela Creager, Elizabeth Lunbeck, and Londa Schiebinger eds., (Chicago: University of Chicago Press, 1999).

[66] Rader and Gilbert, "How does gender matter?". Fox Keller notes that the early and largely unrecognized work of women scientists on embryological questions in the first half of the century "was hard, often back-breaking work, and widely assumed to be unrewarding. What more natural job to assign to women?: "Developmental Biology as a Feminist Cause?", 23.

[67] Rader and Gilbert, "How does gender matter?".

[68] Fox Keller, "Developmental Biology as a Feminist Cause?", 22.

[69] Charles Rosenberg, "Martin Arrowsmith: The Scientist as Hero," in Charles Rosenberg, *No Other Gods: On Science and American Social Thought*, Revised and Expanded Edition (Baltimore and London: The Johns Hopkins University Press, 1997), 123-131.

[70] N Ford Walker, "The Development of Human Genetics at the University of Toronto," *Proceedings of the Genetics Society of Canada*, Vol. 3 (1958), 65 (NA, MG 28 I456).

[71] Kevles, *In the Name of Eugenics*, 233

[72] Jan Sapp, *Where the Truth Lies: Franz Moewus and the Origins of Molecular Biology*, (Cambridge University Press, 1990).

[73] At McMaster, Uchida joined Murray Barr's ex-student and colleague, David Carr, who had left Western in 1967. On Uchida see: Ronald Davidson and Jaimie Dianda, "Regional Development – Hamilton and Region (Ontario Central West), in Soltan, ed., *Medical Genetics in Canada*, 81-86.

[74] Kevles, *In the Name of Eugenics*, 249. This general sequence of stages in the development of medical genetics is recounted in numerous participant histories. See, for example: James V. Neel, "Our Twenty-Fifth," presented at the 25th anniversary meeting of the ASHG at Atlanta, October 24-27, 1973, *American Journal of Human Genetics*, 26 (1974), 136-144.

[75] Robert Aronowitz defends the language of 'social construction' in Aronowitz, *Making Sense of Illness:*, 10-12.

[76] Barr graduated in medicine from the University of Western Ontario (UWO) in 1933. He received an M.Sc. for work in neuro-anatomy in 1938 and prepared for doctoral work at the University of Minnesota in the late 1930s, but these plans were derailed by the war which he spent as a medical officer with the Royal Canadian Air Force. After the war, Barr again pursued doctoral studies, this time at McGill, but his expanding responsibilities in the growing Department of Anatomy at Western after 1945 put an end to further formal education. For biographical details on Murray Barr, see: Murray L Barr, "Human Cytogenetics; Some Reminiscences," Roots, *BioEssays*, 9:2,3 (August-September 1988), 79-82; Paul Potter and Hubert Soltan, "Murray Llewellyn Barr," *Biographical Memoirs of the Fellows of the Royal Society*, London, 43 (1997), 31-46.

[77] In his memoirs, Barr notes that "Dr Hall was a young man with an impressive research background at the Banting Institute, University of Toronto; in correspondence with him during he first part of 1945, I learned of his plan to appoint well-trained young men in several departments and to place an increased emphasis on research." (NA, MG 30 B111, Vol. 1, File 1-2, 1979).

[78] The end of Barr's career was also much affected by institutional changes at Western. As Chair of the Department in the 1960s administrative work, including that relating to the relocation of the medical

school, helped to curtail his research program. Barr had been chair of the Department of Microscopic Anatomy in the years that it existed, from 1953 through 1964, but this was a small department. When this merged with Gross Anatomy in 1964, and Barr became chair of the much larger Department of Anatomy, until he retired from this post in 1967, administrative work was apparently onerous.

[79] Evelyn Fox Keller has argued that central to the making of genetics was the forging of "a way of talking about genes." This way of talking is identified by Keller as the "discourse of gene action," in which the gene is "part physicist's atom and part Platonic soul – at one and the same time a fundamental building block and an animating force." This discourse, Fox Keller argues, successfully imbued the nuclear gene with ultimate authority, relegating all other processes to a secondary ontological status, while still permitting the fundamental ignorance about what genes "actually do," to be ignored: "It enabled geneticists to get on with their work without worrying about their lack of information about the nature of such action – to a considerable degree, it even obscured the need for such information." Evelyn Fox Keller, *Refiguring Life: Metaphors of Twentieth-Century Biology*, (New York: Columbia University Press, 1995), 9, 10, 11.

[80] On "the problem of idiosyncrasy" in disease see: Aronowitz, *Making Sense of Illness*, 7-10.

[81] Rayna Rapp, "Risky Business: Genetic Counseling in a Shifting World," in J Schneider and R Rapp, eds., *Articulating Hidden Histories: Exploring the Influence of Eric R. Wolf* (University of California Press, 1995), 176

[82] Aronowitz, *Making Sense of Illness*, 143-4, 124, 8.

[83] Gerald Grob has suggested that modern medical genetics parallels "the older [nineteenth century] concept of predisposition or diathesis.": "Psychiatry's Holy Grail," 217.

[84] Aronowitz, *Making Sense of Illness*, 118.

[85] *Ibid.*, 116, 127, 140.

[86] Charles Rosenberg, "Banishing Risk: Continuity and Change in the Moral Management of Disease," in Allan Brandt and Paul Rozin, eds., *Morality and Health* (New York and London: Routledge, 1997), 44.

[87] On these developments see: Horace Freeland Judson, *The Eighth Day of Creation: Makers of the Revolution in Biology* (NY: Simon and Schuster, 1979).

[88] Kay, *The Molecular Vision of Life*, 93

[89] AG Motulsky, "Medical and Human Genetics 1977: Trends and Directions," *American Journal of Human Genetics*, 30 (1978), 124, 126, 127.

[90] Victor McKusick, "Medical Genetics: A 40 Year Perspective on the Evolution of a Medical specialty from a basic science," *Journal of the American Medical Association*, 270:19 (Nov 17, 1993), 2351.

[91] Victor McKusick, "Introduction," in Victor McKusick and Robert Clairborne, eds. *Medical Genetics*, (New York: HP Publishing Co., Inc., 1973,1974, 1976), xvii. The list of misconceptions was also published in: *Annals of Internal Medicine*, 75:4 (1971), 642.

[92] McKusick, "Introduction," xiii.

Chapter 1

Making the Indigenous Tradition: Human Genetics and Human Biology in Toronto, c. 1935 – 1950

Introduction

Our story begins in the mid-1930s when, inspired by the birth of the Dionne quintuplets, Norma Ford Walker began to re-direct her research interests from the study of insects to the study of human inheritance. After the quintuplets' birth in 1934, and as part of the international fascination with these children, a scientific study was coordinated through the St George's School for Child Study at the University of Toronto. Norma Ford Walker, together with John MacArthur also of the Department of Biology, was called on to conduct the "biological" study of the quintuplets. Such a study involved the analysis of the zygosity of the children, to determine whether all were the product of the same fertilized ovum. In the view of Ford Walker and her collaborators, what was being determined was whether these children were genetically "identical."

The collaborative scientific study of the Dionne quintuplets connected Ford Walker to a local community of researchers interested in human biology and genetics who were linked to other similarly-engaged workers in the U.S. and Britain.[1] Ford Walker's colleagues in this project were on the margins of the classical genetics enterprise, cynical about mainline eugenics, and interested to investigate the role of both

environment and heredity in human inheritance. Whether gained through this high profile project, or previously possessed, Ford Walker emerged from the Dionne study with expertise in the conventions of classical genetics, a heterodox approach to genetic study, and a technical skill that would serve as the primary resource for her research school for more than twenty years: dermatoglyphics, or the study of skin patterns on the hands and feet.

This chapter explores the first fifteen years of research conducted by Ford Walker and her emerging research school. With the aid of international colleagues in the biological and medical sciences, and through such institutions as the university, the hospital and custodial facilities, members of the Ford Walker school used dermatoglyphic techniques in pursuing two distinct methods – the twin method and what I will call 'the Mongol method.' These methods supported etiological inquiry which presumed the relevance of both genetical and environmental influences and was agnostic on the question of simple causation.

In investigating these historical processes, I suggest answers to several perplexing questions. In the first instance, the Ford Walker school shares few features with the then-dominant British school of human genetics. The first such question must therefore be: what was the science that was being conducted? I argue that it was a species of human genetics, but it was an identifiable variety and deserves to go by the name 'the indigenous tradition.' A second and related question concerns the identity of the practitioners. The fact that these were, to a considerable degree women, is taken to be both meaningful and consequential. The marginality of the Ford Walker school within the international

community of human geneticists was reflected and sustained by its production in Toronto as 'women's work.'

The Dionne Years

The birth of the Dionne quintuplets in May 1934 was met with international attention.[2] As Cynthia Wright has argued, the quints were a sounding board for a range of concerns.[3] Together with the issues of Anglophone-Francophone hostility, economic depression and opportunity, and gender relations and the family, the quints were fodder for the nature-nurture debates. As subjects in an extended research program, their bodies and behavior were measured, observed and controlled in an effort to answer urgent questions. Establishing the "identical" nature of these children fell to Ford Walker and her senior colleague in the Department of Biology, John MacArthur. Drawn into this project with little prior experience in the study of the human animal, Ford Walker forged skills and collegial connections and was profoundly influenced by the intellectual milieu in which the Dionne study was pursued.

The research program was dominated by child study experts and led by William Blatz, the "energetic director of the St George's School [for Child Study]." Study of the quints provided Blatz with the opportunity to "demonstrate the efficacy of modern child rearing methods and educational practices. Blatz's enthusiasm for the potential of this research project," Kari Delhi argues, "was palpable: "never before in the history of

human genetics," [Blatz argued], "have five identical children been born into circumstances where the opportunity not only may but must be provided for following their growth and development under controlled conditions"."[4] Delhi suggests that Blatz was committed to demonstrating the influence of environment in the children's lives, in accordance with his attachment to scientific child rearing practices. "Much was made of the "discovery"," she writes, "that the girls possessed distinct personalities." Despite the difficulty that "ordinary" people had in telling the girls apart, Delhi argues that psychological science, "was able to confirm the existence of unique and different individuals, even within a group that appeared "the same"."[5] Yet this commitment was critiqued by some prominent geneticists, Delhi adds. Horatio Newman, an American geneticist interested in multiple births, who had been invited by William Blatz to join the research advisory committee, publicly criticized the environmental explanations being proffered by Blatz, suggesting that, "to the geneticist ... the quints are turning out rather better than might be expected."[6]

Madge Macklin, Canada's premier human geneticist, and an outspoken eugenicist, also saw opportunity for a more hereditarian than environmentalist interpretation of these children. Reviewing the *Collected Studies on the Dionne Quintuplets* for the *Journal of Heredity* she noted that "the psychologists are striving to show the greater effect of environment in differentiating these children into five distinct patterns. To the geneticist, who admits that environment plays a large role in this, the striking similarity of the curves of motor, adaptive, personal-social behavior and language development plotted by psychologists who certainly were not trying to prove

the importance of an inherited background, is most significant."[7] Popular interest in the quints resonated with similar concerns. The seemingly miraculous survival of the Dionne children was seen to be due both to their "hardy stock" and to the ministrations of modern medicine and the apostles of "scientific motherhood."[8]

John MacArthur and Ford Walker recognized the salience of their work for these debates. They noted that, of the many biological problems their study might help to solve, the goal of "separating and evaluating the influences of heredity and environment in the development of various physical and mental characteristics," was of premier importance.[9] To do this involved determining "as certainly as possible just how the quintuplet set was constituted," in order to assess whether the quints shared "identical" inheritance.[10]

Yet though much hung in the balance, the diagnosis of the Dionne's zygosity was far from technically simple. "It is somewhat disillusioning to learn," MacArthur and Ford Walker wrote, "that there is no single simple qualitative test, or absolutely decisive and infallible diagnostic mark, by which to tell whether a pair of twins is fraternal or identical." [11] Though noting that "identical twins, arising by division of the same fertilized egg cell mass or embryo, quite invariably carry the same chromosomal factors and are of the same genotype," there was no way to assess these genetic materials. MacArthur and Ford Walker turned to such devices as the "similarity method," selecting phenotypic characters for comparison that were "least modified by other than hereditary factors" to assess zygosity.[12]

The authors had wanted to examine as many biological characters as possible in the entire family, but achieved only limited access. The "most satisfactory data" proved

to be the hand and foot prints. Dermatoglyphic patterns were seen to evidence some "strongly inherited characters" and these inherited patterns were made more useful by their resistance to environmental change, being fixed before birth. But these inherited patterns were still complex markers of inheritance – even "identical twins" were expected to have distinct finger prints since "two or more embryos from a single egg develop inequalities, though they carry the same inherited potentialities."[13]

Dermatoglyphic evidence from the quints was evaluated in several ways. First, the authors used finger print patterns to calculate a theoretical "genotype" of each of the quints. All five children were seen to possess the same "genetic formula" for finger prints of "VVRRUU."[14] A second set of procedures for evaluating the dermatoglyphics involved efforts to calculate, both subjectively and quantitatively, the relative similarity of the prints. By this method, the quints were seen to be generally similar and to comply with the standard whereby there was "less difference between a hand of an identical twin and a hand of its mate than there is between the left and right hands of either individual."[15] But the most decisive use of dermatoglyphic evidence involved the comparison of dermal characteristics between the quintuplets by comparison with their sibs. This permitted identical inheritance to be distinguished from "family likeness," by demonstrating that "hereditary dermatoglyphic characters" which showed "strong resemblances" in the quints were notably different in immediate family members "due presumably to segregation."[16]

These methods were indebted to the theories of classical genetics, then dominant in North America. They presumed chromosomal inheritance, the material gene, and

Mendelian patterns of transmission and segregation.[17] The dermatoglyphic evidence, together with supportive evidence from the fetal membranes, the foot prints, the blood groups, and assorted other aspects of the girls' appearance and mannerisms, demonstrated that the "five all carry the same inheritance."[18] But in addition to its diagnostic function, dermatoglyphic evidence also facilitated attention to developmental variation. The quints might be genetically "identical," MacArthur and Ford Walker noted, but some "non-inherited variations" were also apparent. The girls were not doubles, and the process of development evident in dermal patterns ensured that some inequalities appeared despite the identical "inherited potentialities."[19]

Twin Studies, Dermatoglyphics and Human Genetics

The 'biological study' of the Dionne quintuplets initiated Ford Walker into the academic study of human heredity. While her interest in such questions had been evidenced in public talks from the late 1920s, it was not until the mid-1930s that Ford Walker switched her research program at the university from invertebrate zoology to human heredity. The social and intellectual environment of the Dionne study shaped Ford Walker's initiation into the field of human genetics in particular ways.

First, though the Dionne project was a high profile undertaking, this was an anomalous situation for a community of workers who operated on the margins of North American science. In Canada, the University of Toronto was, with McGill University, the

chief repository of the research ideal, and it was Toronto that came to "dominate Canadian science by the interwar years."[20] Yet Canadian science was still backward in these decades.[21] Historian of education, AB McKillop, argues that progress in advanced research in the inter-war period was "modest,...beyond the rhetorical acceptance of the research ideal."[22] It was constrained both by the limited financial supports available, and by a cultural commitment to the humanities as "the formal base of the scholarly pyramid."[23]

Second, many of the workers involved in the Dionne project were rather cynical about the claims of mainline eugenics. Angus McLaren, in his study of the eugenics movement in Canada, has characterized William Blatz as profoundly "skeptical" of the claims of mainline eugenics, and John MacArthur as "perhaps the best qualified opponent of the eugenicists."[24] Horatio Newman is characterized by Daniel Kevles as a person who "had been a strong hereditarian and eugenicist" but who, by 1937 at least, "rather sympathized with the dictum that what heredity could do, environment could also do."[25]

Finally, the intellectual milieu of the Dionne study supported particular kinds of genetics research. The St George's School, through which this collaborative project was coordinated, was one of five centers in the US and Canada which worked to establish a professional science of child psychology in the 1920s and 1930s.[26] Hamilton Cravens argues that these schools of child development were homes to a "new mentality in the life sciences," which privileged interdisciplinarity and a gestalt vision of the whole and its parts, and fostered attention to heredity and environment as interactive rather than oppositional forces.[27] This was a community of researchers who presumed the

significance of both genetics and environment as causal forces in human heredity. Indeed, Ford Walker's colleagues in this project introduced her to research tools which supported broad etiological enquiry. Though Ford Walker was clearly familiar with the premises of classical genetics, the approach which she came to employ, building on twin studies and dermatoglyphic techniques, stretched the boundaries of the classical approach.

Horatio Newman was a biologist working at the University of Chicago. He was an expert in the application of dermatoglyphics to twin diagnosis.[28] Newman attended the University of Toronto in his undergraduate years and retained Canadian links, above and beyond the Dionne study. In the late 1920s, in Oshawa, Ontario, Newman located his first set of identical twins reared apart, having searched for just such a natural experiment for years. Notably, John MacArthur was the Toronto expert called on by the media to comment on this extraordinary case.[29] Newman eventually located nineteen sets of identical twins reared apart and with two educational psychologists at the University of Chicago he collaborated in an important study on the heritability of intelligence. Comparing these nineteen twin sets with a control group of identical twins reared together, Newman and his colleagues found themselves "disillusioned" with their original hereditarian hypotheses. Daniel Kevles argues that their study, published in 1937, pointed to the indivisibility of nature from nurture in producing characters such as intelligence.[30]

John MacArthur was an Associate Professor of Genetics in the Department of Biology at the University of Toronto.[31] He was trained by the iconoclast Charles Manning Child,[32] who was like Newman also at the University of Chicago.[33] Child, like many other American geneticists in the first three decades of the 20th century, pursued

research interests which diverged from the dominant tradition of American genetics as defined by Thomas Hunt Morgan and the Columbia school.[34] Though less of an iconoclast than his mentor, MacArthur's research in agricultural genetics, mammalian genetics and studies of human heredity, involved him with the kinds of complications which research with *Drosophila* was designed to avoid: specifically, a service relationship towards agriculture and medicine.[35] Indeed MacArthur embraced such connections. In the latter-half of the 1930s he worked to produce a commercial greenhouse tomato immune to brown mould. The successful product was introduced at the Vineland Horticulture Experiment Station in the 1939-40 academic year as "vetomold."[36]

MacArthur's interest in human genetics was not so clearly tied to medical institutions as his agricultural work was to commercial breeding. Yet he had an enduring interest in human heredity. Beginning in the late 1920s, and continuing into the early 1940s, MacArthur conducted research on "abnormal human heredity," collected "family histories" and supervised the work of students in human biology and genetics.[37] He became, according to two expert commentators, an "experienced student of twins."[38] Finally, MacArthur also had a research interest in mammalian genetics. He supervised and conducted work with rats, and in the late 1930s, he collaborated in such research with the patriarch of mammalian genetics, William Ernest Castle, when the latter had retired from Harvard to work at the University of California, Berkeley.[39]

Genetics research with the complex organisms which MacArthur preferred not only indebted biologists to concerns beyond the academy, such research also expanded

the scope of questions. The "'characters' that absorbed the attention of many agricultural breeders seemed physiological," Barbara Kimmelman writes: "breeding to increase yield, for particular size, shape, and color, for disease resistance, and to increase or decrease particular nutritive content. These were largely complex phenotypic characters with explicit commercial significance."[40] Karen Rader argues that Castle had mentored a generation of mammalian geneticists with a "skeptical attitude toward Mendelism and a deep commitment to comprehensive genetic knowledge."[41] One group of Castle's students worked with mice. Their experiments were "slower-paced." Yet they worked with "less genetically efficacious organisms," Rader argues, "because these materials promised a different kind of result – knowledge of physiological genetics, evolution, and (for some) complex human heredity." Engaged by such questions, MacArthur tackled not only mammalian genetics with model organisms, but also research with the human animal itself.

The involvement of Newman and MacArthur in the Dionne project was due to their expertise in twin study, one of the techniques which Kevles characterizes as central to human genetics research in the 1930s and 1940s.[42] Newman and MacArthur approached twin study with a particular tool, dermatoglyphics, which had application beyond the support of twin diagnosis and which supported broad based inquiry into etiological processes in human biology.

In their 1943 monograph, *Finger prints, Palms and Soles: An Introduction to Dermatoglyphics*, Harold Cummins and Charles Midlo of Tulane University noted that the study of dermatoglyphics was a "relatively neglected aspect of human biology." Yet

their text, the main one in the field, was committed to demonstrating the versatility of this technique and its potential. "The [skin] configurations," Cummins and Midlo wrote, "are formed in the early fetus and they persist unchanged."[43] They could be used for personal identification, for twin diagnosis, in cases of questioned paternity, in assessing racial variation, in studies of inheritance, and in assessing constitutions potentially including such constitutional characteristics as sex, handedness, disease susceptibility, character, temperament, criminality and degeneracy.

"As objects in the study of inheritance," Cummins and Midlo wrote, "dermatoglyphics present certain advantages." Features in skin patterns "may not be an ultimate anatomical unit," Cummins and Midlo added, "yet these features are at least among the smallest characteristics readily accessible for testing the limits of hereditary control." The value of dermal patterns in the study of heredity also derived from their variability, making them "favorable for comparison among members of families." Dermatoglyphics were age and environmentally stable, persisting unchanged after being established during early fetal development, and were unlikely to be a factor in selective mating.

The versatility of this technique was, to some extent, a function of the complexity of the processes involved in the development of dermal patterns. This complexity also posed challenges for "genetic analysis of dermatoglyphics." Understood to be affected by many genes and to be conditioned by embryological processes, including such factors as skin thickness and tension, the mechanisms of heredity were necessarily obscure. Moreover, distinguishing differential involvement of such generic factors as sex and race

in the patterns of individuals or groups, from the more specific concerns of interest such as family or constitution, was consistently difficult.[44]

Among those whose work Cummins and Midlo cited as they reviewed the potentials of dermatoglyphics was that of John MacArthur and Horatio Newman, particularly in relation to twin diagnosis. They also acknowledged, more personally, their debt to "colleagues in research" like Ford Walker, who had, by the mid-1940s, placed this flexible technique at the foundation of her research school.[45]

"Students of human heredity," Daniel Kevles has argued, "treasured well-defined, sharply segregating traits as immune as possible both to uncertainty in identification and to environmental influence."[46] There was therefore, he adds, "considerable interest stimulated in the early thirties by the discovery that human beings possessed a heritable sensitivity to the taste of the compound phenylthiocarbamide, or PTC."[47] Ford Walker was not immune to the benefits of simply inherited phenotypic characters. She used PTC strips in her public talks to convince her audience of the heritability of characteristics like taste.[48] Indeed, Ford Walker may have begun her research interest in human heredity because of PTC.[49] But she used PTC in her published research to emphasize the inheritance of complex characteristics.[50] And most of her work used a research tool, dermatoglyphics, which met none of Kevles' criteria and stretched the bounds of classical genetic inquiry. In taking up dermatoglyphics, Ford Walker embraced a tool better able to demonstrate broad etiological influences than the workings of single genes, and more likely to suggest the involvement of environmental and developmental influences than to prove their absence.

Beyond Twin Diagnosis: Dermatoglyphics and the Dionne Quintuplets

MacArthur's and Ford Walker's biological study of the Dionne quintuplets established the identical zygosity of the children and confirmed in the authors a commitment to twin diagnosis and research. In their published study on the Dionne's, the authors reviewed the published literature to produce a list of known quintuplet births. Thereafter, both researchers contributed to the literature in the area of twin diagnosis but their interests soon diverged. MacArthur paid particular attention to perfecting dermatoglyphic techniques for twin diagnosis, confirming the reliability of this method.[51] Ford Walker took pleasure in continuing to contribute to the list of known quintuplet births in subsequent publications.[52] But she was less interested than MacArthur in dermatoglyphic techniques. Her contribution to improving the methods of twin diagnosis was a long-term study of fetal biology.[53] She studied, for example, the "physical characters of a case of united foetuses," and the "blood-vascular system in the placentae of multiple births."[54] This research, which she initiated in the 1936-37 academic year and continued through the 1950s, helped to clarify the relationship between fetal membranes and zygosity and to address developmental questions about twinning in monozygotic cases.

Ford Walker was an advocate of the twin method. She proselytized about the need for accurate determinations of zygosity if the twin method were to be of value for

medical research.[55] And as a senior scientist, she published an overview paper outlining the methods for zygosity diagnosis.[56] But Ford Walker quickly went beyond simple twin diagnosis, using the fact of accurately diagnosed twins to illuminate the heritability of disease. And early in her career in human genetics she began a study of "Mongolism" using dermatoglyphic analysis which would produce a new tool for measuring developmental anomaly.

Investigating "the Mongol"

Beginning in the 1937-38 academic year, Ford Walker began to acquire graduate students with an interest in human heredity. She put her first two graduate students to work examining the dermal patterns "in mongolian idiots."[57] The following year, one of these two women students, Grace Workman, finished her Master's thesis,[58] and Ford Walker reported the beginnings of her own long-term research in the field. She began a study of dermatoglyphics in Mongols and their kindred which continued for several years, merging into studies of "etiological factors in mongolism," and including, by the 1950s, questions of "diagnosis."[59] Unfortunately, there are no records of these studies, and we must turn to the work of Ford Walker's students to observe the developing methods in the Ford Walker school.

Grace Workman's study confirmed and sought to expand upon the recent, as yet unpublished findings of Harold Cummins of Tulane University, who had shown that the

"disturbance in general growth" long apparent in Mongols could be traced to a "disturbance of growth" established as early as the third and fourth fetal months.[60] The importance of Cummins' discovery, Workman argued, was in making it possible "to time the disturbance of growth and indicate that the mongoloid constitution was established in the early foetal months."[61]

Workman's thesis was devoted to three arguments: first, confirming Cummins' findings of a distinctive set of dermatoglyphic patterns common to Mongolian idiots; second, seeking to explain the patterns of disturbance in terms of the embryogeny of dermatoglyphics; and third, examining the dermatoglyphics of persons born to women at late maternal age to assess the independent effect of late maternal age on dermatoglyphic patterns.

The first part of Workman's study then, confirmed the important question of the timing of the "disturbance of growth" apparent in Mongolism. Workman's analysis of the dermal patterns of Mongols added to Cummins' evidence, and earlier research on the fusion of skull bones, to confirm that "mongolism is established prior to the third foetal month, possibly as early as the 39th day."[62] A close examination of the embryogeny of these palmar patterns led Workman to the conclusion that "in the mongoloid hand an early stage of development is preserved until after the dermal ridges are laid down and that growth and development have been retarded in some way."[63]

While the first half of Workman's thesis contributed to an understanding of the developmental process by which Mongols were made, Workman devoted the latter half of her study to exploring the cause of the condition, which at that time "remain[ed]

obscure."[64] From a review of the literature, she suggested that three interpretations were possible. Mongolism might result from "inherited factors," the evidence for which were higher frequencies of such births than expected in some families, together with some evidence of inherited familial traits in mongolism. Alternately, mongolism might be due to "environmental factors active prior to birth." Workman cited a recent Ontario study which provided evidence of the influence of thyroid disturbances, and pointed to the evidence for the influence of advanced maternal age and the adverse condition of the mother – in short, "factors affecting the ovum." The final cause was the combination of both the environment and heredity. Workman cited Lionel Penrose on evidence derived from twin studies concerning an "inherited susceptibility to the effect of adverse environment."[65]

Workman's own research addressed the well-accepted influence of advanced maternal age in the production of Mongolism. She assumed that, "If the disturbance of growth in the mongoloid palm is dependent upon the factor of advanced maternal age alone, with no accompanying hereditary factor, then one might expect to find a similar tendency towards disturbed growth in the palms of persons born to older mothers."[66] But in assessing the dermatoglyphics of non-mongoloid persons born to mothers of late maternal age, Workman was unable to find any "correlation in normal persons between pattern expression and maternal age." Workman's findings suggested that "Advanced maternal age must, therefore be significant only as related to some factor or factors such as heredity or endocrine disturbance."[67] Advanced maternal age alone could not explain the peculiar dermal patterns apparent in the Mongol.

In this study, Workman confirmed Cummins' findings that the Mongol had suffered from a profound developmental disturbance during fetal development and that the dermatoglyphics provided a legible sign of that process. Dermatoglyphics, in this project, served a developmental function. Unlike twin diagnosis, where general dermal patterns were believed to be strongly inherited and where broad similarities demonstrated 'identical' inheritance, the dermal patterns in the Mongol testified only to developmental processes, while remaining agnostic on the issue of cause. Indeed, dermal analysis of Mongols confirmed the complexity of systems of causation, and the seeming irrelevance of simple models of genetic control. In the 1940s, Ford Walker would find opportunities to use this complex etiological framework in studies of disease. And she would find – in constitutional medicine – a parallel, yet medical, etiological framework.

Just as John MacArthur had embraced a service orientation in agricultural genetics, Ford Walker embraced a service orientation in her work in human genetics – establishing links to those institutions which housed specimens of human biology, such as hospitals and custodial institutions. Grace Workman, for example, had gained access to "mongoloid idiots" at the Ontario Hospital School in Orillia. In addition to providing access to research material, such co-operative work facilitated attention to disease and disability and helped forge a medical orientation among researchers who were, by training, biologists.

Building a Service Orientation: Human Genetics in the Hospital

Norma Ford Walker was housed within the Faculty of Arts (after 1960, Arts and Science) throughout her academic career. It was not until the 1970s that the university's medical geneticists were housed within the Faculty of Medicine at the University of Toronto. The medical orientation of the school was thus initially fostered through association with hospitals and other patient facilities.

Ford Walker's studies of fetal membranes to aid in twin diagnosis were necessarily pursued "in co-operation with four Toronto hospitals."[68] When she began her study of Mongols and their kindred, Ford Walker reported the "co-operation of several Toronto and New Jersey hospitals."[69] Meanwhile, a "biological study of a pair of monozygotic mongoloid twins" was conducted in co-operation with a collaborator from the "Northern New Jersey Mental Hygiene Clinics" in 1939-40.[70] In the same year, Ford Walker reported collaborative work with the Toronto Hospital for Sick Children.[71] This latter connection would prove enduring.

Ford Walker's collaborative ventures with Sick Kids were rewarded with an appointment as part time consultant on staff, beginning in 1940 and continuing until the early 1960s.[72] Ford Walker attributed her association with the Hospital for Sick Children to the "active interest of Dr Alan Brown...physician-in-chief" of the hospital.[73] As an individual, Alan Brown – remembered as a pioneering pediatrician in his own right – was an important influence. He served in the 1940s as a research collaborator, and proved to be a source of research ideas.[74] But the association between medical genetics and the

pediatric hospital was not unique to the link between Alan Brown and Ford Walker. Such connections were also made in other communities throughout North America. The hospital in general, and the pediatric hospital in particular, were important in several ways for those interested in "practical applications" of human genetics in medicine.[75]

In the first instance, the hospital facilitated the cross-fertilization of the medical and biological sciences. Trained as a zoologist, Ford Walker looked to her medical collaborators for diagnostic expertise, and for explanatory frameworks about disease causation drawn from the scholarship of academic medicine. But pediatric facilities, as distinct from the general hospital, provided more than just clinical and scholarly expertise. The populations served by the pediatric hospital were especially interesting to researchers such as Ford Walker. Through the Hospital for Sick Children, Ford Walker gained access to extraordinary cases of disease and disability, notably monozygotic twins with discordant anomalies and rare childhood diseases. But Ford Walker was not solely interested in Sick Kids for rare conditions. She also gained access to extensive medical records on common diseases. Moreover, many of the extraordinary cases of childhood disease that Ford Walker attended to were not strictly genetic.

In the late 1960s, Margaret Thompson wrote that "Most of the severe genetic diseases are evident at birth or begin in childhood."[76] By this accounting, pediatric facilities were of obvious significance for medical genetics. But Thompson's interpretation is not entirely apt. We should be cautious about assuming that genetic diseases, as currently understood, were the focus of Ford Walker's attention. Indeed,

rather than being a home for formally genetic disease, the pediatric hospital was the home of congenital disease – diseases that were inborn.

The chief importance of the pediatric hospital for medical genetics was the encouragement provided to studies of human heredity through what reads to us now as the etiological ambiguity implicit in the notion of "congenital."[77] For Ford Walker, and the research tradition that she built, the conceptual blurring of congenital and genetical that a pediatric facility institutionalized was of enhanced value. It made sense of a theoretical framework which conceived of environment and heredity as forces which were mutually relevant in hereditary causation. The blurring of congenital and genetical, in other words, made sense of causal explanations which addressed all facets of the "nature-nurture" debate. Moreover, this blurring was also appropriate to a tool for assessing human inheritance, dermatoglyphics, which incorporated developmental concerns.

The resources of medical facilities, the theories of academic medicine and the productive ambiguity of the concept of congenital disease helped to advance the techniques that Ford Walker and her students and colleagues had worked to develop in the latter-half of the 1930s. Through these resources, twin studies were fleshed out into a twin method which advanced knowledge about the etiology of disease. Through these resources also, the studies of dermal patterns in Mongols were developed as a Mongol method. The disturbed dermal patterns of the Mongol served as a prototype of fetal disturbance that helped to explain developmental anomalies in diseased bodies.

Ford Walker's earliest studies at Sick Kids dealt with pyloric stenosis, a congenital condition of intestinal blockage resulting in dehydration and malnutrition but amenable to cure through surgery. She began with a study of two pairs of twins with the condition in 1938-39, then expanded the study to include 12 pairs of twins and more than 400 individual cases recorded in Sick Kids' files.[78] Ford Walker and her co-authors published two articles on this condition in 1941, one of which was used to argue for the "genetic basis" of this condition, the other of which demonstrated the influence of a particular environmental factor in making the condition manifest.[79]

These studies drew on medical resources in more ways than one. In addition to drawing cases of pyloric stenosis from the files of Sick Kids, Ford Walker and her co-authors made sense of this evidence in relation to constitutionalist arguments advanced within the halls of academic medicine. As Sarah Tracy has argued, constitutional medicine emerged as a reaction against the seeming dominance of an infectious-disease paradigm and asserted the relevance of the human "constitution" in disease causation.[80] The work of Ford Walker and her Sick Kids colleagues was in conversation with one of the premier American advocates of constitutional medicine, William Sheldon.

Sheldon had published a study in 1938 which reviewed 36 sets of twins with pyloric stenosis. His study indicated that "identical" twins were usually both affected by the condition, while in fraternal twins, it was more likely that only one member of the set would be affected. In addition to suggesting a hereditary influence in disease causation, Sheldon demonstrated an environmental influence by showing the disproportionate

incidence of twinning (of either kind) in children with this condition – twin pregnancies were understood to create a greater developmental burden for member of the set.[81]

Ford Walker's study was modeled on Sheldon's, but with the key addition of a demonstration of methods for assessing zygosity. Sheldon's cases, together with another ten "possibly monozygotic" cases gleaned from the literature, had provided questionable evidence about etiology by providing questionable evidence about zygosity.[82] Ford Walker's study was, in the first instance, a demonstration of the need for accuracy in twin diagnosis. But it was also a demonstration of the use of twins as a method for assessing the roles of heredity and environment in producing disease. [83]

Ford Walker's and her colleagues' first study presented a review of twin cases from HSC's files where both members were affected with pyloric stenosis. In the twelve cases reviewed, the differing sex of the twins proved that nine sets were clearly fraternal and one same sex twin set was of questionable zygosity. The bulk of the study was devoted to analysis of the two same-sex twin sets with pyloric stenosis available for detailed study through Sick Kids whose identical zygosity could be established using dermatoglyphics, the similarity method and analysis of the birth membranes.

In this study, Ford Walker was also able to use the findings from the dermatoglyphic analysis of Mongols to advantage. The fetal disturbances that made their mark in the palm prints of Mongols corroborated the fact that developmental disturbances could cause dermatoglyphic variations. This evidence made sense of a marked dissimilarity in the palms of one twin set: Ford Walker et al theorized that one member of these otherwise "identical" twins had been subjected to some disturbance as a result of

the odd arrangement of the fetal membranes.[84] Moreover, in both members of the second twin set, a particular palmar configuration was present that was generally peculiar to Mongols. Once again this dermatoglyphic configuration provided evidence of fetal disturbance – in this case a disturbance that imposed a "double handicap" (of fetal disturbance and pyloric stenosis). This evidence made implicit sense of the fact that one member of this twin pair did not recover from surgery and died.

The second published study on pyloric stenosis addressed the environmental thesis more fully.[85] Having contributed, with others, to the demonstration of the genetic basis of this disease, it was important, Ford Walker argued, to investigate the role of birth order in this disease: to "weigh the evidence for the importance of the prenatal environmental factors associated with primogeniture in the production of the disease."[86] Reviewing case file data on order of birth in 405 cases of pyloric stenosis, Ford Walker et al demonstrated a higher proportion of first borns among cases of pyloric stenosis than would be expected by chance. "The importance of primogeniture as an etiologic factor in pyloric stenosis," they argued, "is at least indicated."[87]

This kind of study – of monozygotic twins with seemingly inherited anomalies – was particularly dependent on institutions such as Sick Kids for the location and analysis of such rare events. Ford Walker's continued association with Sick Kids ensured that more such cases came her way. The year after publishing the two studies on pyloric stenosis in twins, Ford Walker came across a set of monozygotic twins discordant for retinoblastoma and cleft palate while pursuing a survey of cleft palate. She and her

student Grace Giles first undertook the 'genetic study' of the twins in 1942. Though not published until 1950, this study was patterned on the pyloric stenosis study of almost a decade earlier. Ford Walker established the monozygosity of the twins, she clarified the heritability of cleft palate and retinoblastoma, she then set out to explain why two seemingly heritable conditions were dissimilar in "identical" twins using the Mongol data to make sense of this disparity.[88]

In these studies, the Mongol data helped to make twin diagnosis more robust, serving to explain divergent dermal patterns in a twin set that Norma Ford Walker believed was monozygotic. "Identical" inheritance was preserved despite extreme developmental and physiological aberration.[89] Significantly, these studies also helped to make the dermatoglyphic anomalies of the Mongol into a *method*, whereby Mongoloid dermal patterns could be used for diagnosis more generally. Such dermal patterns were an analogy for, and sign of, developmental anomaly in a disease such as pyloric stenosis. They testified to the presence of distress during fetal development.

Common Disorders and Constitutions

Pyloric stenosis was a condition more likely to be encountered in a pediatric hospital than elsewhere. But though an uncommon condition, it was not a rare genetic disease. It was not, in other words, the kind of genetic condition which justifies the connection between medical genetics and the pediatric hospital in the late 20th century.

Rather, pyloric stenosis was important to Ford Walker because it was a congenital condition – because it built on the etiological ambiguity of the concept 'inborn.' Ford Walker's work confirmed the condition's heritability, but also its sensitivity to environmental insult. She did not seek to disentangle the mechanics or relative importance of the two influences.

Dermatoglyphic patterns had an acknowledged place in constitutional studies. Cummins and Midlo defined constitution in their 1943 monograph as comprising "all the structural, physiological and psychological traits of an individual. Constitution is determined in part by inherited factors and in part by environment." They noted that "Dermatoglyphics represent a part of the structural constitution. They are heritable, though prenatal environmental influences may mask or modify the genetically prospective traits."[90]

Cummins and Midlo were interested to consider certain "special aspects of constitution, including sex differences, the unlike trends of variation in right-handed and left-handed persons, and the distinctive trends associated with certain diseases."[91] Though the dermatoglyphic patterns in individuals would not be diagnostic of these tendencies, statistical correlations could be found linking dermal patterns to these conditions in populations, in a manner parallel to dermal patterns in racial populations. Without specifying the role of environment and heredity, dermal patterns could provide insight into whether the condition of interest was congenital. "The central question here," Cummins and Midlo elaborated, "is whether persons so afflicted are distinguished from the non-diseased by characteristics of the dermatoglyphics. If such distinctions exist they

are of the utmost moment in analysis of the constitution of disease, because they demonstrate that susceptibility to the disease, like the distinctions in dermatoglyphics with which it is correlated, is inborn."[92]

As her pyloric stenosis study suggests, Ford Walker was already familiar with constitutionalist arguments by the early 1940s, and her student, Grace Workman, had described a Mongoloid "constitution" in the late 1930s. But in the mid-1940s, Ford Walker took this connection further, building direct links to American advocates of constitutional medicine. Ford Walker and a student pursued constitutional research on two distinct diseases: polio and epilepsy. The intention of both studies was to assess the existence of a particular "constitution," visible in the dermal patterns of affected individuals, which demonstrated an inherent susceptibility to these common, complex and thus clinically significant diseases. Disease or disablement could be recognized as constitutional where dermal patterns in affected bodies demonstrated some degree of the signs of disturbance so powerfully manifested by "the Mongol." The Mongol served as an archetypal disease constitution by which other constitutions might be identified, and thus confirmed the significance of Mongol dermal patterns as a method.[93]

In 1945, Norma Ford Walker applied to the University of Toronto for a grant to support research on "constitutional types susceptible to poliomyelitis." This project had grown, Ford Walker stated, "out of earlier studies made in this department on constitutional types found in mongoloid imbeciles." The project was inspired also by a Dr George Draper of Columbia University and the Presbyterian Hospital in New York (and

"physician to the late President Roosevelt" Ford Walker added) who was providing Ford Walker with a hypothesis and data.[94]

Draper was a notable American proponent of "constitutional medicine." Indeed, he is seen by Sarah Tracy as one of the "architects" of that program of "post-Pasteurian medicine" in the 1920s and 1930s.[95] By the time of Ford Walker's polio study, Draper was on the eve of retirement, to be succeeded at the "Constitution Clinic" he founded at Columbia by William Sheldon, whose work on pyloric stenosis had served as the model for Ford Walker's earlier study of the same condition. According to Tracy, William Sheldon became notorious after replacing Draper at the Constitution Clinic. His more anthropometric techniques and explicitly racist proclamations were, Tracy argues, in part responsible for constitutional medicine's demise.[96]

Draper had long been interested in polio. Indeed, he claimed that his conversion to constitutional medicine occurred while fighting the 1916 polio epidemic in New York, when "he noticed that many of the children infected with the polio virus shared similar features, as did their parents."[97] According to Ford Walker, Draper theorized that "certain recognizable physical types are particularly susceptible to the infection of Poliomyelitis." Drawing on her expertise with dermatoglyphics, including Mongol dermal patterns, Ford Walker translated Draper's hypothesis into a testable experiment about dermal developmental patterns: "If Draper's hypothesis were true," she argued, "the growth patterns of such types was already operating before birth in the early foetal months of development."[98]

Draper provided Ford Walker with finger and palm prints of 250 polio patients and Ford Walker enlisted the aid of the Toronto Board of Public Health in identifying another 400 students who had had the disease and could be printed locally. Drawing on her knowledge of the embryology of dermatoglyphics, Ford Walker intended to "indirectly, through a study of these [dermal] patterns, ... reconstruct the early growth pattern in the young embryo." [99] Her early findings were positive; Ford Walker suggested "that definite trends exist and that the digital patterns show a gradual increase in size with increasing susceptibility."[100] Though never published, this study lasted several years, and was referenced by Ford Walker's students as suggesting the existence of disease-susceptible constitutional types.[101]

In the same year Ford Walker was embarking on the study of constitutional types in polio, her student, Wijnada Moonen, completed her Master's thesis on a similar problem: "Digital Patterns in Epileptic Patients." The bulk of Moonen's study was devoted to assessing "whether persons subject to this type of seizure exhibit any constitutional trends in their fetal growth as may be shown in their digital dermatoglyphics." She also sought "to examine any evidence of inheritance of epilepsy."[102]

Like the study of polio, the clinical orientation of this study was apparent in the selection of a complex and relatively common disease for inquiry. Yet Moonen's concern with clinical priorities was even more evident. She credited Alan Brown, Sick Kid's Chief of Pediatrics, with having inspired this inquiry. He had "pointed out the need of

understanding convulsive seizures in young children, for at the present time a physician may see two infants apparently equally ill (with some inflammatory disease such as Otitis Media or Nasopharyngitis) and one of these infants has a convulsive seizure, while the other has not. The problem then presents itself," she added, "as to whether there is a recognizable constitutional difference in these two patients and also whether constitutions susceptible to convulsive seizures are inherited."[103]

Moonen gathered the patients for this study chiefly from two of the Ontario Hospital Schools (Woodstock and Orillia) and also from the Toronto Western Hospital, with controls drawn from the Department of Zoology files.[104] Her study compared the finger prints of the non-epileptic controls with "deteriorated," "non-deteriorated" and "mentally deficient" epileptic patients. With the data generated from analysis of these prints, Moonen sought to find any statistically significant differences between groups. Finding some such differences in pattern distribution and size, differences which were more pronounced in the Orillia group, Moonen attempted to provide some explanation for these differences in embryological processes involving pad elevation and ridge formation. Part one of the study thus demonstrated a constitutional difference between epileptic and non-epileptic persons that was exacerbated in those persons defined also as mentally retarded.

Having established the presence of a disease constitution, Moonen went on to assess the etiology of this condition. Though much family data suggested the minimal importance of heredity, Moonen turned to the twin method for more conclusive evidence. Citing evidence on twins, including one twin set she had discovered and diagnosed as

monozygotic, Moonen pointed to a "greater degree of involvement of both members in monozygotic twins than in dizygotic twins."[105] But though overt evidence of epilepsy was absent in many family members of the afflicted, and in many cases of monozygotic twins, thus disputing the role of heredity, Moonen was impressed by evidence of otherwise hidden abnormalities in the seemingly "normal" twin or relatives. One group of researchers had used EEGs to demonstrate a high incidence of "definitely abnormal records" in the relatives of patients with epilepsy; they also demonstrated abnormal tracings in the seemingly unaffected twin in seven monozygotic twin sets. For Moonen this evidence, together with the data suggesting the significance of such factors as maternal age, suggested that "The predisposition to epilepsy is inherited, but other inherited as well as environmental factors are responsible for the manifestation of the condition."[106]

For Norma Ford Walker, Grace Workman and Wijnada Moonen, establishing the fact of a disease constitution did not imply a specific etiology. The heritability of the Mongol constitution, or the constitutions susceptible to polio or epilepsy, was of interest to researchers but was not implied by the fact of such constitutions. Dermal patterns might usually be laid down according to inherited developmental processes,[107] but distinctive dermal patterns apparent in the case of disease and disability might be due to hereditary or environmental factors. As Cummins and Midlo put it, "Investigation of constitution in dermatoglyphics necessarily confines itself to a consideration of

phenotypes – the traits as expressed in individuals – without discriminating the determinations of the traits by inheritance and their modification by environment."[108]

The Diversity of the Indigenous Tradition

The studies of human constitutions in polio and epilepsy took their place beside a wide array of work conducted by members of the Ford Walker school in the 1940s. John MacArthur had been Ford Walker's collaborator, and to some extent competitor, in the field of human heredity in the 1930s, but in the 1940s, he retreated from the field. Ford Walker found herself the sole academic in Toronto qualified to supervise advanced studies in human heredity, and one of the most accomplished human geneticists in Canada. Beginning in the 1943-44 academic year, the number of advanced students that she supervised was never less than four, and in 1947-48, was double that minimum.

Ford Walker herself pursued a wide array of studies in this decade. She collaborated with Lionel Penrose while the latter was resident in London, Ontario during the war, reporting three years of collaborative work involving family studies of PKU and efforts to find linkage between hair color and blood groups.[109] Alongside occasional collaborations such as this, Ford Walker's research program emphasized the flexible research tool of dermatoglyphics to address four main areas of study: constitutions, etiological factors, inheritance studies and placental membranes for twin study.

Ford Walker fostered a service orientation toward academic medicine and the hospital in the 1940s, and she and her students conducted work on human diseases and disabilities that were of potential interest to clinicians. She studied constitutional predisposition to polio, etiological factors in such conditions as mongolism, harelip and cleft palate and schizophrenia, and sporadic studies on the inheritance of such conditions as three-jointed thumbs, or myositis ossificans progressiva.[110] She set her students to the study of disease conditions: constitutional types predisposed to rheumatic fever, congenital atresia of the neo-lacrimal duct and hereditary pseudoglioma among a group of Ontario Indians.[111] And she had a number of students studying the "inheritance" of convulsive seizures, speech defects, allergies, and celiac disease.[112]

Her most notable student in this respect was Margaret Thompson, who completed her doctorate in 1947 and became Ford Walker's *de facto* heir in the 1960s. Thompson performed the genetical component of a joint clinical, dental and genetical study of celiac disease at Sick Kids.[113] Thompson's study involved a clinically significant condition, of reasonable frequency and of potentially complex etiology and was made possible through clinical interest, diagnoses and institutions.[114] Thompson identified the influence of "unfavorable" environmental factors at work in the prenatal period,[115] noting that the dermatoglyphics of celiac children demonstrated a less severe version of the "marked deviations from the normal shown by the dermatoglyphics of mongoloid imbeciles."[116] She studied twins and familial incidence to assess the evidence for a genetic influence and suggested that "the condition may depend upon a recessive gene, perhaps with incomplete expression." The most noteworthy finding of Thompson's study was an

unexpected familial association of celiac disease with diabetes. Celiacs, Thompson concluded, were "of the diabetic genotype," celiac disease appeared in children of this genotype "under suitable environmental conditions," and all celiac children were "potential diabetics."[117] If the "diabetic gene" were truly involved, celiac disease might, Thompson suggested, be a "pleiotropic effect."[118] In her published article on celiac disease, Thompson argued that the "underlying constitutional defect" is a "genetical susceptibility to celiac disease," with "an unfavourable uterine environment" serving as one of the factors "favoring its development."[119]

But while Ford Walker's research school evidenced a sustained interest in human disease and disability, Ford Walker was not exclusive in her attention. In fact, in those press reports in which she was identified as a specialist in heredity, from the late 1920s through the 1940s, mention was not made of disease conditions. Instead, Ford Walker was featured for her knowledge of dermatoglyphics, her ability to decipher the zygosity of twins, and her ability to speak wittily about such inherited human features as taste, tooth development, eye color, blood groups and fraternal twinning. She was highlighted, in other words, for her human genetics concerns.[120]

In the same decade that she built ties to Sick Kids, and laid the foundation for a strong medical genetics orientation in her research school, Ford Walker also built ties to the Faculty of Dentistry. Beginning in 1940, Ford Walker began a series of dental studies, collaborating for two years with the Dean of the Faculty of Dentistry who had been involved in the Dionne study.[121] Using PTC, they demonstrated the common inheritance of the "taste gene," and theorized the common inheritance of the same "gene complex"

for taste type in the Dionne quintuplets.[122] They also demonstrated the inheritance of a "developmental pattern of eruption of the permanent teeth" resulting in malocclusion in the quints.[123] Through the remainder of the decade, Ford Walker retained her interest in dental studies and supervised graduate work, including a Ph.D. and MSc, of students in the Faculty of Dentistry.[124]

Ford Walker also built links to anthropology in this decade, using dermatoglyphic techniques to illuminate racial constitutions.[125] Ford Walker initiated her own racial studies in the late 1940s, examining dermal configurations in "Northern Indians and Eskimos,"[126] and in the early 1950s she began more sustained work on racial distinctions in Mongolism.[127] Finally, in the latter-half of the 1940s, Ford Walker supervised two graduate students, Gerhard Siemens and Roy Wolfe, with an interest in human biology and anthropology – what we might call physical anthropology.[128]

Like Margaret Thompson, Gerhard Siemens, completed his Doctorate in 1947, but his study concerned dermatoglyphics in Jews. He reported racial differences between Jews and the control series of non-Jewish whites Ford Walker had on file, and also reported intra-racial differences between sub-populations of Jews.[129] In 1947, when Siemens finished his Ph.D. thesis, Roy Wolfe completed a Master's thesis on the dermatoglyphics of the Six Nations Indians of Southern Ontario. Wolfe set out to demonstrate evidence of "miscegenation" in the Six Nations population in Southern-Ontario, confirming the hypothesis that "a child who "looks full-blooded" will have more purely Indian dermatoglyphic characteristics than a child who is obviously of mixed parentage."[130]

These studies of racial populations were concerned first and foremost with confirming the evidence of racial constitutions in dermal patterns. But they were also attuned to Ford Walker's interest in medical research. Siemens' statistically-significant findings of distinctive racial dermal patterns could be used to control for the confounding effects of race in studies of disease. "The analysis of dermal patterns will be used increasingly in the study of disease as a means of measuring rates of foetal growth," he argued, "....[making it] essential to know the normal variations for all groups of people."[131] Meanwhile, Wolfe sought to "furnish data for the files of Dr Norma Ford Walker, for use in her work on the relations of rates of foetal growth (as determined by dermatoglyphic patterns) to inherited susceptibility to infantile paralysis, rheumatic fever and other diseases."[132]

Ford Walker's twin studies were also attuned to her interest in disease and disability. Accurate determinations of zygosity, which her ongoing studies of placental membranes would help to support, made possible the determination of the heritability of disease. But Ford Walker's twin studies, like her racial studies, were not solely attuned to medical questions. Ford Walker co-operated in a study organized by Elizabeth Chant Robertson of the university's Department of Pediatrics, to assess the effect of nutritional supplements (Vitamin B) on the growth, vision and learning abilities of children, between 1945 and 1947.[133] Ford Walker's part in the project was similar to the role she had played in the initial Dionne study. She was to "make the biological determination as to types of twinning" using dermatoglyphics as well as the similarity method.[134] The published paper reported on the study of 44 pairs of "identical twins" ("subjects as closely matched as

possible"). It found some short term improvements in weight and height and response to learning tests over the short term, but no statistically significant improvements over the longer term and thus disputed existing literature which, through study of orphans, had found such improvements.[135] This study advanced Ford Walker's capacities in twin diagnosis,[136] it was also one of Ford Walker's few interventions into the area of behavior genetics – often seen to be a dominant mode of inquiry in twin studies and human genetics.[137]

Ford Walker's studies on placental membranes could also be used to address developmental and embryological questions. In particular, Ford Walker had long taken an interest in twinning time, producing with MacArthur a best guess about the timing and order of twinning among the Dionne quints.[138] The most elaborate example of this kind of work involved a study of two sets of conjoined twins, each of whom separately visited the Canadian National Exhibition (in 1936 and 1938). The study was begun in the late-1930s but not published until 1952.[139] Ford Walker used dermatoglyphics, together with information about fetal membranes, blood groups and general similarity where available to address what she saw as continued confusion about the zygosity of conjoined twins. Though "geneticists and embryologists are in general agreement that conjoined twins originate from one zygote," she wrote, "there still appear in scientific journals articles supporting the claim that such twins result from two zygotes which have become united during development." This confusion resulted from the "marked dissimilarity" between conjoined twins, and yet "excellent theoretical explanations have been advanced to support the uniovular theory."[140] In this paper, Ford Walker engaged embryological

questions about the dissimilarities in zygotes of "identical inheritance" which came about through developmental processes, notably twinning time.[141]

Ford Walker's study was chiefly concerned with differences between the twins that were evident in dermal patterns. Drawing on the Mongol method, she argued that these were "particularly useful" in studies of asymmetries in twins because "These skin patterns, although inherited, are also subject to modification as the result of disturbance of foetal growth occurring at the third and fourth months of development."[142] Ford Walker was able to demonstrate changes in dermal patterns which derived from disturbances due to delayed twinning time. Since both sets of conjoined twins were "pygopagus" (or joined at the buttocks and lower backs) it was assumed that the "division of the posterior part of the body" had been considerably delayed.[143] This developmental delay was apparent in skin patterns in the feet that differed in symmetry from those of the hands. The chief contribution of this study was embryological. The assumed identical heredity of the twins in this series served simply as a control on genetic variation in this natural experiment of environmental influence.

What Science is This?

By the late-1940s Norma Ford Walker presided over a methodologically sophisticated and productive research school. Using the ever malleable tool of dermatoglyphics, she and her students and colleagues had developed a set of methods

which worked together, and independently, to address complex issues of human inheritance and development. The twin and Mongol methods could be used to investigate a broad range of etiological factors: single and complex gene effects, embryological development, fetal disturbance, constitutional types, and environmental influence. The Ford Walker school had pursued its work and made itself of value at the university, at the hospital, in academic medicine, dentistry and anthropology. It was a research school, it had biomedical relevance, it assessed the human animal, and it had developed a sophisticated indigenous tradition incorporating a particular set of methods. But was this human genetics?

In 1945, a summary of research projects in genetics underway at the University of Toronto was presented by Ford Walker's colleague, John MacArthur, to the chair of the Department of Zoology. The report stated that "three lines of investigation are currently stressed in Genetic Research at this University": the "genetic factors controlling body size, growth and reproduction in mammals," the "methods of auto-sexing...in the various breeds of chicks," and "genetics and plant breeding with the Tomato."[144] Notable by its absence in this report is any mention of the work of Ford Walker and her students, or indeed, any mention of genetic research with the human animal.

When Ford Walker and John MacArthur began collaborating on the Dionne study, her work in this field was listed with his in the annual report for the Department of Biology under the category "Genetics."[145] The next year, 1936-37, the annual reports began a new category through which to identify such work: "Genetics and Human Biology."[146] By the 1940-41 academic year, however, the newly named Department of

Zoology had split this category into two.[147] John MacArthur, who thereafter ceased his research on the human animal, retained the category "Genetics," while Ford Walker was classified under the category, "Human Biology." Indeed, her title at the Department of Zoology was "Associate Professor of Human Biology."[148] This departmental classification continued through the 1946-47 academic year, after which, sub-fields of research within Zoology were no longer identified. By this departmental logic, then, Ford Walker was a human biologist not a human geneticist, and her exclusion from MacArthur's report is warranted.

Yet at the time MacArthur prepared his departmental report, a series of commentaries suggest that Ford Walker might not have accepted this narrow definition. "Studies in human biology," Ford Walker wrote in 1944, "are concerned in large part with problems of *inheritance*."[149] Her student, Margaret Thompson, corroborated this bias. She identified the goal of her study as the assessment of "the inheritance of coeliac disease,"[150] and yet she identified herself as a "human biologist," who must also investigate "factors such as maternal age and birth order..."[151] A 1944 report in the *Toronto Star* identified Ford Walker as "Canada's foremost authority on multiple births." She was a professor in the Department of Biology who "specializes in genetics."[152]

The brilliant British polymath and influential geneticist, J.B.S. Haldane, in his writings on the promises and perils of human genetics, might be seen to agree with this position. He argued repeatedly that students of human heredity had to address both nature and nurture in their work. He sometimes made this argument in tabular form – presenting data on the prevalence of polydactyly in four distinct breeding lines of guinea-pig

measured, on the vertical axis, against maternal age. "This table is very instructive as a warning against a one-sided interpretation of human data," he wrote in his important 1942 text, *New Paths in Genetics*.[153] "The extreme eugenist will read it horizontally, the extreme environmentalist vertically. The biologist," he added, "will read it both horizontally and vertically."[154]

In suggesting that the human geneticist must be a biologist first and foremost, Haldane made room for Ford Walker within the human genetics fraternity. The breadth of her inquiry – capturing genetic and environmental causation in human biology – was appropriate to the early decades of work in human genetics, and to the urgency of the nature-nurture debates. Yet though enjoining breadth in etiological investigation in his 1942 text, Haldane emphasized a narrow range of tools – the formal genetics of pedigrees, statistics and linkage maps.[155] His colleague, Lancelot Hogben, suggested a wider range of tools appropriate to human genetics research "as an exact science" in 1931 and included twin studies in his list. But he also emphasized the importance of studies of family pedigrees, and assessments of population consanguinity – tools with which Ford Walker was little concerned.[156] Ford Walker worked primarily with dermatoglyphics – a credible but marginal research tool. Though, as a human biologist, Ford Walker would be accepted by international colleagues herself as a geneticist, her preferred research tool situated her on the edges of this fraternity.

MacArthur and Ford Walker had, for a time, shared professional responsibilities for human genetics at the University of Toronto. When MacArthur ceased such work, and

passed the torch of human heredity research to Ford Walker, the direction of research was altered. While McArthur had been somewhat heterodox, Ford Walker was more so. She downplayed, to a greater extent than MacArthur, the more conventional tools of classical genetics, and took the broad questions of human biology further than MacArthur had. Both workers had shared an interest in dermatoglyphics, in themselves and for twin diagnosis. But McArthur had an interest in studying the heredity of certain conditions, something that likely involved pedigree studies, which Ford Walker paid little attention to. Ford Walker took the marginal research tool of dermatoglyphics as her central technology. Her work concerned embryology and development and complex environmental and heritable influences. Moreover, it was exclusively focused on human bodies and lives. In emphasizing human biology above a more exclusively genetic focus, Ford Walker helped to render her work invisible as *genetic* research.

The invisibility of Ford Walker's work was supported by the social relations of gender.[157] In the mid-1940s, when Ford Walker's research was passed-over in MacArthur's report, the science that was disregarded was conducted almost entirely by women. By 1945, Ford Walker had supervised eight women students and no man. Until he abandoned studies in human heredity in the early 1940s, John MacArthur had supervised three women students in research in human biology, and one student, likely male, whose focus was primarily the albino rat, but who included a component on the comparable human disease.[158] Ford Walker's school was a marginal research tradition, embracing a marginal technology and spread thinly across a diverse array of human

phenomena. It adopted a service role towards a variety of allied disciplines. It was manifestly 'women's work.'

In the final analysis, disciplinary identity is produced by institutions. From this standpoint, Ford Walker cannot be clearly identified with human genetics until after the Second World War. As a founding member of the American Society of Human Genetics in 1948, Ford Walker helped to produce the institutional framework that would make disciplinary identification relatively straightforward. And, in 1949, her title at the University was changed to Associate Professor of Human Genetics.[159]

But Ford Walker did forge a school of medical genetics, and by the mid-1950s, at the latest, she was calling it this. Moreover, the work of this 1950s school shared the conceptual contours of the mid-1940s work. Some of the work by Ford Walker and her students in the 1950s was initiated in the 1940s. Moreover, into the 1950s, the Ford Walker school continued to incorporate interests in broader and more complex questions than traditionally attributed to genetics. Whatever MacArthur may have thought, then, the Ford Walker school was *doing* genetics in the 1940s.

Conclusion

Beginning in the mid-1930s with the biological study of the Dionne quintuplets, Ford Walker began the process of building a human and medical genetics research community in Toronto. She forged an indigenous research tradition that was heterodox in

its genetical inquiries – entertaining genetic mechanisms more in the breach than in the observance. The indigenous tradition embraced a broad explanatory framework wherein environmental, hereditary and developmental processes were observed. This etiological framework in biology found a parallel etiological framework within academic medicine in constitutional studies. Ford Walker's research school spread itself across a wide range of inquiries in human genetics – applying the flexible tool of dermatoglyphics in physical anthropology, behavior genetics, dentistry and medicine. But the service role adopted towards medicine would prove enduring.

Ford Walker's was a marginal research school. It was marginalized by its development within a national research environment with a limited devotion to what McKillop has christened the 'culture of utility,' and with limited financial resources. It was marginal in its detachment from the mathematical genetics of the then-dominant British school of human genetics – preferring dermatoglyphic analysis and the twin and Mongol methods. Finally, the marginality of the Ford Walker school was marked and sustained by gender. As a pioneer scientist at the University of Toronto, Ford Walker made room for women at the research university, but she did so by focusing on a lesser science – the messy and medically relevant science of human genetics.

Endnotes: Chapter 1

[1] MacArthur was trained in Chicago and clearly retained links with American colleagues. He collaborated with William Ernest Castle in studies of: "linkage of the gene controlling hereditary jaundice in rats." Cited in University of Toronto *President's Reports*, 1938-39, 1939-40. Moreover, MacArthur clearly had some connections with the British geneticists. JBS Haldane noted that MacArthur had assessed a branch of a family being studied in Britain in: *New Paths in Genetics*, (New York and London: Harper and Brothers, 1942), 168.

[2] Ford Walker kept clippings on the Dionne quints and her collection testifies to the enormous media attention that these children received. Unfortunately, these clippings are all that Ford Walker left behind in the way of personal papers: (UT, B79-0045, Boxes 1-4).

[3] Cythia Wright, "They Were Five: The Dionne Quintuplets Revisited," *Journal of Canadian Studies*, 29:4 (Winter 1994-95), 5-14

[4] Cited in: Kari Dehli, "Fictions of the Scientific Imagination: Researching the Dionne Quintuplets," *Journal of Canadian Studies*, 29:4 (Winter 1994-95), 87.

[5] *Ibid.*, 98.

[6] *Ibid.*, 98-99.

[7] Madge Macklin, "Quints' Progress: Do they "prove" Heredity of Environment?" *Journal of Heredity*, Vol. 29 (1938), 290. Delhi's interpretation of Blatz's agenda is in conflict with Hamilton Cravens' interpretation of the role of these child study centers. Cravens emphasizes the dichotomy of determinism-indeterminism, especially group determinism, over the heredity-environment controversy which seemed, by the 1930s to be resolved in favor of a mutual influence. With the exception of the original center, in Iowa, Cravens argues that the others, including Toronto, were pressing a group determinist argument about child intelligence and development. The reaction of geneticists like Newman and Macklin to this work suggests, however, that the heredity-environment tension was far from resolved. Hamilton Cravens, "The Case of the Manufactured Morons: Science and Social Policy in Two Eras, 1934-1966," in H Cravens et al, eds., *Technical Knowledge in American Culture: Science, Technology and Medicine Since the Early 1800s* (Tuscaloosa and London: The University of Alabama Press, 1996),154

[8] Katherine Arnup notes that "References to their [the quints] hardy stock abound in the literature of the day." The bulk of her article, however, examines the ways in which the promoters of professional authority in childhood capitalized on the Dionne quintuplets to intensify their interwar message. Katherine Arnup, "Raising the Dionne Quintuplets: Lessons for Modern Mothers," *Journal of Canadian Studies*, 29:4 (Winter 1994-95), 83 ft 33, 66.

[9] John MacArthur and Norma Ford, "A Biological Study of the Dionne Quintuplets: An Identical Set," in W.E. Blatz et al, *Collected Studies on the Dionne Quintuplets* (Toronto: University of Toronto Press, 1937), 3.

[10] *Ibid.*, 3.

[11] *Ibid.*, 6.

[12] *Ibid.*, 4, 5. The similarity method is discussed by Harold Cummins and Charles Midlo, *Finger Prints, Palms and Soles: An Introduction to Dermatoglyphics*, (Philadelphia: The Blakiston Co., 1943), 235.

[13] MacArthur and Ford, "A Biological Study," 7, 9, 16.

[14] *Ibid.*, 12.

[15] *Ibid.*, 18.

[16] *Ibid.*, 16. In addition to the main diagnostic goal in this paper, MacArthur and Ford Walker reviewed the published literature on quintuplet births. They presented data on sex ratios, the age and parity of the mother, and the differences between fraternal and identical twinning in terms of inheritance. They used this data to confirm the theory that a "tendency" or "proclivity" towards fraternal twinning was inherited, and tended to occur in women at later age and higher parity. Since the mother of the Dionne quints was young and had no family history of twinning, the tendency toward inheritance of fraternal twinning was used to further corroborate the argument of monozygosity in the Dionne quints. MacArthur and Ford, "A Biological Study," 37, 43.

[17] Peter Bowler, *The Mendelian Revolution: The Emergence of Hereditarian Concepts in Modern Science and Society* (Baltimore: Johns Hopkins University Press, 1989), 128-9.
[18] MacArthur and Ford, "A Biological Study," 47.
[19] *Ibid.*, 16. MacArthur pursued these questions in greater detail later. He attended to the environmental impact of the "repressive" uterine environment and considered the consequences once the quints were outside the womb where environmental inequalities had decreased and the "*hereditary constitutional growth factors*" are more free to express themselves, though the intra-uterine history might have life-long impacts. John MacArthur, "Genetics of Quintuplets: I. Diagnosis of the Dionne Quintuplets as a Monozygotic set," *Journal of Heredity*, 29 (1938); John MacArthur and Allan Roy Dafoe, "Genetics of Quintuplets: II. Trends of Growth in the Dionne Quintuplets," *Journal of Heredity*, 30 (1939).
[20] AB McKillop, *Matters of Mind: The University in Ontario, 1791-1951* (Toronto: University of Toronto Press, 1994), 343, 344.
[21] Louis-Philippe Bonneau, JA Corry, *Quest for the Optimum: Research Policy in the Universities of Canada*, The Report of a Commission to Study the Rationalisation of University Research, Vol. 1, (Association of Universities and Colleges of Canada, 1972), 7.
[22] McKillop, *Matters of Mind*, 345.
[23] Private American foundations played a crucial role in supporting research, even in Canada. The St. George's School for Child Study, through which the scientific study of the Dionne quintuplets was organized, had been established with money from one of the Rockefeller philanthropies. Delhi, "Fictions of the Scientific Imagination," 91. On the cultural and financial constraints on research in Canadian universities see: McKillop, *Matters of Mind*, 324, 325.
[24] Angus McLaren, *Our Own Master Race: Eugenics in Canada, 1885-1945*, (Toronto: McClelland & Stewart, 1990), 155, 156. MacArthur expressed some support for eugenic measures in the 1920s and early 1930s, such as the use of birth control to prevent "deformed parents" from having children: "Dr Gallie's Proposal has Noted Supporter: Prof MacArthur, UofT, Also Favors Birth Control for Deformed Parents." *Toronto Star*, March 20, 1930 (UT, A73-0026, 248, 90). Yet McLaren argues that from the mid-1930s, MacArthur made public statements which "pilloried" members of the Eugenics Society of Canada: *Our Own Master Race*, 156. In taking this position, MacArthur differed from Canada's premier human geneticist, Madge Thurlow Macklin, in seeking to articulate an analytic distinction between the "geneticists" and the "eugenicists." He judged the inadequacies of most human genetics work by the "rigorous standards of geneticists working with plants or animals." MacArthur's review of *Eugenical Selection: A Reorientation of the Problem*, was highlighted as a "Review by a Geneticist" and positioned next to the "Review by a Eugenicist" provided by William Hutton, the medical health officer of Brantford, Ontario, who sat on the executive of the Eugenics Society of Canada. John W MacArthur, "Eugenical Sterilization, Second Review by a Geneticist," *Social Welfare*, 17 (March 1937), 15. See also: JW MacArthur, "Review of *Heredity and Politics* by JBS Haldane," *Social Welfare*, 17 (June 1938), 106-8. On Hutton see: McLaren, *Our Own Master Race*, Chapter 6. McLaren does not differentiate between mainline and reform eugenics in his discussions. But it is more accurate to portray John MacArthur as a reform eugenicist than an anti-eugenicist. While bitingly critical of compulsion in his review of a report on eugenical sterilization – a position he shared with the report's authors – MacArthur did not dispute the authors' support for voluntary sterilization "in a limited number of selected cases...for both biological and social reasons." Nor did he oppose the imposition of barriers to "unwise procreation" through marriage legislation or "increased segregation by hospitalization." John W MacArthur, "Eugenical Sterilization, Second Review by a Geneticist," *Social Welfare*, 17 (March 1937), 16. Moreover, in his review of JBS Haldane's book, *Heredity and Politics*, MacArthur noted his approval of that reform eugenicist's "modern" and "conservative views" on the applicability of genetic science to the solution of human problems. Haldane, he noted, "has consistently maintained that the biologist is not *yet* in a position to undertake to provide safe guidance in future human evolution"(emphasis added). J. W. MacArthur, "Review of *Heredity and Politics* by JBS Haldane," *Social Welfare*, 17 (June 1938), 107, 108, 106. Emphasis added. For Haldane's more enthusiastic thoughts on the possibility of human engineering, see his: *Daedalus, or Science and the Future: A Paper Read to the Heretics*, Cambridge on February 4th, 1923 (London: Kegan,

Paul, Trench and Trubner, 1924), cited by Mark B. Adams, "Biological Futurism in Science and Literature," paper presented to the Penn Humanities Forum, University of Pennsylvania, Sept 21, 1999.
[25] Kevles, *In the Name of Eugenics*, 141.
[26] Delhi, "Fictions of the Scientific Imagination," 91. See also: Hamilton Cravens, "The Case of the Manufactured Morons," 153
[27] Hamilton Cravens, "Behaviorism Revisited: Developmental Science, the Maturation Theory, and the Biological Basis of the Human Mind," In Keith Benson, Jane Maienschein and Ronald Rainger, eds., *The Expansion of American Biology* (Rutgers University Press, 1991), 134, 135. Cravens suggests that these schools were hereditarian, a thesis which Kari Delhi – in the case of the Toronto school – would likely dispute. The school with which Ford Walker was affiliated tended more to an environmentalist interpretation, Delhi argues. I disagree with Craven's assumption that this new era, driven in part by new developments in genetic science, necessarily disarmed eugenics. For this argument see his: *The Triumph of Evolution: American Scientists and the Heredity-Environment Controversy, 1900-1941* (University of Pennsylvania Press, 1978), Chapter 3.
[28] Horatio Newman, "The Finger prints of twins," *Journal of Genetics*, 23 (1930), 415-446; "Palmar Dermatoglyphics of twins," *American Journal of Physical Anthropology*, 14 (1930), 331-378; "Palm-print patterns in twins," *Journal of Heredity*, 22 (1931), 41-49. Cited in Cummins and Midlo, *Finger Prints, Palms and Soles*, 292.
[29] His manuscript for the *Journal of Heredity* was, Newman claimed, only the second scientific report. The first report having been published by Muller in the mid-1920s. "Twins if Separated Differ as the Grow," *Star*, May 21 [or 22] 1929, (UT, A73-0026, 347, 06); "Oshawa Twins arouse interest in Toronto: Dr JW MacArthur of Toronto University Explains "Identical Twins"," *Toronto Star*, February 26, 1928 (A73-0026, 248, 90).
[30] Kevles, *In the Name of Eugenics*, 141, 206.
[31] According to the University of Toronto *President's Report* for 1929-30, JW MacArthur was promoted from the rank of Assistant Professor to Associate Professor in Genetics in the 1929-30 academic year. McLaren notes that MacArthur was born in Buffalo and trained at Chicago. He taught genetics at the University of Toronto from 1923 through 1948. McLaren, *Our Own Master Race*, 214, n.43.
[32] Child worked with the flatworm planaria – an extremely plastic organism, capable of regenerating itself from minute fragments and lacking the sequestered germ line demanded by Mendelian-Weismannism theory. See: Greg Mitman and Anne Fausto-Sterling, "Whatever Happened to *Planaria*? C.M. Child and the Physiology of Inheritance," in Adele Clarke and Joan Fujimura eds., *The Right Tools for the Job: At Work in the Twentieth-Century Life Sciences*, (Princeton: Princeton University Press, 1992).
[33] Jane Maienschein has suggested that a "Chicago style of Biology" was established at the turn of the twentieth-century, that was committed to problems of development ad heredity. "Similar questions were asked," she writes, "namely, what morphological patterns occur, and what physiological processes shape the development of the whole individual? Specifically, how do the organism and its parts act as a whole?" The Chicago style was also marked by its emphasis on graduate instruction and independent and early research work. Insofar as there is a Chicago style, we might interpret the holistic approach to human genetics and biology developed by Ford Walker as stemming from that style. Jane Maienchein, "Whitman at Chicago: Establishing a Chicago Style of Biology?" In R Rainger, K Benson and J Maienschein, eds., *The American Development of Biology* (Philadelphia: University of Pennsylvania Press, 1988), 173
[34] On Morgan and his dominance see: Rob Kohler, *Lords of the Fly: Drosophila genetics and the experimental life* (London: University of Chicago Press, 1994).
[35] Classical genetics, Lily Kay has argued, was built through a self-conscious effort to produce and sustain academic biology as a distinct and autonomous discipline. Attention to *Drosophila* asserted the independence of biology from its traditional service role towards agriculture, and medicine, in particular. Lily Kay, *The Molecular Vision of Life: Caltech, the Rockefeller Foundation, and the rise of the new biology* (New York: Oxford University Press, 1993), 80-81; see also P Pauly, "The Appearance of Academic Biology," Journal of the History of Biology, 17 (1984), 369-397. While the enthusiasm for scientific medicine promoted the initial development of academic biology in the late 19th century, Pauly

argues, biology only achieved strength as an independent discipline in institutions where medicine was weak or absent.

[36] University of Toronto, *President's Report*, 1939-40, 42.

[37] The annual University of Toronto *President's Reports* indicate that JW MacArthur engaged in sporadic research and supervised some work in human heredity, though he does not appear to have published in the field. His work in the field, prior to the Dionne quintuplet study includes: the study of "abnormal human heredity" in 1926-27; the "collection of family histories of inherited characters in man" in 1928-39; the "heredity of human aphalangy" in 1929-30; in 1931-32 he supervised a Miss Kendall in the study of "heterochromidin of the iris in a human family"; in 1934-35 he did work on "human heredity of dystrophy of hair and nails in a Quebec family with Dr Maurice Hobbs of St Johns," and under his direction Mrs. ME Richardson studied the "role of heredity in families with mentally deficient children."

[38] Cummins and Midlo, *Fingerprints, Palms and Soles*, 237

[39] MacArthur's interest in rat genetics is evidenced from University of Toronto *President's Reports* from at least the mid-1930s. After retiring from Harvard in the mid-1930s, Castle assumed a position as research associate in genetics at the University of California Berkeley. MacArthur's collaborative work with Castle dates to this California period. The collaboration is noted in the annual University of Toronto *President's Reports*.

[40] Barbara Kimmelman, "Organisms and Interests in Scientific Research: RA Emerson's Claims for the Unique Contributions of Agricultural Genetics," in Adele Clarke and Joan Fujimura eds., *The Right Tools for the Job: At Work in the Twentieth-Century Life Sciences*, (Princeton: Princeton University Press, 1992), 213.

[41] Karen Rader, "'The Mouse People': Murine Genetics Work at the Bussey Institution, 1909-1936," *Journal of the History of Biology*, 31 (1998), 335.

[42] Kevles lists the main techniques as blood groups, family surveys or pedigrees, mathematical methods and twin studies. He cites workers like Lancelot Hogben, one of the members of the then-dominant British school of human genetics, as including twin study in his 1931 list of appropriate methods: Kevles, *In the Name of Eugenics*, 209, 198. Enthusiasm for twin study as a means of assessing human inheritance was widespread. Indeed, Herman Muller's earliest human genetics research in the mid-1920s involved identical twins reared apart. Muller is said to have acknowledged "Galton's wisdom in suggesting the use of twins for nature-nurture studies." Elof Axel Carlson, "Eugenics and Basic Genetics in H.J. Muller's Approach to Human Genetics," *History and Philosophy of the Life Sciences*, 9 (1987), 62. In addition to conducting such work, John MacArthur proselytized about the value of twin studies. MacArthur's enthusiasm for twin studies was apparent not only in his own work, but in his commentaries: "That even inherited conditions are not "fated," and that the environment may play an important and necessary eliciting role is suggested by the studies of identical twins." John W MacArthur, "Eugenical Sterilization, Second Review by a Geneticist," *Social Welfare*, 17 (March 1937), 15.

[43] Cummins and Midlo, *Finger Prints, Palms and Soles*, vii.

[44] *Ibid.*, 213-4.

[45] *Ibid.*, vii.

[46] Kevles, *In the Name of Eugenics*, 196.

[47] *Ibid.*, 196.

[48] "Zonta Hears Dr N Ford Talk About Human facts," *Mail*, Jan 9, 1936 (A73 0026, 105, 61). From at least 1942, the American Genetic Association sold "leaflets to demonstrate heredity" which bore samples of PTC treated paper. Advertisements for these leaflets argued that "the "Taster test" served as an introduction to human genetic differences in many classrooms. The test is so easily made with the treated paper, and arouses such great interest that it appears to have a definite place in group demonstrations of such differences." See advertisement, American Genetic Association, "Leaflets to Demonstrate Heredity," *Journal of Heredity*, 34:3 (March 1943), 65.

[49] Ford Walker was quoted in a newspaper article explaining that "in her study of heredity she had begun to experiment first with PTC and then with other things. "It's really a sideline," she said. "I found I didn't know much about it, so I began to explore a little." That 'sideline' has led the Canadian Dietetic Association to invite her as a guest speaker at their first annual convention this week at the Royal York.":

"Junior OK Though He Dislikes Spinach: Merely Matter of Heredity Dr Norma Walker [sic] says," *Star*, May 21, 1936 (A73 0026, 105, 61). In the first year that Ford Walker reported studies in human heredity, she was working with MacArthur on dermatoglyphics in multiple births and the inheritance of physical characteristics in such births, and also "Investigations of taste reactions in young children and in monozygotic twins: University of Toronto, *President's Report*, 1935-36.

[50] In a co-authored study, Ford Walker used PTC to demonstrate that all five Dionne quints possessed the "taste-gene" and thus corroborated other evidence of monozygosity. This study was also used to suggest why persons who could taste PTC experienced different kinds of taste. A person's whole "gene-complex" influences the taste-gene, Ford Walker and her co-author argued, "Or in other words the genes 'live in different houses.' Since monozygotic multiple sets have a common inheritance and hence a common gene-complex," they added, "the members of such a set should theoretically taste alike" Since the quints did, the authors suggested the PTC test showed the common inheritance of an 'identical' gene-complex. Norma Ford and Arnold D. Mason, "Taste reactions of the Dionne Quintuplets," *Journal of Heredity*, 32 (1941), 365, 367..

[51] MacArthur reported research on "Methods of diagnosis of twins and multiple birth sets by the use of skin ridges and other characters" in University of Toronto, *President's Report*, 1937-38 and published on this work: JW MacArthur, "Reliability of dermatoglyphics in twin diagnosis," *Human Biology* 10, 1938, 12-35. Cummins and Midlo comment on MacArthur's confirmation of the technique's reliability in another study: *Fingerprints, Palms and Soles*, 237-8.

[52] See for example: Norma Ford and Gioacchino Caruso, "Two unrecorded cases of quintuplet births, Canadian and Italian," *Canadian Medical Association Journal*, 39 (1938); Norma Ford Walker, " A further description of a set of quadriovular quadruplets," *American Journal of Obstetrics and Gynecology*, 54 (1947); Norma Ford Walker, "Determination of the Zygosity of the Waddington Quintuplets Born in 1786," *American Journal of Human Genetics*, 2 (1950).

[53] Interest in questions of fetal development was also suggested in the study of the Dionne quints, MacArthur and Ford Walker had suggested the value of assessing the embryological processes involved in the timing and order of twin development. But though they produced a best guess about the order of each quint's separation from the original fertilized egg, they expressed doubt "whether this can be successfully done at present." MacArthur and Ford, "A Biological Study," 36, 35. In later work, authored by MacArthur, the non-identical nature of identical sets was further explored.

[54] University of Toronto, *President's Report*, 1936-37, 48. The next year, Ford Walker reported "further investigation of the of the blood vascular system in the placentae of multiple births" University of Toronto, *President's Report*, 1937-38, 55. See also University of Toronto, *President's Report*, 1938-39, 46

[55] The Research Institute of the HSC, *First Annual Report*, Jan 1 to Dec 31, 1954, 10. (HSC).

[56] Norma Ford Walker, "Determination of the Zygosity of Twins," *Acta Genetica Statistica Medica*, 7:1 (1957), 33-38.

[57] Miss M Macdonald studied "Plantar patterns in mongolian idiots compared with their palmar patterns," and Miss G Workman studied, "Palmar patterns in mongolian idiots and the occurrence of similar patterns in normal individuals.": University of Toronto, *President's Report*, 1937-38, 55.

[58] Grace W. Workman, A Study of Palmar Dermatoglyphics of Mongoloid Idiots, University of Toronto, MA Thesis,1939. Workman remained for another year, working with Ford Walker on "Continuation of study of disturbance in growth during early foetal months in mongoloid imbeciles": University of Toronto, *President's Report*, 1939-40, 42.

[59] University of Toronto, *President's Report*, 1938-39, 46: "palmar patterns of the kindred of mongoloid patients (in co-operation with several Toronto and New York hospitals)"; University of Toronto, *President's Report*, 1939-40, 42: "disturbance of growth, as indicated by dermal configurations, in 200 parents and siblings of mongoloids (in co-operation with several Ontario and New Jersey hospitals)"; University of Toronto, *President's Report*, 1940-41, 119: "dermal configurations of the kindred of mongoloids (with the co-operation of several Ontario and New Jersey hospitals)"; University of Toronto, *President's Report*, 1941-42: "dermal configurations of the parents and siblings of 80 mongoloids (with the co-operation of several Ontario and New Jersey hospitals)"; University of Toronto, *President's Report*, 1942-43, 79: "Etiological factors in mongolism, studied indirectly through dermal configurations and the

occurrence of the condition among sibs"; University of Toronto, *President's Report*, 1943-44: "Etiological factors in mongolism, studied indirectly through dermal configurations and the occurrence of the condition among sibs"; University of Toronto, *President's Report*, 1944-45: "etiological factors in mongolism ...". This statement continues in Ford Walker's reports through 1948-49. After a year's hiatus, she begins to report studies of mongolism on and off, where her concern is both "etiological factors" and "diagnosis."

[60] Workman, "A Study of Palmar Dermatoglyphics of Mongoloid Idiots," 3. Cummins published his findings as: "Dermatoglyphic stigmata in mongoloid imbeciles," *Anatomical Record*, 73 (1939): 407-415. Cummins and Midlo cited Workman's study: "Studies on two independent series,' they wrote, "by Cummins and by Workman, agree in all essential respects.": *Fingerprints, Palms and Soles*, 279.

[61] Workman, "A Study of Palmar Dermatoglyphics of Mongoloid Idiots," 4, emphasis in original.

[62] *Ibid.*, 11.

[63] *Ibid.*, 56.

[64] *Ibid.*, 3.

[65] *Ibid.*, 8, 12, 13.

[66] *Ibid.*, 6, emphasis in original.

[67] *Ibid.*, 74.

[68] University of Toronto, *President's Reports*, 1936-37, 48; 1937-38, 55; 1938-39, 46

[69] University of Toronto, *President's Reports*, 1938-39, 46. Ford Walker actually reported "New York" hospitals this first year, but it was likely a typographical error. She cited New Jersey hospitals consistently in subsequent years: 1939-40, 42; 1940-41, 119; 1941-42.

[70] University of Toronto, *President's Reports*, 1939-40, 42

[71] "Primogeniture as an aetiological factor in pyloric stenosis, based on a review of more than 400 cases, including a study of 12 pairs of twins.": University of Toronto, *President's Reports*, 1939-40, 42

[72] N Ford Walker, "The Development of Human Genetics at the University of Toronto," *Proceedings of the Genetics Society of Canada*, Vol. 3 (1958), 65 (NA, MG 28 I456). The Dionnes may have been important in cementing this link. Roy Dafoe, the country physician to the quints in Calendar, was regularly in contact with his brother William Dafoe, an obstetrician/gynecologist in Toronto. William Dafoe was himself a close friend of Dr Alan Brown, and these two regularly discussed the quints. Katherine Arnup, "Raising the Dionne Quintuplets," 69.

[73] Ford Walker, "The Development of Human Genetics at the University of Toronto."

[74] Brown was cited as a co-author on several publications with Ford Walker and was thanked by her students in their thesis acknowledgements for providing research ideas. The timing of this work and the tone suggest that these collaborations were substantive. However, Brown's biographer records suspicions about his actual involvement in many of the research projects and publications which bore his name, see: AB Kingsmill, *Dr Alan Brown: Portrait of Tyrant* (Toronto: Association Medical Services Inc., 1995).

[75] "Knowledge of the inheritance of dermatoglyphics," Cummins and Midlo note in their text, "prepares the way for practical applications." Ford Walker was certainly more interested in these than in the discussions of the mechanics and peculiarities of inheritance in dermatoglyphics: *Fingerprints, Palms and Soles*, 235.

[76] Margaret Thompson, "Genetic Counseling in Clinical Pediatrics: What to do with Inquiries about Heritable Disorders," *Clinical Pediatrics*, 6 (April 1967), 199.

[77] JBS Haldane complained about the confusion between the two terms in: *New Paths in Genetics* (New York and London: Harper & Brothers, 1942), 115.

[78] University of Toronto, *President's Reports*, 1938-39, 46; University of Toronto, *President's Reports*, 1939-40, 42.

[79] Norma Ford, Alan Brown and JF McCreary, "Evidence of Monozygosity and disturbance of growth in twins with pyloric stenosis," *American Journal of Diseases of Children*," 61 (1941); Norma Ford, Mary Ross and Alan Brown, "Primogeniture as an Etiologic Factor in Pyloric Stenosis," *American Journal of Diseases of Children*, 62 (1941). The case of pyloric stenosis was cited by Norma Ford in her article on the "The Value of Clinical Records" where she argued for the production of detailed case files, even where the information seemed irrelevant to clinical practice, in order to support "studies in human biology [which] are concerned in large part with problems of *inheritance*." Norma Ford, "The Value of Clinical Records in Medical Research," *The Canadian Hospital*, 21 (1944), 31, emphasis in original.

[80] Sarah Tracy, "An Evolving Science of Man: The Transformation and Demise of American Constitutional Medicine, 1920-1950," in Christopher Lawrence and George Weisz eds., *Greater than the Parts: Holism in Biomedicine, 1920-1950* (New York, Oxford: Oxford University Press, 1998), 161. Tracy is here citing George Draper's definition of constitution.

[81] W Sheldon, "Hypertrophic pyloric stenosis in one of uniovular twins," *Lancet*, 2 (1938), 1048.

[82] Ford et al, "Evidence of Monozygosity and disturbance of growth," 42.

[83] The faith that monozygotic twins shared an "identical" inheritance (a faith Charlemains and Pons suggests was unfounded) made them ideal for considering both simple and complex patterns of inheritance. Charlemains and Pons suggest that the "classic twin method" involved comparisons between identical and fraternal twins. By this definition, the Ford Walker school was not always using the classical "twin method." But I am less interested in categorical definitions here than in a general trend of research that saw "identical" twins used as a device for etiological and developmental questions. See: Christiane Charlemains and Jean Claude Pons, "What Monozygotic Twins Tell us about Genetic Determinism," *Race, Gender and Class*, 5:3 (1998), 14.

[84] This study also made use of the protocol for the collection and preservation of placenta from Toronto hospitals; the unusual placenta of one of the sets of identical twins with pyloric stenosis helped to explain the disturbance of growth apparent in his skin patterns.

[85] In the first study, Ford Walker and her co-authors suggested that Sheldon was correct in seeing twinning as an environmental factor in the development of pyloric stenosis: "[T]he environmental handicap imposed before birth on members of multiple sets," they argued, "is one factor inducing the condition of pyloric stenosis." Ford et al, "Evidence of Monozygosity and disturbance of growth," 43.

[86] Ford et al, "Primogeniture as an Etiologic Factor," 747.

[87] *Ibid.*, 750, 751. Alan Brown's clinical experience was cited as disputing the thesis of family limitation, since "parents of affected children accept the condition as one of the milder abnormalities which can be corrected by surgical intervention." They used Ontario and Toronto census data as a control,

[88] Ford Walker suggested that cleft palate and retinoblastoma were inherited as dominants with reduced penetrance, yet there was no sign of either phenomenon in the family history of the twins. "It may be," Ford Walker argued, "that in some instances either retinoblastoma or cleft palate is non-hereditary, arising as a result of unfavorable environmental factors." Ford Walker detected signs of developmental disturbance. Both twins were seen to have some palmar patterns that were more commonly seen in Mongoloid imbeciles; moreover one twin, the one affected with retinoblastoma, showed signs of even more marked disturbance of growth. She presented two particularly Mongoloid signs – a speckled iris and partial fusion of digits in the feet. Norma Ford Walker, "Discordant Monozygotic twins with Retinoblastoma and Cleft Palate," *American Journal of Human Genetics*, 2 (1950), 375-384. This study is cited in the University *President's Reports* for 1939-40, 1940-41.

[89] Cummins and Midlo made use of this study to in their discussion of twin diagnosis, to confirm the method's efficacy. "Ford, Brown and McCreary," they write, "report on a pair of twins presenting every evidence of monozygosity except in dermatoglyphics. In this case the parakinetic mechanism responsible for dermatoglyphic unlikenesses is identified with a functional handicap in intrauterine development, which is shown to be probable in view of demonstrated abnormal relations of the fetal membranes." *Fingerprints, Palms and Soles*, 238.

[90] *Fingerprints, Palms and Soles*, 269

[91] *Ibid.*, 269.

[92] *Ibid.*, 276.

[93] They also developed the use of Mongol dermal patterns for diagnosis of suspect Mongols, a capacity that would become steadily more important in the 1950s. A 1942 publication concerned a rare set of twins with mongolism to whom Ford Walker gained access by learning of the case through the psychological literature. Norma Ford Walker used dermatoglyphics and the similarity method to assert the monozygosity of the twin pair. She also used the dermal patterns of the children to confirm the diagnosis of mongolism. She then used the fact of "close intra-pair resemblance" to argue for "a genetic element in the causation of mongolism." Citing her work with Brown on pyloric stenosis, she suggested that an environmental disturbance sufficient to cause mongolism would have left its mark in a more differentiated set, whatever

the zygosity. If the Mongolism of these two young women had been caused by an environmental disturbance during prenatal development, Ford Walker was suggesting, the dermal patterns, and the children's physiology, would demonstrate more anomalies despite their "identical" heredity. Norma Ford and Sylvia Frumkin, "Monozygosity in Mongoloid Twins," *American Journal of Diseases of Children*, 63 (1942), 857.

[94] N Ford Walker, Application for Grant in Aid of Research, June 27, 1945, (UT, A74-0022, Box 10, File: Advisory Committee on Scientific Research – Applications, 1945).

[95] Tracy cites "psychiatrist and consummate holist" Iago Galdston: Tracy, "An Evolving Science of Man," 163.

[96] *Ibid.*, 162.

[97] *Ibid.*, 166.

[98] N Ford Walker, Application for Grant in Aid of Research, June 27, 1945, (UT, A74-0022, Box 10, File: Advisory Committee on Scientific Research – Applications, 1945).

[99] *Ibid.*

[100] Dr NF Walker, Reports on Faculty research, Department of Zoology, Faculty of Arts, unexpended balance of October 31, 1946 (UT, A74-0022, Box 20, File: UofT Advisory Committee on Scientific Research, 1947-48); see also N Ford Walker, Application for Grant in Aid of Research, no date [1946], (UT, A74-0022, Box 10, File: Committee on Scientific Research, 1946).

[101] Ford Walker cited her work on constitutional types susceptible to polio in University of Toronto, *President's reports* from 1944-45 through 1950-51. James Miller wrote, "There is evidence (Walker, unpublished) that polio victims in certain epidemics have similar dermal configurations which deviate from the normal." James Miller, Disturbance of Fetal Growth in Cerebral Palsy: A Study of the Dermatoglyphics of 146 Patients, University of Toronto, MA Thesis, 68-9. (UT, T79 0100, File 12)

[102] Wijnada Moonen, "A Study of Digital Patterns in Epileptic Patients," University of Toronto, MA Thesis, 3, 2. 1945 (UT, T79-0091, File 59), 2.

[103] *Ibid.*

[104] Moonen thanks Penrose, Director of Psychiatric Research, for providing access to material, "A Study of Digital Patterns," 8.

[105] *Ibid.*, 52. It's notable that Moonen didn't subject the twin studies she cited from the literature to critical review, even though Ford Walker had argued that most evaluations of zygosity in the literature were inadequate.

[106] *Ibid.*, 53.

[107] Moonen's interpretation of the production of dermatoglyphic patterns was developmental. She cited Cummins and Midlo that "The character of specific configurations is determined indirectly. It is assumed to depend on developmental circumstances such as stress and tension in the growth of the part, the thickness of the embryonic epidermis and the distribution of the cushioned area....These factors, which condition specific configurations, are themselves under the control of genes, hence the genetic regulation of ridge alignment is accomplished indirectly through them." *Ibid.*, 10.

[108] *Ibid.*, 269, emphasis in original.

[109] Such work was listed in the annual reports and does not appear to have resulted in publications: "Ford, N and Penrose LS Study of possible linkage in the inheritance of hair colour and blood groups." University of Toronto, *President's Report*, 1941-42 and 1942-43, 79. Another joint project was entitled: "Study of the kindred of two phenylpyruvic sisters." *President's Report*, 1940-41, 119.

[110] This condition is now understood as a variably expressed autosomal-dominant disease in which muscles grow hard, causing progressive rigidity of body parts. See: *Cecil Textbook of Medicine*, JB Wyngaarden and LH Smith, Eds. (WB Saunders Co., 1988), 2277

[111] These studies are cited in the University of Toronto, *President's Report*, 1947-48.

[112] The studies of the inheritance of allergies and convulsive seizures were only reported for 1943-44, but the study of coeliac disease was reported from 1944-45 through 1947-48, and the inheritance of speech defects was reported from 1943-44 through 1948-49.

[113] Progress Report – April 1946, Margaret W. Thompson, UT, A24-0022, Box 19, File: Graduate Studies, School of (5-46-14). According to this report the joint study began in February 1945.

[114] The clinical complexity of the condition was apparent in the discussion of the clinical features of the disease and the historical difficulty in distinguishing it from the similar fibrocystic disease of the pancreas. The two conditions were distinguishable primarily on the basis of pathologically evident pancreatic lesions and the clearly familial inheritance of fibrocystic disease. While celiac disease enjoyed a later age of onset and a better prognosis for survival, Thompson noted that "its etiology remains obscure." Margaret W. Thompson, "Some Etiological Factors in Celiac Disease," University of Toronto, Ph.D. Dissertation, 1947, 2. Thompson's dissertation was even prefaced by thanks to the "celiac children and their parents" who had provided the material and "acted as research assistants.": Thompson, "Some Etiological Factors," Acknowledgements.

[115] This prenatal orientation was not due to the irrelevance of postnatal environmental factors in the etiology of the disease. Indeed, Thompson cited one of her co-investigators as the source of the argument that fewer cases of celiac disease were coming to the attention of Sick Kids because "predisposing severe streptococcal infections have become increasingly rare, owing to new developments in chemo therapy." Thompson, "Some Etiological Factors in Celiac Disease," 7.

[116] *Ibid.*, 58.

[117] *Ibid.*, 98, 99.

[118] *Ibid.*, 99, 100.

[119] Margaret W. Thompson, "Heredity, Maternal Age, and Birth Order in the Etiology of Celiac Disease," 159. In her publication Thompson acknowledged the tentative nature of her findings. She suggested that "an association between diabetes mellitus and celiac disease is suggested though not proven by our data." Margaret W. Thompson, "Heredity, Maternal Age, and Birth Order in the Etiology of Celiac Disease," 164.

[120] Certainly, this is the impression that is conveyed by the clippings preserved by the University of Toronto Archives. The coverage of Ford Walker is pretty extensive for the 1920s and 1930s - brief mentions of public talks are included. The coverage is significantly less for the 1940s and material is clearly missing in the 1950s and into the 1960s. Whether these files are fully representative of press coverage of Ford Walker in the decades of the 1920s through the 1940s I do not know. See: (UT, A73 0026, 105, 61).

[121] University of Toronto, *President's Reports*, 1940-41, 1941-42.

[122] Norma Ford and Arnold D. Mason, "Taste reactions of the Dionne Quintuplets," *Journal of Heredity*, 32 (1941), 367.

[123] Norma Ford and Arnold Mason, "Heredity as an aetiological factor in Malocclusion, As shown by a Study of the Dionne Quintuplets," *Journal of Heredity*, vol. 34 (1943), 64

[124] Mrs. BB Cunningham (nee Miss Barbara Bott) pursued work on "Dental malocclusion in relation to disturbance of growth from 1941-42 through 1943-44; Miss Win Lan Liu completed an MSc in Dentistry in 1949 on "A study of the closure of space following the premature extraction of deciduous teeth in man"; Mrs. ME Hatton (nee Miss M Philpotts-Brown) completed a Ph.D. thesis in 1952 in Dentistry on "A comparison of the patterns of clinical eruption of the deciduous teeth in man with growth in width of the dental arches."

[125] Loring Brace, "The Roots of the Race Concept in American Physical Anthropology," in Frank Spencer, ed. *A History of American Physical Anthropology, 1930-1980,* (Academic Press, 1982), 11-29.

[126] University of Toronto, *President's Report*, 1949-50, 1950-51

[127] She reported that "Work on an objective diagnosis of mongoloid imbeciles has continued and cases of both Japanese and Chinese patients have been added to the series." University of Toronto, *President's Report*, 1952-53, 122.

[128] Siemen's major subject was "Human Biology" with Ford Walker, but his two minor subjects were "Anthropology," and "Cultural Geography." See his "Program of the Final Oral Examination for the Degree of Doctor of Philosophy, inserted in his dissertation: GJ Siemens, "A Study of Certain Genetic Traits Found in the Dermatoglyphics of Jewish People," University of Toronto, Ph.D. Thesis. April 1947.

[129] Siemens, "A Study of Certain Genetic Traits," 1.

[130] Roy Israel Wolfe, "A Study of the Dermatoglyphics of the Six nations Indians of Southern Ontario," MA Thesis, University Of Toronto, 1947, 86. (UT, T79 0093, File 53). This effort to use dermatoglyphics to grade races was expanded upon in an Appendix in which Wolfe addressed himself to questions of "primitiveness." He noted that studies of primates had demonstrated an index of primitiveness based on the

intensity of skin patterns. This marker (pattern intensity) when applied to human populations, produced a sequence that largely confirmed anthropological knowledge and was thus seen as a "valid racial criteria." Yet there was one significant problem: "A serious difficulty about the ranking," Wolfe noted, "is that the order is reasonable, but the whole list is reversed." After reconfirming his notions of the sequence of evolution of human races, Wolfe embarked on a "re-evaluation of the phylogenetic development of digital patterns" by drawing on evidence from clinical constitutional studies. Ford Walker, Wolfe reported, had suggested "that the evolutionary trend in man may well be towards a slower foetal growth" and pointed to the "precocious" post-natal development of "Negroes" as evidence. Wolfe also cited the evidence from studies of "mongoloid imbeciles" and Moonen's study of epilepsy as evidence of differential speed of pre-natal growth. With the aid of these clinical studies, Wolfe was able to reverse the order in the sequence of human "primitiveness" – thus sustaining the logic of racial hierarchy with which student and teacher were most comfortable.

[131] Siemens, "A Study of Certain Genetic Traits," 1.

[132] Wolfe, "A Study of the Dermatoglyphics of the Six nations Indians."

[133] This study was reported in 1945-46 and 1946-47 as "effects of added thiamine on the learning ability of identical twins": University of Toronto, *President's Report.*

[134] N Ford Walker, Application for Grant in Aid of Research, June 27, 1945, (UT, A74-0022, Box 10, File: Advisory Committee on Scientific Research – Applications, 1945).

[135] EC Robertson, C.M. Tatham, Norma Ford Walker and M. Reid Weaver, "The Effect of Added Thiamine on Growth, Vision, and Learning, Using Identical Twins," *Journal of Nutrition*, 34 (1947), 692.

[136] The study gave Ford Walker the opportunity to study a large cohort of twins: 72 like-sexed twin pairs were painstakingly reviewed. Ford Walker reported having "collected sufficient data to calculate the arithmetic means, standard deviations and errors for digital ridge counts, digital patterns, palmar lines and palmar patterns. These standards," she added, "will be generally useful in all similar diagnoses." This study also presents," she added, "important evidence to show that uniovular twins may at times have a dichorionic placenta." Dr NF Walker, Reports on Faculty research, Department of Zoology, Faculty of Arts, unexpended balance of October 31, 1946 (UT, A74-0022, Box 20, File: UofT Advisory Committee on Scientific Research, 1947-48).

[137] Ford Walker did supervise a Ph.D. dissertation, completed in 1954 by AJ Butler on "Linkage of Intelligence and twelve hereditary characteristics in man." But she did not focus on these questions. Her career would seem to contradict the assertion made by Daniel Kevles and Charlemains and Pons, that twin studies were generally concerned with intelligence and behavior: Kevles, *In the Name of Eugenics*, 206; Charlemains and Pons, "What Monozygotic Twins Tell us," 14. This also contradicts Diane Paul's assertion that, in this period, "medical genetics is behavior genetics": "The Rockefeller Foundation and the Origins of Behavior Genetics," in Diane Paul, *The Politics of Heredity: Essays on Eugenics, Biomedicine and the Nature-Nurture Debate*, (Albany, NY: State University of New York Press, 1998), 65.

[138] Interest in questions of fetal development was suggested in the study of the Dionne quints. MacArthur and Ford Walker had suggested the value of assessing the embryological processes involved in the timing and order of twin development. But though they produced a best guess about the order of each quint's separation from the original fertilized egg, they expressed doubt "whether this can be successfully done at present." MacArthur and Ford, "A Biological Study," 36, 35.

[139] Ford Walker reported work on the "Godino united twins" and a "case of united foetuses born prematurely in Toronto" in1936-37. She assigned this problem to a student one year. Miss Glenna Stewart had the project "Palmar and plantar patterns in conjoined twins," University of Toronto, *President's Report*, 1940-41, 119. In 1952-53 Ford Walker reported two studies of conjoined twins: "in co-operation with the Neuropsychiatric Institute of the University of Illinois a study was made of the asymmetries of foetal growth of a pair of craniopagus twins, before they were separated surgically," and "in cooperation with the Lahey Clinic, Boston, a further study of a pair of pyopagus twins was made."

[140] Norma Ford Walker, "A Discussion of the Zygosity and Asymmetries of two pairs of Conjoined Twins," *Acta Geneticae Medicae et Gemellologiae*, 1 (1952), 136

[141] This was, Ford Walker suggested, part of a larger study "of birth membranes, foetal circulations, dermal configurations and other physical characters in investigating the association of *dissimilarity* between

monozygotic twin pairs and their *twinning-time*." Norma Ford Walker, "A Discussion of the Zygosity and Asymmetries," 136. Emphasis in original.
[142] *Ibid.*, 137.
[143] *Ibid.*, 141.
[144] John MacArthur, Research Projects in Genetics, June 21, 1945. (UT, A74-0022, Box 10, File: Advisory Committee on Scientific Research – Applications, 1945).
[145] University of Toronto, *President's Report*, 1935-6, 51.
[146] See the University of Toronto, *President's Report* for 1936-37; 1937-38; 1938-39; and 1939-40.
[147] Pauly characterizes the shift in name from Biology to Zoology as a narrowing of scope that, in one institution at least (Columbia, reflected the increasing power of medicine and thus the declining power of biology in the late 19th century. Whether similar power dynamics were at work in Toronto is, unfortunately, beyond the scope of this study. Philip Pauly, "The Appearance of Academic Biology," *Journal of the History of Biology*, 17 (1984), 388.
[148] N Ford Walker, "The Development of Human Genetics at the University of Toronto," 65.
[149] Norma Ford, "The Value of Clinical Records in Medical Research," *The Canadian Hospital*, 21 (1944), 31, emphasis in original
[150] This was the title of Thompson's study in the University of Toronto, *President's Reports*, 1944-45 through 1947-48. In her dissertation Thompson de-emphasized the hereditary side in conformity with the more expansive title of her finished project: "to discover whether celiac disease depends in part for its expression upon hereditary factors." Thompson, "Some Etiological Factors in Celiac Disease," 1.
[151] *Ibid.*, 1. Thompson's Major was Human Biology.
[152] Dora Conover, "Suggest means to test Pampas Quints Reality," *Toronto Star*, March 22, 1944 (UT, A73 0026, 105, 61).
[153] Kevles notes that this was a "benchmark book." Kevles, *In the Name of Eugenics*, 198.
[154] JBS Haldane, *New Paths in Genetics* (New York and London: Harper & Brothers, 1942), 119. Haldane makes the same argument in his more polemical *Heredity and Politics* (New York: W.W. Norton & Co., 1938, 33-34.
[155] See especially Chapters 4 and 5 in: J.B.S. Haldane, *New Paths in Genetics* (New York and London: Harper & Brothers, 1942).
[156] Daniel Kevles summarizes these tools as: "twin studies to sort out the relative role of heredity and environment; measurements of variability within hybrid populations to test for "race"-specific characters; pedigree investigations, especially from medical records, for determining the genetic basis of disease; and surveys of consanguinity, to decide whether certain diseases or physical traits might be the product of homozygous recessives." Kevles, *In the Name of Eugenics*, 198.
[157] Amy Sue Bix, "Experiences and Voices of Eugenics Field-Workers: 'Women's Work' in Biology," *Social Studies of Science*, 27 (1997). This is of some use in seeing the workers as "feminized" their work as having low scientific status – and essentially dealing with human heredity though in an earlier period. This is a reasonable parallel.
[158] See University of Toronto, *President's Reports*, 1931-2, Miss Kendall, "Heterochromidin of the iris in a human family"; 1934-35, 1935-36, 1966-37, 1937-38, completed in 1938-39, Mrs. ME Richardson, "Intelligence quotients in social problem children and their sibs and parents"; 1936-37, CK Gunn, "The acholuric jaundice mutation in the albino rat; its inheritance and its similarity to human disease"; 1936-37, 1937-38, 1938-39, 1939-40, Mrs. FH Miller (nee Miss F Harkness), "Comparison of human hand and foot prints."
[159] "N Ford Walker, "The Development of Human Genetics at the University of Toronto," 65.

Chapter 2

Making Medical Genetics in the 1950s: Sick Kids, Medical Biochemical Genetics and the End of the Indigenous Tradition

Introduction

After World War two, human genetics entered a new era of expansion and disciplinary coherence. The growth of biomedicine gave support to medical genetics, together with a host of other medical sciences and practices. And for their part, human geneticists embraced growth through the creation of new institutions. Norma Ford Walker and her students and colleagues, having developed in relative isolation and obscurity in the inter-war and war-time years, faced a new horizon of opportunity and intellectual consolidation in the 1950s.

Biomedical growth was manifested in Toronto through changes at the Hospital for Sick Children, which expanded its commitment to medical research. Ford Walker had established connections with Canada's premier pediatric facility in the 1940s, and through this association, Ford Walker and her students and colleagues had advanced a human genetics with a medical service role. In the early 1950s a new facility with enhanced space for research was opened – the "new" Hospital for Sick Children. Shortly thereafter, the hospital established a Research Institute to centralize and co-ordinate the

growing community of researchers in the hospital. Human genetics was an acknowledged and institutionally supported aspect of both developments.

Disciplinary growth was apparent in the establishment of the American Society of Human Genetics in 1948, and its journal, *The American Journal of Human Genetics*, in 1949. These institutions were instrumental in propelling human genetics beyond what M. Susan Lindee has characterized as a "ghetto of irrelevance."[1] In this growth, human genetics was aided by scientific interest, and public concern with the genetic effects of radiation, catalyzed by the bombing of Hiroshima and Nagasaki, and intensified by the Cold War in the 1950s. Elof Axel Carlson argues that Hiroshima and Nagasaki did as much to draw medical attention to human genetics as any conceptual or technical developments in the field.[2] M. Susan Lindee adds that the influence of radiation research on post-war genetics generally extended to material support: "By 1959," she writes, "an estimated 15 to 20% of the members of the Genetics Society of America were engaged in AEC [Atomic Energy Commission]-supported research or training programs."[3] Moreover, John Beatty suggests that research and disputes over the genetic hazards of radiation for humans constituted "a useful platform for promoting the new field of human genetics."[4]

The American Society of Human Genetics was also the home of Canadian workers in the field. Norma Ford Walker was a founding member and sat on the editorial board and the board of directors into the latter-half of the 1950s.[5] Moreover, in 1955, the Genetics Society of Canada was established, housing primarily plant and animal geneticists, but also the human variety. Again, Ford Walker was one of the founding

members.[6] In the post-war period, then, Ford Walker was integrated into what was an increasingly self-conscious and North American-wide discipline. It was in the spirit of defining that discipline that Herman Muller, as the first president of the American Society of Human Genetics, outlined the "errors to be avoided," in human genetics and the "trends in modern work" that could and should be followed.[7]

Ford Walker began the 1950s with the institutional identity of a human geneticist. But she headed a research school which investigated questions of human heredity using tools and presumptions that were marginal to the then-dominant British school of human genetics. Moreover, hers was a research tradition that had many, even scattered, interests in diverse applications of human genetics. During the 1950s this would change. The Ford Walker school was profoundly influenced by the local dimensions of expansion in the biomedical sciences. The enhanced institutional supports available at Sick Kids encouraged the Ford Walker school to pursue its medical service role, and the emphasis that the Research Institute placed on collaboration encouraged Ford Walker and her students in their contact with the pre-clinical disciplines, particularly biochemistry. By the mid-1950s, the human geneticists were co-operating with biochemical research that made new sense of classical genetics and helped to displace the complex etiological framework of the indigenous tradition. The influence of the biochemists forged what I will call, to distinguish it from the molecular variety, *medical* biochemical genetics.

The indigenous tradition was profoundly altered by these new developments. This was the era of the 'new genetics' – a new determinism, mechanism and materialism. In this period of generic growth, the particulars of Toronto's indigenous tradition faded and

were largely erased from memory. The indigenous tradition was read, *a posteriori*, as a "classical genetics" research tradition, in conformity with broader North American trends. However, as this Chapter will show, this "tradition" was *produced* during the course of the 1950s. The Ford Walker school which began the decade was very different than the one which closed it.

Expanding Opportunities for Medical Research

After the Second World War, biomedicine was propelled by growth in both the research university and the research hospital. The research university had demonstrated its value in the Second World War and enjoyed a prophetic surge in population due to veteran enrolments shortly thereafter.[8] The University of Toronto absorbed a large proportion of the post-war bulge. Its enrolment doubled, with a student population in the late 1940s that would not be matched again until the early 1960s.[9] Significant financial commitments from governments awaited the 1950s and in the interim the universities lived in what has been characterized as an "atmosphere of genteel poverty."[10] "Personal research by members of the staff ... is curtailed," the Chair of Ford Walker's Department wrote in his annual report for the 1946-47 academic year, "owing to the unusually heavy programme of teaching, both undergraduate and graduate."[11]

By the 1950s, however, universities were able to point to the baby boom generation as a weighty argument in favor of expanded government support. Cold war

insecurities in the atomic age, and the 1957 Sputnik crisis in particular, added considerably to the conviction that the universities were at the heart of a global economic and technological struggle. Sputnik seemed to demonstrate that "all the warnings about North American intellectual flabbiness and educational inadequacies were true."[12] The educational population explosion was also a function of the post-war expansion of white-collar jobs which required a general arts or science education.[13]

The federal government moved to support higher education in the 1950s. Research expanded, along with enrolments, aided in particular by the expansion of research granting bodies. In the early 1960s, federal funding agencies provided over twenty-five million for university research; a decade later, this had grown to almost one hundred and twenty million.[14] Graduate programs, a proxy for university research, grew accordingly. In 1940, McGill and Toronto – the only Canadian universities which were able – conferred 75 doctoral degrees.[15] In 1960, 281 Ph.D.s were granted by Canadian universities. In 1970, there were 1,375.[16]

Medical research was propelled both by the general growth of support for academic research, and by governmental investments in 'health' as a major plank in the building of the welfare state.[17] The post-war period saw a powerful move to define health as a right of citizenship, and biomedicine was promoted as the key. As Ilana Löwy and Stanley Joe Reiser have demonstrated, research was seen as central to the development of biomedical knowledge and treatment capacity.[18] Already by the 1930s in the United States, it was conventional wisdom "that patients in a research and teaching setting received more and better care than patients in hospitals not concerned with these

pursuits." [19] After World War II this enthusiasm grew: "At most university hospitals and medical schools during this decade," Reiser notes, "research had become the keystone of the medical arch."[20]

In Canada, a key promise of post-war reconstruction was the creation of a national health care system. Failing to achieve provincial agreement to a hospital and medical care insurance scheme, the federal government forged ahead with the National Health Grants Program in 1948. This program was a major boost to biomedicine. It provided state support for the education of medical professionals and those in allied disciplines – funding professional schools, professors and students; it supported the growth of hospitals and the expensive machinery that filled them; it financed service programs for particular diseases like TB and cancer and in areas like mental health and maternal and child health; finally, the federal state provided aid to research on the nation's health – some of the research funds went to evaluating pilot projects or to public health research, but much of it went to demonstrably biomedical research.[21]

The research funds available through the provincially administered National Health Grants Program consistently exceeded the funds available through Canada's official biomedical research funding bodies, yet these too grew in the post-war period. In 1960, after considerable lobbying, Canada's Medical Research Council emerged from it's supplementary role within the National Research Council as a fully fledged and independent research body.[22] The MRC, and its predecessor, the Division of Medical Research within the NRC, proved to be an important source of funds for genetic research in Canada.

The National Health Grants Program and the MRC were not the only Canadian supporters of research. As the provincial governments turned increasingly to the support and co-ordination of research, semi-autonomous provincial research organizations were established, such as the Ontario Mental Health Foundation, created in 1960. In London, Murray Barr turned often to local private Foundations which gave him considerable flexibility in responding to new research interests.[23] In Toronto, Norma Ford Walker used supplementary funds from the Hospital for Sick Children to amplify the value of external grants. She also turned to a new source of funds in the post-war period - the voluntary health organization – which engaged in advocacy, mutual support and public education in relation to specific disease entities and also the funding of research on specific medical conditions.

Of course, Canadian developments did not occur in a vacuum. Of major importance were parallel developments in the United States. There was in the US the example of massive state funding for biomedical research with the growth, in particular, of the NIH.[24] The American largesse was a perceived opportunity, since American money for biomedical research flowed readily into Canadian institutions into the 1960s. It was also a perceived threat, since Canadian researchers claimed to be at risk of a so-called brain drain of national capacity. The American example thus served as a constant reminder of the virtually unlimited need for more investment in medical research, and a rhetorical weapon for advocates of such investment. Finally the American model of the disease-specific voluntary organization was highly influential in the development of Canadian associations.[25]

The expansion of medical research and medical capacity were intimately connected – as was manifestly apparent in the agenda of the National Health Grants Program. In Toronto and London, university faculties of medicine grew in size, as did hospitals and other patient care and custodial institutions.

Expanding Opportunities in Toronto

The climate of growth and opportunity that existed at a national and continental level was also manifested locally, in institutional change at the Hospital for Sick Children. In February 1951, the "new" Hospital for Sick Children was officially opened – characterized as "certainly the largest and, almost certainly, the most modern pediatric centre in the world."[26] Financed through an outpouring of government and public support, a key justification for this investment was an expansion in the number of beds, almost doubling from 320 to 632, and thus a massive expansion in clinical capacity. But alongside the increase in service capacity was the corollary enhancement of Sick Kid's research and teaching capacity.[27] The new hospital devoted almost an entire floor of the available 14 to laboratories: 106 rooms replaced 21, "providing," its proponents argued, "new impetus for the research which has come to play such an important role in the Hospital's life."[28]

Genetics was among those departments which benefited from this increase in space. A Genetics Department, concerned with the study of "problems of heredity," was

allocated room with the other laboratories.[29] Indeed, Ford Walker maintained that Sick Kids was the first hospital in the world to have included a department of genetics in its building plans.[30]

The research interests advanced in the new facilities were further enhanced through the incorporation of a Research Institute (RI), officially opened on January 1, 1954. While research had been conducted in the hospital previously, indeed there were research labs and a Director of Research, the Institute represented a new institutional commitment. All research in the hospital was to be coordinated through the Institute, with a central budget, and overseen by the Institute's Director and a Committee of Research. Such a structure was expected to facilitate more research at the hospital, to reduce the administrative burden on workers, and to enhance co-operative research.[31]

Research centers in hospitals had first emerged in the United States in the early 20th century. Keith Wailoo argues that these facilities allowed clinicians to move beyond the narrow demands of specialties which necessarily, in seeking to advance themselves, worked to segment disease conditions.[32] The "cooperative environment" of these centers, Wailoo argues, "nurtured a flexible research ethos. Isolated from clinical politics, researchers focused on the study of specific physiological mechanisms to establish the legitimacy of one disease perspective over another."[33] The research institute permitted collaboration because the source of much dissension – disagreements over a specialty's 'ownership' of a clinical condition and its management – was removed from the mix. The production of this co-operation relied, then, on a changing emphasis on knowledge production in relation to patient care. "Clinical research," Keith Wailoo notes, "placed

decision-making into the hands of the inquisitive individual researcher, placing knowledge production above patient care per se."[34] The research hospital thus collaborated with the research university, with which it was generally affiliated, in the growing emphasis on academic medicine.

In developing its Research Institute, Sick Kids was influenced by comparable facilities throughout North America. The hospital administration commissioned Dr Basil MacLean of the Strong Memorial Hospital of the University of Rochester, N.Y. to produce a "Study on the Hospital for Sick Children" in 1953. His report had as one of its chief recommendations the establishment of a Research Institute.[35] This recommendation encouraged the hospital's newly minted Medical Policy Committee to investigate "six different hospitals active in the research field" in Montreal, Philadelphia, Boston and Rochester during the summer of 1953.[36]

In their visits to other hospital-based research facilities, members of the Medical Policy Committee identified the parameters of good research. They were convinced that "the most fruitful and productive work is performed by whole-time workers." Yet there was some anxiety about what whole-time research work or non-medically trained researchers, like Ford Walker and her students, might bring in their wake. Members of the Medical Policy Committee who toured the six institutes criticized the Research Institute of the Montreal General Hospital, in particular, for its leadership by a "well-known biochemist" who was "not medically qualified" and whose research was "all on the academic plane...[with] little immediate bearing on human disease."[37]

Yet research was to exist in service of clinical needs. TGH Drake, Director of the Research Laboratories, which were the precursor of the Research Institute at HSC, when announcing the research facilities available in the "new" Sick Kids stated that "In the future, as in the past, research problems which are being investigated in the hospital laboratories, must have their beginning and end with the well or sick child."[38] But in its "First Annual Report," the Director put the matter rather differently, declaring that while emphasis was put "on the study of the commoner forms of disease and disability in childhood ... [it would] from time to time be necessary to engage in investigative work of a more fundamental character in the laboratories of the Hospital."[39] Full-time research workers were to engage in sustained enquiry and to benefit from and advance some of the pre-clinical sciences. The Research Institute would house the research work already underway in various departments of the hospital; it would also provide a home for those pre-clinical sciences not usually found in a hospital. The departments of Biochemical Research, Genetics and Virus Research, for example, existed only in the Research Institute.

The Research Institute could provide those working on approved projects with stable financial support – an essential prerequisite for full-time research. The Institute relied for its base budget on hospital funds and moneys from the Pediatric Research Foundation – which received the profits from patents on earlier developments, notably pablum. But this was a financial base to be built upon through access to funds that were increasingly available from governments and charitable organizations after the war. The Research Institute was established, in part, to take advantage of these external funds.

Moreover the Research Institute sought to organize these funds in the most expedient ways possible.[40]

Irene Uchida and the Perseverance of the Indigenous Tradition

The institutional resources offered by the new Sick Kids and the Research Institute had a major impact on members of the Ford Walker school. But the tools and assumptions of the indigenous tradition were not suddenly or completely overturned. Nor was there a total shift towards medical genetics to the exclusion of all other inquiries in human genetics. In fact, Ford Walker's own research on racial questions expanded in the 1950s. And Ford Walker's students and colleagues, who took advantage of available medical links, retained their interest in dermatoglyphic tools and complex etiological questions.

Uchida and the Cardiac Clinic

Irene Uchida is emblematic of the indigenous tradition's resilience in the face of post-war change. Starting her work in the 1946-47 academic year with a "study of constitutional types susceptible to rheumatic fever," she completed her Ph.D. dissertation in 1951 on "a study of environment and heredity in the etiology of rheumatic fever."[41] After receiving her doctorate, Uchida worked at the Institute as a research associate until 1959, becoming Ford Walker's colleague and helping new students in their work.

Uchida's dissertation had relied on collaboration with the Cardiac Clinic at Sick Kids, and the co-operation between the Genetics Department and the Cardiac Clinic continued over the course of Uchida's research career at HSC and resulted in other research projects on cardiac disease in twins and in Mongols. The association between Uchida and the Cardiac Clinic was a model of the clinically-oriented research collaboration which helped to institutionalize medical genetics within the hospital. It was also a model that built on the tools and the etiological concerns of the indigenous tradition.

Uchida's association with the clinic provided her with access to such essential resources as patients, expert clinical diagnoses and medical relevance. This dependence was testified to in Uchida's acknowledgements and by numerous co-authored publications. But while the clinic was a resource for Uchida, Uchida was also a resource for the clinic. The "genetic analysis" that Uchida provided gave answers to the etiological questions of other medical researchers. Indeed, throughout the 1950s, an odd assortment of publications by Norma Ford Walker and her students and colleagues suggests that many departments of the Hospital saw the geneticists as resources for etiological analysis. Moreover, as the Genetics Department expanded its practical work with patients – largely in diagnosis and heredity counseling – it too became a source of patients for collaborative research work.

Yet the etiological analysis that Uchida and her colleagues in the Genetics department provided was of a particular sort. In the three sets of studies that Uchida pursued in association with the cardiac clinic through the 1950s – on rheumatic fever, cardiac anomalies in twins, and cardiac anomalies in Mongols – her analysis of etiology

was broadly framed, concerned with both hereditary and environmental influences, and prepared to assign the principal influence to the environment. Moreover, in considering hereditary factors, Uchida and her colleagues were wont to consider complex rather than single gene effects and to attend to processes of embryological development. Uchida drew on a diverse array of tools, both indigenous to the Ford Walker school and generic, using the twin and Mongol methods, and pedigree and mode of inheritance data. Uchida's near-decade of research at Sick Kids demonstrates the fruits of close collaboration between the Ford Walker school and the hospital and suggests the continued validity of the indigenous tradition. When Uchida left Toronto at the end of the 1950s to lead new Departments at the University of Manitoba and then McMaster University she assumed the role of vanguard in new developments. But while in Toronto, she preserved more traditional approaches and demonstrated the value of these tools within the medical milieu.

Rheumatic fever

Irene Uchida argued that her doctoral research responded to the "urgent need for a critical examination of the claims made by various authors regarding the relative importance of heredity and environment in the etiology of rheumatic fever." Her dissertation addressed the thesis that the "susceptibility to rheumatic fever is transmitted as a single autosomal recessive gene." This thesis, which had been developed in the late 1930s, was widely publicized and long accepted. It had been reported in genetics and

popular texts. It also, Uchida noted, had been used to inform prediction tables of affected offspring that were distributed by a major insurance company.[42]

The clinical dimensions of Uchida's project loomed large and she reserved her first thanks for the "rheumatic patients and their families whose co-operation and constant interest made this study possible."[43] Moreover, Uchida devoted attention to a discussion of the "clinical aspects of rheumatic fever" and asserted the importance for "genetic analysis" of expert clinical diagnosis.[44] Rheumatic fever was an "extremely widespread infection involving the fibrous tissues and certain serous membranes of the body." It might manifest itself clinically through "heart disease, polyarthritis, chorea and subcutaneous nodules" as well as more general symptoms of "fever, aching joints, abdominal pains, loss of weight and appetite, frequent nosebleeds and increased sedimentation rate."[45] The cause of rheumatic fever was unknown. It was clear that the disease demonstrated some familial patterns: it was more prevalent among poorer classes, and many researchers believed that it was precipitated by an infection. But Uchida noted that "the relative importance of the streptococcus and the virus, of environmental conditions and heredity is still being discussed."[46]

Uchida's analysis of etiology began with a review of the population characteristics of the disease, its incidence and age at onset, and its distribution by sex, race, class and geography. This portion of Uchida's study set the stage for her review of rheumatic fever cases among those Toronto children and their families who were amenable to careful study at the Hospital for Sick Children: a total of 58 families. Uchida restricted her study to "white" families which belonged to the "lower economic strata"

and her pedigrees were limited to the review of those generations who were living.[47] Such "rigid standards" provided "strict control of the material used" and, Uchida argued, made her results more compelling.[48]

Uchida's study of the environmental factors involved in rheumatic fever addressed both the post-natal and the pre-natal dimensions. Her attention to post-natal factors such as economic conditions, communicability and climate was unusual for a member of the Ford Walker school. But in attending to prenatal factors, Uchida conformed with the developmental orientation of the Ford Walker school while differing from other students of the disease. This portion of Uchida's study was reliant on the Mongol method: "In some conditions such as mongolism and congenital abnormalities," Uchida wrote, "the prenatal environment is of more importance than the post-natal." Though there was "no reference in the literature to this aspect," Uchida's study paid close attention to "prenatal environmental factors."[49]

Uchida found evidence for the causal effect of prenatal disturbance in the high incidence of rheumatic fever and thyroid dysfunction among the mothers of children with rheumatic fever; she also examined such traditional factors as maternal age, birth order, multiple pregnancies and abortion rate. Uchida used the Mongol method to search for signs of these prenatal disturbances in the dermal patterns of affected persons, arguing that "mongoloid imbeciles who are the victims of developmental retardation can usually be identified by characteristic dermal patterns."[50] But her "analysis of foetal growth" through comparison of prints from her sample with Ford Walker's University student controls was inconclusive.[51]

Uchida addressed the question of the role of inheritance in rheumatic fever carefully. She considered three kinds of evidence, both from her sample and from the literature: the "tendency of rheumatic fever to run in families," twin studies, and various suggested modes of inheritance.[52] The structure of Uchida's analysis left considerable room for complex hereditary "factors"; only the analysis of modes of inheritance demanded attention to specific genetic mechanisms.

Published surveys indicated that, at least in some families, the incidence of rheumatic fever was higher than chance alone would allow. Uchida's own sample of 58 families also demonstrated a higher frequency of the disease than in the Toronto population generally.[53] But, as Uchida noted, "The controversial point lies in the cause of this familial tendency. There are those who accuse heredity, others point to contagion while still others blame common environmental influences for the familial tendency."[54] Uchida's evaluation of her own sample suggested that "since no difference was found between the proportion of affected offspring of rheumatic and non-rheumatic parents, the indications are that the important etiological factors are environmental rather than genetic."[55]

If the analysis of familial incidence was less than definitive, Uchida argued that "One of the best methods to test for the presence of genetic factors is the study of twins."[56] Drawing on the twin method, Uchida argued that differences in "phenotypic expression" among monozygotic twins "are the result of environmental influences, prenatal and postnatal."[57] While Uchida's own sample could contribute limited data on twins with rheumatic fever, she cited evidence from the published literature which

suggested the "powerful influence of environmental factors." At the same time, the frequencies of concordance and discordance in the expression of rheumatic fever between monozygotic and dizygotic twin pairs indicated that "heredity does play some role in the etiology of rheumatic fever" though on balance "heredity and contagion play a role secondary to that of environment."[58]

The final evaluation of the place of heredity in rheumatic fever involved the assessment of a range of theories for the mode of inheritance of the predisposition to rheumatic fever. Demonstration of a plausible genetic mechanism would provide "A strong argument for the importance of genetic factors in the development of a trait," Uchida argued.[59] The three extant theories involved sex-linked inheritance, single autosomal dominant inheritance and single autosomal recessive inheritance. Uchida's careful review of these theories in light of her sample, and a careful review of the data provided by the proponents of recessive inheritance, indicated that "no single mode of inheritance has been established nor is there much indication that a simple explanation is possible."[60]

"It has been possible in the past," Uchida argued, "to reduce certain normal and abnormal characters to simple genetic principles." However, such simple genetic effects were rare. Studies of those "abnormalities which seem to follow the simple rules of dominant and recessive inheritance," Uchida argued, "....are rapidly giving way to examination of conditions which do not fit into any simple category." Indeed, "Even those conditions which were believed to follow definite modes of inheritance are causing

us trouble," she added. Conditions in which persons who were known to possess a certain gene but not to demonstrate the gene's effects had "brought into being the term "penetrance"." Moreover, assessments of the incidence of a certain phenomenon had to take into consideration the existence of "phenocopies": those "conditions which cannot be distinguished by their clinical entity and yet are cause by different etiological reasons.[61]

Uchida presented herself as one of a generation of genetic analysts who were aware of the complexities of heredity. She was attentive, she suggested, to the difficulty of discerning a simple mode of inheritance: it seemed logical that the same condition might be produced through a number of different modes of inheritance. Uchida was particularly concerned to recognize complex patterns in situations where environment was known to be an influence – such as "those conditions which are inherited as a predisposition to the late development of the trait," for example, rheumatic fever.[62]

"The gene," Uchida argued, "is merely one force in the midst of a multitude of others, genetic and environmental. When a gene potential is high, little difficulty is encountered [in analysis of etiology] but in most cases the path from the gene in the germ cell to its final dissolution in the grave is twisted and uncertain."[63] Uchida was forceful in her conclusion. "Rheumatic fever," she argued, "is a sociological problem rather than an eugenical one....it is to the benefit of all, rheumatic families and society, to suppress rheumatic fever by providing better living conditions in those places in which rheumatic fever is rife."[64]

Uchida's dissertation research drew on the full range of tools available to members of the Ford Walker school. She addressed both environmental and hereditary influences, preferring the latter in this instance. Yet ironically, though arguing for attention to complex genetic processes, Uchida pursued precisely the kinds of techniques – pedigree analysis and mode of inheritance modeling – which had not been emphasized by the indigenous tradition. This gesture pointed toward a shift that would make more room for what we might call, paraphrasing Evelyn Fox Keller, 'the discourse of *single* gene action.'

Twins

Uchida's plea for placing social emphasis on environmental efforts at prevention was made without denying the influence of heredity in producing susceptibility to rheumatic fever. Such an influence was testified to by available published data on twins. Uchida shared the faith of the Ford Walker school, then, in the value of twin data to discern genetic forces where genetic mechanisms were too complex for pedigree analysis alone.

If twin data could be used to suggest a place for hereditary forces, it could also be used to disprove such forces. In line with her sympathy for environmental etiologies, and working in collaboration with pediatricians involved with the Cardiac Clinic, Uchida published two studies, in 1951 and 1957, which reviewed cases of congenital cardiac

malformations in twin pairs to argue against "the theory of genetic transmission as reported in some studies of family groups."

Uchida's first article on this subject concerned only a single monozygotic twin pair discordant for a cardiac anomaly.[65] But she later obtained the assistance of the Cardiac staff to pursue a systematic review of twins with cardiac anomalies who had attended Sick Kids for treatment.[66] Publishing this review in 1957, Uchida and her co-author, Richard Rowe, of the Cardiac Clinic presented data from 26 twin pairs, 13 of whom were monozygotic and the other 13 dizygotic. In all twenty-six pairs, only one member of each was affected by a congenital cardiac anomaly. "Discordance among monozygotic twins," Uchida and Rowe suggested, "tends to discount genetic factors in the etiology of a trait. The results of this twin study, therefore, indicate that although in certain families congenital heart disease may be genetic in origin the majority of cases are caused by some uterine factor or factors as yet unknown."[67]

Both studies were reliant on the twin method. Uchida used Ford Walker's diagnostic protocol – dermal patterns, blood groups, and the similarity method, were used in the assessment of zygosity. Uchida also used the ongoing study of placenta by Ford Walker and herself – the availability of a large series of latex-injected, and thus preserved, placenta meant that the fetal membranes of some twin pairs could be investigated.[68] This allowed Uchida to demonstrate the importance of placental configuration in twin diagnosis and the potential developmental influence of "prenatal environmental factors unique to twins" in the production of cardiac anomalies.[69] Uchida and her co-author argued against simplistic beliefs about "identical" twins: "It was once

thought," they wrote, "that one of homologous twins never suffered from a malformation not shared by his fellow." This flawed interpretation of "identical" twins had been corrected by the more current knowledge "that environment may modify a given hereditary trait."[70] Monozygotic twins were "in respect of their genetic constitution ... one and the same individual." But this genetic sameness was subject to developmental and environmental influences such that "When one member of a monozygotic pair presents a particular abnormality not shared by his fellow, it is safe to conclude that the cause of the discordance is not genetic."[71]

Mongols

For her studies of individuals with rheumatic fever, and in particular for her review of twins with cardiac anomalies, Uchida was reliant on the Cardiac Clinic for the location of research material. But by the 1950s, the Ford Walker school had developed an applied service capacity within the Hospital for Sick Children and had developed its own patient population which might serve as research material. This practical service was of two kinds. First, like other North American centers, the Genetics Department provided genetic counseling to individuals and couples concerned about their chances of having a child with a genetic anomaly. The other practical service provided was less usual. The Genetics Department offered a diagnostic service identifying Mongols using Ford Walker's index of dermal patterns.[72] The third study that Uchida undertook in

collaboration with the Cardiac Clinic benefited from the practical capacity of the Genetics Department: it was a study of Mongols with cardiac malformations.

Though unusual, this diagnostic service was significant: almost all suspected Mongols born in Toronto had their diagnosis confirmed or disconfirmed though this service.[73] But ironically, when this diagnostic service was developed at Sick Kids, Mongolism was not a strictly genetic phenomenon. The claims of the geneticists to 'ownership' of this condition were based on their ability to produce effective diagnoses and to an enduring indigenous tradition of methodological reliance on the Mongol. Though the distinctive dermal patterns diagnostic of Mongolism testified to a developmental disturbance that was not necessarily genetically caused, a developmental and broadly etiological Genetics Department was a logical home for this diagnostic test. The study of cardiac anomalies in Mongols pursued by Uchida and her pediatrician collaborators was premised, then, on these conceptual and institutional relations.

The diagnostic service for suspected Mongols offered by the Genetics Department gave the geneticists, and through them their collaborators, unprecedented access to a particularly useful population of Mongols. Most researchers, including Norma Ford Walker's student, Grace Workman, in the late 1930s, gained access to populations of Mongols in institutions for the mentally retarded; such populations were necessarily biased because of the very high mortality of infants and children affected with Mongolism at the time. The clinical service at Sick Kids, by contrast, gave researchers access to an unbiased sample of "almost every mongoloid baby born in Toronto."[74]

The study of cardiac anomalies in Mongols was begun as a pilot project in 1954. Children whose suspected Mongolism was confirmed in the Genetics Department were then sent to the Cardiac Clinic for further study: "In the 12 month period some 58 mongols have been examined. Two-thirds of these have been found to have congenital heart disease." [75] The study proper commenced in 1955 and data were collected until 1957. Analysis of the data took longer; a summary analysis was published in 1961.[76]

The study was intended to serve both the geneticist and pediatrician and thus was undertaken in two parts: the "Genetic Study" and the "Cardiac Study." The "Genetic Study" involved, first, the diagnosis using "a new method, the most reliable to date": Ford Walker's index of dermal patterns. These diagnostic dermal patterns would also be analyzed for signs of developmental disturbance linked to cardiac anomalies. Such analysis, it was hoped, would help to "pin-point more accurately the time and extent of disturbance of growth not only in these defective children, but also by application in normal children with congenital heart disease." This part of the study was to be accomplished by comparing the dermal patterns between Mongols with and without heart disease, and between those with specific types of heart disease with and without Mongolism.[77]

It was the genetic potential of this work that academic reviewers were most interested in. In 1955, one reviewer wrote, "If this study will stimulate interest in the cause of mongolian idiocy I am in favour of supporting it. I think it will. Is it genetically determined?" Another reviewer wrote that "Too little careful work is being done in the important field of human genetics and all well done studies will yield information which,

in light of the increasing application of atomic energy, may in the future have more and more importance." The next year, the same reviewer wrote that "There is no question in my mind that Dr Walker and her group are doing first class work in connection with genetics and the understanding of hereditary defects."[78]

Uchida's analysis of the dermal data from Mongols did suggest "a greater disturbance of fetal development in the mongols with congenital heart disease."[79] But though some dermal patterns appeared to be different, and the difference to be statistically significant, Uchida never appears to have completed the comparison with non-Mongol subjects with congenital heart disease which could have verified these suggestive findings.[80]

Like the "Genetic Study" the "Cardiac Study" involved diagnosis, using "modern investigative methods." Data from these diagnoses would establish the incidence, and types, of cardiac anomalies in Mongols, replacing existing data from analysis of more biased populations. It was hoped that the study might also provide greater knowledge about certain types of heart conditions and about heart function in newborns.[81] The cardiac study appears to have achieved these objects. Data on the incidence and type of cardiac anomalies in Mongols was soon available. Moreover, the cardiac study produced data on mortality among Mongol infants and children. Finally, Richard Rowe was able to conduct studies on a number of the Mongol children who were without cardiac anomalies; access to Mongol children likely made such analyses possible. Transformed into "normal" children for the purposes of cardiac function, these children were subjected

to high concentrations of oxygen in order to "study the effects on pulmonary and systemic arterial pressures."[82]

In retrospect, the "Cardiac Study" appears to have been more successful than the "Genetic Study". While Uchida produced no monograph on the genetic study, and the summary publication she co-authored with Rowe presented "data of genetic interest" only "in brief," Rowe and his colleagues produced at least three publications from this work.[83] This imbalance likely reflected Uchida's growing awareness that the "Genetic Study" had produced very little of what might, on the eve of the 1960s, count as genetic data.[84]

This project had originally been genetic because of its institutional home in the Department of Genetics. Moreover, it had been genetic because geneticists in Toronto had a near-monopoly on accurate and reliable diagnoses of Mongolism. Finally, it was genetic because of an indigenous tradition that understood the "genetic" to encompass environmental, hereditary and developmental processes. If the genetic study was, by the end of its tenure, a failure, this was not a result of poor methods or inadequate data. It was a result of the original intent of the study itself. For the goal of the "Genetic Study" had never been to assess hereditary factors, much less mode of inheritance. Instead, it promised insights of a primarily developmental sort in accordance with the presumptions and tools of the indigenous tradition.

The ultimate failure of the genetic component of the cardiac study, and Uchida's loss of interest as she set out in pursuit of cytogenetic glory at the end of the 1950s,

signals the declining relevance of the answers promised by the methods of the indigenous tradition. This declining relevance was facilitated in Toronto by the emergence of a biochemical orientation with new ways of conceiving of genetic disease.

Building Medical Biochemical Genetics

The University of Toronto had long had a metabolic orientation which built on the Insulin years. In 1959, when Uchida's longstanding collaboration with the Cardiac clinic came to a shuddering halt, the *University of Toronto Medical Journal* declared that "today Toronto stands as one of the foremost metabolic research centres in the world."[85] This metabolic orientation was manifest also at the Hospital for Sick Children, though it was initially of a more practical, nutritional kind. The HSC counted among its principal achievements, the pasteurization of milk in Ontario in the 1930s, the invention of pablum ("the first pre-cooked infant cereal, furnishing adequate amounts of minerals and vitamins, in addition to calories"), and a successful campaign to minimize childhood rickets through the addition of Vitamin D to the diet of children.[86] The enhanced research capacity of the "new" Sick Kids built on this legacy through a special metabolic unit "complete with its own pantry and laboratory," and through co-operative research with such University departments as the Connaught Laboratories and the Banting Institute.[87]

When the Research Institute began operation, it made a special commitment to biochemical research.[88] As the First Annual Report of the Research Institute put it, "The

major part of the work of the Research Institute is carried out in the Biochemical Research Laboratories, in co-operation with various Wards and Departments of the Hospital."[89] It was this biochemical orientation which was to prove so influential in the remaking of medical genetics in Toronto in the 1950s. Through the leadership of biochemists in the study of metabolic disease, through collaborative ventures between the human geneticists and the biochemists, and through the adoption of biochemical tools and assumptions by the human geneticists, the indigenous tradition was transformed into a classical genetics 'tradition' which took seriously the discourse of single gene action.

If Toronto geneticists were propelled into association with biochemical concerns in the 1950s as a result of local institutional change, such intellectual alliances were not unique to Toronto. Indeed, across North America and in the British school, medical geneticists adopted biochemistry as a resource for understanding genetically-controlled metabolic diseases like PKU, and looked to biochemical markers to provide signs of heterozygote carriers. Biochemical genetics was crucial to the making of medical genetics, then, but what kind of biochemistry was this?

In the 1940s, as the standard stories in the history of 'basic' genetics would have it, a new science of biochemical genetics was developed. The American team of George Beadle and Edward Tatum produced the 'one-gene-one-enzyme' theory of gene action and demonstrated its validity in a new and powerful experimental organism: the bread mould, *Neurospora*. This work, which showed that genes 'act' by producing specific enzymes – one enzyme for each gene – supported the turn to research on the material

gene and the move away from a transmission-only genetics; it was central to the making of biochemical genetics, which was, in turn, the basis of molecular genetics. For this contribution, Beadle and Tatum were rewarded with a Nobel Prize in 1958, which they shared with Joshua Lederberg. The standard stories also tell that, in making this discovery of the first importance, Beadle and Tatum were really only re-discovering the long-neglected work of the true 'father' of biochemical genetics: Archibald Garrod. Garrod was an English physician, active in the first half of the twentieth-century. His great work was on the 'Inborn errors of Metabolism': a series of rare, recessively inherited diseases where the clinical defect could be traced to a specific error of metabolism.[90] Garrod takes his place beside Mendel, as Jan Sapp points out, in the great stories of neglect and rediscovery that populate the landscape of genetics.

By the 1950s, when members of the Ford Walker school began their tentative collaborations with the biochemists, we might assume that the biochemists would be aware of the one-gene-one-enzyme hypothesis and committed to its veracity and implications. We might assume, also, that the inherited metabolic phenomena that the biochemists had begun to investigate would have been of obvious genetic significance, indeed, biochemical genetic significance, and that the Ford Walker school was demonstrating is backwardness by failing to lead such inquiries. Yet Jan Sapp has deconstructed the myth from the reality in the standard accounts and suggests that other presumptions might be warranted.[91]

First, Sapp argues, Archibald Garrod was no 'father' of biochemical genetics: he made no declarations about 'gene action' or about genetic theory. Indeed, as a

physiologist in the first decades of the twentieth century he had little interest in, and likely little enthusiasm for, the highly contested narratives of gene action asserted by the classical school; just as Mendel was no Mendelian, Garrod was no 'Garrodian'.[92] Second, the story of Garrod as a 'precursor' must be understood as a "founding father fable," one invented by Beadle as a way to support a contested theory, by suggesting its timeless obviousness. As Sapp puts it, "Garrod and the physiologists of his day had no intention of formulating a general theory of heredity based on genes and enzymes. To some, the reality of the gene was dubious, and to many, genes and enzymes alone could not control the orderliness of metabolic reactions in the cell or organism."[93] Third, an understanding of some association between enzymes and genes was a commonplace from the beginning of the century, and not a discovery: "The idea that hereditary factors controlled metabolic activity by way of enzymes was ... pervasive," Sapp has written.[94] What was new, and contested, in Beadle and Tatum's work was the breadth of their claim – that *all* genes worked *only* through control of *single* enzymes. Finally, Sapp has shown that controversy about the one-gene-one-enzyme theory continued into the late 1950s; the continuing belief among some geneticists in the 1940s and 1950s that this theory was over-simplified was, in fact, what encouraged Beadle's persistent recourse to Garrod as a long-dead and non-competitive, but seemingly all-knowing, predecessor.

In light of Sapp's de-bunking, the situation in Toronto demands a more nuanced analysis. Were the biochemists promoting 'biochemical genetics'? If so, then a biochemical approach should have advanced a rather different model of genetics than the classical school – encouraging the move beyond the metaphoric to the material gene, and

asking questions about what genes actually do. Yet there was actually little support for a physiological human genetics in Toronto. Moreover, it is not clear that the story-line of 'backwardness' can be used to make sense of the disinterest of the Toronto workers?

I will argue that what was being produced in Toronto was actually a distinctly *medical* science of biochemical genetics: a *medical* biochemical genetics. This science was not interested in 'gene action' – in the biochemistry of the gene and its functioning. Rather, this science was one that demonstrated the value of using biochemical tools in contemplating Mendelian processes. Consequently, this medical science, in its collaboration with the Ford Walker school, created a classical genetics orientation that had been under-exploited in Toronto's human genetics research previously. Medical biochemical genetics helped to make the classical genetics model make sense in the medical context in a way that had not previously seemed possible by producing unprecedented enthusiasm about the capacity of a profoundly simple narrative of heredity to adequately describe and, in the case of some conditions, to actually treat, genetic disease. Contrary to any simple theory of knowledge transfer from the 'basic' to the 'applied' spheres, which would support the adjectives of 'backward' or 'prescient,' the medical scientists used the available tools to answer the questions that made sense to them. This was a distinct, not a confused, science.

Ironically, this medical science also saw Garrod as its 'father' – drawing presumably on the myth made pervasive by Beadle. Yet here this mythical predecessor seems more appropriate. As a medical scientist Garrod's concern with clinical phenomena resonated with the attention to the human organism prevalent at Sick Kids.

Moreover, Garrod's disinterest in gene action was paralleled by the disinterest in such processes by these 1950s workers. Like Garrod, and unlike Beadle and Tatum, medical biochemical genetics was interested more in the conventional knowledge of an association between genes and metabolism, rather than a specific theory of gene-enzyme interaction. The importance of Garrod for the medical science of biochemical genetics suggests, then, another way in which this "founding father fable" served Beadle and Tatum's efforts: it provided a narrative linking genetics and biochemistry that was relevant to medical scientists, and thus produced a community of enthusiasts for 'biochemical genetics' in the 1950s, even though the biological and medical scientists were using this terminology in quite distinct ways.

Making Medical Biochemical Genetics In Toronto

One of the institutional innovations made possible by the establishment of the Research Institute was the appointment of full time research workers. "By the employment of these men," the First Annual Report of the Research Institute stated, "a major step forward has been taken in pediatric research in Canada. They have positions which are not dependent on the award of an annual grant, and it should, therefore, be possible to provide for continuity of research programmes on a longer-term basis than has hitherto been possible. These men have available to them all the facilities necessary for productive research and much should be accomplished."[95]

Of the small number of research workers appointed full time to the Research Institute when it began, a large number were of a biochemical orientation (though many were not Ph.D. trained biochemists, I will, for purposes of expediency, refer to them as "the biochemists"). The First Annual Report for 1954 listed the activities of these individuals: Andrew Sass-Kortsak was a certified pediatrician whose work was focused on nutritional and biochemical disorders. At the hospital since 1949 he was appointed a full time member of the Institute in 1954 and headed the Metabolic Ward which opened in 1955 and which permitted in-patient care of research subjects under controlled conditions. Dr Donald Fraser was also a pediatrician, and a Ph.D. Appointed to the Department of Pediatrics at the University of Toronto, he was a full-time research associate of the Institute whose work focused on calcium and phosphorus metabolism.[96] Dr. Sanford Jackson was Chief Biochemist at the Hospital. He, like Sass-Kortsak, was a full time research member of the Institute. He played a role in many of the studies conducted at the Institute and had a particular interest in fluorine metabolism and in the biochemical constituents of the blood.[97]

The Research Institute served as a crucial institutional link between workers with a metabolic orientation and the Ford Walker school. Collaborations extended beyond those formally affiliated with the Research Institute, but even they were built through the networks linking the University and the Hospitals in Toronto, networks which the Research Institute facilitated. Members of the Ford Walker school were helpful, directly and indirectly, in drawing out the genetic interpretation of metabolic phenomena. In the process, what had previously seemed to be too simplistic a model of genetics for medical

purposes came to appear profoundly efficacious: for explanation, diagnosis, and even treatment. In the process also, members of the Ford Walker school came to emphasize classical genetics questions which had previously been of minor importance to the indigenous tradition.

By the early 1950s, the full-time workers at the Research Institute, whose primary interest was in nutritional, metabolic and biochemical disorders, found themselves investigating more obscure forms of these diseases that could be seen to have a hereditary component. Sass-Kortsak's interest in liver disease led him to galactosemia (an inherited inability to digest the milk sugar galactose) and Wilson's disease (an inherited disorder of copper metabolism); Fraser's interest in calcium and phosphorus metabolism led him to rickets resistant to dietary intervention (some of which were inherited conditions). These conditions were amenable to classical genetic analysis, but in much of this work, the involvement of the human geneticists was minimal.

From the inception of the Research Institute, Donald Fraser was reported to be working on forms of rickets that were resistant to treatment with vitamins.[98] A particular interest of his was "hypophosphatasia," which had first been described, in 1948, by a worker from Sick Kids – it was a rare rickets-like disorder involving inadequate mineralization of the bone. The disease came to be understood as a genetic disorder over the course of the 1950s but Fraser pursued no specifically genetic research during this period, and did not rely on his Toronto human geneticist colleagues for initial genetical commentary.[99] Only when called upon to do a review of the disorder for a "Symposium

on Inborn Errors of Metabolism," in the latter-half of the 1950s, did Fraser turn to Ford Walker to conduct the review of the limited genetic information available from published studies.[100]

A sustained research interest of Sass-Kortsak's was Wilson's disease: an inherited metabolic error involving the inability to rid the body's tissues of copper, resulting in liver disease and sometimes neurological complications. By the time Sass-Kortsak began his work on this disease in 1957, it was already understood by him and others as one of the inborn errors of metabolism.[101] He took an interest in the genetics of the condition and by 1958 he was investigating family members "with the aim of finding a biochemical abnormality in the carrier state."[102] By 1959 Sass-Kortsak's "main line of investigation," was said to be, "directed to elucidate the nature of the basic genetic defect in Wilson's disease."[103] He noted that the likely genetic mechanism involved "an autosomal recessive gene," suggested the value for genetic counseling of detecting the abnormality in the heterozygote, and pointed to the need for more detailed family studies.[104] Yet, this work proceeded without apparent collaboration with Toronto geneticists.

Meanwhile the geneticists continued to do work in the vein of the indigenous tradition through much of the 1950s. In the 1954 Annual Report of the Research Institute, which noted Fraser's interest in vitamin D resistant rickets, for example, the study of the "genetic aspects of diseases of children" included everything but such biochemically-oriented work. Ford Walker, Uchida and the stable of graduate students were addressing such questions as twin and Mongol diagnosis, dermatoglyphics in erythroblastotic

children and children with cerebral palsy, pedigree analysis in a family affected by nephrogenic diabetes insipidus, co-operation with the cardiac service in assessing the role of genetic and environmental factors in the etiology of congenital heart disease, and co-operating with the surgeons in assessing genetic factors in Legg-Perthes disease.[105]

Still, by the latter-half of the 1950s, there was evidence of increasing administrative interest in the biochemical orientation. The Annual Report of the Research Institute in 1956 insisted that it was "In the field of biochemical genetics" that Ford Walker was giving assistance to Dr Fraser in his review of hypophosphatasia.[106] In 1957, Ford Walker "our geneticist" was reported to be studying the congenital anomalies, and in association with Dr Fraser was also examining "A most interesting field – the inheritance of congenital metabolic defects."[107] In 1958, "Dr Norma Ford Walker and her group," were said to be continuing "the study of inheritance of disease and abnormality, particularly in the field of inherited biochemical disturbances of childhood."[108]

The biochemists referred to the genetic-metabolic disease conditions as "inborn errors of metabolism," acknowledging the authorship of the field by Archibald Garrod and framing the area of inquiry as "biochemical genetics."[109] Victor McKusick, in his contribution to a "Symposium on Inborn Errors of Metabolism," noted that "Sir Archibald E. Garrod, [was] the acknowledged founder of biochemical genetics in man."[110] As enthusiasm grew, the Toronto geneticists supported the work of the biochemists through family studies and pedigree analysis.[111]

Collaboration between genetical and biochemical workers also went on outside the bounds of the Research Institute. Indeed, it is these collaborations that were especially memorable.[112] These collaborations did not involve conditions that went under the rubric of disease. Instead they were biochemical variations in blood and in the human response to drugs. The references to "inborn errors," and to Garrod are absent, but these collaborations also allow a closer look at the nature of the genetical knowledge being developed and exchanged.

In the first half of the 1950s, Oliver Smithies, while at the Connaught Medical Research Laboratories of the University of Toronto, developed a new method for detecting proteins: starch gel electrophoresis. In doing so, and in experimenting with human serum, he also revealed a new form of blood grouping: blood groups based on serum protein types, as distinct from the existing blood grouping technologies which were based on red blood cells. In 1955, in announcing this technical capacity, Smithies suggested that "Heredity factors may determine the serum groups of adults." But genetical questions were not of sole importance, as the possibility that serum groups changed with age could not be dismissed in this work.[113] At this early stage, Smithies expressed his thanks to Andrew Sass-Kortsak at the Hospital for Sick Children for aid in gaining blood samples, but Ford Walker was not an acknowledged contributor.[114]

Ford Walker's involvement became apparent, however, in two publications. Her role was to aid in the structuring and evaluation of family studies, and to provide the theoretical equipment to interpret the data in Mendelian terms and in accordance with conventional syntax. The first joint publication by Smithies and Ford Walker commented

on Smithies' earlier findings, noting that the ratio of the three serum protein groups in the over 40 persons studied was 1:2:1 – a Mendelian ratio.[115] This publication also presented the analysis of new data from 18 family groups in Mendelian terms and proposed the thesis "that the serum group of an individual is controlled by two autosomal genes with incomplete dominance."[116] In their second joint paper, Smithies and Ford Walker re-asserted this thesis, and suggested a syntax for the description of the "haptoglobin system" – a syntax that identified and posited clear relationships between the "phenotypes" and "genotypes" thus far observed.[117]

Where Ford Walker was an acknowledged co-author in the important work by Smithies, she had a lesser role in relation to the work of Werner Kalow. Kalow was one of the key architects of the field of "pharmacogenetics": a field which contemplated the genetic dimensions of patient responses to pharmaceutical interventions. Kalow's work in the latter half of the 1950s and into the 1960s was concerned with enzymes in the blood which were correlated with different physiological reactions to specific drugs. His research on this phenomenon was housed within the Department of Pharmacology at the University of Toronto. He gained access to serum from varied hospital and public sources, though not the Hospital for Sick Children. Yet Norma Ford Walker was a resource in the latter-half of the 1950s and though never a co-author, Kalow acknowledged her assistance. Before Ford Walker provided assistance to Kalow, he had already undertaken some family studies and become familiar with some genetic syntax.[118] But Ford Walker helped to confirm his genetic thesis.[119] She "guided the planning and

evaluation of the genetic studies"; provided "[I]nvaluable advice to the collection of data."[120] She also provided assistance in the diagnosis and use of twins.[121]

The work Ford Walker co-authored with Smithies lacked clarity about the "gene" as distinct from the "allele." Though defining the genetic mechanism as "two autosomal genes with incomplete dominance," alternate language was used which made apparent the fact that two distinct genes were not really envisioned (i.e. two distinct forms of one gene at the same location on the chromosome were contemplated rather that two genes with different locations on the chromosomes). In discussing the possibility that more variants might be discovered in future, Smithies and Ford Walker, in their 1956 paper, identified their genetic hypothesis with the phrase "either of the alleles."[122] This fuzziness in distinguishing gene and allele was also apparent in the work Kalow undertook with Ford Walker's assistance. Kalow and Staron, in their 1957 publication, used the language of allele and gene interchangeably: the evidence was explained by "two allelic autosomal genes," "two genes," or "two autosomal alleles."[123]

The terminological fuzziness in discussing the gene that Ford Walker allowed should not be seen as a failure, for this was a question of convention, not a reflection of known materiality. Yet the convention of distinguishing between gene and allele had a particular effect. To discuss alleles differently from genes is to insist on the issue of location; it is to insist on the materiality of the gene. To identify alleles is to point to the presence of a material gene at a particular locus, with variable manifestations. In later work, Oliver Smithies switched terminology. Citing his 1956 paper with Ford Walker in

1960, he and his co-authors referred to the thesis as one involving "two autosomal alleles."[124] Notably, in this work, the authors also used the concept of "locus."[125]

Ford Walker's collaborators had technical skills to detect enzymes. Ford Walker's contribution was to explain the enzymatic evidence in Mendelian terms. This work involved the tools of classical genetics: pedigrees, Mendelian ratios, and genetic syntax. These were tools that Ford Walker had demonstrated competence with from her earliest publications in the late 1930s, but which had not been much emphasized in her research school since.[126] If Smithies and Kalow held biochemical knowledge about a relationship between genetic control and protein structure, then this knowledge was not in evidence in these collaborations. There is no mention of the one-gene-one-enzyme hypothesis, no discussion even of gene action. Moreover, Ford Walker's use of terminology demonstrated a certain disinterest in the materiality of the gene – a materiality that the new era of biochemical genetics is imagined to have made relevant. As with the classical genetics' pioneers, the gene was, for Ford Walker and her collaborators, a primarily metaphorical phenomenon.

The classical genetic agenda encouraged in these collaborations had an effect on the work of the geneticists, not only in fostering new research, but in re-shaping older work. Ford Walker quickly added the analysis of serum proteins to her diagnostic protocol for twins, and such tests were apparent in the work of her students. But the transformation of the indigenous tradition into a classical genetics research school is most

evident in the work of Ford Walker's students. Two of her Doctoral students in the mid- to late-1950s, Hubert Soltan and Nancy Simpson, were quick to demonstrate their classical genetic capacities and their ability to use the new, powerful and attractive tools of biochemistry. They did not cease to use the tools of the indigenous tradition, but these were minimized in importance and dis-articulated from the older intellectual orientation.

Biochemistry in the Indigenous Tradition: Re-making Members of the Ford Walker School

Hubert Soltan and Nancy Simpson both began their Doctoral work in the mid-1950s under Ford Walker's supervision and with "Human Genetics" as their major subject. Both were formally associated as full time research fellows with the newly minted Research Institute, both completed and defended their dissertation in 1959, and both went on to serve as key members of the Canadian medical genetics community in southern Ontario: Soltan to London, by way of a brief sojourn in Halifax, and Simpson, after some years in Toronto devoted to biochemically-oriented research, to Kingston.

Hubert Soltan completed a dissertation on "Some Genetical Aspects of the Duchenne form of Muscular Dystrophy." Simpson's dissertation was entitled, "A Genetical Study of Juvenile Diabetes." Both studies were clearly a product of the institutional relationship between the Department of Zoology and the Hospital for Sick

Children and both demonstrated the broad contours of the transformation of the indigenous tradition, though rather differently.

Hubert Soltan began work on the genetics of "muscular or neuromuscular diseases."[127] His primary technique was the study of family pedigrees to assess the mode of inheritance. He collected pedigree data through the muscular dystrophy clinic at the Hospital for Sick Children, and then expanded his search for subjects with the aid of other sources.[128] Soltan was reliant on the collaboration of other workers at the HSC who were interested in the phenomenon of muscular dystrophy. These workers confirmed the clinical diagnosis, and performed other tests. But while Soltan complied with the interests of his clinical collaborators in investigating the field of muscular dystrophy generally – collecting data from almost 300 families – by 1958, his genetical study concentrated on a smaller group of subjects, those 121 families affected with Duchenne Muscular Dystrophy.[129]

This narrowing of intellectual focus allowed Soltan to comprehend relatively simple genetic phenomena – a single gene disorder. His dissertation drew on classical population genetics to estimate the mutation frequency of the gene involved in sex-linked DMD. He also analyzed issues of linkage, examining the evidence from his small sample of DMD families where there was also color-blindness to confirm the evidence in the literature that "the gene does in fact lie on the X chromosome."[130] Soltan used biochemical tests in the hopes of detecting female "carriers" of the disease: "It would be of great practical importance in genetic counseling to be able to detect women who are

heterozygous carriers of the sex-linked recessive gene of Duchenne muscular dystrophy before they produce a dystrophic child," he noted.[131]

Soltan's orientation to classical genetics did not divorce his work entirely from the indigenous tradition. He used both the Mongol and twin methods and assessed dermal patterns to detect evidence of prenatal disturbance. Such evidence, if found, would assign a prenatal age of onset to Duchenne Muscular Dystrophy. Yet this research formed a small part of the total project and the negative findings were seen to support existing clinical evidence: the disease being less severe and generalized than Mongolism at birth.[132] In short, the Mongol method constituted a less 'interesting' portion of the research project. Soltan used dermal patterns as part of his attempt to diagnose the zygosity in three sets of twins with the disease. Yet dermal patterns were only a secondary factor in the diagnosis, and were of lesser significance than the new blood protein data.[133] Soltan also examined some of the environmental factors in the disease, yet his contemplation of "environmental" factors was deliberately narrow. The Mongol method, were it to work, was invoked to provide evidence only of an earlier age of onset than generally believed – not to identify environmental impacts during development. Moreover, the actual efforts to test for environmental factors considered only birth rank and parental age, and the former was intended as a factor in inducing mutations. Finally, Soltan explicitly argued against the phenocopies hypothesis, which suggested the presence of environmentally-induced forms of the disease where family history was absent. Distancing himself from this school of thought, Soltan noted that "[t]he most satisfying theoretical explanation for the environmentalist would be that an induced

biochemical abnormality had occurred very early in life and that this abnormality was identical with the one caused by the defective gene in clearly inherited cases."[134] Soltan preferred the mutation hypothesis, and as noted above, provided calculations about the mutation rate of the DMD "gene."

The Research Institute facilitated extensive collaboration across disciplines and Soltan's research was no exception. He worked with a "muscular dystrophy research group at the Hospital for Sick Children."[135] Within this team, which included at least metabolic, neurological and orthopedic research, each group had independent goals. Neurologists used biochemical analyses in aid of differential diagnosis, for example.[136] The use of biochemical analysis for carrier detection was part of the genetic study. But only as a secondary goal, in the absence of positive findings, did Soltan note the potential for biochemical findings to serve as a diagnostic aid in early, and thus clinically non-evident, cases of the disease.

Genetics was not the lingua franca of the many participating researchers. It was one of a set of approaches – not the chief conceptual framework. Soltan did make reference to the one gene one enzyme hypothesis – "a specific enzyme whose production is controlled by a specific gene" as he put it – but this did not imply attention to a material gene in the tradition of 'basic' biochemical genetics.[137] Soltan did not credit the gene with ultimate cause. Though recognizing a clear genetic role in this disease, Soltan argued that "The primary cause of muscular dystrophy is unknown."[138]

Soltan's work on the genetics of DMD was an early foray into a research focus that would grow in intensity in Toronto – and would move decisively towards molecular genetics. Though Soltan's work was not directly continued, his collaboration with E.G. Murphy of the muscular dystrophy research group at the hospital was continued by Margaret Thompson when she returned to Toronto in 1963. Indeed, research on the genetics of DMD was by the mid-1980s to be one area in which Toronto workers excelled.

Meanwhile, Nancy Simpson, Soltan's student colleague, demonstrated a rather less radical shift away from the indigenous tradition in her dissertation research. Yet once this was finished, Simpson undertook a collaboration with Werner Kalow through the mid-1960s which moved her decisively into the realm of medical biochemical genetics.

Nancy Simpson's doctoral study concerned diabetes – a topic that she later termed the "geneticist's nightmare."[139] In attending to such a disease, Simpson conformed with the prevailing concern of the indigenous tradition with complex clinical phenomena – phenomena with significant environmental as well as genetical causes. Yet, this was the only aspect of Simpson's work that was indigenous in orientation: her chief method was pedigree analysis and her use of the Mongol and twin methods was supplementary.

Simpson's attention to such a complex phenomenon as diabetes crippled her efforts to obtain conclusive data on the mode of inheritance. Yet, Simpson's study drew on and expanded a brief but strong tradition of classical human genetic research in Canada that derived from the residence of the pacifist, Lionel Penrose, in London, Ontario during the war.[140] Ironically, Margaret Thompson had also been involved in the

Penrose connection. While in London, where she worked briefly in the late 1940s and early 1950s after leaving Toronto and before moving to Alberta, Margaret Thompson had collaborated with E.M. Watson, a professor of pathological chemistry, on the study of diabetes.[141] Together, they analyzed, and added to, data that Watson had previously worked on with Penrose.[142] Since Thompson's doctoral work on celiac disease had suggested a genetic connection to diabetes, this collaboration was a logical development. Yet, it had also been, for Thompson, an immersion in a more classical genetic orientation than her training within the Ford Walker school had emphasized – an orientation that Simpson then drew on.

Simpson built her study around patients who had been seen at the Hospital for Sick Children and diagnosed with juvenile diabetes, many of whom now had children. In addition to family studies, Simpson assessed the blood groups, and serum haptoglobins of the probands and their relatives, where possible, to see if any significant differences with controls could be found.[143] She conducted dermal analyses of some of the subjects and their families to consider the question of maternal environment. Twins were also a minor resource.

Simpson concluded that her evidence "adds strength to the controversial hypothesis that diabetes (whether onset is early or late) is controlled by the same recessive gene."[144] This conclusion was like that of Thompson and Watson before her. But by the time she had published an article on the genetics of this complex disease,[145] Simpson was involved with Werner Kalow in a research project that demonstrated the

sophistication of the new classical genetics trajectory: a focus on simple gene effects, using biochemistry as a central technology.[146]

Similar collaborations completed the transition from the indigenous tradition to the new medical biochemical genetics for other of Ford Walker's students. Diane Wilson Cox (née Diane Wilson) completed a Master's thesis under Ford Walker's supervision in 1960. Andrew Sass-Kortsak, who had noted the need for more genetic studies in the late 1950s, took a strong mentoring role towards her.[147] During 1961 and 1962 she updated her knowledge in biochemistry by taking course work, and she studied Wilson's disease in Sass-Kortsak's laboratory, "particularly the biochemical abnormality in the heterozygote."[148] She did her doctorate at McGill, gaining further expertise in biochemistry and when she returned to Sick Kids in 1967she returned to Sass-Kortsak's laboratory, working on "ceruloplasmin and the genetic control of its production," collaborating in an interdisciplinary project on Wilson's disease.[149] By the early 1970s she was publishing with Sass-Kortsak on Wilson's disease.[150]

Conclusion

Within human genetics, biochemistry did not represent a shift to molecular genetics. Rather, it gave new vigor to classical Mendelian explanations. Where Uchida, in her Ph.D. dissertation in the early 1950s, had suggested a trend of turning away from the

search for simple single gene effects, and where much of the indigenous tradition represented a quest for such complexity, the biochemists represented a return.

The indigenous tradition was altered under the influence, but this transformation was neither immediate nor total, and not all local distinctiveness was lost. The indigenous tradition continued to be vibrant until the end of the 1950s, as Irene Uchida's work makes especially evident. But the interest in complexity, in development, and in the place of environment which her work exemplified, subsided in favor of an invigorated classical genetics, concerned with Mendelian models and the material gene. Without abandoning dermatoglyphics and twins, the medical geneticists in Toronto increasingly adopted techniques better able to demonstrate these Mendelian and materialist presuppositions. Studies of pedigrees became of vital importance, and deciphering the mode of inheritance the primary goal of human genetic research. Biochemistry worked to support the metaphor (for it was still a metaphor) of the active single gene.

A distinct medical biochemical genetics supported the creation of a classical genetics orientation, but by the late 1960s, this distinct science was coming to be despised as a failure of comprehension and application, rather than a separate vision. In a 1968 report by the MRC on "Canadian Medical Research," the chapter on Medical Genetics noted that "the biochemical genetics of disease seems to be under-represented in this country." Murray Barr and F Clarke Fraser, who wrote this chapter, pointed out that the existing research in this field wasn't *really* "biochemical genetics": "If one excludes from the field those who are really doing medical biochemistry on a disease that happens to be

genetically determined, and considers only those who are also concerned with the underlying gene, there are very few problems under study."[151]

Endnotes: Chapter 2

[1] M. Susan Lindee, personal communication, May 8, 1998.
[2] Elof Axel Carlson, "Eugenics and Basic Genetics in H.J. Muller's Approach to Human Genetics," *History and Philosophy of the Life Sciences*, 9 (1987), 68.
[3] M. Susan Lindee, *Suffering Made Real: American Science and the Survivors at Hiroshima* (Chicago and London: University of Chicago Press, 1994), 105.
[4] John Beatty, "Genetics in the Atomic Age: The Atomic Bomb Casualty Commission, 1947-1956," in K Benson, J Maienschein and R Rainger, eds., *The Expansion of American Biology* (Rutgers University Press, 1991), 313.
[5] On the founding of the ASHG, see: HJ Muller, "Progress and Prospects in Human Genetics, A Preface to this Journal," *American Journal of Human Genetics*, 1:1 (September 1949), 1-18.
[6] TJ Arnason and LPV Johnson, "A Short History of the Genetics Society of Canada," *Proceedings of the Genetics Society of Canada*, 3:1 (August 1958), 4. (NA, MG 28 I45L vol. 1). Margaret Thompson was also a charter member of both Societies: *Proceedings of the Genetics Society of Canada*, Inaugural Meeting, 1956 (NA, MG 28 I 456, Acc. 1989/0186, Box 1). In her CV Thompson states that she was a Charter Member of both Societies, see: (UT, A79-0061/005 (44), File: 44. MRC, Thompson and Buchwald).
[7] These are among the subtitles in Muller's preface to the new journal: HJ Muller, "Progress and Prospects in Human Genetics," 2, 7.
[8] AB McKillop, *Matters of Mind: The University in Ontario, 1791-1951*, (Toronto: University of Toronto Press, 1994), 557, 548, 551.
[9] *Ibid.*, 548, 551.
[10] Claude Bissell, *Halfway up Parnassus: A Personal Account of the University of Toronto, 1932-1971* (Toronto: University of Toronto Press, 1974), 44, 45. Claude Bissell was president of the University of Toronto from 1958 through 1971. McKillop, *Matters of Mind*, 563.
[11] University of Toronto, President's Report, 1946-47, 95.
[12] Bissell, *Halfway up Parnassus*, 48.
[13] Doug Owram, *Born at the Right Time: A History of the Baby Boom Generation* (Toronto: University of Toronto Press, 1996), 179.
[14] Louis-Philippe Bonneau, JA Corry, *Quest for the Optimum: Research Policy in the Universities of Canada*, The Report of a Commission to Study the Rationalisation of University Research, Vol. 1, (Association of Universities and Colleges of Canada, 1972), 8.
[15] McKillop, *Matters of Mind*, 346.
[16] Bonneau and Corry, *Quest for the Optimum*, 8, 9.
[17] As the first Annual Report of the Research Institute at Sick Kids noted, "the research programme of the Hospital was expanded considerably, especially following the end of World War II, when increased contributions for research became available from various departments of the Government of Canada, as well as from private organizations." The Research Institute of the Hospital for Sick Children, *First Annual Report*, January 1 to December 31, 1954 (HSC), 3.
[18] It was believed that "the only truly efficient way to improve therapy is to increase the amount of fundamental medical knowledge." Ilana Löwy, *Between Bench and Bedside: Science, Healing, and Interleukin-2 in a Cancer Ward* (Cambridge Mass., London Eng.: Harvard University Press, 1996), 16
[19] Stanley Joel Reiser, "Human experimentation and the convergence of medical research and patient care," *Annals of the American Academy of Political and Social Science*, 437 (May 1978), 12.
[20] Reiser adds that "Research in medicine was supported at this time not only for its contributions to the accumulation of knowledge, but also for its value in the education of students and practitioners." Reiser. "Human Experimentation," 15.
[21] Alison Li, "J.B. Collip and the Making of Medical Research in Canada," University of Toronto, Ph.D. thesis, 1993.

[22] See the series of studies on the co-ordination of medical research through the NRC in *Scientia Canadiensis*, 15:2 (1991): Georgina Feldberg, "The Origins of Organized Canadian Medical Research: The National Research Council's Associate Committee on Tuberculosis Research, 1924-1938"; Terrie M Romano, "The Associate Committee on Medical Research of the National Research Council and the Second World War"; Alison Li, "Expansion and Consolidation: The Associate Committee and the Division of Medical Research of the NRC, 1938-1959".

[23] In a letter Barr discusses the financing of his research. He states that "although the MRC of Canada funded much of the work, there was substantial assistance from private sources. Studies related to cancer were funded by money collected by the Canadian Cancer Society - a voluntary organization - and disbursed by the NCI of Canada, Assistance from two local sources were especially valuable because these left me free to use the money where it was most needed at any given moment. One of these sources was the McDermid Research Fund, established from the estate of the late DH McDermid of London; the other was the AE Silverwood Foundation Research Fund." (NA, MG 30B111, File 3.2. Barr, ML. Personal Correspondence. 1975, letter to a Mr. SA Martin, School of Business Administration, August 29, 1975).

[24] Victoria Harden. *Inventing the NIH: Federal Biomedical Research Policy, 1887-1937*, (Baltimore and London: Johns Hopkins University Press, 1986), Epilogue.

[25] Certain associations were formed under the direct influence of American efforts – the Huntington's society, for example, was organized in Canada in association with a speaking tour by Marjorie Guthrie in 1973 – the wife of the singer Woody Guthrie who had died of the disease. Other societies took the American case as a clear precedent – such was the situation for the 'parents' rights' organization that coalesced around issues of childhood intellectual disability in the 1950s. Bonnie Cornell, "Folksinger's widow fights fatal disease," *Toronto Star*, Oct 28, 1973, (OA, MS 755, Reel 534)

[26] This was the sixth building in the hospital's seventy-five year history. RD Atkinson and RL Smith, "The Hospital for Sick Children," *University of Toronto Medical Journal*, 28:5 (February 1951), 173, 174.

[27] This was in compliance with "The duty of the hospital towards the Faculty of Medicine of the University of Toronto": TGH Drake, "The Hospital for Sick Children, Toronto: It's Medical future," *Ontario Medical Review* (October 1951), 30.

[28] Atkinson and Smith, "The Hospital for Sick Children," 174.

[29] JHW Bower, "Serving Sick Children," *Ontario Medical Review*, (October 1951), 26; Atkinson and Smith, "The Hospital for Sick Children," 180.

[30] Norma Ford Walker, "The Development of Human Genetics at the University of Toronto," *Proceedings of the Genetics Society of Canada*, Vol. 3 (1958), 65 (NA, MG 28 I456).

[31] Refusing Basil McLean's recommendation that the Research Institute be separately incorporated, the Medical Policy Committee established an administrative entity that centralized a previously more ad hoc set of activities under a Research Director and Research Committee. The Research Institute existed primarily through the creation and enforcement of a distinct research budget, set apart from teaching and from clinical practice with its complexities of private as distinct from public patients. See Minutes of the Medical Policy Committee, Jan 20, 1953, (HSC).

[32] This point was also made by advocates of such research centers at the time: "Such centers claimed to be removed from narrow specialty debates about diagnostic and therapeutic rules of conduct." Wailoo notes that, in fact, "New institutional arrangements placed researchers far from crowds of clinicians and competing specialists. The by-product was reordered thinking about such diseases as cancer and pernicious anemia." Wailoo, *Drawing Blood*, 110, 118..

[33] Wailoo adds that new findings "emerged from a new research context and depended heavily on their [the researchers'] ability to use technologies of diagnosis and therapy free from the bureaucracy and day-to-day moral economies of clinical work." *Ibid.*, 119.

[34] *Ibid.*, 120.

[35] The other main recommendations apparently involved the School of Nursing, and Thistletown, the HSC's rural facility. Unfortunately this report is not available in the HSC Archives. It is mentioned in various committee minutes and thus the general content is apparent. See: Medical Policy Committee, Minutes of Meeting, January 20, 1953, (HSC).

[36] "To the Medical Policy Committee," Report of Dr Andrew J Rhodes and Mr. CA Sage on Hospitals visited in connection with the proposed Research Institute of the HSC, July 13, 1953; appended to July 16, 1953 minutes of the Medical Policy Committee, (HSC).
[37] They were generally permitted to supplement their salaries by consulting work for private paying patients in the hospital. "To the Medical Policy Committee," Report of Dr Andrew J Rhodes and Mr. CA Sage on Hospitals visited in connection with the proposed Research Institute of the HSC, July 13, 1953; appended to July 16, 1953 minutes of the Medical Policy Committee, (HSC).
[38] Drake, "The Hospital for Sick Children," 30. See also: Atkinson and Smith, "The Hospital for Sick Children," 180.
[39] The Research Institute of the HSC, *First Annual Report*, Jan 1 to Dec 31, 1954 (HSC).
[40] Having heard much about the "hidden costs of research" from Basil McLean and from other research facilities they visited, members of the Medical Policy Committee advocated the standard they had been told was being promoted in the United States, where funders paid the cost of overhead. "It is important," the authors of the report on the 6 research facilities noted, "that a serious effort be made to impress upon governmental and other organisations the necessity for adding to any grant a reasonable sum for overheads. This might be one of the most important educational projects to undertake in Canada at the earliest possible date." "To the Medical Policy Committee," Report of Dr Andrew J Rhodes and Mr. CA Sage on Hospitals visited in connection with the proposed Research Institute of the HSC, July 13, 1953; appended to July 16, 1953 minutes of the Medical Policy Committee, (HSC). This was an issue that was quickly taken up by the research committee that was formed to oversee the Research Institute. See: Minutes, Committee on Research, Dec 1, 1953 (HSC). Indeed the advocacy role played by Sick Kids in this and other respects (such as the Gundy report) points to its central role in Canadian history in "educating" the public and their governments about medical research.
[41] University of Toronto, *President's Report*, 1946-47. Irene Uchida, "A Study of Environment and Heredity in the Etiology of Rheumatic Fever," University of Toronto, Ph.D. Thesis, 1951
[42] *Ibid.*,1.
[43] *Ibid.*, Acknowledgements
[44] *Ibid.*, 9, 14.
[45] *Ibid.*, 9, 10.
[46] *Ibid.*, 7.
[47] *Ibid.*, 32, 29.
[48] Irene Uchida, "Possible Genetic Factors in the Etiology of Rheumatic Fever," *American Journal of Human Genetics*, 5 (1953), 63.
[49] Uchida, "A Study of Environment and Heredity," 55
[50] *Ibid.*, 58.
[51] *Ibid.*, 12
[52] *Ibid.*, 80
[53] Uchida, "Possible Genetic Factors in the Etiology of Rheumatic Fever," 64.
[54] Uchida, "A Study of Environment and Heredity," 82
[55] *Ibid.*, 128.
[56] *Ibid.*, 92.
[57] *Ibid.*, 92.
[58] *Ibid.*, 94, 96.
[59] Irene Uchida, "Possible Genetic Factors in the Etiology of Rheumatic Fever," 64.
[60] Uchida, "A Study of Environment and Heredity," 128.
[61] *Ibid.*, 130.
[62] *Ibid.*, 131
[63] *Ibid.*, 135.
[64] *Ibid.*, 141, 135.
[65] Irene Uchida and Richard D Rowe, "Discordant Heart Anomalies in Twins," *American Journal of Human Genetics*, 9 (1957), 138. See also: Constance C Forsyth and Irene Uchida, "Auricular Septal Defect in one of Monozygotic Twins," *Archives of Disease in Childhood*, 26 (1951).

[66] This article provides minimal information about the location of these twins: whether they all attended the hospital between 1951 and 1957 or whether some were identified through a review of files. Uchida does note that one case did not attend the HSC for treatment but was a referral from interested practitioners; she also notes that the case published in 1951 was included in the review. Nonetheless, she notes that, from the years 1952 to 1954, "Cardiac Staff ... were aware of the twin study in progress," so we can assume something like sustained interest. Uchida and Rowe, "Discordant Heart Anomalies in Twins," 137.
[67] Uchida reported that, though family history was investigated in all cases, there were no instances of a positive family history. *Ibid.*, 138.
[68] Uchida continued to add to the collection in the late 1950s. "During the past year, Dr Irene Uchida has added 250 twin placentae to our collection," Ford Walker wrote in 1959. See: The Research Institute of the Hospital for Sick Children, *Fifth Annual Report*, January 1 to December 31, 1958, p. 52. (HSC)
[69] Uchida and Rowe, "Discordant Heart Anomalies in Twins," 137.
[70] Forsyth and Uchida, "Auricular Septal Defect," 586.
[71] *Ibid.*, 586.
[72] Ford Walker finally published this index in 1957 and 1958, but its use in Toronto long preceded its publication.
[73] Richard Rowe and Irene Uchida, "Cardiac Malformation in Mongolism: A Prospective Study of 184 Mongoloid Children," *American Journal of Medicine*, 31 (November 1961), 732. It's significance is attested to in the recollections of colleagues. Michael Partington wrote that, "To the paediatrician ... newly arrived in Toronto from England in 1959, this reliance on Dr Walker's dermatoglyphic diagnosis by clinicians was novel and unusual." Margaret Thompson, Nancy Simpson and Michael Partington, "Norma Ford Walker," in Hubert Soltan, ed., *Medical Genetics in Canada: Evolution of a Hybrid Discipline, Essays on the Early History*, (The University of Western Ontario, Regional Medical Genetics Centre, London, 1992), 30.
[74] Rowe and Uchida, "Cardiac Malformation in Mongolism," 732.
[75] Norma Ford Walker, "Application for a Grant from the Banting Research Foundation," May 11, 1955 (UT, B79 0061, Box 80, File 54-7)
[76] Rowe and Uchida, "Cardiac Malformation in Mongolism."
[77] Norma Ford Walker, "Application for a Grant from the Banting Research Foundation," May 11, 1955 (UT, B79 0061, Box 80, File 54-7). Ford Walker, who had submitted the applications to the Banting Research Foundation for the funds to conduct the study, identified her and by association this study's field of research as "Medical Genetics." Review comments by Dr Ferguson and Dr Dauphinee, Review of Application of Dr NF Walker, n.d. [c. May 1955]; Review comments by Dr JA Dauphinee, Review of Application of Dr NF Walker, n.d. [c. May 1956] (UT, B79 0061, Box 80, File 54-7).
[78] Review comments by Dr JA Dauphinee, Review of Application of Dr NF Walker, n.d. [c. May 1956] (UT, B79 0061, Box 80, File 54-7).
[79] Norma Ford Walker, letter to Dr WGB Casselman, The Banting Research Foundation, September 12, 1957; this letter conveyed a brief final report from Uchida and Rowe dated September 11, 1957 (UT, B79 0061, Box 80, 54-7).
[80] The final publication on this issue, and final report to funders stated that "The significance of these results is being tested by analysis of the dermal patterns of non-mongoloid subjects with heart malformations." But no publication exists on the subject and it is unlikely that Uchida, who left Toronto for greener pastures in Manitoba in 1959, pursued this work. Rowe and Uchida, "Cardiac Malformation in Mongolism," 734. This publication is a repeat of the Final Report submitted by Rowe and Uchida to the National Health Grants Program which funded the data analysis from 1960 through 1961, April 17, 1961 (OA, RG 10-22, Box 18, File RG 10-22-0-199).
[81] Norma Ford Walker, "Application for a Grant from the Banting Research Foundation," May 11, 1955 (UT, B79 0061, Box 80, File 54-7)
[82] Richard D. Rowe, "Progress Report – Study of the Cardiovascular System in Mongoloid Infants," n.d. [c. May 1, 1956] (UT, B79 0061, Box 80, File 54-7).
[83] Rowe and Uchida, "Cardiac Malformation in Mongolism," 726. In this paper, the following three publications are cited as derived, at least in part, from the Mongol cardiac data: JD Keith, RD Rowe, P

Vlad, *Heart disease in infancy and childhood*, (New York: Macmillan C., 1958); RD Rowe and LS James, "The normal pulmonary arterial pressure during the first year of life," *Journal of Pediatrics*, 51:1 (1957); LS James and RD Rowe, "The pattern of response of pulmonary and systemic arterial pressures in the newborn and older infants to short periods of hypoxia," *Journal of Pediatrics*, 51:5 (1957).

[84] Uchida and Rowe analyzed their data for evidence of familial patterns, but found none. Rowe and Uchida, "Cardiac Malformation in Mongolism," 727.

[85] WN Dale, "Medical Research at the University of Toronto (Part I)," *University of Toronto Medical Journal*, 37:2 (December 1959), 33; see also: G Chertkow, MLA Auerback, "Medical Research at the University of Toronto, Part I," *University of Toronto Medical Journal*, 27:5 (February 1950), 221-222.

[86] Atkinson and Smith, "The Hospital for Sick Children," 174.

[87] Bower, "Serving Sick Children," 25, 27

[88] The Research Institute built on and expanded existing capacity in the study of disorders of metabolism and nutrition. Such work had been ongoing in the biochemical research labs for many years prior to the development of the Institute, and constituted a major plank in the expanding capacity of the Research Institute. Minutes of the Committee on Research, December 29, 1953 (HSC, CRM, Vol., 1953-1959)

[89] First Annual Report of the Research Institute, Jan 1 to Dec 3, 1954, 6-7. A top priority was the organization of a clinical investigation group to consider "nutritional and metabolic disorders of childhood.": Hospital for Sick Children, 78th *Annual Report*, 1953 (reprinted from Feb 1954 issue of *Modern Medicine*), (HSC).

[90] See: Horace Freeland Judson, *The Eighth Day of Creation: Makers of the Revolution in Biology* (NY: Simon and Schuster, 1979).

[91] Jan Sapp, *Where the Truth Lies: Franz Moewus and the Origins of Molecular Biology*, (Cambridge University Press, 1990), See especially Chapter 2, "Founding-father Fables."

[92] Victor McKusick did actually use this term, see: Victor McKusick, "Introduction," in Victor McKusick and Robert Clairborne, eds. *Medical Genetics*, (New York: HP Publishing Co., Inc., 1973,1974, 1976), xv.

[93] Sapp, *Where the Truth Lies*, 39

[94] *Ibid.*, 43.

[95] *First Annual Report of the Research Institute*, Jan 1 to Dec 3, 1954, 5, (HSC).

[96] *Ibid.*, 4.

[97] *Ibid.*, 7.

[98] "Dr Donald Fraser," it was reported, "is continuing an investigation of calcium and phosphorus metabolism in cases of resistant rickets and other interesting conditions." Therapeutic efforts are reported in the annual report and in publications: *Fifth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1958, 23 (HSC); D Fraser and RB Salter, "Diagnosis and Management of Various Types of Rickets," *Pediatric Clinics of North America*, (May 1958), 417-441.

[99] In his presentation before the combined meeting of the American Pediatric Society, British Pediatric Society, Society for Pediatric Research and Canadian Pediatric Society in 1955, Fraser relied upon a member of the audience to comment on the genetics of the condition. Dr Edna Sobel from Boston noted that "Dr Fraser asked me to comment on genetics. I am still not sure that we can call this a genetically determined disorder, since the possibility of a toxic factor has not been eliminated entirely.": D Fraser and ER Yendt, Metabolic Abnormalities in Hypophosphatasia, Society Transactions, *American Journal of Diseases of Children*, 90 (1955), 553.

[100] "The genetic data have been interpreted by Professor N Ford Walker," Fraser noted: Donald Fraser, "Hypophosphatasia," *American Journal of Medicine*, 22 (May 1957), 740.

[101] *Fourth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1957, 20 (HSC).

[102] *Fifth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1958, 17 (HSC).

[103] He noted that this was "a condition which we here recognized as an important cause of juvenile cirrhosis." *First Annual Report of the Research Institute*, Jan 1 to Dec 31, 1954, 8 (HSC).

[104] A Sass-Kortsak et al, "Observations on Ceruloplasmin in Wilson's Disease," *Journal of Clinical Investigation*, 38 (1959), 1672; A Sass-Kortsak et al, "A Study of Heterozygosity in Wilson's Disease," Society Transactions, *American Journal of Diseases of Children*, 98 (1959), 631.

[105] *First Annual Report of the Research Institute*, Jan 1 to Dec 31, 1954, 10-11, 14, (HSC). Meanwhile other "genetic" work was going in the RI. Researchers in the field of "psychological medicine and neurology" were said to be examining childhood schizophrenia and to have made many "interesting observations" particularly "in regard to the possible role of genetic factors in the etiology of this condition." *First Annual Report*, 13.
[106] *Third Annual Report of the Research Institute*, Jan 1 to Dec 31, 1956, 13 (HSC).
[107] *Fourth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1957, 6 (HSC).
[108] *Fifth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1958, 10 (HSC).
[109] See, in particular: Donald Fraser, "Hypophosphatasia," *American Journal of Medicine*, 22 (May 1957), 730; A Sass-Kortsak et al, "Observations on Ceruloplasmin in Wilson's Disease," *Journal of Clinical Investigation*, 38 (1959), 1672.
[110] Victor McKusick, "Mechanisms in Genetic Diseases of Man," *American Journal of Medicine*, 22 (May 1957), 677.
[111] By 1957 Sass-Kortsak was also involved with Harry Bain and Irene Uchida in a "family study of essential hypercholesterolemia." *Fourth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1957, 10 (HSC). Uchida published a genetic study of this: Irene Uchida, "The genetics of hypercholesterolemia," *Proceedings of the Tenth International Congress of Genetics*, 2 (1958), 298. Dr A Hunter an emeritus professor in pathological chemistry had a longstanding interest in the determination of histidine. By 1956 he had devised a procedure for determining the presence of histidine in urine and was set to employ this in the study of "various abnormal condition." *Third Annual Report of the Research Institute*, Jan 1 to Dec 31, 1956, 9 (HSC). By 1961 two unusual cases had been found, and with Michael Partington and another colleague from the hospital, Hunter published a report on a heretofore un-identified "familial disturbance of histidine metabolism." H Ghadimi, MW Partington and A Hunter, "A Familial Disturbance of Histidine Metabolism," *New England Journal of Medicine*, 265:5 (August 3, 1961), 221.
[112] MW Thompson, N Simpson and M Partington, "Early Pioneers – Norma Ford Walker," in Hubert Soltan, ed., *Medical Genetics in Canada*, 32-3.
[113] O Smithies, "Zone electrophoresis in starch gels: group variations in the serum proteins of normal human adults," *Biochemical Journal*, 61 (1955), 639. See also: O Smithies, Grouped Variations in the Occurrence of New Protein Component in Normal Human Serum," *Nature*, 175 (Feb 12, 1955), 307-8.
[114] O Smithies, "Zone electrophoresis in starch gels," 639.
[115] This ratio was simply presented as, I would suggest, self-evident proof of Mendelian processes; the conclusion was not drawn out.
[116] O Smithies and N Ford Walker, "Genetic control of some serum proteins in normal humans," *Nature*, 178:4496 (Dec 31, 1955), 1266.
[117] O Smithies and N Ford Walker, "Notation for serum-protein groups and the genes controlling their inheritance," *Nature*, 178:4535 (September 29, 1956), 695.
[118] See: W Kalow, "Familial Incidence of Low Pseudocholinesterase level," *The Lancet*, 2 (September 15, 1956), 576-7.
[119] In later publications, he cited the publication by himself and Staron which acknowledged Ford Walker's assistance, as establishing the genetics of the condition; see: W Kalow and RO Davies, "The Activity of Various Esterase Inhibitors Towards Atypical Human Serum Cholinesterase," *Biochemical Pharmacology*, 1 (1958), 183.
[120] W Kalow and N Staron, "On the Distribution and Inheritance of Atypical forms of human serum cholinesterase, as indicated by Dibucaine numbers," *Canadian Journal of Biochemistry and Physiology*, 35 (1957),1317; W Kalow, "Progress Report on Project 605-5-220," p 4, received Dec 6, 1955, (OA, NHGP, RG10-22, Box 16, File177). Kalow and Gunn wrote that "Dr Norma Ford Walker, Department of Human Genetics, University of Toronto, encouraged this work with interest and stimulating criticism.": W Kalow and DR Gunn, "Some statistical data on atypical cholinesterase of human serum," *Annals of Human Genetics*, 23, (1958-59), 247.
[121] "Identical twins, as established in the Hospital for Sick Children, Toronto, by Dr Norma Ford Walker." Kalow and N, "On the Distribution and Inheritance of Atypical forms of human serum cholinesterase,"1311.

[122] It should also be noted that Smithies and Ford Walker expressly acknowledged the assistance of key figures in the field of blood group genetics, like Bruce Chown and Ruth Sanger, "for their helpful comments on the notation here proposed." O Smithies and N Ford Walker, "Notation for serum-protein groups and the genes controlling their inheritance," *Nature*, 178:4535 (September 29, 1956), 695.
[123] Kalow and Staron, "On the Distribution and Inheritance of Atypical forms of human serum cholinesterase," 1314, 1315. This is also true for a later publication: W Kalow and DR Gunn, "Some statistical data on atypical cholinesterase of human serum," *Annals of Human Genetics*, 23 (1958-59), 239, 243, 247.
[124] H Harris, SD Lawler, EB Robson and O Smithies, "The occurrence of two unusual serum protein phenotypes in a single pedigree," *Annals of Human Genetics*, 24 (1960), 64.
[125] *Ibid.*, 66. O Smithies, "Third allele at the serum β-globulin locus in humans," *Nature*, 181 (1958), 1204. This was not always the case. In still later work, Smithies alternated between the terms gene and allele: Oliver Smithies et al, "Inheritance of Haptoglobin Subtypes," *American Journal of Human Genetics*, 14 (1962), 14.
[126] Some indigenous capacities, such as the diagnosis and evaluation of inheritance through twins, was of aid in these collaborations.
[127] *Third Annual Report of the Research Institute*, Jan 1 to Dec 31, 1956, 14 (HSC).
[128] Hubert Soltan, "Some Genetical Aspects of the Duchenne Form of Muscular Dystrophy," University of Toronto, Ph.D. thesis, 1959, p. 45.
[129] *Fourth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1957, 29 (HSC).
[130] Soltan, "Some Genetical Aspects," 138.
[131] He also noted that the average family size in such families, "must lead to the conclusion that eugenic considerations have not entered into the planning of these families – families which are acutely aware of the nature and prognosis of Duchenne muscular dystrophy." Soltan, "Some Genetical Aspects," 125, 145.
[132] *Ibid.*,144.
[133] *Ibid.*, 145. Hubert Soltan, "Muscular Dystrophy in three pairs of twins," *Acta Geneticae Medicae et Gemellologiae*, 8 (1959), 434-442. Ironically, Soltan's difficulty in diagnosing the zygosity of one set of twins demonstrated the continuing value of dermal analysis: blood group analysis in this case suggested monozygosity, it was the dermal differences that argued against it.
[134] Soltan, "Some Genetical Aspects," 35.
[135] *Ibid.*, acknowledgements.
[136] *Fourth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1957, 27-28 (HSC).
[137] Soltan, "Some Genetical Aspects," 13.
[138] He hypothesized that the "primary cause" of muscular dystrophy was the presence of a defect in the metabolism of vitamin E: *Ibid.*, 12, 13.
[139] Margaret Thompson, Nancy Simpson and Michael Partington, "Early Pioneers – Norma Ford Walker," in Soltan, ed., *Medical Genetics in Canada*, 32.
[140] Hubert Soltan, "Early Pioneers – Lionel Penrose," in Soltan, ed., *Medical Genetics in Canada*, 36-9.
[141] MW Watson, LE Laakso and EM Watson, "Studies of the Inheritance of Diabetes Mellitus," *Canadian Medical Association Journal*, 63 (December 1950), 556-8; EM Watson and MW Thompson, "Heredity and Diabetes," *American Journal of Digestive Diseases*, 18 (1951), 326-330; MW Thompson and EM Watson, "The Inheritance of Diabetes Mellitus," *Diabetes*, 1:4 (July-August 1952), 268-75.
[142] LS Penrose and EM Watson, "A sex-linked tendency in familial diabetes," *Proceedings of the American Diabetes Association*, 4 (1945), 165-79.
[143] Nancy Simpson, "A Genetical Study of Juvenile Diabetes," University of Toronto, Ph.D. Thesis, 1959, 34.
[144] *Ibid.*, 119.
[145] She disagreed with her dissertation's main findings – suggesting that different genes were involved in the juvenile and adult forms of the disease. Nancy Simpson, "The genetics of diabetes: a study of 233 families of juvenile diabetics," *Annals of Human Genetics*, 26 (1962), 1-21.
[146] She was an Assistant Professor in Pharmacology: W Kalow, "Hereditary variants of hydrolitic enzymes in man and their metabolism of centrally acting drugs," application for a research grant, October 15, 1962

(OA, RG 67-2, Box 6, File Dr Kalow). Nancy Simpson and Werner Kalow, "Serum Cholinesterase Levels in Families and Twins," *American Journal of Human Genetics*, 15 (1963), 280-7; Nancy Simpson and Werner Kalow, "The "Silent" Gene for Serum Cholinesterase," *American Journal of Human Genetics*, 16 (June 1964), 180-8; Nancy Simpson and Werner Kalow, "Comparison of Two Methods for Typing of Serum Cholinesterase and Prevalence of its Variants in a Brazilian Population," *American Journal of Human Genetics*, 17 (March 1965), 156-62.

[147] Sass-Kortsak sought to have Wilson Cox' status within the Research Institute raised from that of a junior to an intermediate fellow in 1962, he also sought financial support for her to travel to the annual meeting of the GSC to present a paper from her Master's thesis. Minutes of the Committee on Research, February 7, 1962 (HSC, CRM. Vol. 1960-1966).

[148] Curriculum Vitae of Diane Cox, December 1969, enclosed in Memorandum Re; New Appointments in Genetics, attached to the Minutes of the Committee on Research, May 27, 1970 (HSC, CRM, Vol. 1967-1973)

[149] Sass-Kortsak, Plans for Further Development and Expansion of Research Activities in the Department of Paediatrics, December 1967, attached to Minutes of the Committee on Research, December 13, 1967 (HSC, CRM, Vol. 1967-1973)

[150] DW Cox, "Genetic and environmental influences on the serum protein ceruloplasmin," McGill University, Ph.D. thesis, Montreal, 1968; Diane Wilson Cox, "A Screening Test for Wilson's Disease and its Application to Psychiatric Patients," *Canadian Medical Association Journal*, 96 (Jan 14, 1967); DW Cox, N Aspin and A Sass-Kortsak, "Identification of Wilson's disease heterozygotes using copper-64 or copper-67 (Abstract), *Proceedings 4th International Congress of Human Genetics*, Paris, September 1971, 190; Diane Wilson Cox, F Clarke Fraser and Andrew Sass-Kortsak, "A Genetic Study of Wilson's Disease: Evidence for Heterogeneity," *American Journal of Human Genetics*, 24 (1972).

[151] *Canadian Medical Research: Survey and Outlook*, MRC Report #2 (Ottawa, September 1968), 189.

Chapter 3

Making Medical Cytogenetics in the 1960s: Making the Autosome Anomalies

Introduction

In the first Presidential Address to the new American Society of Human Genetics, in 1949, Herman Muller strongly advocated a cytological-turn in human genetics. His charge was not fulfilled for a decade. Human chromosomes became an object of investigation in the mid-1950s and medical interest was piqued in the late 1950s with the discovery of anomalies in the human chromosome complex. Reflecting on these developments, the pioneering American medical geneticist, Victor McKusick, noted sardonically that he and his fellow workers had finally found "our organ."[1] Medical geneticists could now join the ranks of other medical scientists in the possession of a specific body part. They could claim tangible evidence of the workings of heredity.

The early years of medical cytogenetics were an age of discovery as new chromosome anomalies were mapped and made sense of. Lacking the technical capacity to individually identify each chromosome, as was the case for much of the 1960s, medical cytogenetics focused on numeric anomalies and gross chromosomal malformations and translocations. It was not until the 1970s, with more advanced

banding techniques, that each chromosome and its parts could be individually identified so that even minor structural anomalies could be detected through routine investigation.

For Toronto and London, Ontario workers, the attractions of medical cytogenetics seemed obvious, and they sought to develop or adopt the technical capacity that would allow them to participate in this new venture. In Toronto, the new bandwagon was hitched to the engine of a research school that had integrated genetics and biochemistry into a resolutely classical genetics enterprise – a research school that had largely divested itself of its indigenous tradition and was solidly integrated into a North American-wide medical genetics community. London, by contrast, was marginal to this community at the end of the 1950s, despite indigenous expertise with the sex chromatin, which was understood to be comprised of chromosomal material. For Murray Barr and his students and colleagues in London, Ontario, the emergence of medical cytogenetics provided a *new* opportunity for affiliation with medical genetics.

Through mutual aid, the Toronto and London workers built some of the pioneering capacity in medical cytogenetics in Canada. Indeed, so successful were the London, Ontario workers, that they took their place among the small fraternity of international pioneers in the early years of medical cytogenetics. The prestige of the Toronto school was established in other ways. In the 1960s, Toronto-trained workers fanned out across the country, often creating new institutional capacity in human genetics. Some of these individuals, notably Irene Uchida, would come to be dominant players in the new field.

Workers trained and based in Toronto and London adopted the basic tools of medical cytogenetics from the broader community of researchers. But they brought their own skills and concerns to bear in the process. Toronto-trained workers applied an interest in heredity and family to the world of cytogenetic anomalies. They made particular use of dermatoglyphic evidence, and built on indigenous expertise with the Mongol. In the process, they made sense of chromosome disease through a familiar language of reproductive risk, they helped to renew the meaning of the seemingly outdated technique of dermatoglyphics, and to transfer the symbolism of the Mongol onto a new syndrome category – that of the autosome anomalies.

By contrast, the London workers emerged into the new world of genes and chromosomes, at the end of the 1950s, from a world dominated by the discipline of endocrinology and the agency of hormones. Yet the skills and assumptions they brought to the new field seemed remarkably suitable. They utilized their skill with sex chromatin, and their gendered symbolism of sexual pathology, in the reading of chromosomes, and transferred their concern with intersexuals onto the bodies and lives of the freshly-minted category of the sex chromosome anomalies.

In this and the subsequent chapter I reproduce the bifurcation that these workers produced in the early years of medical cytogenetics: that between the so-called sex chromosome anomalies, and the so-called autosome (or non-sex chromosome) anomalies. This Chapter examines the re-tooling efforts in both communities and then focuses on the research on what came to be called the autosome anomalies. In the following Chapter, I discuss the research pertaining to the corollary disease category, produced at the same

time and through explicit and implicit comparison: the category of the sex chromosome anomalies.

Retooling in Medical Cytogenetics

London

Sociologist Augustine Brannigan argues that a theory of scientific discovery should not seek to explain how discoveries happen, but instead, how happenings become discoveries.[2] By this measure, Murray Barr's identification of the sex chromatin in 1948 became a discovery because of its relevance to socially and clinically compelling questions about sexual ambiguity. Bernice Hausman has argued in her important book, *Changing Sex: Transsexualism, Technology and the Idea of Gender*, that the 1950s were an important period in the interpretation of sex, gender and sexuality. In the face of new technical capacity, medical science became increasingly competent in the clinical management of patients with ambiguous sexual anatomy – hermaphrodites who, in the 1950s, were beginning to go by the name intersex. In this period medical science also lent itself to the treatment of those with ambiguous sexual identities – the new phenomenon of transsexualism.[3]

In the 1950s, the Barr body, as the sex chromatin has come to be called, was given meaning in the world of congenital errors of sex – the medical management, interpretation and production of human intersexuality. It stimulated research interest in

and was used to define types of intersexuality,[4] and Murray Barr, its discoverer, played a central role in these efforts.[5] When Barr and his students and colleagues retooled in cytogenetics on the eve of the 1960s, they drew on their cytological capacity developed through work with the sex chromatin and brought the gendered meanings that were invested in the Barr body with them into the new era. Indeed, these gendered metaphors of sexual pathology would lie at the heart of the reading of sex chromosome anomalies as an identifiable clinical category.

Reading the Barr Body

After the 1948 discovery of the sex chromatin, Murray Barr set out to assess what this deeply staining body was, and what it meant. He postulated that the sex chromatin represented the compacted and deeply staining portions of both X chromosomes. By this logic, the male's XY sex chromosomes might also be compacted and form a dense particle of chromatin in the cell's nucleus, but it would usually be too small to see. The association between the sex chromatin and the sex chromosomes was not demonstrated convincingly until the late 1950s when the sex chromatin was seen to represent a single X chromosome. The full articulation of its function, the "Lyon" hypothesis, which still governs its interpretation, was not fully articulated until 1961. But Barr's belief that the sex chromatin represented the female's two X chromosomes, though not an established fact,

was widely shared. The thesis was sufficient to place this marker at the apex of a model of sexual development, and make it a productive instrument for research and clinical medicine.

Sex differentiation, according to the evolving model used by Barr in the 1950s, came about under the direction of a series of actors. These actors were, first, the sex chromosomes (and sex related genes), second, the sex hormones, and third, the environment. Early in the 1950s, Barr referenced a two stage model. First were "certain chromosomes which bear genes with special significance in the primary determination of sex. These are called the sex chromosomes." It was "the particular combination of sex chromosomes and the genes which they bear [which] determine whether the initial indifferent gonad develops into an ovary or a testis." But while genes were seen to make a sexually-differentiated gonad, "Subsequent sex differentiation ... is largely under hormonal control."[6] By the mid-1950s, under the influence of the sexologists John Money and John and Joan Hampson from Johns Hopkins, Barr had confirmed the third stage of his model. "The third phase in sexual development," he wrote, "extends from infancy to maturity and is the period when all facets of psychosexual attitudes are gradually fitted into place. Environmental influences appear to be especially important here."[7]

During the 1950s, Barr and his colleagues focused on hormonal action (and the environment) and not the chromosomes as causal of the sexual pathologies. As one of Murray Barr's graduate students put it, "Broadly speaking, the sex hormones produce effects that override sex chromosome constitution."[8] This "transcendence of hormonal sexuality over genetic sexuality," was seen to be confirmed by the cases of congenital sex anomalies that came to Barr's attention.[9] They were taken to confirm a thesis that was

defined some decades later by John Money, as the "Adam principle": the thesis that "to differentiate a male something must be added."[10] Barr did not use this term, but it aptly names the particular cultural burden carried by this hypothesis. The stories about how sex is made were very much in line with what Emily Martin has termed, "scientific fairy tale[s]," in which female processes were slower, softer and ultimately, lesser.[11]

The chief clinical value of the Barr body in the 1950s was in providing evidence of a person's 'true sex,' even where bodily pathology meant that such truth could not be medically or socially realized. It was not until the end of the 1950s that the sex chromatin, as a technology of true sex, was re-invented as a technology with direct application to the discipline of medical genetics. Meanwhile, the London, Ontario workers had been intimately involved in the hormonal reinterpretation of two of the syndromes that would be discovered to be cytogenetic anomalies in 1959: Turner's and Klinefelter's syndrome. Using the sex chromatin as a technology of true sex, these two clinical conditions were brought into the family of intersexuals in the mid-1950s. In this period, they came to represent extreme examples of congenital sexual anomaly: radical sex reversal.

Making the Intersex: The Barr Body and Gonadal Dysgenesis

In 1955, a team from Johns Hopkins, with assistance from Murray Barr and his team in London, published a comprehensive review of a syndrome they called "gonadal

dysgenesis."[12] This syndrome involved patients with "normal but infantile female external genitalia," with "no evidence of female secondary sex characteristics." The condition was generally associated with "rudimentary ovaries" and "decreased stature" and the names of "ovarian agenesis," "Turner's syndrome," and "Bonnevie-Ulrich syndrome" had been applied to it.[13] The authors' purpose in publishing this article was to clarify the understanding of the syndrome, proposing a new name and a new theory of the disorder's etiology that made sense of all available evidence. A crucial piece of new evidence that this article considered was the fact that the majority of patients with this disorder had the male sex chromatin pattern.

"Individuals with this syndrome," the authors wrote, "had always been considered to be females." Yet there had long been experimental evidence which "emphasized the importance of the embryonic testes in counteracting the inherent tendency of the fetus to feminize," and had for some years suggested an alternate explanation – "that some patients with this disorder should be chromosomal males."[14] The authors confirmed in this important review article that the older hypothesis was, in fact, true. Henceforth, these previously female persons were to be understood as intersexuals.[15]

This 1955 article understood the evidence provided by the sex chromatin to be clear – these patients did not just have male chromatin patterns, they *were* chromosomal males. Understood this way, such evidence had manifold implications. It meant that "titles implying only an ovarian defect or deficiency should be abandoned." The authors proposed instead the sex-neutral title "gonadal dysgenesis," for these patients.[16] Moreover, since, as they wrote, "Normally, the development of all the sexual structures conforms to the

chromosomal sex established in the zygote at the time of fertilization," these patients provided decisive evidence for the Adam principle – "that female differentiation of the genital ducts and external genitalia always occurs in the absence of fetal testes." "These patients," they wrote, "exemplify the essential and primary role of the testis in human embryonic sex development."[17] They were the human analogue of the well-known experiments with fetal castration in rabbits from the 1940s, in which castrated male fetuses developed as females.[18] The authors went further still, and argued that in fact, these patients should be regarded "as the most severe and extreme form of male pseudohermaphroditism."[19]

Having so decisively re-interpreted the meaning of this syndrome in scientific terms, the authors closed with some cautionary comments about clinical matters. "The sexual orientation [of the patients]," they argued, "has been entirely feminine, irrespective of the chromosomal sex pattern." They added the caution that, "The authors consider it most important that the patients and their families should not be informed concerning their chromosomal sex when a male chromatin pattern is found, in view of present-day misconceptions of the importance of chromosomes in determining psychosexual outlook."[20] Indeed, Barr suggested a linguistic strategy to his clinician colleagues, arguing that instead of the terms "female nuclei or male nuclei" and "genetic female and genetic male" the "less committal expressions" "chromatin positive or chromatin negative" should be used, to avoid placing a "psychological burden" on patients of a truth about their sex that their physical condition might not approximate.[21]

Murray Barr, who had reviewed all the sex chromatin evidence for the article by Grumbach and his colleagues accepted and adopted their terminology and interpretation. Barr wrote that "About 80 per cent of patients with gonadal dysgenesis have male nuclei, which suggests that they developed in the female direction when deprived of the masculinizing hormone or inductor of embryonal testes."[22] These details made sense of all aspects of Barr's three stage model of sex development, with the sex chromatin indicating 'true' chromosomal sex, the Adam principle explaining the 'failure' to masculinize, and the detachment of sex from gender and sexuality (with the latter two internally and heterosexually consistent) explained by the environmental control of psychosexual identity.

The circle of sex researchers was a tight one. The same research which underpinned this study by the Johns Hopkins team of endocrinologists underpinned one of the ground-breaking 1950s articles by the pioneering sexologist team of Money and the Hampsons. All of the 11 patients studied by them who were "chromosomally male," "were found unequivocally to fulfill the cultural and psychological expectations of femininity. The salient finding to emerge from the study," they added, "was that a person's conviction of himself as a man or herself as a woman – the gender role and erotic orientation – is a variable quite independent of genes and chromosomes."[23]

Making the Intersex: The Barr Body and the Men with Small Testicles

The episode with Turner's syndrome women was not the only one which involved a rather radical reinterpretation of some extraordinary bodies. In fact, in 1955, Murray Barr was involved in the effort to redefine another syndrome. But this time the situation was the reverse of that apparent in "gonadal dysgenesis" patients. Instead of apparent females demonstrating a male sex chromatin pattern, apparent males were shown to have a *female* sex chromatin pattern. The conclusion was the same, however. These cases too were re-made as intersexuals. [24]

In 1956 Barr and colleagues began to describe apparently male patients who could be shown to have a *female* sex chromatin pattern. The patients described had a range of symptoms. The key defining element was significant atrophy of the testes and hence infertility. There might also be a "female" distribution of fat and hair, and sometimes obesity and gynecomastia (growth of breasts). Such patients had, since 1942, generally been grouped together under the name "Klinefelter's syndrome"."[25]

In first describing the new findings, Barr and his co-workers made clear their surprise at the phenomenon of chromosomal females having testicles: "Although some true hermaphrodites with both testicular and ovarian tissue have chromatin positive nuclei, until the inception of the present work, patients with chromatin positive nuclei and testicular tissue only had not been observed."[26] The first interpretative strategy adopted by Grumbach, Barr and others was to view these cases as "true hermaphrodites:" "The complex of a masculine phenotype usually with normal or fairly normal secondary sexual characteristics, malformed seminiferous tubules, and female-type nuclei may be considered a variant of true

hermaphrodism."[27] But Barr was later satisfied to simply define these cases as examples of "a congenital error of sex development."[28]

The interpretative difficulty experienced by Barr and his colleagues resulted from the fact that the available evidence did not integrate as readily with their three stage model of sex-making as had those patients with "gonadal dysgenesis." If these patients did have a female chromosome pattern – which Barr thought most likely – then how could the Adam principle make sense of a masculinized female?[29] It was true that female pseudohermaphrodites might have masculinized external genitalia, but their gonads helped their sex chromatin to speak the truth about their sex. Here were patients who had both masculinized secondary sex characteristics – a veneer past which research science could see – and masculine gonads. If, as the Adam principle suggested, females were those who *failed* to masculinize because of the absence, or the inadequacy, of testicles, how could there be testicles in a female? There was no ready experimental analogy – no castration experiment – that could make sense of this.

The lack of a hormonal explanation that was congruent with the Adam principle forced Barr back to the under-used chromosomal and genetic explanations in his model of sex development. While Barr's model theorized that the sex chromosomes made the gonads, and thus played a key role in making sex, most sexual pathologies were seen to arise through gonadal and hormonal problems, and not through chromosomal or genetic aberration. This case was an exception, however. In the absence of a credible hormonal explanation, the case of the chromatin positive Klinefelter's was interpreted as demonstrating pathology farther back in the sequence of sex making – in the genes. "It

seems more likely," Plunkett and Barr wrote, "that the abnormality is the result of a fault in the sex-determining genes in a zygote which bears two X chromosomes."[30]

The following year, Barr was more decisive. "It has recently been shown that a proportion of sterile males with hyalinisation and fibrosis of the seminiferous tubules have female nuclei," he wrote. "They appear, therefore, to represent an almost complete female → male sex reversal from an early stage in embryonal development." Barr added that "Since the condition appears to be a female → male sex reversal, Nelson (1956) is technically correct in suggesting that it be designated as "female pseudohermaphroditism with gonadal dysgenesis. But in the practical situation," Barr added, "the patients are clearly males, and a terminology that suggests otherwise is best avoided."[31]

Switching Decades: From Intersexuals to Sex Chromosome Anomalies

Murray Barr and his sometime student and then colleague, David Carr, had hoped to pursue cell culture work in the late 1950s, to examine directly the chromosomes that the sex chromatin signified indirectly. But they had been unable to solicit someone with what were then rare skills. Eventually, David Carr developed these technical skills and remade himself as a medical cytogeneticist. But outside London, Ontario, other researchers with an interest in the cytology of intersexuals were making more headway. Daniel Kevles describes the efforts of a number of different workers in England who were motivated both by sex chromatin findings in intersexes, and the clarification of the

normal human chromosomal complement in 1956, to investigate chromosomes in Klinefelter's and Turner's cases.[32]

Paul Polani, a physician at Guy's Hospital, was especially interested to investigate the cytogenetics of Turner's syndrome. He had been the first worker to report that these women were "chromatin negative" – having male sex chromosomes according to Barr's sex making scheme. But, Daniel Kevles suggests that Polani was not deceived: "There was," Kevles writes, "...scientific doubt that chromatin negativity could be taken as a definite sign of genetic maleness."[33] Polani thus investigated a sex-linked trait, color-blindness, in these women and then in Klinefelter's men, following up Barr's observation of the chromatin positive state of the latter individuals. And Polani solicited the aid of Charles Ford, a cytogeneticists in a radiobiological research unit of the British Medical Research Council, to pursue the direct examination of chromosomes in these individuals. In their first effort, Polani and Ford failed to discover the Y chromosome in a Klinefelter's male, counting only two XXs among the normal complement of 46. Preparing to try again, they were beaten to the discovery of the XXY chromosome complement in Klinefelter's by Patricia Jacobs, a young cytogeneticist from Edinburgh.

Kevles's narrative suggests that the sex chromatin diagnoses were never taken completely seriously. Polani was seeking a chromosomal aberration, Kevles implies, and was not satisfied with his first, retrospectively false, finding of chromosomal sex reversal in the Klinefelter's case. Moreover, Kevles does not acknowledge the enormity of the intersexual diagnosis in the Klinefelter's and Turner's cases, writing of intersexuality blandly as "people of one sex who displayed some characteristics of the other."[34] Since

some sort of chromosome anomaly was always, somehow, expected by these British workers, Kevles implies, the intersexual diagnoses had no enduring significance.

I take the opposite interpretation of this episode. While Barr did note the possibility of varied chromosome constitutions in these cases of sex reversal, he saw this as an improbable explanation. In the 1950s, an elaborate explanatory framework had been built around the interpretation of the role of sex chromosomes in the making of human sex, and the interpretation of sex chromatin data was congruent with this framework. The 1959 findings of anomalous sex chromosome constitutions in Turner's and Klinefelter's syndromes upset the scientific schema of sex. This reinterpretation was decidedly *not* anticipated, though it could be absorbed.

In 1959, Murray Barr published a review piece in the prestigious journal *Science*, on the "Sex Chromatin and Phenotype in Man." In this paper, Barr briefly summarized the knowledge about the "hermaphrodite group" and then turned his attention to "errors of sex development in which there is an extreme divergence between the phenotype and the nuclear chromatin pattern." These included two cases in which the "phenotype is predominantly female although the intermitotic nuclei have a male chromatin pattern and probably contain the XY sex chromosome complex": "gonadal dysgenesis" (Turner's syndrome) and "testicular feminization." Barr also highlighted the situation in which there was a "discrepancy between the phenotype and nuclear structure ...[in] the reverse [direction]": "seminiferous tubule dysgenesis" (Klinefelter's syndrome).[35] In the bulk of this paper, then, the sex chromatin was seen to signify a female or male sex chromosome

pattern unambiguously, and to provide definitive evidence of intersexuality in these clinical conditions.

But this 1959 article was on the cusp of the unexpected interpretative transition that was to be enabled by the discoveries of Patricia Jacobs and others. Barr's piece had been written for a January function, but by the time it was published in the fall it was necessary to add an addendum which pointed to new interpretative directions unleashed by the evidence that chromosomal anomalies could be associated with particular human syndromes – notably Down's, Turner's and Klinefelter's. Attention to these chromosomal anomalies motivated a reinterpretation of the significance of the sex chromatin. The sex chromatin could no longer signify simply the 'normal' XX sex chromosome complement, it also referenced the aberrant sex chromosome constitutions of XXX, XXY, XXXY, and so on. With this, the sex chromatin added a new capacity to that of diagnosing 'true sex' – diagnosing defect – and the sex chromosomes were re-read as causal of pathology.

These new developments also inspired a rethinking of theories about the genetic making of sex. "These observations," Barr wrote, "necessitate a revision of the currently accepted hypothesis of genetic sex-determining mechanisms in man.... It now appears that the Y chromosome, far from having a passive role in sex determination, contains potent male-determining genes."[36]

In the 1960s, the London researchers, Murray Barr chief among them, came to present a taxonomy of sex errors that placed the sex chromosomes at the causal apex. All forms of sex anomaly, whether due to chromosomal error, genetic error or hormonal

error, were included as subsets of particular chromosomal constitutions. In the 1950s, Barr had not talked about the varied intersex conditions as chromosomal anomalies. At that time, the sex chromatin, which signified the female sex chromosome constitution unambiguously, could only identify that an error of sex had occurred, not explain why it had occurred. After 1959, however, when the sex chromatin could provide explanations for errors – by indicating deviations from the usual sex chromosome complement – Barr re-wrote his interpretation of the errors of sex, seeing them now as types of sex chromosome anomaly – as *caused* by sex chromosome anomalies. Carr, Barr and Plunkett made the case in 1961; arguing that "[sex] chromosomal anomalies fall into two categories, the first being abnormal only in the sense that the sex chromosome complex is contrary to the predominating features of the phenotype." This first category then, encompassed all of the older "errors of sex development" such as testicular feminization, or the adrenogenital syndrome. The second category of sex chromosome anomaly involved aberrations in the number or structure of the sex chromosomes themselves; these were the new-era sex anomalies, involving the re-interpreted Klinefelter's and Turner's syndromes.[37] Medical genetics textbooks, such as that by James and Margaret Thompson adopted this taxonomy – classifying intersexes into two groups "intersexual conditions with normal chromosome complement" and "intersexual conditions with abnormal chromosome complement."[38]

In presenting the sex chromosome anomalies as one aspect of a total picture of sex errors, researchers like Murray Barr and David Carr were engaged in the co-production of themselves as human geneticists, and of the sex errors as lying within the

province of medical genetics. This approach suggested the continued value in the new era of cytogenetics of expertise with sex chromatin and intersexuals, and the continued relevance of an epistemological framework which emphasized gendered metaphors of sexual pathology, even as some older interpretations were deemed false. Writing in the *Canadian Medical Association Journal* in 1960, Barr and Carr asserted their continuing expertise in the proper management of sex anomalies, instructing clinicians about the "etiology and pathogenesis of sex anomalies," with particular attention to "those anomalies having as their basis an abnormal sex chromosome complex." These "genital anomalies," the authors noted, though rare, are "a source of particular concern to the parents of an affected child, and the patient may bear a heavy burden on reaching maturity because the defect usually interferes with satisfaction of the basic instinct of reproducing one's kind."[39]

The integration of older skills and frameworks into sex chromosome analysis was not restricted to London. "Chromosome analysis of intersex problems," Pat Conen of Toronto's Hospital for Sick Children wrote in a *Canadian Medical Association Journal* editorial, "can be considered an extension of the sex chromatin test."[40] The establishment of cytogenetics facilities at Sick Kids in light of the 1959 developments was intended for chromosome studies of two kinds – the study of "cases of multiple congenital anomalies" and the study of "intersex conditions."[41] In Toronto, London and elsewhere, the technical value of the sex chromatin helped to justify the linkage. Expertise with the sex chromatin

was a vital adjunct to chromosome analysis throughout most of the 1960s –helping to identify the hard to distinguish X chromosome.[42]

The cytogenetics era involved new technical capacities, new interpretations of pathological causation, and resilient sexual symbolism. Having been converted into representatives of extreme sexual pathology, Klinefelter's and Turner's syndromes carried those metaphors with them into the new context of medical cytogenetics, helping to confirm the distinctiveness of sex chromosome anomalies as a coherent meta-category of disease. I examine this process in greater detail in the subsequent chapter.

Retooling in Medical Cytogenetics

Toronto

While Murray Barr and his team were embroiled in the shifting cytological interpretation of the intersex, some human cytogenetic study was taking place at the University of Toronto.[43] But it was not until 1959 and the explosion of *medical* cytogenetics that the human geneticists in Toronto took much note. From the first, these workers hoped primarily to catch up in a new and exciting field of study. In seeking funds from the National Health Grants Program, Sick Kid's classical genetics team – Ford Walker, Donald Fraser and Donald McLean – stated their desire to take advantage of "the development of new techniques for examination of human chromosomes reported in the period 1956-1959 [which], immediately opened important new avenues of study in

the field of human genetics." The award, they argued in their final report, had "made possible the establishment and operation of facilities for culturing and examining human chromosomes," and supported several studies.[44]

The bulk of this work was taken on by Patrick Conen, a pathologist in the Research Institute. He "undertook certain clinical studies of patients with multiple congenital anomalies, and did much to direct the service and diagnostic aspects for the patients attending this Hospital."[45] Alex Bell, an MD, research fellow in Genetics, and Master's student whom Ford Walker was helping to supervise, was an auxiliary worker. He was said to be pursuing investigations that were "fundamental in nature." He undertook an "investigation of the effects of X-irradiation on [the chromosomes in] normal human leucocytes in culture."[46] Tied to both genetics and pathology, Bell manifested the links between these two Departments, and supported the joint enterprise of developing medical cytogenetic capacity as a genetical discipline at Sick Kids.

Pat Conen had been hired to the hospital in the late 1950s to pursue studies in Electron Microscopy, but took up cytogenetics with a flourish. At a time when appropriate technical skills were rare and in great demand, Conen's interest and capacity were fortuitous. He was one of the self-taught amateurs in cytogenetics which the sudden attention to medical cytogenetics in 1959 made possible. In the late 1950s and early 1960s, during what I call the discovery phase, the opportunity for identification of extraordinary human chromosome constitutions was available to any who could master the technical skills and gain access to the clinical material.

Conen drew on and supported the complementary skills developing in London, Ontario. Under the auspices of the head of Pathology, William Donohue, a long-time colleague and friend of Murray Barr, Conen met and exchanged technical notes with Barr and David Carr who were busily trying to establish their cell culture techniques in 1959.[47] The links between these two communities were manifested in the development, beginning in 1961, of the Great Lakes Chromosome Conference – annual meetings for the exchange of knowledge which initially involved only the Toronto and London workers, but have grown to include a greater range of Canadian and American Workers.[48] The links between Toronto and London were also strengthened when Hubert Soltan, Ford Walker's ex-student, was hired on at Western as their first 'real' geneticist in 1962.

In both communities, the pioneering development of cytogenetic capacity encouraged a proselytizing spirit. Conen and Barr independently published editorials in the *Canadian Medical Association Journal* which instructed medical scientists on the basic techniques and interpretations in medical cytogenetics, and advocated the value of this new capacity for medicine and genetics.[49] Murray Barr wrote in 1959 that "The importance of these new developments can hardly be overestimated since they show that abnormal chromosome complements, in addition to mutant genes, are etiological factors in errors of human development that have a genetic basis."[50] Moreover, research from both centers contributed to technical developments in cytogenetics, and David Carr was of sufficient international status by 1963 to warrant participation in one of the series of international conferences held to produce standardized nomenclature for the "normal human karyotype."[51]

Though not the sole practitioner, Pat Conen was at the heart of human cytogenetics in Toronto in the 1960s. He established clinical capacity at Sick Kids, played his part in disseminating that capacity in Canada, and contributed reports to the research literature of the varied cytogenetically-correlated clinical anomalies and chromosomal phenomena discovered at the hospital. Conen collaborated with Toronto-based and Toronto-trained geneticists in this work, and through such collaborations, he was partially adopted into the medical genetics fold. Meanwhile, Toronto-trained geneticists, like Irene Uchida and Hubert Soltan, also re-tooled themselves in this period, adopting cytogenetic techniques. By the 1960s, Toronto capacity was no longer restricted to the Toronto locale.

In a 1950 newspaper article, Ford Walker's educational orientation had been highlighted. "My chief job is teaching," Ford Walker was reported as saying as she "picked up a set of files and notes and started off to a lecture." "But sometimes," she added, "I wish I could stop teaching and just do research. It's much more fun.""[52] While Ford Walker's teaching load may have constrained her research, it produced an intellectual legacy that bore fruit in the 1960s. In this decade, Ford Walker's students were particularly successful in finding and developing new homes for themselves in institutions throughout Canada.

Two of Ford Walker's doctoral students who had completed their work under the auspices of the indigenous tradition successfully remade themselves in the 1960s. Margaret Thompson, who received her Ph.D. in 1947, returned to Toronto from Alberta in 1963 and revitalized her research program. Irene Uchida, who completed her Doctorate

in 1951, had spent the remainder of that decade as Ford Walker's colleague at Sick Kids. In 1960 she, and Elizabeth Curtis, one of Ford Walker's Master's students, moved to the University of Manitoba to head the medical genetics work at the university and children's hospital. Before arriving in Manitoba, Uchida pursued re-training in cytogenetics at the University of Wisconsin and became an important researcher in that sub-field. Hubert Soltan and Nancy Simpson, both of whom received their Ph.D.'s in 1959 as students of the new classical genetics orientation in Toronto, moved to jobs in Ontario universities in the 1960s. In 1962, Hubert Soltan assumed his appointment in London, Ontario, in Murray Barr's department. There, he brought his genetics skills to bear in medical cytogenetics research. Nancy Simpson did not move from Toronto to Queen's University in Kingston until the mid-1960s, when she left to head a new department in medical genetics.[53]

Of all of Ford Walker's intellectual heirs, Irene Uchida and Hubert Soltan were most involved in cytogenetic studies, and their cytogenetic work clearly reflected their human genetics education and specifically Toronto training. They asked classical genetics questions, bringing pedigree studies and gene locus and linkage analysis to cytogenetic work. But they also preserved older techniques, such as dermatoglyphic analysis. Indeed, the Toronto-trained workers were particularly prominent promoters of this resilient technique. Far from being displaced by cytogenetic studies, as a purely internalist and technical reading of the history of science would suggest, dermatoglyphics was preserved and even enjoyed something of a renaissance in the 1960s, though it lacked the interpretative framework invested in it by Toronto's indigenous tradition.[54]

Finally, Toronto-trained workers also brought institutional traditions and metaphors to their work in medical cytogenetics. The sex chromosome anomalies were produced as a category that was invested with gendered metaphors of sexual pathology developed through the interpretation of intersex patients within an endocrinological community. The corollary category 'autosome anomalies' relied on the association with errors of the autosomes (or non-sex chromosomes), and found its symbolic content in the condition of Mongolism and its institutional legacy in the management of these persons by human geneticists.

The Toronto research school had long had an interest in Mongolism. Within the indigenous tradition, the Mongol served as a method for making sense of complex genetic, environmental and developmental processes. By the 1950s, as the indigenous tradition began to fade, research on the Mongol still enhanced the capacity and reputation of genetics within the hospital community in Toronto, providing an important sphere of practical activity at Sick Kids and a resource for medical research. Notably, the Mongol held this privileged institutional and technical position long before it was a clearly 'genetic' condition. So in 1959, when the mechanism of the anomaly was exposed as Trisomy 21, the significance of the Mongol for genetics was further consolidated. In the new era of cytogenetics, the Mongol, and its diagnostic instrument, dermal patterns, came to stand as representative of the new genetics dispensation: emphasizing mechanistic processes, and genetic causation.

The Mongol served as an institutional and technical link for members of the Toronto school, across the divide of 1959. But the Mongol was also a metaphor, and the symbolic meaning with which it was invested was also durable. The term "Mongolism" was coined in the 1860s, in the context of debates about the polygenic or monogenic origins of humanity. The physician John Langdon Haydon Down described a syndrome that, as Daniel Kevles puts it, "along with severe retardation, included an enlarged head and a prolonged, or epicanthic, fold to the eyelid." Declaring the persons afflicted with this condition to be reversions to the Mongols of Asia, Down understood the capacity of Europeans to breed more 'primitive' types to be proof that the human species had a single origin.[55]

The racialized terminology for this poorly understood condition persevered even as researchers worked to dispute the association between Mongoloid 'imbeciles' and the racial group of Mongols.[56] And the discovery of a chromosomal mechanism underlying Mongolism encouraged a definitive effort by a coalition of workers to plead, in 1961, for an end to the use of this term.[57] It took more than a decade for the majority to follow suit, but in the 1970s 'Down's syndrome' or 'Trisomy 21' came to be more commonly used than the racially-inflected name.[58]

For Toronto workers, the racial metaphor was not just a superficial gloss. Indeed, beginning in the early 1950s, and into the mid-1960s, Ford Walker took a direct interest in the relations between Mongolism and race. Her work focused on the demonstration of "racial" distinctions in dermal patterns of Mongols, to support diagnosis of children with Mongolism from different racial backgrounds.[59] Ford Walker researched dermal patterns in

Asiatic and Negro mongoloids; supervised a Master's thesis, completed in 1960, on Dermal patterns in Negro Mongoloid imbeciles; and published papers on dermal patterns in Italian Canadian Mongols in the early 1960s.

At the inaugural meeting of the Genetics Society of Canada, in 1956, Ford Walker drew on some of this research to present a paper which suggested that the term "Mongoloid" might be more racially appropriate than was usually assumed. "Over the 10 years while studying mongoloid imbeciles," she argued, "we have given considerable thought to the term "mongoloid imbecility" and we have in the past taken the position that the name was an unfortunate one. The Asiatic people have resented it, and we had agreed with other workers that the name should be changed to one suggesting a retention of fetal characters." However, she argued that recent research contradicted this position. The "term, mongoloid imbecile is, from the European standpoint," Ford Walker pointed, "more appropriate than we had supposed." Indeed, she continued, "A comparison of Asiatic and European controls indicates that in the fetal growth of European mongoloid imbeciles there are some physical features of these retarded children which can be truly termed "mongoloid"."[60]

Ford Walker did not repeat this rather controversial claim. For the most part, she adopted the stance of a liberal on racial questions: defending inter-racial marriages, for example, as producing 'hybrid vigor.' But though not deliberately racist, Ford Walker took racialist meanings seriously. In the 1950s, for example, genes that were associated with the development of disease were described as "black genes."[61] Similarly, the discussion of the Mongolian features of the Mongol indicates that Ford Walker was engaged with the

racialist symbolism of 'the Mongol.' The significance of this racialism is hard to decipher, yet it would seem to have added to the burden of defect that was attached to this anomalous human condition – intensified the stigma. The Mongol stood literally, through the Mongol method, and figuratively, through the racialized metaphor, for defect.

As members of the Ford Walker school entered the new era of cytogenetics, they carried this symbolic meaning with them – a symbolic meaning that they likely shared with other Euro-American workers. But the Toronto workers also carried with them the Mongol method. Just as the London, Ontario workers continued to assert the value of sex chromatin analysis in the study of sex chromosomes, the Toronto workers emphasized the value of dermatoglyphic analysis in the study of autosomes. Together with the logic of the terminology of sex chromosomes and autosomes, dermatoglyphic analysis helped these workers to make sense of coherent categories of 'autosome anomalies.'

The 'autosome anomalies' were united technically through dermatoglyphic analysis. But they were also united through their association with Mongolism as a condition of unalloyed severity. This severity was, on the one hand, a function of mental retardation which, without reference to degree, seemed to be understood as inherently severe.[62] On the other hand, this severity was a function of what appeared to be a naturally high lethality.[63] Citing mortality rates of 50% in the first year of life, David Carr wrote in 1965 that, "It is obvious that there is a high mortality among liveborn individuals with Down's syndrome."[64] The 'severity' of defect in the Mongol was premised on and worked to disallow, or simply make irrelevant, analysis of the condition in a way that would support its internal heterogeneity, and render the term 'severe' insufficient as a clinical description. On the

contrary, the 'severity' of defect in the Mongol was paralleled with the 'severity' of defect in other 'autosome anomalies,' confirming the association between these distinct phenomena as members of a larger category of disease.

Toronto and London, Ontario workers shared the faith in the categorization of chromosome anomalies into the 'sex chromosome anomalies,' on one hand and the 'autosome anomalies' on the other. This categorization enforced homogeneity within each category and established a hierarchy of severity: "The current literature," Barr argued in 1960, "suggests that abnormalities of the sex chromosome complex cause mental deficiency less consistently than do autosome anomalies."[65] Pat Conen added in 1961. "To date it has been shown that abnormalities of the autosomes may produce marked congenital malformations, while in contrast, sex chromosome abnormalities may be associated with only minimal physical changes."[66]

Producing Anomalies: "Autosome anomalies" and Syndrome Making

Much of the work of medical cytogenetics after 1959 was devoted to the discovery of new anomalies and the production of syndromes and their variants. But cytogenetic research involving Mongols was obliged to do more than report the association between clinical and chromosomal evidence. This association had been demonstrated, quickly confirmed and readily accepted.

Toronto and London workers nonetheless embarked on research involving the Mongol. The cases they found interesting, and the questions they sought to answer, provide insight into the narratives of 'the Mongol' then prevalent, and the particular inflexion imposed on these narratives by genetical workers. The consolidation of the narratives of the Mongol were then instrumental in managing the meaning of the new disease phenomena that became available through the work of cytogenetic discovery.

As a pathologist at a major children's hospital, Pat Conen had access to congenital anomalies and disease, and responded to institutional priorities in relation to conditions like childhood cancer and cleft lip and palate.[67] Human cytogenetics, Conen argued, would provide information of various sorts. It would elucidate the cause of congenital and other defects, including malignant disease. It would provide information on the parameters of the 'normal' human chromosome complement. And, through the careful correlation of chromosome anomalies with physical and functional anomalies, it could aid in mapping the human chromosomes.[68]

Pat Conen came in contact with the Mongol through those extraordinary cases brought to his attention in the hospital.[69] He published two reports on individual cases which posed diagnostic difficulty. One was a Chinese infant, and one an old woman.[70] Though the cytogenetic evidence was not ambiguous, other signs had been. Conen's explicit goal, then, was to confirm the value of chromosomal investigation for clinicians. Chromosomes would provide diagnosis, he argued, where dermatoglyphic evidence was ambiguous and clinical signs uncertain.

Diagnosis of the Chinese infant had been difficult because his appearance at birth seemed "within the limits of normal." Alex Bell, one of Conen's co-authors, used Ford Walker's dermatoglyphic index but could not make a definite diagnosis because "of the child's racial origin." Citing unpublished research by Ford Walker comparing the dermatoglyphics of "Asiatic and Caucasian Mongoloid Imbeciles" the authors argued that dermal patterns "vary among the different racial groups."[71] In the similar diagnostic dilemma involving a fifty-three year-old woman, diagnosis was made difficult not by the presence but by the *absence* of a racialized physiognomy: "In adulthood," the authors noted, "...the characteristic facies becomes difficult to recognize." The word "mongolism," they pointed out, "would never have been used if only adult cases had been studied". Moreover, the woman's age worked against the diagnosis of Mongolism in still another way: "it has been estimated," the authors wrote, "that even today a sizable proportion of persons with mongolism die by the end of the first year of life, most frequently because of a severe congenital heart malformation or else because of increased liability to infection."[72] In this case dermatoglyphic studies, again provided by Alex Bell, were diagnostic of Mongolism, but it was only the cytogenetic evidence that could overcome the barriers to diagnosis posed by a 'normal,' racial appearance.

Ironically, this case study was presented as an argument *against* the use of appearance as a diagnostic criterion, and indeed, in support of the argument that the name of the condition was inappropriately racialized: "The objection to a descriptive term such as mongolism," the authors noted, "is that the description is inaccurate, the resemblance to a racial Mongol being only superficial." Moreover, the term was embarrassing to

"Oriental populations." "We suggest," they concluded, "that the chromosomal abnormalities be accepted as the only essential feature of the syndrome of mongolism."[73] Ironically in presenting their case studies, Conen and his colleagues had demonstrated their faith in the racialist understanding of this condition, in the presumption of clinical confusion in those instances where the 'racial' portrait was not apparent.

In addition to this racialist narrative, Conen and his co-authors had gestured towards the severity of the condition – indeed, towards its 'natural' lethality – in their surprise at the existence of the aged Mongol. This interpretation was further developed in work Conen, and in a separate study, Margaret Thompson, conducted on the association of Mongolism with Leukemia. For Conen, this study was part of a larger research project concerning the use of cytogenetic evidence in the diagnosis and prognosis of cancer, work which flourished in many communities as a result of the discovery of the "Philadelphia chromosome" – a chromosomal fragment frequently seen in the blood and marrow cells of patients with a particular type of leukemia (and bearing no relation to the individual's inherited chromosome constitution).

Conen and his colleague, Bayzar Erkman, reported on eight "mongoloids in whom a diagnosis of leukemia was made," all of whom had died (the expected prognosis). They discussed the diagnostic process, contradicting Conen's earlier publication in noting that two of the cases involved patients of "oriental origin" making the chromosome studies of "diagnostic value," whereas "the other six patients were Caucasian, and mongolism was easily diagnosed clinically." [74] But the bulk of the paper engaged with debates that had flourished at least since the late 1950s when published

epidemiological evidence had suggested that "combined mongolism and leukemia was approximately 20 times more frequent than expected."[75] Conen and Erkman were supporting the argument of some "difference between leukemia in mongoloids and nonmongoloids," in being more frequently congenital and of a specific type.[76] In her earlier and briefer analysis of the "well known" fact that "mongols are particularly susceptible to leukemia," Thompson reported a family with two Mongol children, one of whom had leukemia, in support of the theory of "some genetic predisposition toward non-disjunction" in these families. Though this case was far from conclusive, it encouraged the search for more data.[77]

Though both Thompson and Conen shared the presumption of the 'severity' of Mongolism as a human disease, Thompson's interest in the familial dimensions of Mongolism – reproduction and the transmission of the disease and related risks – contrasted with Conen's more clinical approach. In this, she demonstrated the particular concerns of the geneticist. While in Alberta, in the early 1960s, Thompson published two other brief case reports on the Mongol which addressed this concern. They provided available clinical, cytogenetic, dermal and reproductive information on two "fertile female mongol[s]," confirming the risk of transmission of this defect as 50% in accordance with the genetic prediction, but "add[ing] nothing to our knowledge of the familial transmission of translocations."[78]

More sustained genetics research on the Mongol was conducted in London by Barr's students and colleagues. Such work generally involved the Ford Walker school

geneticist, Hubert Soltan, and on one occasion involved collaboration with Ford Walker herself. The familial and hereditary interest of the London research was clear in the focus on the relatively uncommon phenomenon of "translocation mongolism." As Fred Sergovich, Hubert Soltan and David Carr put it in an early publication: "The hereditary transmission of the abnormal translocation chromosome is of special interest." "[T]he matter is of practical importance," they added, "in genetic counselling."[79]

The London workers had a particular interest in mental deficiency – Murray Barr having spent considerable time in the latter half of the 1950s conducting research in institutions for the mentally retarded. Cytogenetics seemed to Barr to promise enhanced attention to this important but under-examined phenomenon. In an editorial on "Cytogenetics in Mental Deficiency Research," Barr wrote that "There is encouraging evidence in reports from several countries that scientific investigators are becoming increasingly aware of the magnitude of the problem of mental deficiency....Of the many approaches to the problem that must be explored," he noted, "cytogenetics is of special interest because the knowledge that visible chromosomal abnormalities are etiological factors in mental deficiency is of such recent origin."[80]

In translocation Downs, the extra chromosome 21 is not present as a free chromosome, but rather, is attached to another chromosome (twinned). Such a mechanism makes possible the existence of carriers of what are called balanced translocations, where an individual has one twinned chromosome, but lacks one free chromosome 21 such that the total presence of genetic material matches the normal complement. Though unaffected themselves, these carriers of balanced translocations are at risk of transmitting

the twinned chromosome to some of their progeny in an unbalanced manner; they are at greatly increased risk (1 in 3, theoretically), of having trisomy 21 children.

In a series of publications, and in an unpublished Ph.D. dissertation supervised by Murray Barr, the London workers presented data on translocation mongolism.[81] They examined both inherited translocations, and those translocations which developed *de novo*. A key goal was to achieve a more accurate assessment of the *actual* risk of familial transmission. Their data suggested a risk of transmission that was less than theoretically expected. It also confirmed that the elevated incidence of mongolism among some families was generally not attributable to the mechanics of translocation inheritance. As they put it, "the great majority of mongols who have mongoloid relatives are of the regular trisomic type....[and] where translocation patients had mongoloid relatives, these relatives proved to be regular trisomic mongols in all four families studied."[82] Such data provided tentative support for the thesis that "certain factors (genetic or environmental) which predispose to non-disjunction and chromosome breakage may accumulate in certain families. The chromosome anomaly which occurs may then manifest itself both in translocation and standard trisomic karyotypes in different branches of the family."[83]

Though the London workers focused on cytogenetic technologies, dermatoglyphic analyses – generally conducted by Hubert Soltan – were prominently reported and deliberated on in many of their studies. Indeed, dermatoglyphic evidence seemed to enjoy something of a renaissance in the 1960s. "For many years," Irene Uchida and Hubert Soltan wrote in their 'evaluation of dermatoglyphics in medical genetics',

> dermatoglyphics has been accepted as a useful tool in the differentiation between monozygotic and dizygotic twins. Yet until relatively recently its use as an aid in the diagnosis of mongolism was greeted by many with skepticism. With the rapid development of human cytogenetics and the discovery of chromosomal aberrations in man, the value of dermatoglyphics in clinical medicine has been proved.[84]

The preservation of a tool that, despite this polemical defense, even Uchida and Soltan conceded was to some extent technically outmoded, demands explanation.[85] In the first instance, there is the explanation that it was not *entirely* outmoded. In the early 1960s, as cytogenetic capacity was under development, with many technical improvements that would enable direct identification of each chromosome still a decade away, cytogenetic evidence was very difficult to interpret. Throughout this period, a karyotype was an attempt to organize the scattered chromosomal evidence available in a human cell into a coherent plot of 46 (or more, or less) chromosomes. The karyotype was constructed in accordance with international conventions seeking to identify individual chromosomes through comparison with their peers by size, location of centromere, presence of satellite bodies and other visible features. It was, to say the least, an inexact science. The sex chromatin proved to be an indispensable tool throughout the 1960s because it supported the "reading" of the X chromosome. Dermatoglyphic evidence was presented as having a similar function in supporting cytogenetic interpretation.

Ford Walker and her London colleagues presented a case where two Mongols were born within successive generations of the same family with no apparent explanation for this increased incidence. Dermatoglyphic findings of "striking mongol features" in non-Mongol family members were used to tentatively suggest the presence of chromosome mosaicism in the parents. Cytogenetic evidence did not demonstrate mosaicism but workers were well aware of the technical difficulties of doing so – such that the thesis produced by dermal evidence could not be cytogenetically disproved.[86] This publication also rendered transparent the generally obscured racial dimensions of Ford Walker's dermatoglyphic index, as the people in question were "a North American Negro family" who were presumed to demonstrate "interracial mixture," and thus posed "problems" for data interpretation.[87]

The continued technical relevance of dermatoglyphics was particularly apparent amongst the adept – those who had already invested professional energies into the task of developing proficiency. As was the case with Murray Barr and his colleagues with the sex chromatin, those with technical prowess with dermatoglyphics sought for opportunities to assert and demonstrate the continued relevance of their pet technology. And in making such arguments about technical relevance, the dermal analysts offered and supported new hypotheses that this tool could be used to test. They suggested, in particular, various genetic explanations for the dermal patterns of specific syndromes. In seeking to preserve their tool then, members of the Ford Walker school dis-articulated it from indigenous-tradition theories of pattern production, which emphasized complex and developmental processes, in favor of the new theoretical emphases on the material and directly acting gene.

Dermal analysts took advantage of the narratives of gene action and chromosome location to re-write dermal pattern production in the language of classical genetics. Uchida and Soltan noted that "the formation of the dermal ridges would be determined by many genes spread over many chromosomes. In mongolism, the presence of the extra chromosome, with its large number of genes, causes abnormal development in many organ systems, including the dermal ridges. One would expect, therefore, that the presence of extra chromosomes causing other syndromes might well produce characteristic peculiarities in dermal pattern formation."[88] Some studies attempted even more focused genetical analysis. In an early study presenting one "pedigree" of translocation mongolism, Sergovich, Soltan and Carr took up Lionel Penrose's genetic hypothesis about the production of dermal characteristics. Their conclusion, that they could provide "no direct positive evidence for the hypothesis that a locus is present on chromosome 21 with an allele which controls the height of the axial triradius," nonetheless demonstrated their faith in a mechanistic and simple-acting vision of the genetics of such patterns.[89] In yet another study, Soltan and a co-author attempted, unsuccessfully, to use dermal evidence to detect any "small deletion" or "position effect" that might arise from the potentially different genetical composition of translocation and trisomy Down's syndrome.[90]

All of these ways of preserving and producing relevance for dermatoglyphic evidence in the cytogenetic age supported and deployed its metaphors. The relevance of dermatoglyphics in the age of chromosomes was in its historic capacity to know the Mongol. This knowing had now been granted a fresh scientific justification – chromosome anomaly – which both produced the Mongol, and its distinctive dermal patterns. Other

chromosome anomalies were, by extension, logical subjects for dermal review. Dermatoglyphic evidence thus worked to produce the category 'autosome anomalies' – drawing on both the material and the metaphorical Mongol.

Of all Toronto-trained, and Toronto and London-based workers, Irene Uchida undertook the most significant work of cytogenetic discovery in the production of new 'autosome anomalies.' From Manitoba, where she went to direct the Department of Medical Genetics at the Children's Hospital of Winnipeg (and participate in the Department of Pediatrics at the University of Manitoba) in 1960, Uchida embarked on a period of very productive research. She collaborated with the geographically-proximate 'Wisconsin group,' with whom she had worked for a year as a Rockefeller scholar retooling herself as a cytogeneticist. Members of the Wisconsin group were the discoverers of "D" Syndrome.[91] In addition to her own work of discovery, then, Uchida collaborated with members of the Wisconsin group, namely Klaus Patau and David Smith, to identify "distinctive dermal configurations" in "the new autosomal trisomy syndromes."[92]

This work drew explicitly on the Mongol example: "If the existence of a mongoloid dermal pattern is the consequence of a highly polygenic determination of such patterns, one should expect trisomics for other chromosomes to display dermal peculiarities of their own," Uchida, Patau and Smith argued. With some evident delight, they recorded the confirmation of that thesis: "From a genetic point of view," they argued, "it is remarkable that every one of the three types of trisomy that has been identified in man results in recognizable

dermatoglyphic alterations just as it results in mental retardation and, less regularly, in heart defects."[93]

Of note in these deliberations was the genetic narrative, on the one hand, and the categorizing expectations, on the other. The chromosomal trisomies that were investigated were autosomal, and severe. Such was the burden of this expectation that one of the newly discovered trisomies "in man" was *not* investigated. The XXX female had been reported in 1959, but in involving the sex chromosomes, and being described as a "Super Female," it is perhaps no surprise that triplo-X fell outside the scope of this dermal analysis.[94]

Uchida worked to produce autosome syndromes through cytogenetic discovery and description. She took a particular interest, in the early 1960s, in 18 Trisomy syndrome (what Conen called "E" syndrome), having discovered an infant with both triplo-X and trisomy 18 in 1961.[95] But she also published reviews of the syndrome. In a review of eight 18-Trisomy cases, Uchida and her colleagues demonstrated the emerging faith in this anomaly as constitutive of a coherent syndrome: "Among the numerous reports of multiple congenital malformations suspected to be caused by autosomal trisomy," they wrote, "one syndrome other than mongolism, the 18-Trisomy syndrome, in our area at least, stands out as a relatively common, well defined entity." "In time," they added, "cytologic studies may be as superfluous in the diagnosis of the 18-trisomy syndrome as in most cases of mongolism."[96] Uchida would have agreed with Fred Sergovich and his London colleagues that "Each autosomal trisomy causes a distinctive phenotype which enables it to be recognized, as a rule, on clinical examination."[97] Dermal analysis could serve as an aid in such diagnosis.

Meanwhile, in Toronto, Pat Conen and his colleagues at Sick Kids took advantage of their institutional location to identify and report upon numerous cases that conformed to and differed from the new 'syndromes.' Conen took a particular interest in the "D" syndrome – a trisomy in the then-hard to distinguish 13-15 group of chromosomes. He and his colleagues reported several cases that came to their attention, noting "The remarkably similar pattern of multiple anomalies present in all the reported cases of this syndrome [which] strongly suggests that the same genes on the same chromosome are present in triplicate."[98] Conen and his colleagues also reported on translocation D syndromes, noting the "characteristic clinical features" in these infants, assessing the "pedigrees," and commenting on the "increased risk of abnormal offspring."[99] Conen and the workers in his lab were aided by Irene Uchida or Margaret Thompson in the analysis of dermal patterns in these cases, and Conen and his colleagues compared these data with the diagnostic guide Uchida and her Wisconsin colleagues had developed for these syndromes.[100] Finally, Conen and a co-author also published reviews which attempted to estimate the incidence of both "D" and "E" syndromes, noting that "Accurate estimates of the frequency of autosomal abnormalities other than mongolism have not yet been made because of their relative rarity. With the increasing awareness of the patterns of multiple anomalies of the D and E syndromes," they added, "the diagnoses may be suspected more often, strengthened by finding characteristic dermatoglyphics and confirmed by chromosome analyses."[101]

What made these discoveries into syndromes, then, were characteristic clinical signs, and sometimes characteristic dermal patterns. But what made them into *autosomal* syndromes was their 'severity.' Indeed, the D and E syndromes were seen as generally

lethal. As Conen and Erkman noted in their reviews, E syndrome cases "have a characteristic pattern of anomalies and usually die in infancy," while D syndrome "is lethal."[102]

The London workers played a particularly important role in confirming the narratives of 'severity' and especially of 'lethality' in the autosome anomalies. Murray Barr and his students and colleagues were institutionally oriented towards the phenomenon of intellectual disability, a phenomenon understood as intrinsically severe. Though less active in the production of new autosomal syndromes,[103] these workers focused attention on institutional and population-based categories, such as the "mentally retarded," arguing for their inherent interest to the science of cytogenetics: "chromosome errors," as Barr put it, "rank first among the *known* causes of severe retardation."[104] Andrew Chen, who took his Ph.D. in Barr's department, worked to produce the population of "full-term low birth weight" infants as inherently worthy of cytogenetic analysis, noting the "association between full-term low birth weight and mental retardation" and the "high proportion of infants affected with chromosome disease ... born with low birth weight."[105]

Of international significance in supporting the narratives of lethality was the work of David Carr on "chromosome studies in spontaneous abortions."[106] In his first published report on the high incidence of chromosome anomalies amongst abortuses, he noted that "The finding of lethal chromosome abnormalities in children with multiple chromosome anomalies, for example the D and E syndromes, suggested the possibility of similar findings in abortuses or stillborn infants." Noting that chromosome abnormalities were far more

common in spontaneous abortuses than among newborns, and detecting some chromosome anomalies among abortuses that had never been found in a live-born person, Carr concluded "that chromosomal abnormalities are a significant cause of early embryonic wastage.[107]

Because of the difficulties of identifying specific chromosomes in the 1960s, Carr's work categorized most anomalies according to their letter group. These included D, E and G trisomies (the G group included 21 and 22 and thus Downs) – those chromosome constitutions which were among the most frequently detected in newborns with congenital malformations. There were also trisomies involving chromosome groups that were not seen among the liveborn, such as A, B and F. Then, there were extraordinary chromosome constitutions such as triploidy, involving 69 chromosomes per cell, and tetraploidy, involving 92 chromosomes per cell, and other miscellaneous structural and numerical aberrations. But the most common chromosome anomaly detected was X-monosomy, or XO, otherwise known as Turner's syndrome. This was, as Carr noted in his dissertation, "the only sex chromosome abnormality found."[108]

Carr's work suggested that many chromosome anomalies were 'naturally' lethal, but his evidence suggested that one of the sex chromosome anomalies was more lethal than many autosome anomalies – a fact that contradicted the hierarchy of severity imagined by the categories of 'sex chromosome anomaly' and 'autosome anomaly.' Indeed, Turner's syndrome was a frequent exception to the rules implied by the distinct categories. In their evaluation of the place of dermatoglyphics in medical genetics, Uchida and Soltan corrected the earlier omission of the dermal patterns of 'sex chromosome anomalies' by Uchida and her Wisconsin colleagues. Available evidence on the sex chromosomes was reviewed:

"Only in Turner's syndrome," they reported, "...is there any suggestion of the presence of distinctive dermal patterns."[109]

But this exception proved the rule, and despite its awkward fit, Turner's syndrome did not disrupt the category of 'autosome anomaly.' Yet it did demonstrate the contingency of these categories of disease – categories which *were* produced, and which *did* embody a hierarchy of severity. Clearly, the evidence available at the time could have supported different effects.

Conclusion

The London, Ontario workers emerged, at the end of the 1950s, from a research arena dominated by the discipline of endocrinology, and the agency of hormones, into the new world of genes and chromosomes. They utilized their skill with sex chromatin, and their sexualized symbolism, in the reading of the chromosomes, and transferred their concern with intersexuals onto the bodies and lives of a category they helped to generate: the category of the sex chromosome anomalies.

Both Toronto and London workers addressed the 'autosome anomalies.' Mongolism was a distinct concern, as were the "D" and "E" syndromes. David Carr's work to demonstrate the prevalence of chromosome anomalies in human spontaneous abortions was internationally significant, and supported the production of the 'abortus' as a new population for cytogenetic review. These workers relied on local and generic

narratives and technologies of the Mongol for the production and re-production of the category 'autosome anomalies.' And their presumptions of internal homogeneity within this disease category supported the naturalization of narratives of defect and lethality in these conditions.

As Toronto workers sought to assimilate medical cytogenetics into human genetics, they adopted and re-produced narratives and technologies from genetic science. Though the genetical ownership of cytogenetics was never in doubt, it still required the work of production. The age of cytogenetic discovery, as new chromosome anomalies were catalogued and clinical syndromes produced, involved workers from both Toronto and London. Both sets of workers brought skills, assumptions and methods to this new work, and helped to produce the enduring disease category of autosome anomaly. This category also relied for its coherence on its opposite – the sex chromosome anomalies.

Endnotes: Chapter 3

[1] Victor McKusick, "The Growth and Development of Human Genetics as a Clinical Discipline," *American Journal of Human Genetics*, 27 (1975), 262.
[2] Augustine Brannigan, "The Reification of Mendel," Social Studies of Science, 9, (1979).
[3] "As endocrinology and plastic surgery developed," Hausman writes, "doctors could be more active in their treatment of intersexual subjects; clinicians could intervene at the level of anatomy and physiology to enable their patients to simulate one or the other sex." Bernice Hausman, *Changing Sex: Transsexualism, Technology and the Idea of Gender*, (Durham and London: Duke University Press, 1995), 7, emphasis in original.
[4] Keith Moore, one of Barr's graduate students, who worked with Barr in the 1950s on the clinical research in intersexuality enabled by the sex chromatin, argued that the sex chromatin stimulated interest in intersexuality. Keith Moore and Clifford Edwards, "Medico-legal aspects of intersexuality: criteria of sex," *Canadian Medical Association Journal*, 83 (September 24, 1960), 711.
[5] Murray Barr collaborated with a diverse community of researchers around the world, including those American researchers whose work was to define the field of 'congenial errors of sex' for subsequent generations, such as John Money of Johns Hopkins University, and his co-workers, Joan and John Hampson. These sexologists formally articulated a coherent protocol for the medical management of intersexed cases. Money, who has dominated the field in the latter half of the twentieth-century, made further revisions to the protocols with Anke Ehrhardt. See: Suzanne Kessler, "Medical Construction of Gender: Case Management of Intersexed Infants," *Signs: Journal of Women in Culture and Society*, 16:1 (1990), 6. Kessler describes these processes in great detail in her article on sex assignment in New York in the mid-1980s, as told by the specialist medical practitioners involved in the process. See also, Hausman, *Changing Sex*, Chapter 3. For more detail on Barr's work in the 1950s see: Fiona Alice Miller, ""Your True and Proper Gender:" Medical Science Disciplines the Intersex" unpublished MS.
[6] ML Barr, "Sex chromosomes and the neurone," lecture to the Montreal Neurological Society, Nov 28, 1951, pp. 2-3. (NA, MG30 B111, 18-24).
[7] ML Barr, "Psychosexual attitudes in sex reversals," lecture to the Ontario Psychological Association, February 7, 1958, p 3. (NA, MG30 B111, 18-30).
[8] Raymond Prince, "Sex and the cell nucleus," University of Western Ontario, MSc. Thesis, 1952, 39. "The sex chromosomes are concerned with gonadal differentiation," Barr noted; "genes on other chromosomes are feminizing and their feminizing effect is counteracted, under normal conditions, in male embryos by a masculinizing hormone that is elaborated by the foetal testis." ML Barr, "Psychosexual attitudes in sex reversals," lecture to the Ontario Psychological Association, February 7, 1958, p 3. (NA, MG30 B111, 18-30).
[9] Raymond Prince, "Sex and the cell nucleus," 39.
[10] Marianne van den Wijngaard, "The Acceptance of Scientific Theories and Images of Masculinity and Femininity: 1959-1985," *Journal of the History of Biology* 24:1 (Spring 1991), 24. Anne Fausto-Sterling, *Myths of Gender: Biological Theories about Women and Men*, (New York: Basic Books, 1985), 85.
[11] Emily Martin, "The egg and the sperm: how science has constructed a romance based on stereotypical male-female roles," *Signs*, 16:3 (1991), 486.
[12] Barr analyzed the skin biopsies and he reviewed the manuscript, which he thought "splendid": Barr, letter to Grumbach, June 6, 1955 (NA, MG30B111, 1-13).
[13] Melvin Grumbach, Judson Van Wyk and Lawson Wilkins, "Chromosomal Sex in Gonadal Dysgenesis (Ovarian agenesis): Relationship to Male Pseudohermaphroditism and theories of Human Sex Differentiation," *The Journal of Clinical Endocrinology and Metabolism*, 15:10 (October 1955), 1162, 1163.
[14] *Ibid.*, 1161, 1162.
[15] This article was a review article; the fact that many of these cases demonstrated male sex chromatin patterns had been known since 1954.
[16] *Ibid.*, 1162.
[17] *Ibid.*, 1177, 1182.

[18] On Jost see: Alfred Jost, "Problems of Fetal Endocrinology: The Gonadal and Hypophyseal Hormones," in Gregory Pincus ed., *Recent Progress in Hormone Research, The Proceedings of the Laurentian Hormone Conference*, (New York: Academic Press, 1953), 379-418.
[19] Grumbach et al, "Chromosomal Sex in Gonadal Dysgenesis," 1189.
[20] *Ibid.*, 1189. The authors also use this case as evidence to substantiate the Money thesis about gender and erotic orientation not being automatically determined by sex chromosomes or sex hormones.
[21] Murray Barr, "Cytological tests of sex," letter to the editor, *The Lancet*, 1 (Jan 7, 1956), 47.
[22] Murray Barr, "Dysgenesis of the Seminiferous Tubules," *British Journal of Urology*, 29:3 (Sept 1957), 251. See also: Murray Barr, "The Sex Chromatin and its Bearing on Errors of Sex Development," *Canadian Medical Association Journal*, 74:6 (March 15, 1956), 419-422. Barr wrote in a 1959 article that was based on a lecture given on November 5, 1958, "most patients with Turner's syndrome are derived from male embryos that feminized because testes with their masculinizing evocator failed to develop." Murray Barr, "Sex anomalies in general practice," *Ontario Medical Review*, (May 1959), 483; ML Barr, "Role of the fetal testis in the maturation of the reproductive tract," N.D. [1955] presented at annual meeting of Canadian Physiological Society, (NA, MG30B111, 12-21).
[23] John Hampson, Joan Hampson and John Money, "The syndrome of gonadal agenesis (ovarian agenesis) and male chromosomal pattern in girls and women: Psychologic studies," *Bulletin of the Johns Hopkins Hospital*, 97 (1955), 225.
[24] Barr's publications on this include: Earl Plunkett and Murray Barr, Letter to the Editor, "Cytological Tests of Sex in Congenital Testicular Hypoplasia," *Journal of Clinical Endocrinology and Metabolism*, (June 1956), 829; M Grumbach, E Engle, W Blanc and ML Barr, Abstract, "The Sex Chromatin Pattern in Testicular Disorders: Relationship to Pathogenesis and to True hermaphrodism," *Journal of Clinical Endocrinology and Metabolism* 16 (July 1956), 923; Earl Plunkett and Murray Barr, "Testicular Dysgenesis affecting the seminiferous tubules principally, with chromatin-positive nuclei," *The Lancet*, (Oct 27, 1956), 853-856; Murray Barr, "Dysgenesis of the Seminiferous Tubules," *British Journal of Urology*, 29:3 (Sept 1957), 251-257; Earl Plunkett and ML Barr, Abstract, "The occurrence of the sex chromatin in congenital testicular hypoplasia," Meeting of the Endocrine Society, June 1956 (NA, MG30B111, 13-4).
[25] In early publications, Barr reported on two cases, only one of whom definitely fit the clinical syndrome of Klinefelter's; the other was "difficult to classify according to current nomenclature. Possibly the findings in this patient might have been those of Klinefelter's syndrome had he been studied at an earlier age." Plunkett and Barr, "Testicular Dysgenesis," 855.
[26] *Ibid.*, 853.
[27] Grumbach et al, Abstract, "The Sex Chromatin Pattern," 923. See also: M Grumbach, E Engle, W Blanc and ML Barr, Abstract, "The sex chromatin pattern in testicular disorders: relationship to pathogenesis and to true hermaphroditism," [Endocrine Society, June 1956] (NA, MG30B111, 13-4).
[28] Earl Plunkett and Murray Barr, "Testicular Dysgenesis affecting the seminiferous tubules principally, with chromatin-positive nuclei," *The Lancet*, (Oct 27, 1956), 856.
[29] The possibility of variations in the chromosome constitution was broached, but the XX chromosome constitution was deemed more likely. Barr wrote that "Although the exact genetic mechanism is not known, there is good evidence that it operates within the framework of an XX- or an XY- sex chromosome complex, i.e., there is no need to postulate an unusual sex chromosome complex such as XO or XXY." ML Barr, "Chromosomal sex and sex reversal," *American College of Obstetricians and Gynecologists*, Oct 2-4, 1958 (NA, MG30B111, 11-19). Barr and co-authors also wrote that "The error may lie in the presence of an unusual sex chromosome complex, such as XXY..." But they added, "If these patients bear the XX sex chromosome complex, which is more likely..." Plunkett and Barr, "Testicular Dysgenesis," 856. For alternate suggestions from Barr's international colleagues: the XXY constitution was suggested by WD Davidson Clinical Pathologist, King's College Hospital, London England, letter to Barr, Feb 20, 1956, case 43 (NA, MG30B111, 9-3); the XXY or XXXYY patterns were suggested by H David Mosier, the Johns Hopkins Hospital, letter to, Jan 27, 1956, case 47 (NA, MG30B111, 9-3).
[30] Plunkett and Barr, "Testicular Dysgenesis," 856.
[31] Barr, "Dysgenesis of the Seminiferous Tubules," 251, 255.

[32] Daniel Kevles, *In the Name of Eugenics: Genetics and the Uses of Human Heredity*, revised edition, (Cambridge, Mass., London: Harvard University Press, 1985, 1995, 1997), 241-245
[33] *Ibid.*, 242.
[34] *Ibid.*, 242.
[35] Murray Barr, "Sex Chromatin and Phenotype in Man," *Science*, 130:3377 (Sept 18, 1959), 682, 683, 684. Barr does mention in this paper the possibility that XO or XXY sex chromosome constitutions could give sex chromatin evidence that was indistinguishable from XX and XO; even at this point, however, these were lesser hypotheses.
[36] *Ibid.*, 685.
[37] David Carr, Murray Barr and Earl Plunkett, "An XXXX Sex chromosome complex in two mentally defective females," *Canadian Medical Association Journal*, 84:3 (Jan 21, 1961), 131. Barr used other categorizations at times but the sex chromosomes remained causal. For example, in one paper he described 4 types of sex chromosome anomaly: type 1 - missing chromosomes; type 2 – additional; type 3 – mosaics; types 4 – involved "the conditions wherein the sex chromosomes are normal but contrary to the prevailing features of the phenotype, where the fault is at the gene rather than the comparatively gross chromosome level." ML Barr, "Abnormalities of sex chromosome complex in relation to embryological development," p. 1, paper presented at American Academy of Pediatrics, Chicago, Oct 2, 1961 (NA, MG30B111, 11-17).
[38] James Thompson, Margaret Thompson, *Genetics in Medicine*, (Philadelphia and London: WB Saunders, 1966), 117, see Chapter 7 generally. In the fourth edition of this textbook in 1986, in the chapter on the "Sex Chromosomes and their Disorders," Thompson and Thompson categorized thusly: "sex chromosome abnormalities" and "disorders of sexual development with normal chromosomes." James Thompson, Margaret Thompson, *Genetics in Medicine*, (WB Saunders, 1986), 141, 146.
[39] The full quote reads: "Developmental anomalies of the reproductive system are encountered infrequently, in comparison with many conditions that confront physicians. Yet genital anomalies have to be studied carefully. They are a source of particular concern to the parents of an affected child, and the patient may bear a heavy burden on reaching maturity because the defect usually interferes with satisfaction of the basic instinct of reproducing one's kind. These problems should be handled with exceptional discretion and understanding." Murray Barr and David Carr, "Sex chromatin, sex chromosomes and sex anomalies," *Canadian Medical Association Journal*, 83:19 (November 5, 1960), 979.
[40] PEC, editorial, "The clinical significance of research on human sex chromosomes," *Canadian Medical Association Journal*, 84 (Jan 21, 1961), 167. Barr and his co-authors noted "The X chromosome is so similar to autosomes in the 6-12 group that it cannot be distinguished from them with certainty. But," they added, "the number of X chromosomes can be inferred from the sex chromatin pattern in interphase nuclei." ML Barr et al, "The XXXXY sex chromosome abnormality," *Canadian Medical Association Journal*, 87 (Oct 27, 1962), 896.
[41] PE Conen, "Cytogenetic Investigations of Congenital anomalies," Progress Report to NHGP, received Oct 31, 1961 (OA, RG 10-22, NHPG, Box 90, File 1515)
[42] Pat Conen argued this forcefully in his editorial. PEC, editorial, "The clinical significance," 167.
[43] "The first procedures were worked out in part by Mr. Philip Chang, MA." Ford Walker, Fraser and McLean wrote. "Mr. Chang had been trained by Professor KH Rothfels and Professor RC Parker, both pioneers in human cytogenetics at the University of Toronto." "Chromosome patterns in genetically determined anomalies," Final Report, May 21, 1963 (OA, RG 10-22, Box 90, File 1516).
[44] "Chromosome patterns in genetically determined anomalies," Final Report, May 21, 1963 (OA, RG 10-22, Box 90, File 1516). Genetic leadership in these issues was also reflected in the fact that Ford Walker gave the presentation to the hospital trustees on chromosome studies for example. Minutes of the Committee on Research, October 14, 1959 (HSC, CRM. Vol. 1953-1959)
[45] "Chromosome patterns in genetically determined anomalies," Final Report, May 21, 1963 (OA, RG 10-22, Box 90, File 1516). "Clinicians began to use Dr Conen's service to such an extent that a routine diagnostic cytogenetics laboratory was opened under his supervision," wrote Dr Chute in reviewing the history of the Genetics Department. Chute, "Report Re Department of Genetics," September 1964, attached to Minutes of the Committee on Research, September 2, 1964 (HSC, CRM. Vol. 1960-1966).

[46] "Chromosome patterns in genetically determined anomalies," Final Report, May 21, 1963 (OA, RG 10-22, Box 90, File 1516)
[47] They learned from Conen his marrow biopsy culturing method and taught him in turn the clinically much easier leukocyte culture method.
[48] Hubert Soltan, "Ontario Overview," in HC Soltan, ed., *Medical Genetics in Canada: Evolution of a Hybrid Discipline, Essays on the Early History*, (London, Ontario: The University of Western Ontario Regional Medical Genetics Centre, 1992), 88.
[49] ML Barr, editorial, "The Chromosomes of Man," *Canadian Medical Association Journal*, 81 (August 1, 1959), 192-3; MLB, editorial, "Cytogenetics in Mental Deficiency Research," *Canadian Medical Association Journal*, 83 (November 26, 1960),1164-5; PEC, editorial, "Identification and Nomenclature of Human Chromosomes," *Canadian Medical Association Journal*, 84 (June 17, 1961), 1390-2.
[50] ML Barr, editorial, "The Chromosomes of Man," 193.
[51] PE Conen and B Erkman, "Necropsy Spleen Samples for Chromosome Cultures," *The Lancet*, (March 21, 1964), 664-5. DH Carr and JE Walker, "Carbol fuschin as a stain for human chromosomes," *Stain Technology*, 36 (1962), 233-6; Letters to the Editor, "The London Conference on "The Normal Human Karyotype" August 28-30, 1963," *American Journal of Human Genetics*, 16 (1964), 156-8.
[52] "But she continues some study in dental heredity and in dermatoglyphics – the fingerprint side," the article continued: "Multiple births study material for Geneticist," *Globe and Mail*, February 27, 1950 (UT, A73 0026, 105, 61).
[53] In the meantime, through collaboration with Werner Kalow in the Department of Pharmacology in Toronto, her work had become strongly biochemical in orientation.
[54] And dermatoglyphics has not gone away today. See, in particular, the March of Dimes, Birth Defects Foundation collection: CC Plato, RG Garruto and BA Schaumann, eds., "Dermatoglyphics: Science in Transition," *Birth Defects: Original Article Series*, 27:2 (1991).
[55] Kevles, *In the Name of Eugenics*, 160.
[56] There had long been genetical research which had disputed an association between Mongolism and racial "devolution" – research that Grace Workman cited and supported in her Master's thesis, for example. Indeed, the research of Cummins and Ford Walker on racially distinct patterns in Mongolism served as proof that the Mongol did *not* constitute a distinct racial group. And see Kevles, *In the Name of Eugenics*, pp. 160-2.
[57] Gordon Allen et al, "Mongolism," *The Lancet*, 1 (April 8, 1961), 775. The signatories included such key figures as Jérôme Lejeune, Charles Ford, Lionel Penrose and Curt Stern.
[58] Medline did not stop using the term "Mongolism" until 1975. And Charles Bosk's ethnographic study of a team of U.S. genetic counselors suggests the continued salience of the term in the clinical context in the late 1970s and early 1980s. Charles Bosk, *All God's Mistakes: Genetic Counseling in a Pediatric Hospital*, (Chicago and London: University of Chicago Press, 1992), 96. I interpret Bosk's use of the term "mongolism" as a reflection of the usage of those counselors he observed.
[59] According to the University of Toronto, *President's Report*, Ford Walker first reported work on "diagnosis" of mongolism in the 1950-51 year. She soon began work on mongolism in different racial groups to aid in diagnosis: "Work on an objective diagnosis of mongoloid imbeciles has continued and cases of both Japanese and Chinese patients has been added to the series," 1952-53; studies of "the dermal configurations of Asiatic mongoloid imbeciles compared with control series of Asiatics and Europeans," 1953-54; "studies of Asiatic mongoloid imbeciles compared with European patients," 1954-55; "Continuation of studies of Asiatic mongoloid imbeciles compared with European patients," 1955-56; "study of negro mongoloid imbeciles as compared with European, Asiatic and North American Indian patients," 1956-57; "in cooperation with Miss Elizabeth Doidge, records were assembled of negro mongoloid imbeciles (108) in institutions for the mentally retarded in the United States, this study being part of a larger comparative study of mongoloid imbeciles of various racial groups", 1957-58. After this date there were no more research reports included in the *President's Reports*, but Elizabeth Doidge did complete her Master's thesis on Negro Mongoloid Imbeciles in 1960 and she discusses these racial diagnostic questions in her Discussion and Conclusions.
[60] Norma Ford Walker, "The Dermatoglyphics of Asiatic and Indian Mongoloid Imbeciles," Abstracts of Papers, Proceedings of the Genetics Society of Canada, Inaugural Meeting, 1956 (NA, MG 28 I 456, Acc.

1989/0186, Box 1). Emphasis in original. It is notable, that though Conen, Bell and Rance cite this work as "in process" in their study of the Chinese Mongoloid infant, they do not make the argument for the "appropriateness" of the term "Mongol." This may be because Ford Walker changed her mind, or because of the different social climate and personal attitudes of these workers. See: PE Conen, AG Bell and CP Rance, "A review of chromosome studies in the diagnosis of Mongolism: Case Report of a Chinese Infant," *The Journal of Pediatrics*, 60:4 (April 1962), 537.

[61] "Some genes carry disease and physical defects. Heredity counselors call them *black genes*." Sidney Katz, "She knows the kind of children you'll have," *Maclean's Magazine*, 57 (December 1, 1954), 82, emphasis in original. That this was a racialist, rather than simply racist statement is evident in Ford Walker's repeated statements, in this article, about the merits of racial intermarriage, in the face of her client's and general social aversion: 79, 83.

[62] In this there is some continuity with the eugenics movement. Diane Paul has argues that mental defects was considered a far more egregious problem than physical defects. See: Diane Paul, *Controlling Human Heredity: 1865 to the Present*, (New Jersey: Humanities Press, 1995), 122

[63] This "natural" lethality has declined considerably in recent decades, due to more consistent treatment of infections and heart disease. Paradoxically, while the newborn incidence of Down's syndrome is declining in some parts of the world, as a function of prenatal diagnosis and selective abortion, the population incidence of Down's is increasing because of longer life expectancy and, to some degree, later maternal age. See: MP Janicki, et al, "Mortality and Morbidity among older adults with intellectual disability: Health services considerations," *Disability and Rehabilitation*, 21:5-6 (1999), 284-94; P O'Leary, et al, "The impact of antenatal screening for Down Syndrome in Western Australia," *Australian and New Zealand Journal of Obstetrics and Gynaecology*, 36:4 (1996), 385-8; A Nicholson and E Alberman, "Prediction of the number of Down's syndrome infants to be born in England and Wales up to the year 2000 and their likely survival rates," *Journal of Intellectual Disability Research*, 36: 6 (1992), 505-17; CW McGrother and B Marshall, "Recent trends in incidence, morbidity and survival in Down's syndrome," *Journal of Mental Deficiency Research*, 34:1 (1990), 49-57.

[64] David Carr, "Chromosome Studies in Spontaneous Abortions," University of Western Ontario, Ph.D. Thesis, 1965, 11.

[65] MLB, editorial, "Cytogenetics in Mental Deficiency Research," *Canadian Medical Association Journal*, 83 (November 26, 1960), 1164.

[66] PEC, editorial, "Identification and Nomenclature of Human Chromosomes," *Canadian Medical Association Journal*, 84 (June 17, 1961), 1391.

[67] *Ibid.*, 1391. See also reports submitted by PE Conen, October 25, 1963, N.D., (OA, RG 10-22, Box 91, Files 1545). In 1959, the Pathology department was overseeing work on chromosomes – developing new skills in tissue culture and cytogenetics, examining cancerous specimens, and identifying chromosome anomalies in cases of Turner's syndrome, Klinefelter's syndrome and in "Mongols." *Sixth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1959, 38 (HSC).

[68] See reports submitted by PE Conen, October 25, 1963, N.D., (OA, RG 10-22, Box 91, Files 1545). Pat Conen and Alex Bell did some more experimental work in human cytogenetics. Alex Bell investigated the production of chromosome aberrations from X-rays in human blood cultures: Alexander Graham Bell, "An Investigation of Irradiation-Induced Chromosome Aberrations in Human Leukocytes in Culture," MA Thesis, UofT, 1962 (UT, T79 0107, File 54). Pat Conen examined clinical cases of chromosome damage in children seemingly causes by exposure to diagnostic or therapeutic radiation and chemical agents like mustard gas, and affected children whose parents were exposed to radiation through occupations or therapy: PE Conen, "Chromosome damage in an infant after diagnostic irradiation," *The Lancet*, 2 (July 1, 1961), 47; PE Conen and GS Lansky, "Chromosome Damage During Nitrogen Mustard Therapy: A Case Report," *British Medical Journal*, (October 21, 1961), 1055-7; PE Conen and AG Bell, "Chromosome Aberration in an Infant Following the Use of Diagnostic X-rays," *Pediatrics*, 31 (1963), 72-79; PE Conen and B Erkman, "A Mosaic Normal-"D" Trisomy Boy with a Radiation Chimera Father," Abstract, *American Journal of Pathology*, 43 (1963), 28a; PE Conen, B Erkman and Bernard Laski, "Chromosome studies on a radiographer and her family," *Archives of Internal Medicine*, 117 (Jan 1966), 125-132.

[69] This was not always HSC, however. Conen also collaborated on such cases brought to the attention of workers in other hospitals, like Toronto General.
[70] PE Conen, AG Bell and CP Rance, "A review of chromosome studies in the diagnosis of Mongolism: Case Report of a Chinese Infant," *The Journal of Pediatrics*, 60:4 (April 1962), 533-9; LH Opie, WB Spaulding and PE Conen, "Masked Mongolism: Group 21 Trisomy in a Fifty-Three Year Old Woman," *American Journal of Medicine*, 35 (July 1963), 135-42.
[71] Conen et al, "A review of chromosome studies, 535, 537.
[72] Opie et al, "Masked Mongolism,"138.
[73] *Ibid.*, 140, 141. In making this argument they were citing a collective statement on the matter of terminology in Mongolism, published in 1961.
[74] PE Conen and Bayzar Erkman, "Combined Mongolism and Leukemia: Report of Eight Cases with Chromosome Studies," *American Journal of Diseases of* Children, 112 (November 1966), 442, 437.
[75] *Ibid.*, 429.
[76] The authors discussed the possible cause of the association between leukemia and mongolism: it might be due to some relationship between chromosome 21, which was tripled in the Mongol, and the Philadelphia chromosome; it might also be due to the association of both conditions with advanced maternal age. Finally, mongolism might "be merely the most frequent example of an increased risk of malignant disease in patients with genic imbalance due to abnormal karyotypes; this risk," they added, "cannot be tested in many patients with developmental [read, autosomal] anomalies because they die in infancy." Yet there was evidence of increased malignancy in some of the sex chromosome anomalies, and in family members of persons with such anomalies. *Ibid.*, 439.
[77] Margaret Thompson, RE Bell and AS Little, "Familial 21-Trisomic Mongolism Coexistant with Leukemia," *Canadian Medical Association Journal*, 88 (April 27, 1963), 894. At this time, Thompson was temporarily at the Jackson Laboratory, Bar Harbor, Maine, though her collaborators were from her home department in the Faculty of Medicine at the University of Alberta.
[78] Margaret Thompson, "21-Trisomy in a Fertile Female Mongol," *Canadian Journal of Genetics and Cytology*, 4 (1962), 352; Margaret Thompson, "Reproduction in two Female Mongols," *Canadian Journal of Genetics and Cytology*, 3 (1961), 353. Thompson's interest in the fertility of Mongols, and indeed her access to these cases, may have been due to her service on the province's eugenics records board during this period.
[79] FR Sergovich, HC Soltan and DH Carr, "A 13-15/21 Translocation Chromosome in Carrier Father and Mongol Son," *Canadian Medical Association Journal*, 87 (Oct 20, 1962), 853, 857.
[80] MLB, editorial, "Cytogenetics in Mental Deficiency Research," *Canadian Medical Association Journal*, 83 (November 26, 1960),1164.
[81] Frederick Raymond Sergovich, "Chromosome Studies in Translocation Mongolism," University of Western Ontario, Ph.D. Thesis, 1964.
[82] HC Soltan, RG Wiens and FR Sergovich, "Genetic studies and Chromosomal analyses in families with mongolism (Down's syndrome) in more than one Member," *Acta Genetica*, 14 (1964), 256.
[83] FR Sergovich, HC Soltan and DH Carr, "Twelve unrelated translocation Mongols: Cytogenetic, Genetic and Parental Age Data," *Cytogenetics*, 3 (1964), 43.
[84] Irene Uchida and Hubert Soltan, "Evaluation of Dermatoglyphics in Medical Genetics." *Pediatric Clinics in North America*, 10:2 (May 1963), 409.
[85] Uchida and Soltan noted in their conclusion that "Since the discovery of trisomy as the cause of mongolism, dermatoglyphic analyses have given way to chromosomal investigations as a diagnostic procedure. Nevertheless dermatoglyphics remains important for quick screening of infants suspected of trisomy and for confirmation of clinical diagnosis when chromosomal investigations are not possible." *Ibid.*, 421.
[86] A genetic hypothesis, of a "predisposition to chromosome anomalies," was also suggested. Norma Ford Walker, DH Carr, FR Sergovich, ML Barr and HC Soltan, "Trisomy-21 and 13-15/21 Translocation Chromosome Patterns in related Mongol Defectives," *Journal of Mental Deficiency Research*, 7 (1963). 153, 160.
[87] *Ibid.*, 150, 156.

[88] Uchida and Soltan, "Evaluation of Dermatoglyphics," 409-10.
[89] FR Sergovich, HC Soltan and DH Carr, "A 13-15/21 Translocation Chromosome in Carrier Father and Mongol Son," *Canadian Medical Association Journal*, 87 (Oct 20, 1962), 858. Penrose authored this hypothesis with JDA Delhanty, *Annals of Human Genetics*, 25 (1961), 243.
[90] HC Soltan and K Clearwater, "Dermatoglyphics in Translocation Down's Syndrome," *American Journal of Human Genetics*, 17:6 (November 1965), 476. The different genetical compositions in these two types of Down's was anticipated because some deletion of chromosome material generally occurred as a result of translocations.
[91] See: K Patau, et al, "Multiple congenital anomaly caused by an extra autosome," *Lancet* 1 (1960), 790-3; K Patau, et al, "Trisomy for Chromosome 18 in man," *Chromosoma*, 12 (1961), 280-5; DW Smith, et al, "A new autosomal trisomy syndrome: multiple congenital anomalies caused by an extra chromosome," *Journal of Pediatrics*, 57 (1960), 338-45; DW Smith, et al, "Autosomal trisomy syndromes," *Lancet*, 2 (1961), 211-2.
[92] Irene Uchida, Klaus Patau and David Smith, "Dermal Patterns of 18 and D1 Trisomics," *American Journal of Human Genetics*, 14 (1962), 345-52. This research was first presented in 1961, Uchida cited it as: IA Uchida, K Patau and DW Smith, Presented at thirty-first annual meeting of Society for Pediatric Research, Atlantic City, New Jersey, May 4-5, 1961.
[93] Uchida et al, "Dermal Patterns of 18 and D1 Trisomics," 345, 351-2.
[94] PA Jacobs et al, "Evidence for the Existence of the Human "Super Female"," *Lancet*, 2 (1959), 423.
[95] Irene Uchida and JM Bowman, "XXX 18-Trisomy," *Lancet*, 2 (November 11, 1961), 1094; Irene Uchida et al, "A case of double trisomy: Trisomy No. 18 and triplo-X," *The Journal of Pediatrics*, 60:4 (1962), 498-502.
[96] Irene Uchida et al, "The 18-Trisomy Syndrome," *New England Journal of Medicine*, 266:23 (June 7, 1962), 1200, 1201.
[97] F Sergovich et al, "The D Trisomy Syndrome: A Case Report with a Description of Ocular Pathology," *Canadian Medical Association Journal* 89:4 (July 27, 1963), 151.
[98] PE Conen et al, "Multiple Developmental Anomalies and Trisomy of a 13-15 Group Chromosome ('D' Syndrome)," *Canadian Medical Association Journal*, 87 (Sept 29, 1962), 710
[99] Bayzar Erkman et al, "D/D translocation "D" syndrome," *The Journal of Pediatrics*, 67:2 (August 1965), 270, 281.
[100] "The dermatoglyphic findings were characteristic in only two of the six cases from this series with suitable prints." In this article, the authors thanked both Uchida and Thompson for performing the dermatoglyphic analysis: PE Conen et al, "The "D" Syndrome: Report of 4 Trisomic and 1 D/D Translocation Case," *American Journal of the Diseases of Children*, 111 (March 1966), 246. Uchida and Thompson were also thanked for such assistance in: Bayzar Erkman et al, "D/D translocation "D" syndrome," *The Journal of Pediatrics*, 67:2 (August 1965), 281
[101] PE Conen and B Erkman, "Frequency and Occurrence of Chromosomal Syndromes. I. D-Trisomy," *American Journal of Human Genetics*, 18:4 (July 1966), 374; PE Conen and B Erkman, "Frequency and Occurrence of Chromosomal Syndromes. II. E-Trisomy," *American Journal of Human Genetics*, 18:4 (July 1966), 374, 389-98.
[102] Conen and Erkman, "Frequency and Occurrence of Chromosomal Syndromes. II.," 387; Conen and Erkman, "Frequency and Occurrence of Chromosomal Syndromes. I.," 376. The London workers produced only one report on these syndromes.
[103] In their report in a D syndrome case, the London workers noted that "Defective development of the brain and the heart occur frequently in the three major conditions caused by autosomal trisomy." F Sergovich et al, "The D Trisomy Syndrome," 157.
[104] Murray Barr, A New Aspect of Genetics and its Bearing on Mental Retardation, a public lecture given at the University of Saskatchewan. December 9, 1965 (University of Saskatchewan, 1966), 19, emphasis in original. See also: FR Sergovich, "Cytogenetic Practice in a Mental Retardation Clinic," *Canadian Psychiatric Association Journal*, 12 (1967), 35-52.
[105] Andrew Chen et al, "Chromosome Studies in Full-term, low-birth-weight, mentally retarded patients," *The Journal of Pediatrics*, 76:3 (March 1970), 393; Andrew Chen, "Chromosome Studies in Full-Term

Low Birth Weight Mental Retardates," University of Western Ontario, Ph.D. thesis, 1968; Chen was supervised by Sergovich.

[106] David Carr, "Chromosome Studies in Spontaneous Abortions," University of Western Ontario, Ph.D. Thesis, 1965. Carr was an MD who got his Ph.D. under Barr's supervision and became a close colleague. See also: David Carr, "Chromosome Studies as a cause of spontaneous abortion," *American Journal of Obstetrics and Gynecology*, 97:3 (February 1, 1967), 283-93; David Carr, "Chromosome Abnormalities in Spontaneous Abortuses," in George A Jervis, ed., *Mental Retardation: A Symposium*, (Illinois: Charles C Thomas, 1967), Chapter 3; DH Carr, "Chromosome studies in selected spontaneous abortions: 1. Conception after oral contraceptives," *Canadian Medical Association Journal*, 103:4 (August 15, 19, 1970), 343-8.

[107] David H Carr, "Chromosome Studies in Abortuses and Stillborn Infants," *The Lancet*, 2 (September 21, 1963), 603, 605.

[108] David Carr, "Chromosome Studies in Spontaneous Abortions," Ph.D. Thesis, xi.

[109] Uchida and Soltan, "Evaluation of Dermatoglyphics," 419.

Chapter 4

Making Medical Cytogenetics in the 1960s: Making the Sex Chromosome Anomalies

Introduction

Autosome anomalies were not made in isolation. Though informed by their own peculiar logic, their production was reliant, also, on the concurrent production of the sex chromosome anomalies. It was only through the complementary generation of *both* of these disease categories, that the allocation of syndromes could be rendered coherent. Where severity was the organizing principle for the autosome anomalies, sex – specifically, gendered readings of sexual pathology – was the organizing principle for the sex chromosome anomalies. Where the Mongol was the analogy for the autosome anomalies, the intersex served a parallel purpose for the sex chromosome anomalies.

The London workers were consequently deeply involved. Research on the sex chromosomes followed 'logically' from research with sex chromatin and intersexes. Existing metaphors and institutional commitments in the science and clinical practice of sex anomalies shaped the new evidence so that the system retained internal and cultural coherence. Sex chromosome anomalies were integrated into frameworks for managing the 'congenital errors of sex' of the 1950s. Syndromes of sex chromosome anomaly were

forged in relation to older narratives of sex-making, though in slightly modified form. Researchers searched for signs of 'intersexuality' in psyches and bodies; they expected to find gonadal pathology, in conformity with their understanding of gonads as the physiological seat of sex, and wondered at the sexual identities of these ambiguously sexed persons.[1] In the process, the gendered metaphor of sex that was written into the terminology of the 'sex chromosomes,' and the separation of the sex chromosomes from the autosomes implied by this terminology, was consolidated through the making of sexualized syndromes of sex chromosome anomaly.

The sex chromosome anomalies – being read as less severe and more sexual – were subject to more intensive scrutiny. Such scrutiny revealed varied physical, mental and behavioral anomalies in association with particular sex chromosome constitutions – not all clinical signs were constant. More problematic, however, were those anomalies of sex chromosomes which did not reference known clinical syndromes. These phenomena were assumed to constitute disease – the power of chromosomes to define conditions was uncontested. Moreover, they were presumed to constitute diseases marked by sexual pathology. Disturbingly, however, clinical sequelae were not so predictable and depended, to a remarkable extent, on the kinds of research pursued – whether in hospitals, infertility clinics or institutions for the mentally retarded. The syndromes that were defined by these extraordinary chromosome anomalies, then, often lacked coherent or consistent symptom complexes. New research strategies were needed to make sense of such evidence – notably, study of unbiased populations. Struggling to makes sense of these new diseases, workers in Toronto and London, with their international colleagues,

produced these chromosome constitutions as risk-based diseases – defined as diseases by chromosome constitution, but defined clinically only by the risk of a diverse array of pathological outcomes.

Since the First World War, the sex chromosomes have been seen to make sex.[2] That a 'male' XY sex chromosome complex made a male and a 'female' XX sex chromosome complex made a female was, and is, definitional. But some of the details in the mechanics of sex making were malleable. In the 1950s, and again in the 1960s, the story about the genetic making of sex sat at the apex of Barr's model of sex making. But in the 1950s, the capacity of the genes was directed to making sex-specific gonads through a genetic balancing act, and the model of genetic sex-making presupposed an 'inert' Y, though this was rarely mentioned.[3] Instead, researchers seemed to revel in the masculinist narrative of the hormonal Adam principle, where the testicles made the man. In 1959 and thereafter, though the hormonal narrative remained, a new story of male action was added: the Y chromosome now assumed the role of "male-determining potency."[4] As an appropriately gendered tale, this story was henceforth never silent.

A new distinction of agency could be drawn between the 'X' and 'Y' chromosomes. With the 'Y' now clearly 'potent,' the 'X' could be rendered as its gendered opposite, with a reduced capacity to 'determine' sex: a 'Y' could make a man, but an 'X' alone couldn't really make a woman. There was now a new technology of 'true sex,' and the hormonal Adam principle was supplemented by a chromosomal Adam principle in which the Y played the leading role.[5] As Toronto researchers, Margaret

Thompson and her husband James put it in their popular 1966 textbook, *Genetics in Medicine*, "The fundamental rule governing the phenotype of all persons with uncomplicated anomalies of the sex chromosomes is: if a Y chromosome is present, the phenotype is male; if no Y chromosome is present, the phenotype is female. These "males" and "females" may not be normal in all respects, but assignment to the correct sex usually presents no problems."[6] The sex chromosomes sat at the causal apex, defining both sex and sex error.

Re-Making the Old: Reproducing Intersex Syndromes as Sex Chromosome Anomalies

When Barr and his colleagues had applied the sex chromatin test to the 'congenital errors of sex development' in the 1950s, they engaged with and re-interpreted two pre-existing syndromes – Klinefelter's and Turner's. After 1959 these syndromes were again re-defined in the face of both clinical definitions and the now seemingly definitive evidence of the chromosomes. The re-definitions proposed in the 1950s under the influence of the sex chromatin would be re-made in the era of medical cytogenetics.

Turner's Syndrome

In 1959, when researchers in England bore witness to the presence of a single X chromosome constitution in Turner's Syndrome cases, the sex chromatin evidence was re-interpreted. Instead of an XY the sex chromatin could now be understood to reference

a single X.[7] But this re-interpretation of Turner's syndrome was soon complicated by discovery of a multitude of chromosomal variations on the one hand, and a multitude of syndrome variations on the other. Pat Conen in Toronto and Murray Barr and his students and colleagues in London, Ontario participated in the era of discovery and interpretation.

At the Hospital for Sick Children in Toronto, the diagnostic protocol of chromosome analysis was organized to investigate the twin phenomena of congenital defect and intersexuality. This meant that the concept of 'intersexuality' served as an *a Ipriori* framework for analyzing the sex chromosome anomalies. It also meant that many extraordinary bodies were read in relation to syndromes like Turner's that would not, on the basis of clinical evidence alone, have been brought into definitional relation with the syndrome.

Conen and colleagues at HSC published papers on some of the variations that came to their attention in this manner. There was for example, the "intersex" child with an X/XX mosaicism with a primarily male phenotype. This was considered to be an unusual phenotype for what was generally a Turner's syndrome-type chromosomal complex.[8] Two infants were reported with the typical X chromosome constitution, but an atypical form of heart anomaly, which proved fatal; one of these infants had a nearly normal ovary.[9] Many clinical variations of Turner's syndrome were possible, Conen commented in a *Canadian Medical Association Journal* editorial: some women with the X complex might have "histologically normal ovaries," and one woman was reportedly fertile.[10] It was also apparent that many cases of Turner's syndrome were "a mixture of different chromosome abnormalities presenting a similar clinical picture."[11]

Barr and his co-workers in London also came into contact with unusual examples of Turner's syndrome through referral for cytogenetic analysis. Discussing the case of a woman clinically diagnosed as Turner's syndrome and then discovered to have the chromosomal constitution of an X/XX/XXX mosaicism, David Carr and his co-authors assessed the clinical picture for evidence of the anomaly. They reported minimal dysfunction in the "non-sexual sphere" – short stature and "normal intelligence."[12] On the other hand, this young woman possessed poorly developed breasts, little growth of pubic and axillary hair and some degree of "gonadal" dysfunction. The psychological assessment noted "indications of psychosexual immaturity and a lacking in expression of the normal amount of adult feminine drive, feelings and fantasies. In some ways her fantasy life was like that of the preadolescent girl, one who was focusing on academic achievement, intellectual growth and development but showing little interest in interpersonal and heterosexual social situations." Despite these limitations, the patient, who had been married for 8 months at the time of her physical exam, "reported satisfactory marital relations." [13]

The pathology in question for this young woman was clearly sexual, both physically and psychologically. Indeed the sense that Turner's syndrome was the consequence of a sex reversal, as 1950s sex chromatin evidence had suggested, was partially sustained by 1960s chromosomal research. Barr early referred to the sex chromosome constitution of X as "neither male nor female, but incomplete."[14] The women affected by this syndrome continued to be designated as cases of "gonadal dysgenesis."[15] Pat Conen his Sick Kids colleague used the pronoun "it" to describe an

infant with Turner's syndrome who had died, even as they described the infant's seemingly normal ovaries and uterus.[16]

In the 1950s, the Adam principle had made sense of the sexual inversion that was Turner's syndrome. In the 1960s, the hormonal Adam principle was supplemented by a chromosomal narrative and Turner's syndrome was still seen as evidence of an almost male: "absence of a Y chromosome leads to failure of the testis to develop and differentiation of the XO [or X] zygote is along female lines," David Carr noted.[17] But Carr added a crucial caveat to this developmental summary: the person would be phenotypically female, only "if it survives." The association between Turner's syndrome and physical anomalies had been noted and discussed by Barr and his colleagues in the 1950s, but after 1959 the association of Turner's syndrome with physical defect was amplified both through the theoretical association of chromosomal anomaly with genetic disease, and through research practices which brought new bodies into relation with the syndrome through chromosomal findings rather than clinical symptoms.

In the early 1960s, David Carr had obtained the cooperation of physicians and hospitals in London to gather and culture specimens of spontaneous abortuses, subjecting a new population of 'patients' to systematic chromosomal review.[18] This research, which considered the association between chromosomal abnormality and pre-natal lethality, included the observation of a high incidence of X monosomy among abortuses, and expanded on the association between Turner's syndrome and physical anomaly. "That the XO [X] condition might be lethal on occasions is not unexpected," Carr wrote,

"considering the multiple congenital anomalies often found in subjects with this chromosome constitution."[19]

The potential lethality of the X chromosome constitution associated it with genetic disease; it was an aspect of the condition that was not about sex, consequently non-"sex" genes must be at fault: "It is probably genes on the X or Y that are unrelated to sex determination," Barr wrote, "whose absence is generally inimical to embryonic survival."[20] There were, then, two categories of error operating within this one syndrome whose distinction was theoretically and practically significant: the sexual on the one hand, and the "deficiency of genes operating in the non-sexual sphere" on the other.[21]

Just as the chromosomal errors were compartmentalized into two types – sex chromosome and autosome – making sense of particular sex chromosome anomalies meant conceiving of their associated anomalies as of two types – sexual and 'other.' In the case of Turner's syndrome this bifurcation was literal: the syndrome of gonadal dysgenesis was split in two. On the one hand was the typical variety, defined by the presence of 'other' anomalies and by an X constitution, [22] on the other was the rare 'pure' gonadal dysgenesis in which gonadal anomaly was the only clinical symptom.[23]

The first case of pure gonadal dysgenesis was reported in 1959. British workers "found a normal male chromosome complement 46, XY in a 19-year-old woman with primary amenorrhea." According to Barr and his co-authors, "They called this disorder pure gonadal dysgenesis because of the absence of other developmental anomalies."[24]

The anomaly was purely sexual – intersexual – and involved none of the anomalies that accompanied an abnormal chromosome complement such as the single X.

In 1967, Barr and co-authors published a report on a case of "pure gonadal dysgenesis." This case was made notable by its presence in a family where another sibling was affected with male pseudohermaphroditism.[25] The first case in this family had come to Barr's attention in the mid-1950s. A young woman of 16 was referred because of signs of "masculinization." This case was interpreted as a classic instance of male pseudohermaphroditism. At birth, physicians had removed an "enlarged clitoris;" at 16, when the young woman failed to menstruate, experienced deepening of the voice and the growth of excess facial hair, doctors had diagnosed her condition with the aid of Barr's sex chromatin test and begun her on estrogen therapy. Two years later, readmitted to hospital because of "increasing masculine build and hirsutism," laparotomy was performed to remove her undescended testes; this operation also established the presence of a normal uterus and tubes. At 16 the psychiatrist had expressed some concern about her adjustment, stating: "prefers masculine types of games and hobbies as well as a masculine type of literature. No desire for children, likes to wear dresses, but without frills..." But at 22, Barr and his colleagues were able to report that "Signs of masculinization, aside from deepening of the voice, had almost disappeared and the result was an attractive young woman who had been married for 2 years. Psychosexual attitudes were clearly feminine."[26] At that time chromosome analysis confirmed the earlier interpretation of her negative sex chromatin status as an XY sex chromosome constitution.

This young woman had an older sister whose complaint to physicians concerned the absence of menses and failure of breast development. Hormone therapy at age 16 had caused "slight vaginal bleeding and moderate development of the breasts." At 25 years, a buccal smear was sex chromatin negative and this, together with the evidence from her sister, was taken to suggest that she was also a male pseudohermaphrodite. But four years later, this presumptive diagnosis was overturned. Because of the risk of malignancy from undescended testes, an operation was undertaken to remove them, but upon opening her abdomen surgeons were surprised to discover "no evidence of testes. However, in the ovarian position there were whitish streaks...exactly like those seen in typical gonadal dysgenesis or Turner's syndrome."[27] Chromosome analysis then demonstrated a normal male chromosomal pattern. No ordinary male pseudohermaphrodite, this woman was an example of "pure gonadal dysgenesis."

The 1967 article by Barr and his colleagues was written to support the taxonomy which distinguished the pure and impure forms of gonadal dysgenesis. It was intended to suggest a genetic association between male pseudohermaphroditism and pure gonadal dysgenesis: the familial relationship between these two conditions, and the unusual presence in the male pseudohermaphrodite sister of uterus and tubes, were presented as supporting existing evidence of such an association. With the aid of Hubert Soltan, Barr presented a pedigree, performed dermatoglyphic analysis, and theorized about common inheritance – elaborating on the relevance of human genetics for interpreting sex errors.

But even as this paper presented itself in light of new genetic and cytogenetic findings, it fit an earlier endocrinological pattern which had been established in the

1950's studies of hermaphrodites. The story told about the anomalies mirrored almost exactly one told over a decade before: "Patients with XY gonadal dysgenesis," Barr and his co-authors wrote, "are apparently the natural equivalent of Jost's experiments occurring in man." Again they argued, "these patients are genetic males and ... they presumably suffer a spontaneous intrauterine castration early in embryonic development..."[28]

More than ten years after the Johns Hopkins team, with Barr's assistance, had defined Turner's as a case of embryonic castration of the 'truly male,' Barr and his colleagues had found a case that was taken to chromosomally confirm that contention. Even as Barr and his co-workers adopted the tools and approaches of cytogenetics, the older hormonal Adam principle remained viable, and the story of the 'potent Y' could be suspended when, as in this case, it manifestly failed the test. Moreover, even as Barr and his colleagues turned their attention to sex chromosomes, they retained their interest in the 'true sex' project of managing intersexuality.[29] In accordance with this true sex project, both women were recorded on the pedigree chart with the symbol for a male.

Oddly, researchers like Barr had not chosen to define the XY cases of gonadal dysgenesis entirely out of association with a Turner's syndrome that was increasingly understood as defined by a sex chromosome anomaly. Such a re-definition would certainly have reflected the primacy granted to chromosomes in defining syndromes. Of course, the terms gonadal dysgenesis and Turner's existed in some tension in relation to each other. They were often, but not always, used interchangeably. Barr's use of the term gonadal dysgenesis reflected greater attention to sexual anomalies while he reserved the

term Turner's for a broader range of defect. Nonetheless, gonadal dysgenesis and Turner's syndrome were associated, and naming a clinical condition of intersexuality the pure version of a larger chromosomal syndrome, located sex at its ontological center. Such a naming reflected and sustained belief in the association of sex errors with sex chromosome errors.

Klinefelter's Syndrome

The story of the re-making of Klinefelter's syndrome in the 1960s is in many ways quite similar to that of Turner's. Like Turner's, Klinefelter's was a syndrome that was clinically established before chromosome explanations were introduced. In 1942, Harry Klinefelter had published an analysis of the clinical symptom complex which soon came to bear his name. When, in the mid-1950s, Barr's sex chromatin tool was applied to these symptomatically defined men it assessed approximately 2/3rds of them as chromatin-positive, and thus as chromosomal 'sex reversals.'[30] With direct chromosome analysis, after 1959, the chromatin positive cases were re-read as possessing the chromosome constitution XXY. As was the case with Turner's, there was soon a proliferating array of chromosome constitutions to be interrogated for their relationship to Klinefelter's syndrome. Also as had been the case with Turner's syndrome, researchers were aware of clinically defined cases of Klinefelter which did not demonstrate sex chromosome anomalies. In these varied cases, researchers assessed the complex of symptoms apparent in the extraordinary bodies under analysis, considering the two sides

of sex chromosome anomaly – the nature and extent of the defect, and the sexual anomaly.

In the 1960s, the Klinefelter phenomenon continued to be saturated with the gendered metaphors of sexual inversion that had been generated in the 1950s. At the Hospital for Sick Children in Toronto, where Patrick Conen used chromosome analysis as part of a diagnostic protocol and in research-inspired surveys, he approached this syndrome first and foremost as an intersexual condition.[31] Barr and his colleagues engaged in a more sustained analysis of Klinefelter cases than Conen, through surveys in institutions for the mentally retarded. But for the London group too the sexual nature of the pathology remained important. Barr consistently identified the XXY complex as "intersexual,"[32] and the bodies of the men bearing these 'intersexual' chromosomes were consistently interrogated for evidence of sex aberration. Certain clinical evidence was therefore expected: there was the testicular atrophy – the failure in the seat of maleness which was an expected sequelae of sex chromosome aberration; the presence of 'eunuchoid' signs, by which Barr and his colleagues meant 'feminine' distribution of body hair, light build, occasional breast growth, a high pitched voice; there might also be an intersexual psychological identity. One "mentally defective" male patient with Klinefelter's syndrome was reported to have a "self-concept [that] shows many indications of being an asexual one and reflects the preidentification need for a nurturant figure. There seems to be no established internal identity with either sex although, in his role-playing activities, he is descriptively masculine..."[33]

Though Barr acknowledged the "highly variable" nature of the clinical symptoms in Klinefelter subjects, he expected these bodies to be "intersexual" and expressed surprise at the "masculine and mesomorphic development" of one XXY man.[34] This expectation of an intersexual body in the presence of an intersexual chromosome complex ordered research questions. Barr and his colleagues indicated their intention to undertake chromosomal studies on this overly masculine patient to confirm that he bore the XXY complement, but found nothing unusual.[35] In one case, however, the determination to attach sexual pathology to the intersexual sex chromosome complex was productive of research results. This case of a "normal male, aside from the unusual sex chromatin pattern and mental deficiency" had early been reported upon.[36] The masculinity of this man was stressed: he had "a normal male habitus," there was "no gynecomastia. Growth of facial hair was normal and the pubic hair had a masculine distribution. The penis was normally developed and the testes were of normal size."[37] Reporting on this case in her 1958 Master's thesis, Evelyn Shaver had noted that "the patient presented unusual findings – normal testes but chromatin-positive nuclei and a percentage of cells with two sex chromatin masses. This case," she added, "has no relationship to Klinefelter's syndrome..." It was "a different form of sex reversal."[38]

Barr had originally agreed that this was not a case of Klinefelter's, but his twin conviction that the XXY chromosome constitution defined the Klinefelter's syndrome, and that this syndrome involved symptoms of sex anomaly, encouraged him to investigate further and he soon theorized that this must be a mosaic case. Mosaicism was always a possibility in any chromosome anomaly, but finding it required a determined

search. Because Barr saw Klinefelter's as a sexual anomaly, he and his co-workers conducted such a search and were able to demonstrate the presence of two cell lines in this man, one containing the normal XY and the other the abnormal XXXY. "So one can only infer," the authors wrote, "that there were sufficient XY cells in the testes generally, or in some especially important cellular component of the testes, so that the tubules contained adequate numbers of germ cells and the seminiferous epithelium responded normally to gonadotrophins during puberty."[39] Because of his cellular mosaicism, "the patient escaped the Klinefelter's syndrome," by which Barr meant the intersexual physique. But, he added, the patient did not escape "the mental deficiency that is frequently a part of the syndrome."[40]

When Barr first became interested in the Klinefelter syndrome in 1955 it was through the surprise discovery that these apparent men had 'female' sex chromatin. He wrote to the doctor in Italy who first provided him with skin biopsies from these cases that this finding was potentially of "far-reaching significance in the theoretical aspects of sex differentiation and might possibly be of some importance in the study of sterility in males."[41] While this prediction was not untrue, it was notable for failing to mention the relevance of this syndrome for intellectual disability. But this was no oversight – in 1955 this link was not obvious. It was not until the second half of the 1950s that Barr began to address the association between mental deficiency and sex anomalies. As a neurocytologist, with an interest in the functioning of the brain, this work had followed logically on research with the sex chromatin in relation to mental illness.[42]

"It has long been recognized," Murray Barr wrote in his application for a research grant in the fall of 1956, "that mental deficiency is much more common in persons with congenital gonadal defects than in the general population." [43] In researching the association between sex defects and mental defects, Barr initially focused on the archetypal mental defective – the Mongoloid.[44] But in testing the "control" populations of non-Mongoloid mental defectives, Barr's student found an unexpected "sex reversal" in the non-Mongol population which "prompted a mass survey of mental defectives."[45]

Survey research – which was effective in identifying the range of chromosome aberrations possible in the human animal – was one of the key ways of organizing cytogenetic research in the 1960s. It was made possible by technologies which could be rapidly and easily applied to large groups of people. By the latter half of the 1950s, as researchers like Barr developed easier methods for sex chromatin detection such as the buccal smear, and as workers overcame their initial difficulties with the technique and became comfortable with the analysis of sex chromatin, survey research using the sex chromatin had become viable.[46] Barr and his students started to conduct surveys using the sex chromatin in institutions for the mentally retarded in Ontario at this time. Barr utilized the network of Ontario Hospital Schools, promoted the sex chromatin as a standard part of the diagnostic protocol at the Children's Psychiatric Research Institute (CPRI), and conducted at least one survey in an institution for the mentally ill.[47]

Before 1959, surveys using the sex chromatin were productive in identifying a higher than anticipated incidence of Klinefelter's syndrome among inmates of institutions

for the intellectually disabled.[48] This research also discovered some even more anomalous sex chromatin cases – for example, cases in both males and females where the sex chromatin was doubled in many cells. After 1959, when the sex chromatin was re-read as a marker of chromosome variants, survey research using this technique was productive in the analysis of sex chromosome anomalies.

Institutions for the mentally retarded, where much of this survey research was conducted, were well structured to facilitate these scientific fishing expeditions. Not only did researchers have access to large numbers of inmates, they were able to follow-up any interesting findings years later with relative ease, performing batteries of tests on the relevant individuals. In facilitating survey research, these institutions also structured research findings by certifying the clinical fact of mental retardation through the social organization of institutionalization. The syndrome-making process which used data from institutions for the mentally retarded thus emphasized the presence of mental retardation as a direct or risk effect, and located the chromosome anomaly as *the* cause of the syndrome.

Barr argued in 1959 that his survey in two of the Ontario Hospital Schools was intended to "search for subjects with the Klinefelter syndrome, using the oral smear sex chromatin test."[49] He reported that of the "1,506 male defectives" tested, 14 had a "positive sex chromatin pattern," and 13 of these fit the clinical profile of Klinefelter syndrome. This clinical diagnosis could then be used to provide a causal explanation for mental retardation – removing most of these men from the "undifferentiated category" of

mental retardation.[50] This in turn suggested that "the Klinefelter syndrome occurs with a significantly higher frequency among recognized defectives, as compared with the general male population." [51] Indeed, such a survey provided evidence, Barr argued, that chromosomal aneuploidy was "a significant factor in some forms of mental deficiency."[52]

Disciplinary logic demanded that cytogeneticists pay little attention to those Klinefelter men without chromosome anomalies; it was logical then for these workers to define the syndrome through its associated chromosome anomalies.[53] Thompson and Thompson in their textbook presented Klinefelter's and the XXY (and variations on that theme) as synonymous, commenting that "A condition resembling XXY Klinefelter's syndrome in its signs and symptoms may occur in chromatin negative individuals. There are no satisfactory descriptive appellations for this condition, which is usually referred to as *chromatin negative Klinefelter syndrome*, as opposed to chromatin-positive Klinefelter syndrome."[54]

Barr was in good company, then, in his use of the sex chromatin as a diagnostic tool, even though this meant that he would not find all cases of Klinefelter syndrome, but only the subset with positive sex chromatin.[55] Moreover, the clinical diagnosis of Klinefelter was made only after these 14 men with sex chromatin anomalies were identified. Nonetheless the finding of sex chromatin positive men with clinical signs of Klinefelter syndrome and mental retardation was taken to provide a causal explanation for mental retardation. This approach to investigating Klinefelter syndrome supported the interpretation of the chromosomal anomalies as themselves creating the symptomatic effects. The notion that Klinefelter syndrome was caused by a chromosome anomaly, and

the association of the syndrome with the symptom of mental deficiency, were unquestioned effects of the structure of this survey research.

In the early publications using the data from his inmate surveys, Barr had simply added the chromosomal interpretation as a gloss to his chromatin evidence. In instances of single sex chromatin, Barr suggested that these were XXY males. In the few cases of doubled sex chromatin, Barr suggested a more complicated anomaly (XXXXYY was his first guess). As these and other men were subjected to full chromosome review, these guesses were clarified and the kinds of chromosome variants seen to cause Klinefelter proliferated. Upon further review, one case from an original 14 subjects was demonstrated to have an XXXY chromosome complex; another three were found to have an XXYY chromosome constitution; meanwhile the XXXXY constitution was discovered in one child seen at CPRI and another at a hospital.[56]

By 1960 the clinical definition of the Klinefelter's syndrome had become quite loose: "the presence of small testes after puberty" became the sole clinical marker of the syndrome.[57] Such a permissive clinical definition meant that there was no basis for excluding chromosomal variants from the syndrome. Barr made his most concerted effort to construe a distinct syndrome in relation to the XXXXY sex chromosome anomaly. He argued in these cases for "the triad of marked mental retardation, skeletal anomalies and hypogenitalism," but found through a counter-example that this symptom complex did not define the XXXXY genotype exclusively.[58] Chromosomal variants might lead to more severe congenital and mental defects, but they did not constitute distinct

syndromes.[59] This variability prompted Barr and his colleagues to argue that "the basic requirement in the cytogenetics of the [Klinefelter] syndrome appears to be the presence of at least two X chromosomes in combination with at least one Y chromosome."[60]

All of the cases of Klinefelter's syndrome discovered by Barr and his colleagues in their survey research demonstrated mental deficiency by virtue of the process of their discovery. But Barr did recognize some of the biases of his research. He noted that studies in infertility clinics, where many of these patients were diagnosed, put the proportion of Klinefelter's men with mental retardation at about 25%,[61] and in one article he argued against undue emphasis on the "mental retardation aspect of the syndrome ... since some patients are encountered who are successful in exacting occupations."[62] Indeed, Barr argued that "abnormalities of the sex chromosome complex are less likely to have a serious effect on maturation of the intellect than are abnormalities of the autosomes".[63]

At the Hospital for Sick Children too, the structure of Pat Conen's research meant that Klinefelter's was not necessarily attached to mental retardation. Conen was not concerned specifically with Klinefelter's but rather with chromosome anomalies of various kinds. Like Barr then, his work necessarily confirmed the chromosomal basis of this condition.[64] However, unlike Barr, the use of chromosome analysis in research-inspired surveys, or as part of a diagnostic protocol in a hospital, discovered different clinical effects. Reporting on the surprise association between various chromosome

anomalies and syndactyly, Conen noted that his Klinefelter case was reported to have an IQ of 123.[65]

The survey research in institutions for the mentally retarded, together with evidence from the infertility clinic and the children's hospital, meant that mental retardation was understood as a variable component of the Klinefelter syndrome. Behavioral research, cited by Barr, also suggested an increased likelihood of other psychological ailments such as "epilepsy, psychoneurosis and psychosis." [66] Indeed, faith in these potential behavioral sequelae encouraged a probation officer to contact Barr in the fall of 1964 about a young man, "placed on Probation by a London court following his conviction on a charge of false pretences which involved uttering cheques in the amount of approximately $37.00." Officials had learned of the young man's Klinefelter's syndrome through the preparation of a pre-sentence report. Concerned at this fellow's "native shrewdness and cunning" and arguing that his "continuing compulsive behaviour will, we feel, inevitably result in his incarceration," they wrote to Barr seeking assistance. Barr responded quickly. He was familiar with the case, having been responsible for establishing the presence of the "chromosome abnormality that is responsible for Klinefelter's syndrome" in 1962. But while noting that it was "a well established fact that men with Klinefelter's syndrome are more prone than others to various psychiatric and behavioural aberrations such as you describe in this individual," he could offer no assistance.[67] Pathologies of the psyche might not always be present, but increasingly they were the risk effects of this sex chromosome anomaly. This would prove to be especially apparent with the 'new' sex chromosome anomalies.

Making New Sex Syndromes: Producing Sex Chromosome Anomalies

"Four main types of numerical error of the sex chromosomes are now known," Barr and his co-authors reported in a 1969 review. "Two of them result in clinical syndromes that had been delineated well before the advent of human cytogenetics. These are the XO [X] error that is the principal cause of Turner's syndrome in the female and the XXY abnormality (or others in which there are at least two X's and at least one Y) that causes Klinefelter syndrome in the male. The remaining types of numerical error are difficult to deal with," Barr added, "because adverse effects on development may be minimal or absent and because they are variable from one individual to another when they do occur." These two other types were the poly-X female and the poly-Y male chromosome complexes.[68]

With the syndromes of Turner's and Klinefelter's, researchers had assessed the workings of the aberrant chromosomes in relation to existing clinical interpretation: Turner's syndrome presented a well-defined symptom complex recognizable in infancy, and Klinefelter's was associated, at a minimum, with small testes after puberty. In cases of poly-X and poly-Y, however, researchers were adhering exclusively to the logic of the chromosomes in interpreting these phenomena. Definitive clinical knowledge was hard to produce, for these chromosome constitutions were seen to be associated with a range of

defects. As had been the case with Klinefelter's, an association with mental deficiency seemed obvious. Also as with Klinefelter's, the structure of the research process made the degree of that association, and the potential behavioral sequelae, difficult to decipher. But quite unlike Klinefelter's and Turner's, the gonads in these bodies failed to demonstrate pathology, leaving researchers without the expected sexual signifier of the sex defect – indeed, without any consistent clinical symptom at all. All of the clinical sequelae – physiological, mental and psychological – were *risk* effects. These new sex chromosome syndromes, then, constituted a distinctive form of "genetic disease" – one defined not by the necessary presence of pathological outcome, but only by the risk of its presence.

Poly-X Females

Females with an excess of X chromosomes were discovered early in the flush of cytogenetic enthusiasm in 1959. Analysis of these women was immediately guided by the metaphor of sex. When the triplo-X female was first "discovered" she was dubbed a "superfemale" by researchers, drawing an analogy back from what seemed to be nature – the heavily anthropomorphised female banana fly with a triplo-X constitution and "exaggerated secondary sex characteristics."[69] When Carr, Barr and Plunkett announced the "discovery" of the tetra-X female (XXXX) in 1961, Pat Conen joked in an editorial that "It must have been tempting to coin the term "super-duper-female"... but apparently conservatism prevailed."[70] AL Chute, chairman of the Department of Pediatrics at HSC noted in 1965 that "Despite her female appearance, she [the triplo-X female] is generally

defective mentally and not at all what an advertising agency would consider a superfemale."[71]

The sex metaphor so richly employed in the naming of this phenomenon extended to the expectation of a physiological sex anomaly. As cases of "sex chromosome anomaly," these bodies were expected to evidence gonadal error. It was in answer to this unspoken hypothesis that Carr, Barr and Plunkett noted that the triplo-X female "is likely to be normal (and fertile), aside from mental retardation," and reported on "a hitherto unreported sex chromosome complex, namely XXXX" in "two mentally defective but otherwise normal females."[72] Indeed, as Barr and Carr noted with surprise, the triple X sex chromosome complex was clearly "compatible with fertility;" the hospital record of one of their subjects indicated that she had had nine pregnancies.[73]

"We have been doing sex chromatin tests for 16 years and chromosome analyses for nine years, at the request of physicians who suspected a sex chromosome abnormality because of certain clinical findings," Barr reported. But the sexually anomalous bodies that were visible in the clinical context had never been diagnostic of the triplo-X error. The absence of gonadal effects in poly-X cases confirmed the view "now generally held," as Barr put it, "that a clearly defined clinical syndrome has not been established."[74]

Despite the apparent absence of a clinically obvious syndrome, particularly one involving a sexual pathology, a range of symptoms were possible. An early and continued association existed with intellectual disability: Barr and Carr argued that, "the [triplo-X] patients were of low normal or definitely subnormal intelligence." But as with Klinefelter's these cases were found disproportionately through surveys of

"institutionalized mental defectives," a bias that the researchers acknowledged.[75] A review of "the triplo-X female" in 1969 by the London team introduced 12 new cases to the international literature; these cases were found through surveys at Ontario Hospital Schools, the London Psychiatric Hospital, and through routine buccal smears of all new patients seen at CPRI.[76] That all had "mental abnormalities" was, the authors noted "to be expected in view of the method of ascertainment."[77] Indeed of the 155 females from various studies reviewed in this paper, 101 had been found through similar survey techniques.

This ascertainment bias was constantly noted, and it served as evidence of the need for "unbiased" surveys.[78] But the fact of these biases was not taken to dispute the associations between mental and physical defect that inmate populations evidenced, it only rendered the degree of the association questionable. Barr and his co-authors explained the association between triplo-X chromosomes and physical defects arguing that "the genetic error renders the bearer more susceptible than chromosomally normal individuals to developmental defects ranging from mild to severe and of great diversity." They suggested that "the addition of an extra X chromosome ... increases the susceptibility to ovarian dysfunction or pathology.... [though] it is clear that the reproductive system functions normally in the majority of these women..." Finally, the authors argued that "There is no question that the error predisposes the individual to mental abnormality; it is the magnitude of the risk that is virtually impossible to estimate."[79]

Even though there was "no triplo-X syndrome in the clinical sense,"[80] then, there was a syndrome which was defined by the existence both of a chromosomal anomaly and by what were perceived to be elevated risks of a wide range and degree of potential defects, with mental defect chief among them.

Poly-Y Males

The sex chromatin referenced the X chromosome and thus made the X a logical and identifiable target for sex chromatin screening and new chromosomal research. Despite its metaphoric significance, then, research devoted to the Y chromosome was slow to begin. In London, early findings of poly-Y males emerged from buccal smear surveys in various institutions in the quest for sex chromatin (and thus X chromosome) anomalies. Thus these men were initially associated with the Klinefelter's syndrome. A man with an XXYY chromosome constitution, found through a survey of the London Psychiatric Hospital, and reported in 1961, was noted to be "mentally defective," tall with small testes and some "eunuchoid traits."[81] Fitting the clinical diagnosis of Klinefelter's syndrome, this man suggested to Carr, Barr and Plunkett that "the basic cytogenetic requirement for the [Klinefelter's] syndrome seems to be the presence of at least two X chromosomes and at least one Y chromosome."[82] Similarly, chromosomal analysis of the sex chromatin positive males found in Barr's survey of Ontario Hospital Schools revealed that 3 of the 14 had an XXYY chromosomal constitution. All three of these men demonstrated the clinical signs of the Klinefelter syndrome. The cases were discussed in

stereotyped ways, as having "intersexual" chromosome complexes, "eunuchoid" traits, mental retardation, and so on.[83]

Yet though merged with Klinefelter's subjects in this early work, Barr and his colleagues hoped to extract meaningful information about the workings of the Y chromosome from these anomalous subjects. In the case of the men found in the Ontario Hospital Schools survey, they pointed to variations in "skeletal maturation or vascular or cutaneous manifestations in the legs, for example, or characteristics of a biochemical or physiological nature that have not yet been investigated." Hubert Soltan and Irene Uchida tried, but failed, to find distinctive dermal patterns that would be diagnostic of the XXYY chromosome constitution and thus provide a screening test of multiple Ys to parallel the Barr test's capacity to detect Xs.[84]

Overall, signs of distinctiveness seemed minimal – suggesting that an additional Y in the presence of multiple Xs had no decipherable effect. Barr and his co-authors concluded that, "the phenotype [in the XXYY cases] does not differ markedly from that resulting from the presence of a single Y chromosome." Without a clinical portrait, full chromosome analysis was necessary to distinguish XXY from XXYY.[85] The absence of a clear set of distinct sexual symptoms troubled the expectation that the potency of the Y in generating maleness might produce extra maleness in a double dose: "it appears that the addition of a Y chromosome to a male XY complex," they wrote, "far from increasing masculinity in the phenotype, introduces a genetic imbalance that is likely to cause varying degrees of hypogenitalism [small genitals]."[86]

The expectation, held by the London workers, that additional Ys should evidence some form of sexual anomaly formed a widely held research hypothesis. In Scotland, Patricia Jacobs and her colleagues soon announced that such an hypothesis could be sustained. But failing to find sexual anomaly in the physiological sphere, they discerned the behavioral proxy of 'aggressivity' among inmates in institutions for the difficult-to-manage.[87] As Margaret Thompson put it in her speech to the Annual Conference of the Canadian Association for Retarded Children in 1967, "the most striking new finding has been that males with an extra Y chromosome (the "male" chromosome), though almost unknown in the general population, are not uncommon among very tall inmates of institutions for criminal psychopaths."[88] From 1965, when Jacobs and her colleagues first published their account, there was a torrent of research and popular speculation which drew associations between the poly-Y "genotype" and gonadal abnormalities, great height, and mental aberrations, including intellectual disability, a propensity to mental illness and "anti-social" behavioral tendencies.[89]

Researchers in London, Toronto and elsewhere in Canada contributed to this work.[90] Fred Sergovich of CPRI confirmed that XYY males were present in the population of mentally ill men in Kingston's Penetanguishene prison for the criminally insane.[91] He reported to the press that one of these men "was convicted in the brutal shooting of a woman." Sergovich was also reported to have identified 4 young people with the XYY chromosome constitution in London. "One boy of 11," the press reported, "has a learning and school problem.... Another, a youth of 18, has a case file "several inches thick," listing his behaviour difficulties." [92] In Toronto, Pat Conen also identified

some XYY cases through diagnostic screening at the hospital.[93] "Two are infants," it was reported. "The third, an eight-year-old boy, while being tested in the laboratory, pushed equipment around and punched his mother."[94] Reports of this work in the press fed popular fascination with medical science, and the growing conviction of the genetic basis of behavior.[95]

This work clearly caught the imagination of researchers and the public since it seemed to demonstrate such a logical fit between the 'hyper-male genotype' and 'hyper-male behavior.' But this was not an aberrant episode in the history of research on the sex chromosomes. Indeed, the dependence on survey research among inmate populations, and all the biases that such work implied, together with the growing purchase of the concept of genetic disease defined solely by risk effects, made sense of Klinefelter's, the poly-X female and the poly-Y male. Moreover, the association between sex chromosome anomalies and behavioral effects was a general finding, relying again on the concept of risk, and also on the attention to the psyche which anomalies involving sex seemed to demand. Speaking on the topic of the poly-Y male, Barr commented that "sex chromosome abnormalities of all kinds predispose the bearer to psychological aberrations and XYY is probably no exception." Barr advocated more research to answer questions about the precise nature of these risk effects. Specifically, he advocated a rather different modality of research than that pursued heretofore – the newborn survey.[96]

The Era of the Newborn Survey

In the latter half of the 1960s, independently, but in concert with international trends, researchers in Toronto and London, Ontario took up the challenge of ascertainment bias by pursuing surveys of 'unselected' newborns, with the intention of long-term follow-up of children born with chromosome anomalies. In this way, researchers believed that they might better assess the range and severity of the defects attached to these chromosome constitutions and thus resolve questions about the risk effects attached to such anomalies.

Alex Bell of the University of Toronto initiated an ambitious research project in 1967. He utilized the survey capacity of the sex chromatin to make initial selections from the thousands of newborns available for full chromosome review in local hospitals.[97] When, after 1970, a comparable survey technology for the Y chromosome became available, it was added to the repertoire. After the initial screen using sex chromatin or the Y-body test, newborns with anomalous readings were then subject to full chromosome review. Also in 1967, in London, a more modestly sized survey was begun. Fred Sergovich and G Howard Valentine performed full chromosome analyses of all infants born in a single hospital in a single year. The use of full chromosome analysis as a survey technology reflected both the limitations of the sex chromatin as a screening tool, and the degree to which chromosome analysis had become routinized.[98]

The two studies differed in their techniques and approaches. Bell's study was focused on X chromosome, and later Y chromosome, anomalies. The full chromosome

analyses conducted in London, by contrast, captured all gross chromosome anomalies. Indeed, Sergovich pointed to the availability of data from sex chromatin testing to justify the need for studies on autosomal and Y-chromosome anomalies.[99] Despite these differences, however, the similarities between these studies were ultimately more important. Both studies sought to provide reliable statistics on the incidence of specific chromosome anomalies and through follow-up, to provide an unbiased developmental narrative about the 'phenotypes' attached to these chromosomal constitutions.[100] Both projects ultimately concentrated their attention on the follow-up of children with sex chromosome anomalies, and did so into the 1980s. And by the mid-1970s, both studies were integrated into an international collaborative effort among nine independent studies which reviewed the effects of sex chromosome anomalies through long-term follow-up.[101]

Initiated with the expectation that chromosome anomalies *did* constitute definable disease entities, these studies struggled heroically to produce coherent symptom complexes out of a diverse array of uncertain risk effects. They did so in accordance with conventional narratives of gender, and in light of what we might term the 'null hypotheses' formulated by original, biased research. Workers presumed, in other words, that the original research had produced valid evidence about pathological sequelae and sought, through assessment of newborns, to better estimate the incidence, and thus the gravity, of these outcomes as risk effects.

Paradoxically, while the newborn studies were deeply influential in the production of culturally and clinically powerful narratives of genetic disease, medical

geneticists were only marginally involved. Alex Bell in Toronto, and Fred Sergovich in London, who initiated the studies, were members of the community of medical geneticists. But Donald Stewart and Howard Valentine, who lead the follow-up studies, were clinicians first and foremost. Reflecting on the difficulties of coordinating the substantial follow-up study in Toronto, Stewart noted that the medical geneticists at the hospital were distinctly uninterested. It was as Director of the Outpatient Department at Sick Kids that Stewart coordinated the project. Psychologists and pediatricians assisted him. Medical geneticists did not.[102] This disinterest reflects the professional identity of medical geneticist as researchers and not clinicians. Though working actively to construct new disease states, medical geneticists were only marginally involved in the enormously complex clinical and social questions that emerged as a consequence of genetic diagnosis. Thus I review these studies only in brief.

The Toronto and London Studies

"Little is known," Bell wrote in seeking funds for his project, "about the mental, physical and psychological development of patients with sex chromosome anomalies." His study was intended to address this limitation "by sex chromatin screening at birth and by chromosome analyses of all those with abnormal sex chromatin patterns....Annual follow-ups will take place to puberty or beyond. These will include studies of mental, physical and psychological development, IQ distributions, morbidity and mortality, dermatoglyphics and X chromosome markers. In addition endocrine studies can be done,

along with investigations of family dynamics, socio-economic factors and clustering in time and space."[103]

The appraisals of Bell's 1966 proposal to the Ontario Mental Health Foundation were generally supportive. Reviewers were particularly interested in the proposed developmental studies of children identified at birth with chromosome abnormalities: "There is certainly a need of a longtitudinal research study such as is proposed here, in order to appreciate the mental and psychological development of individuals with sex chromosome anomalies," wrote one reviewer.[104] Murray Barr was highly supportive. Noting that "our present concept of the effects of sex chromosome abnormalities are inaccurate because of the way in which reported patients were found," Barr argued that "These defects can be made good only by a study such as the one proposed by Dr Bell."[105] As a member of a site visit team in 1971, Barr reviewed the progress of Bell's research again. Once again he indicated his and the team's assessment of the project's value: "Data arising from a prospective study are needed in order to assist in assessment of prognosis in individual patients." They strongly encouraged the Ontario Mental Health Foundation to continue its assistance so that the infants identified through the screening could be followed up ..."[106]

Sergovich and his colleagues also promoted the value of their survey in terms of the potential for follow-up. However, these authors stressed the need for data on non-X chromosome conditions. "It seems clear," Sergovich and his colleagues wrote, "that to have a more solid basis for determining the role of chromosomes in mental retardation or congenital malformation, one must test large numbers of persons with a wide variety of

disorders in a way that will bring to light variations, not only of the X-chromosome number but also of the autosomes and of the Y-chromosome complement."[107] But despite this statement of general interest, the follow-up of cases was selective and only patients with certain sex chromosome anomalies were followed. The interest in the risk effects of sex chromosome anomalies, and the corollary faith that the autosomal anomalies were of clear and uncomplicated consequence, made this approach sensible. Moreover, the coincidental finding of four XYY males made a follow-up study of obvious interest. Noting that the data on XYY males derived from "highly selected populations of neurologically inadequate male criminals, the authors enjoined caution in "accepting the interpretation that XYY is specifically associated with criminal behaviour..." [108] "In no other syndrome," they added, "is the necessity for prospective study more evident than in the XYY genotype." [109] In presenting initial follow-up data, Valentine and his co-authors argued that "A prospective and long-term follow-up of the physical and mental development of XYY males ascertained at birth in an unselected population of newborn infants would best indicate the true significance of this chromosomal anomaly."[110]

While the technology of the newborn survey was expected to provide definitive data of decisive value, generating and managing the evidence proved to be less than entirely straightforward. Bell's sex chromatin study successfully surveyed 72,739 specimens for sex chromatin anomalies and found 72. The later screening of 5395 males for anomalies involving the Y chromosome turned up 5.[111] These results did provide incidence figures, but assessing the meaning of these incidence figures was complicated.

A key problem involved issues of categorization. Bell could readily identify the incidence of what he called "pure" Klinefelter's syndrome (XXY), or "pure" Turner's syndrome (XO), but these incidence figures could be transformed if the XXYY variant and the XY/XXY mosaic was included with Klinefelter's or the XO/XXr variant (Xr identifies a ring X chromosome) and XO/XX mosaic were included with Turner's. A related concern involved assessing the meaning of anomalous incidence findings. On the one hand, the total incidence figures for sex chromosome anomalies in the Toronto population were lower than those which had been expected on the basis of published data. While this had contributed to Bell's reduced sample size it was, his site visit team noted, "in itself an interesting observation."[112] Though accepting this statistical anomaly as evidence of fact, other statistical anomalies were understood as the effects of chance. One anomaly that was apparent at a much higher incidence than expected involved the XX sex chromosome constitution in two male infants. As Bell noted in 1969, "That they should occur at all would appear impossible in view of the widely accepted belief that the Y chromosome is essential for male development."[113] In his Final Report to the National Health Grants Program, Bell summarized four theories to explain this anomaly, all of which sustained the thesis of the Y chromosome's male determining potency.[114] Whatever the reason for the anomaly, Bell argued that "This condition is extremely rare and our finding of two cases in this series is probably due to chance, and is not a reflection of the true incidence.[115]

Sergovich and his colleagues also identified problems with interpreting their incidence figures. "It is difficult to account for the discrepancy between the results

expected from the pooled-data sources and those found empirically," the authors noted. "Most probably," they added, this problem will not be solved until more newborn surveys are forthcoming from a variety of populations and with large numbers of infants since it is quite possible that racial and geographic differences are important determinants of chromosome anomalies."[116] In listing the credible reasons for cytogenetic differences in populations, Sergovich and his colleagues implicitly discredited theories of environmental causation as non-credible. That this was a contingent decision is evidenced by reviewer comments. In assessing the merits of Bell's first proposal, Barr had been impressed by the possibility of using such data to assess whether chromosomal abnormalities were affected by environmental factors such as time of year or socio-economic status. Citing research by a group in Denver who had identified just such factors, Barr noted that "If these observations can be confirmed in other studies, we will have an important break from the idea of "inevitability" of a certain frequency of chromosomal non-disjunction influenced only by maternal age."[117] But Barr's optimistic appraisal of Bell's research was misplaced. Though Bell made reference to the Denver group's findings of seasonal fluctuations in the incidence of chromosome anomalies, his data were inconclusive and he gathered no data on the socio-economic status of the families whose sex chromatin and chromosomes he studied.[118] Sergovich's disinterest in the thesis of environmental causation was even more surprising since his study produced data that could have been taken to suggest an association between chromosomal abnormality and the marital status of the mother. Of the 10 chromosomal abnormalities discovered, 4 of the infants were born to unmarried mothers. But this finding was not

commented upon.[119] For Sergovich and his colleagues, evidence of chromosomal anomaly was sufficient as a statement of cause in the production of pathology.

Deciding what data 'counted' was a complicated process. But generating data could be even more difficult, involving difficult issues of physician and parental disclosure and consent. These dynamics drove the studies in complex ways, until their eventual termination in the 1980s.[120] Moreover, results were never definitive, but only suggestive. Bell's initial findings were unremarkable. In his Final Report to the Ontario Mental Health Foundation he noted that "little or no difference between the various developmental parameters of these very young children as compared to normal, has been noted." In accordance with the implicit assumption that symptoms in sex chromosome anomalies would somehow be related to sex, Bell added, "Since diagnoses of these conditions is usually delayed to late childhood or puberty, this finding is not surprising."[121]

The remaining follow-up of the cases discovered by Bell was pursued by a team at Sick Kids under the leadership of Donald Stewart, the Medical Director of the Outpatient Department. Stewart and his colleagues followed these infants into early adulthood. Their study was the largest of nine newborn studies that had been initiated internationally in the decade after 1965.[122] Their first publication, in 1979, assessed a small number of XXX females and XYY males, and a large sample of XXY males, and suggested that though there might be some changes in physical and intellectual development, "The evidence for increased psychopathology is...unconvincing."[123] Their

final publication in 1990 reported primarily on the XXY males, most of whom were about 20 years old. They argued that "Our overview leads us to conclude that aneuploid 47,XXY boys are unlikely to reach a level of personal and social development that is consistent with their family background." About their small sample of XXX females they argued that "girls with chromosome aneuploidy who come from adequately functioning families may have fewer behavior and social adjustment problems than their male counterparts." Despite these rather unexciting findings, Stewart and his colleagues were certain that the chromosomal aneuploidy in these cases "plays a significant role in their [the patients'] psychosocial characteristics now that they have reached adulthood."[124]

Donald Stewart and his co-authors offered no conclusions about the XYY males, having lost contact with their final sample of one. But in the review done by the Sick Kids psychologist in 1986 of all the data from the 7 relevant international prospective surveys, XYY males were reported to demonstrate no statistically significant intellectual or behavioral problems by comparison with the control populations. But "Fifteen of the 28 ... boys had educational problems compared to five of 9 ... controls." Noting that this finding was not statistically significant, the psychologist wondered aloud at "why they tended to have poor educational histories" given their average intelligence.[125]

Meanwhile, Valentine's follow-up of the 4 cases found through Sergovich's survey, together with two other cases ascertained beyond the parameters of the initial survey, continued until 1982. In the first follow-up report, Valentine and his colleagues reported the absence of physical anomalies, and noted especially that "None of our babies

showed genital abnormalities."[126] In the psychological sphere they reported that 3 of the 4 were "normal in behavior and intellect; they are not aggressive, destructive or hard to manage..."[127] Nonetheless, though the 3 "normal" boys were "exceptionally affable children," the authors cautioned that "It is difficult to know how much long range comfort one can take for this present normal behavior..."[128] Moreover, the fourth child showed "aggressive and undisciplined behavior," "a worrisome lack of warm interpersonal relationships with peers and to some extent with adults," together with "slower than average language and intellectual performance" and so on.[129] Acknowledging that the child, who had been taken into care at the age of 15 months and then been moved through a series of foster homes, might have other reasons for his behavior, the authors suggested that "If one did not know of the XYY chromosome complement in this boy, one would with every justification ascribe his personality defects to an unsatisfactory heredity on his father's side and a most unstable emotional climate for the first two years."[130]

By 1977 this difficult child had been adopted into a more stable family and he was doing much better. Valentine reported that the six children demonstrated no "physical characteristics that constitute a recognized syndrome." Five of the six children demonstrated entirely normal behavior and social interactions, and the sixth who had "exhibited obviously deviant behavior" through his disturbed infancy and placement in different and inadequate foster homes, had "made a remarkable recovery from a bad start. One can only speculate," Valentine added, "whether an XYY chromosome complement may cause such a "psychic vulnerability" that an adverse emotional climate or

environmental stress would result in a deviant behavior that under more favorable circumstances would not become evident. Such, at any rate, seems to be the case for Case 3."[131]

The association between the XYY chromosome complement and anti-social behavior that the inmate studies suggested to researchers was not disproved by these newborn surveys. The disproportionate numbers of men with XYY and to a lesser extent XXY in penal and penal-mental institutions were taken to demonstrate convincingly that such behaviors were a risk effect; the only thing at issue was the degree of risk.[132] In his final published discussion on the six cases he had followed with increasing concern, Valentine was still not able to decipher the risks attached to the XYY "syndrome," but he had concluded that knowledge of such risks was of little value: "One can only say that ... the implications of the XYY chromosome complement remain uncertain. It seems probable that no generalization will be applicable to all cases and that prenatally, at birth, in childhood, and in adult life the implications of the XYY complement will be speculative. Any abnormalities that come to light from continuation of this and other studies will give only an indication of what *might* be a consequence (and a likelihood of that consequence) but not a prediction of what *will* for certain be a consequence of the additional Y chromosome."[133] For Valentine, at any rate, a genetic syndrome defined solely through risk effects was of no clinical value.

But Valentine was tilting at windmills. Though medical geneticists had played only a marginal role in the long-term work of consolidating clinical information about

these syndromes – in Toronto and London, in any event – they had played a decisive role in the 1960s in producing those diseases in the first instance. What was disputed – and is disputed still – was the range and severity of the risk effects. What has not been disputed is the power of the chromosome constitution to define a disease state – a risk based disease – and the salience of gendered metaphors of sexual pathology in their constitution.

In a 1996 summary of the international newborn studies, produced for a clinical audience, there was much that was different in the interpretation of the varied sex chromosome anomalies.[134] The null hypotheses of the 1960s were caricatured as hyperbolic, the severity of potential pathological outcomes was downplayed, and the opportunity for normality was emphasized. Yet, there was also much in this modern account that was old. Gendered metaphors of sexual pathology persisted, even as they were being dismissed. About Klinefelter's men, the authors argued that "the behavior characteristics frequently noted by the research teams included tendencies toward passive and unassertive behavior." Yet, they added that "[t]here is no evidence of increased homosexuality." Moreover, while learning disabilities were evident, "Mental retardation is not associated," with the condition.[135] With respect to the poly Y men, the authors argued that

> Speech delay was noted in approximately half of the boys, and half of the sample needed part time or full time educational intervention. There was no consistent behavioral phenotype. Several investigators reported an increase in temper tantrums and distractibility among boys. [but] Aggression was not frequently observed in children and adolescents.[136]

Despite the uncertain implications of these diseases, their existence remains uncontested. Moreover, their status as risk-based diseases enjoins moral management. Charles Rosenberg, in writing about what he calls protodisease states, such as high cholesterol or blood pressure, notes that, "Whatever one thinks about their ultimate prognostic or clinical significance ... [these conditions] create new emotional agendas." They imply a "'Patient's Progress' of choice and moral self-definition ... [and] a new social role."[137] Similarly, persons affected by risk-based disease, and their parents, must tread carefully. "[M]ost of these individuals with sex chromosome aneuploidy," the authors of the 1996 review article noted, "fall within the normal range in development and ... marked abnormality is not usually seen."[138] "The impact of the environment is particularly significant," the researchers added. In conclusion, the authors pointed to the importance of moral management.

> Our studies have concluded that these individuals adapt less well to environmental adversity (alcoholism, family conflict, economic instability) than do their karyotypically normal siblings. For this reason, a strong and supportive home environment is especially important.[139]

Stories of X and Y

By the time the newborn studies were underway, and certainly by the time they were finished, the sense that sex chromosome anomalies constituted a distinct category seemed self-evident. If, as I have argued, this category was historically contingent, and

emerged through the institutional and conceptual links made between the sex chromosome studies and the 1950s work on intersexuals, it was not long before this contingency was obscured. The initial work of making sex chromosome syndromes proceeded in tandem with research which assessed the meaning and mechanics of the sex chromatin. Such research made theoretical and practical sense of the links between the congenital sex anomalies of the 1950s and the sex chromosome anomalies after 1959, and clarified the manifest distinctiveness of the sex chromosome anomalies.

In the early 1950s Barr had proposed a what I have termed a 'fusion' thesis – that the sex chromatin represented the fused, resting and deeply staining portions of the two X chromosomes in the female and potentially the similarly behaving X and Y chromosomes in the male. By the early 1960s it seemed clear that the sex chromatin represented a single X.[140] This theory was articulated as a 'general rule' which aided in the interpretation of cytogenetic evidence. As James and Margaret Thompson wrote in their textbook, "sex chromatin appears in all persons with two or more X chromosomes and ... *the number of masses of sex chromatin is one less than the number of X's.*"[141] As Barr and his co-authors noted when reporting on two cases with what they interpreted as XXXXY chromosomes "The X chromosome is so similar to autosomes in the 6-12 group that it cannot be distinguished from them with certainty. But," Barr and his co-authors added, "the number of X chromosomes can be inferred from the sex chromatin pattern in interphase nuclei."[142]

The clarification of the meaning of the sex chromatin aided in the production of a theory to explain why it existed. This theory was formally articulated by Mary Lyon in

1961. According to James and Margaret Thompson the Lyon hypothesis was: "1) that the condensed sex chromatin is genetically inactivated, 2) that the inactivated X could be either the paternal or the maternal X in different cells of the same individual and 3) that the inactivation occurs early in embryonic life."[143] For those dealing with the sex chromosome anomalies, the Lyon hypothesis made sense of, and was corroborated by, the tremendous variety of conditions involving multiple X chromosomes. Reviewing the evidence concerning the Triplo-X female in 1969, Barr and his co-authors utilized these cases to illustrate the "suppression of genetic activity of extra X chromosomes."[144] The Lyon hypothesis explained why "The effect of autosomal trisomy is consistently that of abnormal development .... In contrast, trisomy of the large X chromosome has a much less adverse effect on development and some triplo-X females are phenotypically normal."[145]

That anomalies involving X chromosomes might be inherently less severe – through the protective action of Lyonization – was not, I would argue, sufficient to constitute the disease category of sex chromosome anomaly, especially in light of the evident exception to the rule of benignity posed by the single X chromosome constitution, or Turner's syndrome. The category 'sex chromosome anomaly' relied, in addition, upon metaphors of gender and gene action. The historically shifting, but consistently gendered, ways that these stories were told illuminate the depth of meaning invested in the sex chromosomes – a depth of meaning sufficient to render conditions involving such chromosomes as a coherent categories of disease.

The chief interpretive difference in the narratives of X and Y as the 1950s became the 1960s was the re-framing of the Y as 'potent' in the making of maleness. This macho Y was initially unleashed when the chromatin-positive male was re-interpreted from the female with flawed testicles, to the male holding up under the onslaught of excess X chromosomes through the virility of his single Y.[146] Describing two Klinefelter's cases involving the XXXY chromosome constitution, David Carr and his co-authors wrote that, "The male determining property of the Y chromosome is thus emphasized, for in its presence the testes differentiate from the indifferent gonads of the early embryo, when there are either two or three X chromosomes ..."[147]

Klinefelter's evidenced an enduring battle between the sexes – one that males seemed destined by their chromosomes to win. As Barr put it, "It appears ... that the male-determining factors carried by the Y chromosome, together with such male-determiners as there may be on autosomes, almost entirely override the female-determiners on the two X chromosomes."[148] The interpretation of the sex chromatin as one X helped to unleash the Y chromosome – leaving it free to act in the cell. Moreover, the passivity of the X chromosome under the Lyon hypothesis was both compatible with a feminine reading of the X, and served to explain what was understood as the lesser severity of sex chromosome anomalies as distinct from autosome anomalies, and thus to confirm the meta-category of 'sex chromosome anomalies.' Indeed, the X chromosome itself could be read as feminine. Alex Bell, in describing the evidence of the Barr body to a non-specialist audience, wrote that "This body is a single X chromosome which has been inactivated, condensed so that it becomes microscopically visible, and pushed to the

periphery of the nucleus to be carried as excess baggage."[149] Though less disparaging, Barr's repeated referencing of the X chromosome as the "conservative" member of the XY pair – remaining essentially unchanged as the Y chromosome evolved over the millennia – suggested his adherence to a similar metaphor of feminine passivity.[150]

The negative and passive reading of the action of the X chromosome was retained even where alternate narratives were possible. The phenomena of Turner's syndrome and the poly-X female, for example, were taken to confirm the seeming impotence of the X chromosome – since one X alone could not make a 'complete' female, and more than one did not produce gonadal effects. The London workers disparaged the weakness of a single X: David Carr and his co-authors wrote that, "In females there is usually a failure of ovarian maturation when there is a deficiency of X chromosome material, as in XO and Xx individuals."[151] Carr noted that "an XO specimen is genetically neuter [but] it is phenotypically female if it lives to term."[152] These researchers did not entertain the positive alternative – marveling, for example, at the capacity of the single X to alone cause the gonadal differentiation of the early embryo in the female direction, for example. On the contrary, Thompson and Thompson wrote that: "... a human with the XO constitution is female in appearance and ... upon this background the Y chromosome asserts itself and causes its possessor to be male."[153]

By contrast, positive readings were consistently introduced to the story of Y. Not only was the Y chromosome 'potent' enough to override multiple Xs, it was so potent that the individual so affected was essentially sexually normal – until the test of his manhood at puberty. In the case of Klinefelter's, Barr's estimation of the gonadal error

was the reverse of that for Turner's. Where Barr had initially expected the gonad in Turner's to be sexually undifferentiated, to conform with the impotent X and the incomplete sex chromosome constitution, he emphasized the normality of the testes in Klinefelter's (it was never just a gonad), at least until puberty.[154] The failure of ovarian function in Turner's testified to the weakness of the X chromosome, but the failure of testicular function in cases of Klinefelter did not similarly disqualify the Y chromosomes from claims for its potency.

The narrative of Y potency gave to males the capacity to define the 'true sex.' Thompson and Thompson's popular text, *Genetics in Medicine*, stated that "It was formerly believed that ... the number of X's present ... determined the sex of the individual. It is now known that sex determination in man depends upon the Y chromosome..."[155] Putting the matter more bluntly, the authors added: "The mother ... cannot determine the sex of the child."[156] A paternalist narrative was also apparent in David Carr's work on chromosome anomalies among abortuses. Seeking to explain why "if the Y is only male determining ... X-monosomy [XO is] so lethal?", Carr suggested that the Y chromosome might play a "protective" role: "It is clear that, in some way, the Y chromosome in man is responsible for protecting the X-hemizygote against prenatal death."[157] That a second X chromosome also 'somehow protected the X-hemizygote from prenatal death,' was not mentioned.

So potent was the narrative of Y that it could be seen not only to make males, but even 'better' females. An article in the *Financial Post*, which awkwardly translated Barr's research for popular consumption, described Turner's syndrome females – those

with only one X – as "always short, stocky and plain featured." By contrast, those females in which "masculinity predominates" – cases of testicular feminization for example – "will be tall, beautiful and perfectly proportioned."[158] Barr commented in 1961 about one XY female known to him from his 1950s work on hermaphrodites that "the end result is far from disastrous for these girls are often strikingly attractive."[159] This narrative pops up in the 'rumor' passed on by Alice Dreger from the intersex community "that many "female" high-fashion models are testicularly feminized males."[160]

The masculinist story of Y was not displaced by contrary evidence. Cases of XY 'pure' gonadal dysgenesis were understood as male castrates, not as evidence of the Y chromosome's impotence. The hormonal Adam principle could still be called upon to sustain a vision of masculine potency when the Y chromosome was in trouble.[161] In the same vein, the explanations for the 2 XX males found by Alex Bell all suggested that the Y chromosome – or its proxy, Y-genes – must be lingering unseen in these extraordinary bodies. Moreover, the alarmingly high incidence of this anomaly, which was demonstrated by Bell's survey, was contained by attributing the incidence to chance. Meanwhile, research on poly Y males was organized to validate the assumption of the Y chromosomes' potency, even where the bodies and lives of the affected men seemed recalcitrant. Hyper-masculinity, or aggression, was deemed a risk effect of this chromosome constitution.[162]

The stories of X and Y helped to confirm the essential distinctiveness of the sex chromosomes in relation to the other chromosomes. While all chromosomes might conform to a metaphor of gene action, the sex chromosomes were particularly prone to

stereotyped tales of gendered behavior. And the sex chromosome anomalies, in evidencing sex anomalies, and lesser degrees of 'severity,' confirmed the essential distinctiveness of the sex chromosome anomalies. There were cases, however, which could be taken to contradict the meta-category of sex chromosome anomaly. The poly-X females and poly-Y males, for example, failed to evidence either a sexual aberration, or a coherent symptom complex. In the case of the XO (Turner's) cases, the problem was more the degree of 'severity' – David Carr's work certainly suggested that sex chromosome anomalies could be at least as severe as autosome anomalies: "the XO zygote has a lethality of almost 98%," Carr wrote.[163] That the meta-category of sex chromosomes was preserved despite these exceptions, points both to its historical contingency, and the importance of sex in making sense of disease.

Conclusion

The term "sex chromosomes," Alice Dreger notes in her important work on hermaphroditism, is an "unfortunate misnomer leading to much confusion." Drawing on contemporary scientific knowledge, Dreger suggests that the term is improper because genes related to traits we consider non-sexual are present on the X chromosome and because sexual development is abetted by genes on chromosomes other than the X and Y.[164] For Dreger, the reason why this terminology is "unfortunate" is that it leads people to believe that hermaphrodites must all have missing, or extra sex chromosomes – a false

belief. Dreger is cautioning here that this language has important social consequences – an argument with which I agree. But her suggestion that the scientific facts of the matter should dissuade us from use of the term is overly sanguine. Contemporary scientific knowledge is neither necessary nor sufficient to decide the argument about terminology. Scientific understanding in the 1950s and 1960s also made it possible to see the term 'sex chromosome' as unfortunate or alternately to see it as credible. But the use of the term responded to more demands than just a simple reading of evidence.

The use of the term has supported the generation of a typology of chromosome anomalies, with the sex chromosome anomalies in one camp and the autosomal anomalies in the other, and the interpretation of the sex chromosome anomalies as matters of sex. In so far as there was contingency in the making of sexualized sex chromosome anomalies, however, it was apparent only for a few short years. By the end of the 1960s, the logic of the sex chromosome anomalies as a category apart was so common-sensical that explicit referencing of gendered metaphors was less obvious, and the scientific justification for the category, including the Lyon hypothesis, seemed clear.

Endnotes: Chapter 4

[1] Barr and Carr had argued that "The consequences of the genetic differences imposed by the XX or XY complexes are seen primarily in diverging paths of gonadal development." Murray Barr and David Carr, "Sex chromatin, sex chromosomes and sex anomalies," *Canadian Medical Association Journal*, 83:19 (November 5, 1960), 983. In line with this attention to gonads, they argued that "correlations between sex chromosome complexes and phenotypes give some hint as to the role of the X and Y chromosomes in gonadal differentiation." Murray Barr and David Carr, "Correlations between sex chromatin and sex chromosomes," *Acta Cytologica*, 6 (1962), 37.

[2] Jane Maienschein, "What determines sex? A study of converging approaches, 1880-1916," *Isis*, 75 (1984), 457-480. See also: Stephen Brush, "Nettie M Stevens and the Discovery of Sex Determination by Chromosomes," *Isis*, 69 (1978), 163-172; Marilyn Bailey Ogilvie, "The "New Look" Women and the Expansion of American Zoology: Nettie Maria Stevens (1861-1912) and Alice Middleton Boring (1883-1955), In K Benson, J Mainenschein and R Rainger, eds., *The Expansion of American Biology* (Rutgers University Press, 1991), 52-79

[3] In Barr's 1959 article in *Science*, for example, the fact of an inert Y was noted only in a footnote; it was only stated in the text in the Addendum where it was exposed only to be definitively overturned. Murray Barr, "Sex Chromatin and Phenotype in Man," *Science*, 130:3377 (Sept 18, 1959), footnote 7, 685.

[4] ML Barr et al, "An unusual sex chromatin pattern in three mentally deficient subjects," *Journal of Mental Deficiency Research*, 3 (1959), 84.

[5] As with the hormonal Adam principle, the new chromosomal Adam principle also assumed that "to make a male, something must be added." Admitting that these theories might be modified in time, Barr summarized the then understood biology of sex chromosome anomalies as: "The Y chromosome promotes the development of testes and that two X's are generally required for ovarian development, that a testicular evocator substance is necessary for masculinization of the embryo..." ML Barr, "Abnormalities of sex chromosome complex in relation to embryological development," p. 4, paper presented at American Academy of Pediatrics, Chicago, Oct 2, 1961 (NA, MG30B111, 11-17).

[6] By "uncomplicated" they meant non-mosaic. James Thompson and Margaret Thompson, *Genetics in Medicine*, (Philadelphia and London: WB Saunders, 1966), 116.

[7] ML Barr, editorial, "The chromosomes of man," *Canadian Medical Association Journal*, 81 (Aug 1, 1959), 192.

[8] All three of the infants reported in this brief communication were being reared as males (the presence of penises being the chief issue it appeared), yet all three had chromosomal constitutions that might in other circumstances be read as belonging to Turner's syndrome, namely XO/XY mosaicism, and XX/XX mosaic with partial deletion of the short arm of the X in one cell line. PE Conen and B Erkman, "Two "new" sex-chromosome mosaics XO/XX, XX/XX (deletion of short arm X) and a further XO/XY mosaic," letters to the editor, *The Lancet*, (Dec 14, 1963), 1276-7.

[9] PE Conen et al, "45/XO Turner's syndrome in the newborn: report of two cases," *The Journal of Clinical Endocrinology and Metabolism*, 23:1 (Jan 1963), 1-10.

[10] In reporting these cases, Conen was informing the Canadian medical community of international findings. PEC, editorial, "The clinical significance of research on human sex chromosomes," *Canadian Medical Association Journal*, 84 (Jan 21, 1961), 168

[11] PE Conen and IH Glass, "45/XO Turner's syndrome in the Newborn: report of two cases," *The Journal of Clinical Endocrinology and Metabolism*, 23:1 (Jan 1963), 9. This was not particularly innovative work. Conen's work was heavily criticized in the mid-1960s for being largely irrelevant. One anonymous reviewer wrote that "surely the time is past when a report is necessary on one or two cases of XO Turner's and SSY [sic, likely XXY] Klinefelter's." Three anonymous reviews were sent to Conen for his information after his application for renewal of his National Health Grant was refused, Jean Webb, letter to PE Conen, March 17, 1964, attached to Minutes of Committee on Research, Feb 3, 1965 (HSC, CRM, Vol. 1960-1966).

[12] Barr used the term "non-sexual sphere" in: Murray Barr, "The sex chromosomes in evolution and in medicine," *Canadian Medical Association Journal*, 95 (Nov 26, 1966), 1146; Murray Barr, "The Sex chromosomes in evolution and in Medicine," a lecture presented at the Fiftieth Anniversary Ceremonies, NRC Canada, Ottawa, Sept 21-23, 1966, published in CMAJ, 95 (Nov 26, 1966), 1146.
[13] David Carr et al, "An XO/XX/XXX mosaicism in relationship to gonadal dysgenesis in females," *Journal of Clinical Endocrinology and Metabolism*, 22:7 (July 1962), 672, 673. For the extensive correspondence about this patient between Germany, from which she hailed, and Canada, where she moved as the wife of a Canadian soldier, to LA where she moved yet again with her husband, see: (NA, MG30B111, File 5-4).
[14] Murray Barr and David Carr, "Sex chromatin, sex chromosomes and sex anomalies," *Canadian Medical Association Journal*, 83:19 (November 5, 1960), 983.
[15] Indeed, at first the name was taken quite literally and Barr's 1959 commentaries suggested that the gonads were sexually undifferentiated. Murray Barr, "Sexual Dimorphism in Interphase Nuclei," *American Journal of Human Genetics*, 12 (1960), 123; ML Barr, editorial, "The chromosomes of man," *Canadian Medical Association Journal*, 81 (Aug 1, 1959), 192. In the 1960s, Barr's writings conceded that the gonads were ovaries, but the term "gonadal" dysgenesis continued in use. Barr and Carr, "Sex chromatin, sex chromosomes and sex anomalies," 982. Barr wrote that "'Gonadal dysgenesis' is an alternate name for the disorder [Turner's]." Murray Barr, "The Significance of Nuclear Sexing," in John Howells ed. *Modern Perspectives, World Psychiatry* (New York: Brunner/Mazel, 1968, 1971), 5.
[16] "The second case might have menstruated normally, since the pituitary, ovaries and uterus appeared normal, and it might also have been fertile." PE Conen and IH Glass, "45/XO Turner's syndrome in the Newborn: report of two cases," *The Journal of Clinical Endocrinology and Metabolism*, 23:1 (Jan 1963), 8.
[17] David Harvey Carr, "Chromosome Studies in Spontaneous Abortions," University of Western Ontario, Ph.D. thesis, 1965, 94. Barr identified it as the "inherent tendency of all embryos to feminize in the absence of a masculinizing inductor of testicular origin." Murray Barr, "Sexual Dimorphism in Interphase Nuclei," *American Journal of Human Genetics*, 12 (1960), 123, 124.
[18] He received the cooperation of "all the obstetricians and many general practitioners" to collect material from Victoria Hospital and St Joseph's Hospital; he also received some specimens by mail from other centers in South-western Ontario. Carr, "Chromosome Studies in Spontaneous Abortions," 31.
[19] David Carr, "Chromosome studies in abortuses and stillborn infants," *The Lancet*, (Sept 21, 1963), 605.
[20] Murray Barr, "The Sex chromosomes in evolution and in Medicine," a lecture presented at the Fiftieth Anniversary Ceremonies, NRC Canada, Ottawa, Sept 21-23, 1966, published in *Canadian Medical Association Journal*, 95 (Nov 26, 1966), 1146.
[21] *Ibid.*, 1146.
[22] Of course the association between "gonadal dysgenesis" and "Turner's" was also difficult. Barr and Carr argued that: "The patient with an XO syndrome complex is a female with dysgenesis of the gonads and shortness of stature. The name "Turner's syndrome" is applied when webbing of the neck and cubitus valgus are also present, but for convenience the terms ... will be used interchangeably." Murray Barr and David Carr, "Sex chromatin, sex chromosomes and sex anomalies," 982. See also: Murray Barr, "Sexual Dimorphism in Interphase Nuclei," 123.
[23] "The cases in which gonadal dysgenesis is the only abnormality have been referred to as pure gonadal dysgenesis." PE Conen and IH Glass, "45/XO Turner's syndrome in the Newborn," 7. See also: Jorge J Yunis, "Human chromosomes in disease," in Jorge Yunis ed., *Human Chromosome Methodology*, (New York and London: Academic Press, 1965), 195. "Cases with streak gonads and sexual infantilism, but of normal or high stature and normal female or male sex chromosome complement will be referred to as examples of "pure gonadal dysgenesis"."
[24] Murray Barr et al, "Male pseudohermaphroditism and pure gonadal dysgenesis in sisters," *American Journal of Obstetrics and Gynecology*, 99:8 (Dec 15, 1967), 1047. The sex chromosome constitution in cases of "pure" gonadal dysgenesis, could also be XX. Yunis, "Human chromosomes in disease," 200.
[25] Barr had these cases in hand from the 1950s and commented in a 1961 article about the evidence for a genetic association between "pure" gonadal dysgenesis and male pseudohermaphroditism provided by

these siblings: David Carr, Murray Barr and Earl Plunkett, "An XXXX Sex chromosome complex in two mentally defective females," *Canadian Medical Association Journal*, 84:3 (Jan 21, 1961), 131.
[26] Murray Barr et al, "Male pseudohermaphroditism and pure gonadal dysgenesis," 1048, 1049.
[27] *Ibid.*, 1050, 1051.
[28] *Ibid.*, 1054. Barr was not alone in this belief; Yunis wrote: "Individuals with an XY karyotype could be expected to differentiate along phenotypically female lines if the gonad became dysgenetic at an early state. This is consistent with Jost's observations ..." Yunis, "Human chromosomes in disease," 200.
[29] Indeed Barr did continue some clinical involvement with 1950s intersexes into the 1960s. He continued to assess sex chromatin for clinicians who lacked local capacity (see correspondence, 1961, NA, MG30B111, 4-7). He also continued some limited involvement with "inverts," referring transvestites to sympathetic clinicians (see Barr, letter to Dr Sydney Friedman, Department of Anatomy, UBC, Jan 5, 1960, NA, MG30B111, 4-22).
[30] Estimates of the proportion varied, from about 40% through 75%
[31] Conen reported, for example, on the surprise association between various chromosome anomalies, including the "intersex conditions" of XO and XXY, and physical anomalies of the hands. PE Conen et al, "Chromosome abnormalities in patients with syndactyly," *Canadian Medical Association Journal*, 101 (Nov 15, 1969), 77, 76. This survey of 105 patients with syndactyly is also notable for the absence of IQ testing in most cases; it seems that hospital patients were less readily subjected to batteries of tests than inmates of institutions for the mentally retarded. This meant that judgements of intelligence were often social: "Mental achievement was judged by conversation with the patients during examination and by discussion of their school achievements with their parents." p. 75. Indeed, Conen used a case of Klinefelter's syndrome to unknowingly repeat the warning made by Barr a decade previously about cases of intersexuality – that sex assignment decisions should not be made on the basis of sex chromatin alone. This male infant had genital abnormalities which, taken together with the finding of sex chromatin positivity, might have encouraged sex-assignment to the female role. In this instance, chromosome tests had established the diagnosis of XXY with probably coincidental genital anomalies. Conen's warning was tempered by the philosophic reflection that, "Admittedly any error made would not be so serious in this condition since the patient would be reared as a sterile female subject instead of an almost certainly sterile male subject." PE Conen et al, "47/XXY Klinefelter's syndrome in an infant with abnormal genitalia," *The Journal of Urology*, 91:5 (May 1964), 599. But this particular article was singled out by Margery Shaw and Klaus Patau in their very critical review of Conen's cytogenetics research. This was "muddled writing" and they also pointed out that in 1964, an XXY Klinefelter case "does not deserve five pages of print even though the abnormal genitalia of the patient are an unusual trait." M Shaw and K Patau, Report, Cytogenetics, Jan 11, 1965 attached to Minutes of Committee on Research, Feb 3, 1965 (HSC, CRM, Vol. 1960-1966).
[32] ML Barr et al, "The chromatin-positive Klinefelter syndrome among patients in mental deficiency hospitals," _Journal of Mental Deficiency Research, 4 (1960), 91; ML Barr et al, "The XXXXY sex chromosome abnormality," *Canadian Medical Association Journal*, 87 (Oct 27, 1962), 892; ML Barr et al, "The XXYY variant of Klinefelter's syndrome," *Canadian Medical Association Journal*, 90 (Feb 29, 1964), 575.
[33] DH Carr et al, "An XXXY sex chromosome complex in Klinefelter subjects with duplicated sex chromatin," *The Journal of Clinical Endocrinology and Metabolism*, 21:5 (May 1961), 493.
[34] ML Barr et al, "The chromatin-positive Klinefelter syndrome," 99-100.
[35] This was of particular interest because other researchers had suggested the central role of the two Xs in inhibiting masculine muscular development. It was notable also that this patient had the most "masculine" endocrinology. Barr noted, for example, that it was "probably not a coincidence that the two patients without advanced tubular hyalinisation had the most masculine body habitus and normal excretion of urinary 17-ketosteroids." The authors provided a picture of patient with "strongly masculine physical development and mesomorphic proportions." Next to this is a picture of a more "typical" Klinefelter's patient "with long lower extremities, very little growth of facial hair and gynaecoid distribution of pubic hair." ML Barr et al, "The chromatin-positive Klinefelter syndrome," 99, 100, 103, 99.

[36] ML Barr et al, "An unusual sex chromatin pattern in three mentally deficient subjects," *Journal of Mental Deficiency Research*, 3 (1959), 86.
[37] *Ibid.*, 82.
[38] Evelyn Shaver, "A study of cell nuclei in Mental deficiency," University of Western Ontario, MSc Thesis, 1958. pp. 41, 52
[39] ML Barr et al, "An XY/XXXY sex chromosome mosaicism in a mentally defective male patient," *Journal of Mental Deficiency Research*, 6 (1962), 71. This is case 1 (NA, MG30B111, 9-4).
[40] *Ibid.*, 72. On this case, see also: ML Barr, "Chromosomes in Medicine," Homecoming medical conference, UWO, Oct 18, 1968, pp. 7-8. (NA, MG30B111, 18-4)
[41] Barr, letter to Dr Nicola D'Onghia, Milan Italy, Nov 24, 1955 (NA, MG30B111, 4-21).
[42] Barr pursued many hypotheses in relation to the sex chromatin – its place in malignant processes, its malleability in tissues in relation to sex hormones and stage of development in the life cycle. It is perhaps logical that as a neurocytologist, he would also pursue research on the pathology of the mind using the sex chromatin. As early as 1950, Barr had been interested in beginning a clinical project involving mental disease, though it did not get underway until 1952. This early research involved the examination of neural cytology in the brains of institutionalized psychotics. Barr's psychotic material came from lobotomies performed in London, his controls came from autopsy material from all over southern Ontario. Barr and his students had wanted to see whether the sex chromatin underwent any morphological changes as a result of the pathology of psychosis; they found none. ML Barr, "Investigation of Nucleoprotein metabolism of the brain in mental disease," NHGP, Mental Health Grant, received Dec 5, 1951, (OA, NHGP, RG 10-22, File 96). They concluded their study of neural tissue from 52 psychotic and 46 non-psychotic subjects in 1955 with the observation that "The morphological details of the sex chromatin were identical in psychotic and non-psychotic subjects." Margaret Mylle, Margaret Graham and Murray Barr, "The sex chromatin in neurons of the human frontal cortex and sympathetic ganglia," Abstract, Canadian Neurological Society, June 1955, included with Nov 18, 1955 Progress Report for NHGP, Mental Health Grant, (NA, MG30 B111, 6-4).
[43] ML Barr, Application for a Research Grant, NHGP, Mental Health Grants, Nov 23, 1956, (NA, MG30 B111, File 6-12).
[44] The student who initially took on the task of surveying some of these inmates started out with two survey tools – the blood and oral smear methods of testing sex chromatin. As a parallel exercise, Shaver also performed more elaborate analyses of the blood of the Mongol inmates. Shaver wrote that "Anomalies in sex development in mongoloids are reported to be common with undescended testes occurring in more than half the males and delayed menarche, irregular menstrual cycles and early menopause occurring in the female." Shaver, "A study of cell nuclei," 8.
[45] *Ibid.*, 2. Barr sought funds for further work on this project arguing that "A large population of mental defectives should be screened therefore by means of cytological tests of sex to learn if genetic gonadal deficiency is a factor in mental deficiency of a severity requiring institutional care." He noted that arrangements had been made to survey the inmates of Ontario's Hospital Schools, Dr Claire Buck of the Ministry of Health(?) having "kindly granted permission to proceed." It was Barr's intention to study material from most of the institutionalized mental defectives in the province of Ontario. ML Barr, Application for a Research Grant, NHGP, Mental Health Grants, Nov 23, 1956, (NA, MG30 B111, File 6-12). ML Barr, "Cytological and endocrinological studies in mental deficiency," Progress report, NHGP, Mental Health Grant, Nov 20, 1957, (NA, MG30 B111, 6-15).
[46] That the sex chromatin was not inherently "easy" to read is evidenced by Barr's correspondence and research notebooks from the 1950s. Many workers wrote to him about the great difficulty they experienced in interpreting the cellular evidence. Indeed one of Barr's most important contributions in this decade was in helping to "black box" the technology of the sex chromatin by distributing detailed and standardized instructions for preparing and reading the samples and by distributing photographs and more importantly, prepared slides of tissues, so that other investigators could, with the aid of this material, learn how to read the cellular evidence of sex themselves.
[47] The protocol of subjecting all new cases to a buccal smear at the CPRI was certainly something Barr had been involved: ML Barr, "Cytology laboratory, CPRI," N.D. [1961] (NA, MG30B111, 12-27). He also advocated this kind of approach more widely, writing, "It is recommended that the simple buccal smear sex

chromatin test be made a routine procedure in the study of male mental retardates." ML Barr et al, "The chromatin-positive Klinefelter syndrome among patients in mental deficiency hospitals," *Journal of Mental Deficiency Research*, 4 (1960), 104.

[48] Barr's team was one of many which in the late 1950s reported these findings. When Shaver completed her MSc in 1958 she was able to cite 3 other 1958 published studies in which high incidences of Klinefelter were found among mental defectives; so was a going concern at the time. Shaver, "A study of cell nuclei," 50.

[49] ML Barr et al, "An unusual sex chromatin pattern in three mentally deficient subjects," *Journal of Mental Deficiency Research*, 3 (1959), 78. Barr did not always make such a definitional slip. He stated in another publication that the purpose was "to establish the frequency of chromatin-positive males in certain institutions for the mentally defective in the Province of Ontario." ML Barr et al, "The chromatin-positive Klinefelter syndrome," 89. For Barr's research on Klinefelter's see: Research Notebooks: Klinefelter's syndrome in mental defectives, Book 1, File 10–3; see also Book 2, File 10-4, Book 3, File 10-5 (NA, MG30B111).

[50] ML Barr et al, "The chromatin-positive Klinefelter syndrome," 93. A bar graph of the classifications of mental retardation graphically demonstrates this process of rescue. The longest bar is termed "undifferetiated;" stars occupying 1/6th of the space indicate the newly defined classification of Klinefelter for these patients.

[51] *Ibid.*, 91, 92.

[52] ML Barr et al, "An unusual sex chromatin pattern," 86.

[53] "Klinefelter's syndrome used to be considered to be atrophy of seminiferous tubules and hypozoospermia with a relative conservation of androgenic functions. Since the discovery of sex chromosome anomalies, the criteria have changed. Most authors accept an excess of X chromosomes in a male as the main characteristic and basis for the definition." W Zaleski et al, "The XXXXY chromosome anomaly: Report of three new cases and review of 30 cases from the literature," *Canadian Medical Association Journal*, 94:22 (May 28, 1966), 1152.

[54] JS Thompson and MW Thompson, *Genetics in Medicine*, (Philadelphia and London: WB Saunders Co., 1966, reprinted 1967, 1968), 123, emphasis in original. Jorge Yunis put it even more boldly; he argued: "Before chromosome analysis was available, many cases were diagnosed as Klinefelter syndrome on the basis of clinical findings, although their sex chromatin patterns were male..." Yunis, "Human chromosomes in disease," 194. Harry Klinefelter apparently agreed with the chromosomal hegemony; in reviewing the syndrome that bears his name noted that, "The syndrome in patients with positive chromatin in the buccal mucosa should probably be called Klinefeleter's disease." Harry F Klinefelter, "Klinefelter's syndrome: historical background and development," *Southern Medical Journal*, 79 (1986), 1092.

[55] Indeed Barr confirmed his disinterest in the chromosomally uninteresting subset writing that the "natural history of the Klinefelter syndrome" involved subjects with "an intersexual XXY sex chromosome complex." ML Barr et al, "The chromatin-positive Klinefelter syndrome among patients in mental deficiency hospitals," *Journal of Mental Deficiency Research*, 4 (1960), 90. Again, Barr did use the modifier of "chromatin positive" in relation to Klinefelter on occasion, but the thrust of his research methodology was to exclude the chromatin negative cases from analysis and ultimately from membership in the syndrome.

[56] DH Carr et al, "An XXXY sex chromosome complex in Klinefelter subjects with duplicated sex chromatin," *The Journal of Clinical Endocrinology and Metabolism*, 21:5 (May 1961), 491-505; ML Barr et al, "The XXYY variant of Klinefelter's syndrome," *Canadian Medical Association Journal*, 90 (Feb 29, 1964), 575-580; ML Barr et al, "The XXXXY sex chromosome abnormality," *Canadian Medical Association Journal*, 87 (Oct 27, 1962), 891-900. See Barr's Research Notebook: Male defectives with duplicated sex chromatin, File 9-4 (NA, MG30B111).

[57] ML Barr et al, "The chromatin-positive Klinefelter syndrome," 89.

[58] Later a London colleague together with two other Canadian researchers argued that a distinct syndrome could be constituted. ML Barr et al, "The XXXXY sex chromosome abnormality," 899; Witold Zaleski et al, "The XXXXY chromosome anomaly: report of three new cases and review of 30 cases from the literature," *Canadian Medical Association Journal*, 94:22 (May 28, 1966), 1143-1154.

[59] "[T]he risk of mental defect perhaps increases as more chromosomes are added to the complex." ML Barr et al, "An XY/XXXY sex chromosome mosaicism," 71.
[60] In another section of the same paper the authors put it thusly: "The basic requirement for seminiferous tubule dysgenesis (disregarding in this context the chromatin-negative Klinefelter subject) appears to be the presence of at least two X chromosomes in association with at least two X chromosomes in association with at least one Y chromosomes." DH Carr et al, "An XXXY sex chromosome complex in Klinefelter subjects with duplicated sex chromatin," *The Journal of Clinical Endocrinology and Metabolism*, 21:5 (May 1961), 491-2, 503; Similar arguments are made in many articles see: ML Barr et al, "The XXXXY sex chromosome abnormality," *Canadian Medical Association Journal*, 87 (Oct 27, 1962), 891-2; David Carr, "A probable XXYY sex determining mechanism in a mentally defective male with Klinefelter's syndrome," *Canadian Medical Association Journal*, 84:16 (April 22, 1961), 877.
[61] ML Barr et al, "The XXYY variant of Klinefelter's syndrome," *Canadian Medical Association Journal*, 90 (Feb 29, 1964), 579.
[62] ML Barr et al, "The chromatin-positive Klinefelter syndrome," 92, 93.
[63] *Ibid.*, 103.
[64] Conen did continue to mention chromatin-negatives, but his work focused on the chromosomally abnormal cases: "Sex chromatin studies have suggested that approximately 40% of patients with the clinical features of Klinefelter's syndrome are chromatin positive." PE Conen et al, "47/XXY Klinefelter's syndrome in an infant with abnormal genitalia," *The Journal of Urology*, 91:5 (May 1964), 595.
[65] PE Conen et al, "Chromosome abnormalities in patients with syndactyly," 77, 76.
[66] The chances of these complications, he added, "are higher yet when the complex is XXXY and very high when the complex is XXXXY." Barr, letter to Dr WJ McClelland, Department of Psychology, UWO, July 21, 1964 (NA, MG30B111, 4-11).
[67] BR Oatley-Willis, Provincial Probation Officer, Windsor Ontario, letter to Barr, Oct 23, 1964; Barr responds, Oct 27, 1964 (NA, MG30B111, 4-25).
[68] ML Barr et al, "The Triplo-X female: An appraisal based on a study of 12 cases and a review of the literature," *Canadian Medical Association Journal*, 101:5 (Sept 6, 1969), 247.
[69] PEC, editorial, "The clinical significance of research on human sex chromosomes," *Canadian Medical Association Journal*, 84 (Jan 21, 1961), 168. The term was used also by the Thompsons in their textbook: *Genetics in Medicine*, 120.
[70] PEC, editorial, "The clinical significance of research," 168.
[71] AL Chute, "Some aids in the diagnosis of genetic disorders," *Canadian Medical Association Journal*, 93 (August 7, 1965), 263. By the fall of 1967, if not before, Chute was the Dean of Medicine at UofT.
[72] David Carr, Murray Barr and Earl Plunkett, "An XXXX Sex chromosome complex in two mentally defective females," *Canadian Medical Association Journal*, 84:3 (Jan 21, 1961), 131, 137. Such comments were frequently made, i.e. "This complex does not appear to prejudice normal development of ovaries and the female reproductive system generally..." Murray Barr and David Carr, "Correlations between sex chromatin and sex chromosomes," *Acta Cytologica*, 6 (1962), 37. These two women are discussed as the first 2 cases in Barr's research notebook. The gynecological reports for both women state that they were "referred for pelvic examination because of a sex chromatin irregularity," (NA, MG30B111, 10-2)
[73] Murray Barr and David Carr, "Sex chromatin, sex chromosomes and sex anomalies," *Canadian Medical Association Journal*, 83 (Nov 5, 1960), 985.
[74] Barr's discussion of his 16 and 9 years following up on clinical signs of "sex chromosome error" provides a teleological vision of sex chromosome errors; his work in the 1950s was seen to signify sex inversions of various sorts, not chromosomal anomaly. This narrative does confirm Barr's expectation of "gonadal" defects however, since clinical suspicion of "sex" chromosome error would be so particular only in the case of sex anomaly. ML Barr et al, "The Triplo-X female: An appraisal based on a study of 12 cases and a review of the literature," *Canadian Medical Association Journal*, 101:5 (Sept 6, 1969), 248. See also: "There does not appear to be a triple-X syndrome clinically..." Murray Barr and David Carr, "Human cytogenetics: congenital abnormalities caused by chromosome abnormalities," in JP Greenhill, ed., Obstetrics, 13th edition, (WB Saunders Co., 1965), 1061. And, "...there is no triple-X syndrome in the clinical sense..." Murray Barr, "The sex chromosomes of man," *American Journal of Obstetrics and*

Gynecology, 93 (1965), 615. This comment, when first made, was received with some interest. It appeared in the US Medical News Highlights, and elicited comment from other researchers. See, letter to Barr from Elizabeth Chu, NCI, NIH, August 30, 1967 (NA, MG30B111, 2-1).

[75] Murray Barr and David Carr, "Correlations between sex chromatin and sex chromosomes," *Acta Cytologica*, 6 (1962), 37, 38.

[76] See Barr's research notebook, "Female defectives with duplicated sex chromatin," (NA, MG30B111, 10-2).

[77] ML Barr et al, "The Triplo-X female: An appraisal based on a study of 12 cases," 249. Barr explained the need for his review of the triplo-X phenomena given general confusion about this syndrome of no syndrome. Barr, letter to Dr GJ Dickinson, Editor, *Canadian Medical Association Journal*, (NA, MG30B111, 2-6).

[78] Barr attempted to gather data that might balance the results from his inmate surveys. He sought from the Ontario government a "rough estimate of the number of persons with Klinefelter syndrome (XXY) and the XXX syndrome in Ontario who are at home and who are either normal or significantly normal to get along without institutional care." Barr, letter to Mr. Cyril Greenland, Mental Health Branch, Ontario, Feb 8, 1965 (NA, MG30B111, 4-13).

[79] ML Barr et al, "The Triplo-X female: An appraisal based on a study of 12 cases," 251, 252. The mental retardation was seen to be a general effect of chromosomal imbalance, not of the sex-side of the anomaly. Barr wrote of the triplo-X female that, "there is the spectre of mental retardation as the result of a general and non-specific genetic imbalance, just as there is with the infertile male who has too many sex chromosomes." ML Barr, "Abnormalities of sex chromosome complex in relation to embryological development," paper presented at the American Academy of Pediatrics, Chicago, Oct 3, 1961, p. 7. (NA, MG30B111, 11-7).

[80] ML Barr et al, "The Triplo-X female: An appraisal based on a study of 12 cases," 257.

[81] David Carr, Murray Barr and Earl Plunkett, "A probable XXYY sex determining mechanism in a mentally defective male with Klinefelter's syndrome," *Canadian Medical Association Journal*, 84 (April 22, 1961), 873, 875.

[82] *Ibid.*, 877.

[83] ML Barr et al, "The chromatin positive Klinefelter syndrome."

[84] Irene Uchida, James Miller and Hubert Soltan, "Dermatoglyphics associated with the XXYY chromosome complement," *American Journal of Human Genetics*, 16 (1964), 284-291.

[85] ML Barr et al, "The XXYY variant of Klinefelter's syndrome," *Canadian Medical Association Journal*, 90 (Feb 29, 1964), 575, 580. Barr and Carr wrote in an overview in 1965 that "An XYY syndrome cannot at present be defined clinically." Murray Barr and David Carr, "Human cytogenetics: congenital abnormalities caused by chromosome abnormalities," in JP Greenhill, ed., *Obstetrics*, 13th edition, (WB Saunders Co., 1965), Chapter 74.

[86] ML Barr et al, "The XXYY variant of Klinefelter's syndrome," 580.

[87] Pat Jacobs et al, "Aggressive behaviour, mental subnormality and the XYY male," *Nature*, 208 (1965), 1351. I'm not suggesting that Pat Jacobs was intent on finding hypermasculinity, just that this was a reasonable hypothesis to test for. In fact, Pat Jacobs had clearly not expected much from this syndrome; she wrote to Barr about the latter's discovery of the XXXX female that "one of the few 'common' sex chromosome aberrations left to be found is the XYY – I guess he must be a rather normal male," she added, "or he should have turned up by now." Letter to Barr, from Patricia Jacobs, MRC Clinical Effects of Radiation Research Unit, Edinburgh, Oct 19, 1960 (NA, MG30B111, 4-4).

[88] Margaret Thompson, "Genetical research in mental retardation, 1967," presented at the CARC's 10th National Conference on Mental Retardation, Quebec City, September 19th-22nd, 1967, Roeher Institute Library.

[89] For a favorable review of the research, by an involved researcher, see: WM Court Brown, "Males with an XYY sex chromosome complex," *Journal of Medical Genetics*, 5 (1968), 341-359.

[90] Researchers at Queen's University pursued the XYY males, see the brief reports in: MG Joneja et al, "Another XYY case in a prison population," letter to the editor, *Canadian Medical Association Journal*, 104 (March 6, 1971), 424-5; D Soudek, "XYY phenotype: does it exist?" letter to the editor, *Canadian*

Medical Association Journal, 114 (Feb 21, 1976), 294, 297. Barr played a role in facilitating this work in Kingston. He supported the emigration to Canada of Dusan Soudek, a Hungarian cytogeneticist, in 1968. Soudek was supported by funds from the OMHF; he worked briefly in London and then found more permanent quarters in Kingston. See his project description in his application for funds to the OMHF: D Soudek, "Chromosome studies in male mental retardates with special reference to XYY error," (NA, MG30B111, 3-13).

[91] Of the 230 men reviewed, 2 were found with an XXY, 3 with XYY and one with XYYY chromosome complexes. This research was unpublished, but its main findings were noted in: F Sergovich, "Chromosome aberrations and criminal behaviour: a brief review," The Criminal Law Quarterly, 11 (1969), 307. Barr was key also to the London research. Sergovich got access to the Penetanguishene population when the prison administration wrote to Barr seeking cytogenetic advice after ceasing the administration of LSD to the maximum security prisoners in light of fears of chromosome breakage. Barr brought Sergovich onto the case, arranging for both a review of chromosome breakage and for the XYY chromosome constitution in these inmates. See correspondence: EJ Barker, Assistant Superintendent, OH Penetanguishene, to Barr, Oct 24, 1967; Barr responds, Oct 30, 1967, Nov 3, 1967 (NA, MG30B111, 2-1). There may also have been co-operative work with officials at Oakalla Prison Farm, which ironically followed up on 1950s work by Barr on the sex chromatin in homosexuals. See: letter to Barr from RGE Richmond, Senior Medical Officer, Oakalla Prison Farm, BC, March 7, 1968; response, March 11, 1968. (NA, MG30B111, 2-2).

[92] Sidney Katz, "They say criminals may be bred," *Toronto Daily Star*, Dec 9, 1967 (OA, Reel 299).

[93] Most of the publications on the Y chromosome by Conen and his colleagues related to the development of screening capacities. See: PK Lewin et al, "Dyeing the Y chromosome," *The Lancet*, 1 (March 20, 1971), 596; RB Surana et al, "Minute Y chromosome," *Annales de Génétique*, 14:2 (June 1971), 145-8; Peter Lewin and Patrick Conen, "Fluorescent Y screening if Hospitalized newborns," *Nature*, 233 (Oct 1, 1971), 334-5; Jurgen Kegel et al, "Nuclear sex identification in human tissues," *American Journal of Clinical Pathology*," 57 (1972), 425-30; V Damodar et al, "Value of Fluorescent Y chromosome and sex chromatin tests," *Acta Cytologica*, 17:3 (May-June 1973), 220-23.

[94] Katz, "They say criminals may be bred."

[95] For Canadian press reports see: Mack Laing, "Some men can be born bad," *Toronto Telegram*, Dec 4, 1967 (OA, Reel 299); "Wrong sex chromosomes likely to cause crime, doctor says," *Toronto Star*, June 7, 1969 (OA, Reel 362); Sidney Katz, "This man is a killer – but should he stand convicted of murder?" *Maclean's Magazine*, July 1968, 4; "Toronto Doctors: "Killer" chromosome study set," *Toronto Telegram*, Jan 22, 1971 (OA Reel 459).

[96] ML Barr, "Chromosomes in medicine," Homecoming medical conference, UWO, Oct 18, 1968, 13 (NA, MG30B111, 18-4).

[97] This survey was one in a long line of sex chromatin surveys reviewing X chromosome aberrations, though other anomalies might also become evident upon chromosomal investigation, it also retained an interest in "intersexes". This project was first proposed in 1966. "Also in three cases of ambiguous genitalia, we have been able to provide information as to the nuclear and chromosomal sex." Alex Bell, "Description of proposed research," Application for a grant for research, Sept 25, 1970, (OA, RG 97-2, OMHF, File 134).

[98] In early publications, researchers would provide tremendous detail about their techniques for chromosome analysis – outlining the reagents used, the number of cells observed, the number of karyotypes made, etc.

[99] Sergovich's survey was funded by MRC. Bell's survey was supported by both the Ontario Mental Health Foundation and the National Health Grants Program; jointly they provided approximately $130,000 over five years. The Ontario Mental Health Foundation provided a total of $86,384.22 from 1967 through 1972. The National Health Grants Program provided funds from April 1969 through March 1971; they would have provided up to $20,000 each year. See: calculations appended to Bell's 1971 application to OMHF, (OA, RG 67-2, OMHF, File 134).

[100] Bell hoped to analyze the sex chromatin of over 200,000 newborns over approximately 8 years, find in this way about 400 infants with sex chromosome anomalies, obtain a matched control population, and

subject all of these infants and their families to intense scrutiny at least until puberty. In the end, Bell surveyed just under 80,000 infants; he "discovered" about 80 infants with sex chromosome anomalies and gathered no controls. The only publication that I have been able to find by Bell concerning this project: AG Bell and PN Corey, "A sex chromatin and Y body survey of Toronto Newborns," *Canadian Journal of Genetics and Cytology*, 16:2 (June 1974), 239-250. Sergovich and Valentine studied 2159 newborn babies from April 1967 through March 1968. F Sergovich et al, "Chromosome aberrations in 2159 consecutive newborn babies," *New England Journal of Medicine*, 280:16 (April 17, 1969), 851-855.

[101] For London see: GH Valentine, "The YY Chromosome complement, What does it mean?" *Clinical Pediatrics*, 8:6 (June 1969), 350-355; GH Valentine et al, "The growth and development of four XYY infants," *Pediatrics*, 48:4 (October 1971), 583-594; GH Valentine, "The growth and development of sex XYY children," In A Robinson, HA Lubs and D Bergsma, Eds., "Sex Chromosome Aneuploidy: Prospective Studies," *Birth Defects: Original Article Series*, National Foundation – March of Dimes 15:1 (1975), 175-90; GH Valentine, "The growth and development of six XYY children: a continuative report," In D Stewart and S Conde Greene, Eds., "Children with Sex Chromosome Aneuploidy: Follow-up Studies," *Birth Defects: Original Article Series*, National Foundation – March of Dimes, 18:4 (1982), 219-226. Alex Bell does not appear to have stayed involved with the follow-up studies; this work was taken over by a team at HSC, see: DA Stewart et al, "Growth and development of children with X and Y chromosome aneuploidy: a prospective study," In A Robinson, HA Lubs and D Bergsma, Eds., "Sex Chromosome Aneuploidy: Prospective Studies," *Birth Defects: Original Article Series*, National Foundation – March of Dimes 15:1 (1975), 75-114; DA Stewart et al, "Growth and development of children with X and Y chromosome aneuploidy from infancy to pubertal age: the Toronto study," In D Stewart and S Conde Greene, Eds., "Children with Sex Chromosome Aneuploidy: Follow-up Studies," *Birth Defects: Original Article Series*, National Foundation – March of Dimes, 18:4 (1982), 99-154; DA Stewart et al, "Growth and development from early to midadolescence of children with X and Y aneuploidy: The Toronto Study," In. S Ratcliffe and N Paul, Eds., "Prospective Studies on Children with Sex Chromosome Aneuploidy," *Birth Defects: Original Article Series*, National Foundation – March of Dimes, 22:3 (1986), 119-182; DA Stewart et al, "Growth, development and behavioural outcome from mid-adolescence to adulthood in subjects with chromosome aneuploidy: The Toronto Study," In J Evans, J Hamerton and A Robinson Eds., "Children and Young Adults with Sex Chromosome Aneuploidy: Follow-up, Clinical and Molecular Studies," *Birth Defects: Original Article Series*, National Foundation – March of Dimes, 26:4 (1990), 131-188. The March of Dimes hosted 5 conferences bringing together researchers and their data from prospective studies of children with sex chromosome anomalies. Canadian involvement with these conferences was considerable: the group at HSC hosted the third of these March of Dimes conferences in Toronto (the first two were in Colorado and Hawaii, the fourth was in Edinburgh and the fifth in Minaki, Ontario); the Foundation of the HSC provided some assistance in the conduct of the third and fifth conferences, and the MRC also supported the fifth; the HSC group wrote the summary of clinical findings from the work presented at the third conference and the psychological summary for the fourth conference; finally, the Manitoba group whose studies were included in the fourth and fifth conferences (paralleling the departure of the London research), also edited the collection and provided a summary discussion on the need for further studies for the fifth conference.

[102] Donald Stewart, Interview with the author, Toronto, January 29, 1999.

[103] Alex Bell, Application for a grant for research, October 1, 1966, (OA, RG 67-2, OMHF, File 134). Bell initially proposed to conduct the research at Toronto General Hospital; HSC was a collaborating institution, and Margaret Thompson, then the acting Director of the Department of Genetics at HSC, was identified as the consultant to the project. As it turned out, the research was conducted at the University of Toronto, and by the end of the project the association with HSC was stronger since Pat Conen became involved in the Y-body screening. The follow-up studies were conducted exclusively through HSC.

[104] Appraisal by HF Frank, Superintendent, OHS Smith Falls, letter dated Nov 8, 1966, (OA, RG 67-2, OMHF, File 134).

[105] Appraisal by Murray Barr, 1966, (OA, RG 67-2, OMHF, File 134). JR Miller reviewed the project in 1969 and commended the project as an "excellent study that merits full support" particularly for the

proposed follow-up of "anomalous conditions." Appraisal by JR Miller, UBC, Nov 10, 1969, (OA, RG 67-2, OMHF, File 134).

[106] Murray Barr, DH Carr and HB Kedward, "Report to research committee, Ontario Mental Health Foundation," Nov 24, 1971, (OA, RG 67-2, OMHF, File 134).

[107] F Sergovich et al, "Chromosome aberrations in 2159 consecutive newborn babies," *New England Journal of Medicine* 280:16 (April 17, 1969), 853.

[108] *Ibid.*, 854.

[109] *Ibid.*, 854.

[110] GH Valentine et al, "The growth and development of four XYY infants," *Pediatrics*, 48:4 (October 1971), 583.

[111] AG Bell and PN Corey, "A sex chromatin and Y body survey of Toronto newborns," *Canadian Journal of genetics and cytology*, 16:2 (June 1974), 241-2. Bell reports slightly different numbers in his progress reports to the OMHF. Alex Bell, Final Report to the NHGP, received Sept 29, 1971, page 4. (OA, RG 10-22, NHGP, File 1060). In a later report to the OMHF that responded to the request for more data by the site visit team, Bell reported on 76 sex chromosome studies discovered through sex chromatin testing; the total tested was not provided. Alex Bell, "Computer data and Statistical Analyses," Jan 10, 1972, (OA, RG 67-2, OMHF, File 134).

[112] Murray Barr, DH Carr and HB Kedward, "Report to research committee, Ontario Mental Health Foundation," Nov 24, 1971, (OA, RG 67-2, OMHF, File 134).

[113] Alex Bell, Application for a grant for research, September 10, 1969, (OA, RG 67-2, OMHF, File 134).

[114] He suggested that this anomaly could be the result of a single gene error – the counterpart to testicular feminization; it could result from an unrecognized mosaicism with a Y chromosome active somewhere in the body and at the least at the time of embryogenesis; it might result from the cross-over of genetic material from the Y to the X chromosome; and finally, it might result from the cross-over of genetic material from the Y chromosome to one of the autosomes.

[115] Alex Bell, Final Report to the NHGP, received Sept 29, 1971, pages 5-6. (OA, RG 10-22, NHGP, File 1060). In his more detailed statistical analysis Bell also commented that the XY females and the XX males "are not true sex chromosome anomalies;" Bell likely made no effort to follow these cases closely, he noted that the children were being followed by their pediatricians. Alex Bell, "Computer data and Statistical Analyses," Jan 10, 1972, (OA, RG 67-2, OMHF, File 134).

[116] F Sergovich et al, "Chromosome aberrations in 2159 consecutive newborn babies," 853-4.

[117] Appraisal by Murray Barr, 1966, (OA, RG 67-2, OMHF, File 134).

[118] In his final report Bell noted that "A possible seasonal variation which we had noticed earlier will likely prove to be not significant." Alex Bell, Final Report to the NHGP, received Sept 29, 1971, page 8. (OA, RG 10-22, NHGP, File 1060).

[119] The authors provide "brief clinical notes on chromosomally abnormal infants;" these notes include information about marital status. F Sergovich et al, "Chromosome aberrations in 2159 consecutive newborn babies," 852-3. Valentine later did mention this finding, but only in relation to the XYY cases, only 2 of the then 6 children having been born out of wedlock which Valentine ascribed to chance. Valentine, "The growth and development of six XYY children," *Birth Defects*, 1979, p 186.

[120] For an analysis of these events see: Fiona Miller, "The Impact of Ethics on Research Results: Producing Genetic Knowledge, A Case Study of the Human Sex Chromosome Anomalies," Unpublished MS, Healthy People and Healthy Communities: A Canada-United States Dialogue on Best Practices in Public Health. May 8-9, 1999, Toronto.

[121] Alex Bell, Final Report to the NHGP, received Sept 29, 1971, page 8. (OA, RG 10-22, NHGP, File 1060).

[122] "The largest newborn population studied was in Toronto." S Ratcliffe, "Introduction," "Prospective studies of children with sex chromosome aneuploidy," *Birth Defects*, 1986, xv. Ratcliffe was discussing 7 newborn studies; in this total Winnipeg had been included since the previous March of Dimes workshop and London had been excluded.

[123] DA Stewart et al, "Growth and development of children with X and Y chromosome aneuploidy: a prospective study," *Birth Defects*, 1979, 110.

[124] DA Stewart et al, "Growth, development and behavioral outcome ..." 179, 132.
[125] Charles Netley, "Summary Overview of Behavioural development in individuals with neonatally identified X and Y aneuploidy," *Birth Defects*, 1986, 301.
[126] GH Valentine et al, "The growth and development of four XYY infants," *Pediatrics*, 48:4 (October 1971), 591.
[127] *Ibid.*, 592.
[128] *Ibid.*, 592.
[129] *Ibid.*, 588, 589.
[130] *Ibid.*, 592.
[131] GH Valentine, "The growth and development of six XYY children," *Birth Defects*, 1979, 185, 187-8. In the first follow-up the authors had written: The authors theorized that the XYY individual might simply be pre-disposed to anti-social behavior; he might suffer from a "precarious emotional balance which requires only other inherited personality defects, or an unstable emotional climate to precipitate the impulsive, aggressive and anti-social features that have come to be associated with a YY chromosome complement." "What has one learned from a study of these four randomly ascertained infants?" Valentine and his colleagues asked rhetorically. "No more perhaps than the knowledge that in infancy there may be no clue... to the presence of an extra Y chromosome." GH Valentine et al, "The growth and development of four XYY infants," *Pediatrics*, 48:4 (October 1971), 593.
[132] On this see: RJ Gorlin and H Sedano, "XYY Syndrome," *Modern Medicine of Canada*, 30:1 (Jan 1975), 42-3; John Hamerton, "Human Population Cytogenetics: Dilemmas and Problems," *American Journal of Human Genetics*, 28 (1976), 107-22; John Hamerton, "Ethical considerations in Newborn Chromosome Screening Programs," *Birth Defects*, 1979, 267-78; Thompson and Thompson, *Genetics in Medicine*, Fourth Edition, (WB Saunders Co., 1986), 143.
[133] GH Valentine, "The growth and development of six XYY children: a continuative report," *Birth defects*, 1982, 226, emphasis in original.
[134] This summary was produced by members of the Denver team, who had conducted their own newborn study, and participated in the series of international workshops and publications that brought the various independent trials into conversation. This review paper incorporated the results from the Toronto study, but not from the London study. Valentine withdrew from the international meetings in the early 1980s, because of increasing concern at the ethical improprieties of the work, and a lack of conviction that the clinical information was of value.
[135] Mary Linden et al, "Review: Intrauterine Diagnosis of Sex Chromosome Aneuploidy," *Obstetrics and Gynecology*, 87(3) (1996) 468-475.
[136] *Ibid.*, 470.
[137] Charles Rosenberg, "Banishing Risk: Continuity and Change in the Moral Management of Disease," in Allan Brandt and Paul Rozin, eds., *Morality and Health* (New York and London: Routledge, 1997), 42, 43. Rosenberg makes the argument about moralization in relation to chronic disease in particular. This category, of chronic disease, seems as logical a home for risk-based diseases as any.
[138] Linden et al, "Review: Intrauterine Diagnosis of Sex Chromosome Aneuploidy," 469.
[139] *Ibid.*, 471-2.
[140] Much of the early theoretical work was conducted by Susumu Ohno of the City of Hope Medical Center in Duarte California in the latter half of the 1950s. See: S Ohno, *Sex Chromosomes and Sex-linked genes*, (New York: Springer-Verlag, 1967).
[141] Thompson and Thompson, *Genetics in Medicine*, first edition, 115, emphasis in original.
[142] ML Barr et al, "The XXXXY sex chromosome abnormality," *Canadian Medical Association Journal*, 87 (Oct 27, 1962), 896.
[143] Thompson and Thompson, *Genetics in Medicine*, first edition, 128.This theory had three implications; it provided an explanation of "dosage compensation" – compensating for the differential size and genetic content of the X and Y chromosomes; it suggested that all females had two populations of cells (one with a maternal X inactivated and one with a paternal X inactivated) and were in effect mosaics; and finally, that since the inactivation of the maternal or paternal X chromosome was random, the heterozygous female would demonstrate variable expression of the particular trait.

[144] ML Barr et al, "The Triplo-X female: An appraisal based on a study of 12 cases and a review of the literature," *Canadian Medical Association Journal*, 101:5 (Sept 6, 1969), 256.
[145] *Ibid.*, 256. "In contrast to any other trisomy known in man, triplo X females do not show a reasonably constant phenotype." Yunis, "Human chromosomes in disease," 205.
[146] "Thus it appears that the Y chromosome bears potent male determiners which largely counteract female determiners, even on multiple X chromosomes." ML Barr, "Abnormalities of sex chromosome complex in relation to embryological development," Paper presented to American Academy of Pediatrics, Chicago, Oct 2, 1961, p. 2. (NA, MG30B111, 11-7).
[147] David Carr et al, "An XXXY sex chromosome complex in Klinefelter subjects with duplicated sex chromatin," *The Journal of Clinical Endocrinology and metabolism*, 21:5 (May 1961), 503. See also: D Carr, "Should concepts of sex determination in mammals be revised?" Abstract, Meeting of the Royal Society of Canada, June 5-7, 1961 (NA, MG30B111, 15-8).
[148] Murray Barr, "Sexual Dimorphism in Interphase Nuclei," *American Journal of Human Genetics*, 12 (1960), 124, 125.
[149] Alex Bell, "Sex chromatin survey of Toronto Newborns," no date, (OA, RG 67-2, OMHF, File 134).
[150] Barr attributed this also to Susumu Ohno, see: Murray Barr, "The sex chromosomes in evolution and in medicine," *Canadian Medical Association Journal*, 95 (Nov 26, 1966), 1142; Murray Barr, "The sex chromosomes of man," *American Journal of Obstetrics and Gynecology*, 93 (1965), 609.
[151] David Carr, Murray Barr and Earl Plunkett, "An XXXX Sex chromosome complex in two mentally defective females," *Canadian Medical Association Journal*, 84:3 (Jan 21, 1961), 136-7.
[152] Carr, "Chromosome studies in spontaneous abortions," Ph.D. thesis, 144.
[153] Thompson and Thompson, *Genetics in Medicine*, first edition, 112.
[154] "The testes of prepuberal chromatin-positive males are normal except for a reduction in the number of spermatogonia in the seminiferous epithelium." And, "The first pathological change in the chromatin-positive XXY male occurs in early puberty and the pathology is found in the testes." Murray Barr and David Carr, "Sex chromatin, sex chromosomes and sex anomalies," *Canadian Medical Association Journal*, 83:19 (November 5, 1960), 984. Dave Carr's work on abortuses did eventually show that fetuses with Turner's syndrome did develop ovaries, but they were usually just streaks of connective tissue by the time of birth.
[155] Thompson and Thompson, *Genetics in Medicine*, first edition, 111.
[156] *Ibid.*, 112. This statement mirrors the popular determination to read biology in such a way that "the father, not the mother, determines whether the child will be a girl or a boy.' Helen Claire Howes, "A Boy or a Girl? Sex of the Unborn Child," *Saturday Night*, August 2, 1952, p. 34.
[157] Carr, "Chromosome studies in spontaneous abortions," Ph.D. thesis, 100, 101.
[158] Terence Robertson, "Babies thought 'hopeless' can be restored to normal." *Toronto Financial Post*, July 15, 1961 (OA, Reel 192).
[159] ML Barr, "Abnormalities of sex chromosome complex in relation to embryological development," Paper presented to American Academy of Pediatrics, Chicago, Oct 2, 1961, p. 10. (NA, MG30B111, 11-7).
[160] Alice Dreger, *Hermaphrodites and the Medical Invention of Sex*, (Harvard University Press, 1998), 38.
[161] "One might have predicted," Barr wrote, "that the double dose of Y [in XXYY males] would so dominate the 2 X's as to permit normal testicular maturation at puberty, but this is not so." ML Barr, "Abnormalities of sex chromosome complex in relation to embryological development," Paper presented to American Academy of Pediatrics, Chicago, Oct 2, 1961, p. 8. (NA, MG30B111, 11-7).
[162] But these men also suggested the impotence of the Y chromosome in the "non-sexual" sphere. "The study of individuals who have two Y chromosomes," Barr et al wrote, "suggests that the inclusion of an extra Y, while not innocuous, does not alter radically the course of development that would otherwise be expected. Although our knowledge of the genetic properties of the Y chromosome is no doubt incomplete, the clinical findings in double-Y individuals are consistent with the view that the Y chromosome bears relatively little genetic information, compared with the autosomes, other than that concerned with male sex determination." ML Barr et al, "The XXYY variant of Klinefelter's syndrome," *Canadian Medical Association Journal*, 90 (Feb 29, 1964), 580. Not all researchers were prepared to leave such a conclusion untouched. A study by Sergovich and colleagues in 1971 drew links between male and female anomalies

both of which involved 4 "additional" X chromosomes. Here the link drawn was not sexual, but physical, specifically certain kinds of skeletal anomalies; this research also attempted to use the evidence of similar physical effect to rehabilitate the Y, in the "non-sexual" sphere: "the Y chromosome has a more complex function," they wrote, "than merely the initiation of testicular structures." F Sergovich et al, "The 49, XXXXX chromosome constitution: Similarities to the 49, XXXXY condition," *Journal of Pediatrics*, 78:2 (Feb 1971), 290.

[163] Carr, "Chromosome studies in spontaneous abortions," Ph.D. thesis, xii.

[164] Dreger, *Hermaphrodites and the Medical Invention of Sex*, 4.

Chapter 5

Re-making Medical Genetics: Organizing the Department of Medical Genetics in Toronto

Introduction

In 1961, shortly before her retirement, Ford Walker offered her thoughts on the relations between genetics and medicine. In a co-authored review of extant and needed Canadian research on the human genetics of radiation effects, Ford Walker pointed out that, "Some of the questions asked concerning the genetics of human populations have direct medical implications, but," she cautioned, "this is not true of all of them." Though some of the basic genetic mechanisms to be investigated were of medical interest, many were not. Ford Walker warned that "the more fundamental studies of human populations and their genetic structure may suffer from lack of support as compared with those having direct practical objectives." [1] For Ford Walker, for her colleagues, and for the research school that she had built in Toronto, medical genetics was a sub-species of human genetics. It was relevant for those with a practical interest in human health and disease, but it did not encompass the larger field of fundamental inquiry in human genetics.

Yet, within little more than a decade this consensus would change. Medical genetics would come to be defined as a larger field of inquiry, one not solely limited to the human organism, but encompassing fundamental studies of genetic mechanisms in other organisms, to elucidate general questions of disease causation. Ironically, it was Ford Walker's protégé, Margaret Thompson, who articulated this emerging definition within the shifting institutional and disciplinary parameters of medical genetics in Toronto. Medical genetics, Thompson offered in 1975, "... involves [the] application of genetics to the understanding of normal and abnormal human biology, but does not imply ... that the organism of study is necessarily man. Thus it includes such fields as molecular and mammalian genetics in so far as these fields relate to improving understanding of human biology."[2]

In this Chapter, I document the production of this new form of medical genetics in Toronto. The re-definition of medical genetics institutionalized conceptual and technical changes that had steadily re-made the indigenous tradition since the late 1940s. It was abetted by institutional reorganization at the university, as the Faculty of Medicine moved to foster a closer association between the basic and medical sciences in support of the 'new biology.' These local institutional changes involved negotiations between the hospital and the university, and the creation of a new department which broached the former divide between the Faculty of Medicine and the hospital-based practice of medical genetics. The re-definition of medical genetics in Toronto was a contested process, and

involved political negotiations, as new hierarchies, and strategies of inclusion and exclusion, were negotiated.[3]

Louis Siminovitch, a biophysicist practicing somatic cell genetics, emerges as the central protagonist of this story of local organization. Assisting with and then presiding over the reorganization of genetics research at the University of Toronto from the mid-1960s, he emerged in the 1970s as the Chief Geneticist at Sick Kids and the head of a Department of Medical Genetics that spanned the hospital and the university. This new Department brought into association the biophysically-oriented biological researchers at the university with those human geneticists at the hospital who were able and willing to re-make themselves. It also created room for a new breed of 'clinical geneticist,' oriented solely towards service in what was once a primarily research-oriented field.

The HSC Research Institute: Re-producing Medical Research

The Toronto press took some interest in the opening of the "new" Sick Kids in 1951. Announcing an open house in January, one report highlighted what seemed to be the principle feature of the new building. "Major Research Centre," the headline read: "Hospital for Sick Children Building to be Opened January 15th for Inspection." "The new hospital," the article announced, "will rate as one of the world's major research and treatment centres on children's diseases."[4] When, less that three years later, the new Research Institute was announced, the press once again highlighted the value of research

for treatment: "Co-ordinate all Research to Treat Sick Children," the headline read: "Doctor Predicts Improved Results."[5]

Organizing efforts at Sick Kids in the early 1950s reflected the widespread faith that the advance of medical science necessarily resulted in better treatment for patients, both in the future and even immediately. Yet while press reports reflected this implicit faith, the practical reality within the walls of Sick Kids was more complex. For many medical workers, research was in potential conflict with clinical service.

From the mid-1950s, when the Research Institute was formally established, its scope and size were consistently expanded. But this did not occur without contest. Expansion of the Institute reflected and supported the centrality of research within medicine, but it also supported shifting hierarchies of medical, clinical and basic research. Though the Institute was initiated with a human research orientation that saw research without direct medical application as too fundamental to support, by the late 1960s and 1970s, all clinicians were assigned the expectation of 'clinical research' and the Institute directed its attention to the more basic varieties of research, increasingly with a focus on the non-human organism. Some members of the hospital community balked at the subordination of what we might call 'human-order' knowledge within this hierarchy.

The struggles over organization and reorganization of the Research Institute at Sick Kids, from the mid-1950s through the late 1960s, were important for the reorganization of medical genetics in Toronto for two reasons. First, they stand as general examples of the re-organization of knowledge and practice hierarchies. Second, and more

specifically, they served as the material backdrop to reorganizing efforts in medical genetics in Toronto.

"The Research Institute of the Hospital for Sick Children has been established," the Research Committee stated in 1954,

> for the promotion of research into diseases and disabilities of children, and the programme of the Institute will be carried out in all departments of the hospital, both clinical and laboratory. The purpose of the Institute will be to increase existing knowledge concerning the causes of diseases of childhood and to improve methods of diagnosis and treatment. Research directed towards the development of methods of prevention of such diseases will also be undertaken.

In developing the Institute, its framers sought to carefully delimit its scope. This was an Institute that was to serve, not lead, clinicians:

> In the furtherance of these [above] objectives, it will from time to time be necessary to engage in investigative work of an allied, but more fundamental character, in the laboratories of the Hospital. These studies will be conducted only if it proves necessary to supplement the information being gained by other methods of investigation.[6]

Yet this careful delineation of priorities suggests how difficult was the balancing act that was being proposed – and it was a balance that did not hold. By 1959, advocates for an expanded role for research targeted two forces that limited expansion, specifically, the problems of insufficient workers and shortages of space. In the Annual Report, the Director of the Research Institute declared that he and the research committee had been "considerably exercised" over proposed building plans which they feared would not

"provide adequate space for the proposed increases in the number of research projects, and the working space necessary for the associated increases in personnel."

> It is appreciated that limits must be drawn to the space which may be made available to a research group associated with a service hospital; however, it should be emphasised that the problems of medical research, though they may arise from the study of clinical cases admitted to the hospital, depend on research in the allied basic sciences of Biochemistry, Physiology and Pathology, for their complete comprehension. Though this aspect of medical research may not have been in the consciousness of the Trustees when the project of a Research Institute was elaborated some six years ago, it becomes increasingly apparent that the profitable future of medical research must depend more and more on the work of men who are trained in the fields of basic science .... Unfortunately, this aspect of medical research is too little emphasised in the contacts which the clinician has with medical students under his instruction; it is to be hoped that sufficient student contact may be provided to men who are working in the fields of basic science related to medicine, so that an interest in such science may be aroused in both junior and senior medical students, who may thereby be attracted to an academic career in such fields.[7]

This demand for expansion was not uncontested, however. In 1960, as the committee on research which oversaw the Institute contemplated its organization, tensions between a research and clinical orientation erupted. Some members of the committee recommended reorganization to ensure that "research is to be a tool of the medical departments rather than visa versa."[8] Arguing for increased clinical responsibilities among researchers, and for reducing the role of research Director to that of an administrative assistant, this camp argued that "The trustees of the hospital in setting up the Institute did not conceive that it would become a centre for basic research, but envisaged an Institute which would carry on research in problems arising from the clinical wards....[A]t no time," the minutes added, "when the erection of the Research

Institute was considered was an organisation similar to the Rockefeller Institute model thought of."[9]

Other members of the Committee, led by the Director, argued strenuously for retaining the current organization, and for minimizing the clinical obligations of researchers, noting that "research is now a highly specialized and competitive occupation."[10] Indeed the Director of the Institute was actively working to enhance the orientation of the Institute toward research, arguing that "the time might be ripe to consider the possibility of adding graduate teaching responsibilities to the Institute and developing it as a centre of the University of Toronto for graduate instruction."[11]

It was this latter vision of the Institute that was endorsed by the Board of Trustees and the Institute continued its steady expansion and advanced its research focus.[12] Indeed, in the late 1960s, grandiose plans for expansion were well received by the hospital board: "The trustees would like it understood," the Minutes of the Committee on Research note, "that they support the efforts of the Hospital staff and the staff of the Research Institute to expand and improve clinical services as a result of an expanded research effort."[13] And while the problems of space were constant, being a function of the growth imperative,[14] the problems of personnel were reversed.

In the mid-1960s, after further reorganization had encouraged closer collaboration between the clinical and research aims of the hospital, rather than having too few clinicians interested in research, as had been the complaint in 1959, the problem was the opposite one.[15] By 1967, it appeared that any ambitious clinician must necessarily pursue

research, and this promised to exacerbate ongoing space problems. The Director of the Institute noted "a revolution (albeit a quiet one)" in the

> attitude towards investigation by the bright young clinician of today compared to that of his elder brother even as recently as a decade ago....Consequently heads of patient-service departments in important clinical institutions, such as our own, are increasingly encountering the situation that the bright young men in their respective disciplines cannot be recruited or retained on their staffs unless they are given excellent facilities including well-equipped space for research .... In addition, the young man is demanding more time in which to conduct the research.[16]

By the mid-1960s, then, though conflicts continued, the research imperative was seen to be capable of transforming the definition of clinical practice: All clinicians, to be good clinicians, would be researchers. Moreover, as the Director of the Institute noted, they would be good researchers: their research projects would be able to "compete at every level with programmes conducted by full-time salaried career researchers." "In the future," the Director added, "demands on our resources (particularly space) will be so competitive that we will not be able to permit projects to continue unless they are of this high caliber." The Director saw this "quiet revolution" in clinician concerns as coinciding "almost exactly with our [the RI's] avowed aims. The more clinicians on the Hospital Staff who are deeply involved with sophisticated research programs, the more rapidly will the benefits of the laboratory reach the bedside." [17]

The reproduction of clinicians as researchers encouraged the clarification of research hierarchies within the hospital. Clinicians would be "clinical researchers" and the Research Institute would unabashedly advance 'basic' research. In 1970, the Scientific Advisory Committee to the Research Institute advised that "there is really a need to put

more of the resources into well-trained scientists. The Institute is weighted too heavily by physicians with an interest in research."[18]

By the 1970s, the Research Institute had committed itself to advancing research that was only symbolically associated with patient care, through the promise of 'applicability.' This orientation created more room for Ph.D. scientists with little or no clinical capacity or interest, and for a shift away from the use of patient-based research material to non-human organisms. Clinically-oriented and patient-based research continued, of course, but it now existed side-by-side with the 'basic' non-clinical and non-human research that was increasingly conducted at the hospital. Moreover, it suffered a reduced status as a result.

Building Institutional Capacity – Making the New Medical Genetics

The changing shape of medical genetics in Toronto was modeled on and affected by the institutional shifts within the Research Institute. But the timing of the transition was closely associated with the retirement of Norma Ford Walker, and the transformations occurring at the university Faculty of Medicine.

In the 1950s and early 1960s, Ford Walker had presided over a department that responded with alacrity to the new medical biochemical genetics and cytogenetics. Yet she also retained an indigenous research tradition that was coming to make less and less sense, and to be of less and less interest, in the new era of invigorated classical genetics.

When she retired from her posts at Sick Kids and the university in 1962, her departure created the usual institutional problem of succession. Because of her long reign, however, her departure also created the opportunity for institutional reorganization to match the changing epistemological shape of the field. The protracted efforts at finding her successor, not complete until 1970 when Siminovitch was appointed to head a new Department, illuminate the remaking of medical genetics in Toronto.

Efforts by the hospital to find a successor to Ford Walker began in the late 1950s, anticipating her departure for 1960. The hospital unsuccessfully courted F Clarke Fraser of Montreal, who had headed the Montreal group in medical genetics since shortly after World War II.[19] From this date, and for approximately the next decade, the goal was to find a "medically qualified geneticist."[20] Initial efforts were delayed by Ford Walker's decision to extend her retirement by two years.[21] Yet the real delay was a function of the Institute itself: stalled by questions of internal reorganization and by a tradition which granted leadership in such areas of decision-making to the university.

The university was attuned to its own agenda when it appointed the human geneticist, T Edward Reed, to fill Ford Walker's shoes in the Department of Zoology in 1960. That department's need was for "an academic research-minded Geneticist."[22] The hospital was notified of the university's search for a replacement, since the university wished to have the connection with the hospital continued. But Reed, a population geneticist with a research focus on blood groups, was not medically oriented, and was not, from the perspective of the hospital, an adequate replacement for Ford Walker.[23]

Soon after Reed's appointment to the university, the Director of the Research Institute expressed particular concern that "the Institute does not have a Full Time Geneticist on staff. There is also a need," he noted, "for a qualified basic scientist [in genetics]."[24] When Ford Walker retired in the summer of 1962, Reed was appointed as the acting director of the Department of Genetics for a year.[25] By the fall of 1962, the Committee on Research of the Institute reiterated their opinion that "with developments in the field of genetics" there was a need for a full time Director of the Department of Genetics, and they hoped to make an appointment by the following summer.[26]

Reorganization of the Genetics Department fell victim to the inadequacy of space and the ongoing planning for the future of the Research Institute. The committee was advised in the fall of 1962 that "at the present state of planning the Hospital cannot allocate further space to the Department of Genetics beyond the space which it now occupies." In light of this, Reed's appointment as Acting Director was extended by a further year and the committee reaffirmed its belief that a full-time Director should be appointed when space became available for the extension of the department.[27] The following summer (1963) Margaret Thompson was appointed as a research associate in genetics. Thompson's appointment served as another example of the hospital's deference to the university in deciding appointments to the Genetics Department. The hospital was asked by the Dean to "accommodate Dr Margaret Thompson, wife of Professor Thompson who was being brought to the University Department of Anatomy."[28] Yet it was she who would step into the breach, serving as acting director over the latter-half of the 1960s.[29]

In the fall of 1964, the Head of Pediatrics, AL Chute, produced a report on the Department of Genetics outlining the difficulties it had faced. The chief problem he identified involved the lack of planning in growth. The Department had grown initially in an ad hoc fashion, responding to the interests of Ford Walker and her students, with the initial approval of Alan Brown. Since Ford Walker's retirement, Chute noted, "we have not really controlled the appointments to this service but have accommodated University needs largely through lack of an approved plan of our own."[30] About Reed he was diplomatic: Reed, he noted, had been "rather inundated in his first year by the load of lectures at the University. He had, therefore, little time to give to research here [at the hospital] or to family counselling. Diagnostic dermatoglyphics were also outside his field of interest and expertise."[31]

In conformity with the Institute's goal to integrate research with clinical departments it was suggested that the anomalous situation of genetics, in having no departmental status outside the Research Institute, should be corrected. The Genetics Department should be "primarily a service area" Chute recommended, providing diagnosis and counseling. "Research should be developed by this area as in other service areas as the programme develops." Moreover, "In view of the volume of genetic abnormalities, mental defectives (mongols) [and] congen[ital] anomalies," Chute continued, "... it would seem that we should have a full-time person as director of this department." It was early recognized that finding the right person would be a challenge. "One of the chief difficulties is the acquisition of a Geneticist with a broad interest and knowledge in human genetic problems," Chute noted. "Preferably an M.D. with genetic

training, if not a Ph.D. with demonstrated interest in the service aspects of diagnosis (dermatoglyphics and cytogenetics) and counselling of parents, as well as an interest in investigative work."[32] What was needed was an individual able to fulfil the requirements for "both a service and research Geneticist."[33]

As a result of Chute's report, a Committee on Genetics was struck to consider the issues. The committee soon reported their support for the appointment of a new Director, arguing that genetics "impinge[d] on every field of medicine in all the clinical departments as well as in the basic science area." Included in its core competence were diagnosis and counseling, cytogenetics, clinical and family studies, and biochemical genetics.[34] This report was submitted to the Medical Advisory Committee which approved it but added that "as a principle, the Chief Geneticist should be a medical doctor."[35]

The hospital had specific needs with regard to this appointment – needs which emphasized applied competence in addition to investigative capacity. This desire reflected the mid-1960s situation in the Research Institute, where the goal was greater research, but still focused on the human organism and in the service of the medical patient. But university leadership was still presumed: the new full time Director, together with any future staff, was to "be acceptable to and receive appointments in the new Human Genetics Committee of the Faculty of Medicine" that was proposed at the University.[36] Over the latter-half of the 1960s, that requirement, together with the expectations of potential appointees, crippled the effort to appoint a head and thus to establish the new department.

Meanwhile, by the mid-1960s, the Faculty of Medicine at the university was developing a new agenda with respect to genetics at the university, in preparation for the new Medical Sciences building, to be opened by the end of the decade. Given the pattern of university leadership in genetics at Sick Kids it is not surprising that the shifting patterns that emerged out of this university-based reorganization were ultimately reflected in medical genetics at the hospital.

In the interwar-period, Toronto had prided itself on leading in the pursuit of Flexnerian reforms.[37] Yet, according to then-President Claude Bissell, in the post-war period it was falling into decline. In the early 1960s, the Dean argued that the Faculty of Medicine was slipping badly, largely as a result of the continuing reliance on part-time teachers, the split between the clinical and the basic sciences, and the lack of research facilities. The Faculty had a strongly practical orientation and was not seen, by outside observers, as nurturing academic medicine.[38] In addition to what Bissell termed "the "failing academic strength of medicine," there was pressure to expand the student population to meet the patient demand that would be spurred by the anticipated provincial health insurance plans. These forces encouraged a renewed emphasis on medical science and in the last half of the 1960s, the University of Toronto planned and built its new Medical Sciences Building, which towered over the downtown campus.[39] In this period also, the university took over and developed Sunnybrook Hospital as its own university hospital.[40]

The new Medical Sciences Building at the University of Toronto was to bring together all the basic and clinical sciences in recognition of "the increasing

interdependence of the biological and medical sciences."[41] It was a reorganization that drew its inspiration from the "new biology" that had been built in the US by the late 1950s. The new biology differed from the old biology in its attention to the sub-microscopic, its dependence on physics and chemistry, and its disinterest in the traditional concern with the organism and its emergent properties. By the terms of the new biology, it was not the specificity of organisms that mattered, but the fundamental properties that all organisms shared which provided the 'secret of life.'[42] In Toronto, genetics had previously been taught within the medical school by members of the Department of Zoology. But the creation of a new medical science building, and the corollary new medical science vision – inspired by the new biology – created the opportunity for establishing genetic capacity within the Faculty of Medicine.

Louis Siminovitch, then Head of the Division of Biological Research at the Ontario Cancer Institute, and a full professor at the University of Toronto, set out his thoughts on the "future of genetics" at the university in preparation for this reorganization. "I do not feel," Siminovitch wrote in 1965, "that a Department that contains only medical geneticists can remain top-flight. Such people," he added, "must have intimate contact with geneticists from other areas."[43] In seeking to produce "top-flight" research, then, Siminovitch recommended a Department of Genetics that would include some of those interested in medical genetics with workers on plant, virus and biochemical genetics. He premised these recommendations on the belief that the "classical tie-up between genetics and botany and zoology is diminishing and that, at the

moment, genetics interrelates most closely with biochemistry, microbiology, biophysics, immunology and pharmacology, and possibly physiology."[44]

In the mid-1960s, then, Siminovitch shared with his university and hospital colleagues the belief that medical geneticists were human geneticists with an interest in health and disease. It was a definition given the stamp of official approval in the Survey of "Canadian Medical Research," published in 1968 by MRC.[45] Yet this was not the definition that would prevail into the 1970s.

Siminovitch's recommendation that a Department be created was not immediately accepted, nor his suggestion that it be called Genetics. Yet a 'Group in Cell Biology' was established and he was appointed its first chairman in 1966.[46] Not until 1969 would the Group be granted Departmental status, when space became available in the new building, and until then Siminovitch remained physically at his base within the Department of Medical Biophysics at the Ontario Cancer Institute. Nonetheless, planning for the Group proceeded. These plans responded to Siminovich's concern with the state of genetics research on the campus – his conviction that the medical (read human) geneticists could not be left to their old devices, attached to 19th century natural sciences and divorced from their 'natural' allies in the 'new' pre-clinical disciplines of biochemistry and biophysics. Cell biology was a hodge-podge group, assigned responsibilities for teaching in microbiology, immunology and genetics.[47] In its responsibilities toward these as a triumvirate of still-distinct disciplines, it proved unsatisfactory. But in planning for

research programs which merged this group with medical biophysics, it was a step on the path to a more inter-disciplinary and less human configuration for medical genetics.[48]

When Siminovitch made efforts to organize the cell biology group as a department in the spring of 1969, he developed a research agenda which necessitated inter-disciplinarity: it focused on developmental biology and somatic cell genetics. Yet this inter-disciplinary research program did not encompass the whole team. Only the more "applied aspects" of the cell biology agenda were to be pursued in the hospitals, and those workers were expected simply to "have strong groups in human genetics."[49] In other words, the medical geneticists were not clearly conceived of as partners in the project of research in cell biology. Their role was to pursue applied research, assist in teaching, and perform clinical services. Nonetheless, if the medical geneticists, as individuals, were only partially integrated into the research group, their symbolic status was unifying. Human applications, after all, justified the "eventual aim" of the cell biology agenda. The point, as Siminovitch argued to potential funders, was "of course, to apply our basic information to problems in man."[50]

Siminovitch's involvement with planning for the university's genetics research, and the necessity of considering the place of hospital staff from university-affiliated hospitals in this planning, resulted in his involvement in Sick Kid's efforts to recruit a person to be in charge of Medical Genetics.[51] The plan, in the latter-half of the 1960s, was to appoint a human geneticist who would run medical genetics within Sick Kids. Siminovitch was amenable to allowing the recruited person to chair a similar group in medical genetics within the Department of Cell Biology at the University.[52] But

difficulties in appointing an appropriate person were protracted. Several individuals were offered the job but refused. Many explained their disinterest by pointing to inadequacies in research space, and uncertainties about academic status at the university as departments evolved. As the head of the Research Institute was declaring at this time: "the bright young men in their respective disciplines cannot be recruited or retained on their staffs unless they are given excellent facilities including well-equipped space for research."[53]

In 1970, Siminovitch assumed leadership of the Department at Sick Kids, beginning his appointment October 1st.[54] He was to serve as chief geneticist at the hospital in addition to his role as Chair of the Department of Cell Biology at the University. This appointment solved seemingly irresolvable administrative difficulties between the university and the hospital which had prevented an outside appointment: Siminovitch's status was full professor and his needs in the way of research space and a research team were, to some extent, already accounted for. But Siminovitch's appointment was more than just administratively useful. It also reflected changed intellectual and organizational assumptions.

By the time Siminovitch was appointed in 1970, the new goal of the Research Institute – to emphasize 'basic' research and downplay the role of the research-oriented physician – was congruent with Siminovitch's emphasis on basic research, where human genetics served as an applied discipline and as a symbolic goal. Though the initial intention, at Ford Walker's retirement, had been to find a human geneticist with a

medical dimension, the delay in appointment – a delay of more than five years – allowed the shifting orientation towards research at Sick Kids' Institute to move into alignment with the new priorities of the university researchers. The administrative hiatus had also allowed the medical geneticists at the hospital to remake themselves in accordance with the new priorities. For the most part, these old order medical geneticists, even in the context of limited space and an approved plan, were willing participants in the re-making of medical genetics.

Leadership During the Hiatus

After 1965, Margaret Thompson served as acting head of the genetics department at Sick Kids. Concurrently, she had an appointment as Associate Professor in her old Department of Zoology. By 1968, Thompson had been appointed to Siminovitch's Department of Medical Biophysics, which merged with the Cell Biology Group in 1969 to become the Department of Medical Cell Biology. Reflecting the changing disciplinary orientation of medical genetics at this time, Thompson resigned from the Department of Zoology in 1970.[55]

Margaret Thompson was one of the students of the Ford Walker school who successfully navigated the shifting terrain of her mutating profession. In the mid-1960s, Thompson spent time at the premier facility for the production of North American medical geneticists: Jackson Laboratory in Bar Harbor, Maine. Victor McKusick, himself

the 'father' of medical genetics in America, had helped to establish the influential summer "Short Course in Medical Genetics" at Jackson Lab in 1960. This institution fostered links between mammalian and medical genetics and worked to generate and disseminate a hegemonic tradition of medical genetics both within North America and world-wide.

As a post-doctoral fellow at the Jackson Laboratory, Margaret Thompson expanded her human genetics skills to include mammalian genetics. She participated in mouse genetics research while there and continued this work upon her return to Toronto, even as she also continued her more traditional human genetics work. Louis Siminovitch, an infrequent and indirect resource for Toronto geneticists,[56] worked in collaboration with Margaret Thompson on some of this research in the late 1960s. This collaboration abetted Thompson's fuller integration into the Siminovitch fold in the 1960s and 1970s. She collaborated with Siminovitch-trained geneticists in new research on somatic cell genetics from the early 1970s and was a member of the team which did internationally important research on the molecular genetics of Duchenne Muscular Dystrophy in the 1980s – a condition she began researching using the tools of classical genetics in the early 1960s.[57]

Margaret Thompson shared with Siminovitch the latter's sense that the future of medical genetics lay in association with the new pre-clinical disciplines. During the latter-half of the 1960s, under her leadership, the Department of Genetics at Sick Kids addressed key questions in the organization of medical cytogenetics and biochemical genetics research, and laid the ground-work for further changes in the 1970s.

Medical biochemical genetics became one of the dominant research traditions within medical genetics at Sick Kids in the 1960s. Work on genetic metabolic disease, which brought geneticists, biochemists and clinicians into close association, was seen as a model of inter-disciplinary collaboration. In 1967, Andrew Sass-Kortsak reported on a "Genetic, Biochemical and Paediatric Center for the Study of Inborn Errors of Metabolism" and advocated more work of this kind.[58] These projects were necessarily interdisciplinary, he argued. There were "Geneticists, because these conditions are inherited, biochemists because the basic defects is of a biochemical nature and paediatricians, because these diseases afflict infants and children primarily" [59]

Sass-Kortsak's discussion of genetic metabolic disease was part of a plan for "Further Development and Expansion of Research Activities in the Department of Paediatrics," which presumed the need to pursue "basic" research. While clinical research was not excluded, Sass-Kortsak noted that "exploration of problems in depth will be necessary." Specifically, "Animal experimentation and other strictly laboratory based studies of biochemical, physicochemical, physiological, biophysical and mathematical nature will have to be carried out to shed light on the disease process in question....This approach will require the organisation of teams composed of scientists with a wide spectrum of interests and qualifications," Sass-Kortsak noted. Including "clinical staff physicians," "research oriented physicians," and "full time basic scientists." [60]

These interdisciplinary ventures encouraged the move towards more 'basic' research among the community of medical scientists in the hospital, and for geneticists,

they encouraged studies in human biochemical genetics to be merged with more 'basic' approaches. By 1968, a new interdisciplinary venture was being coordinated involving pediatrics, genetics, virology and biochemistry in the study of fibroblasts "as a medium for study of metabolic reactions in inherited Metabolic Diseases."[61] Further expansion of the metabolic genetics program took place in 1970, just prior to the appointment of Siminovitch as head of the Department. Andrew Sass-Kortsak and Margaret Thompson recommended two new appointments to expand the genetics team within the Division of Pediatrics – giving Diane Wilson Cox a more secure position, and providing a spot for one of Siminovitch's post-doctoral fellows, Manuel Buchwald, in the hospital under Thompson's auspices.[62] The purpose of these additions was to enhance the hospital's research in "productive and promising" fields that had gone ignored: "the field of cell genetics ... [with] its application to prenatal detection of genetic disorders and ultimately to genetic engineering."[63]

These efforts at coordinating genetics research which created space within Sick Kids for some workers also involved exclusion. In his 1967 review of the current and future needs of Pediatric research, Sass-Kortsak had identified the need for research on blood groups. This "may well be regarded," he noted, "as primarily of genetic interest and as such should be covered by the Department of Genetics. However, failing this, there should be a full time research-oriented scientists who is properly qualified in this and attached to the Hematology Department. [64] But by this time, Edward Reed, the human population geneticist who would have been a logical person to meet that research

need within the genetics department had been frozen out. After Margaret Thompson took over as acting head, and Reed transferred his activities to the university, he sought the continued use of research space at the hospital beyond the period approved. But the Committee on Research, and Margaret Thompson, refused. The genetics department had continuing space constraints at this time, so the decision is understandable on those terms,[65] and Reed's vacated space was made available for Thompson's laboratory and research fellows.[66] But this exclusion also reflected Reed's association with the traditional disciplines of Zoology and Anthropology and his classical human population genetics research interests.

But Edward Reed was not the only member of the old medical genetics community who was excluded from the field as it re-made itself. Pat Conen who, since 1960, had presided over the medical cytogenetics enterprise at Sick Kids, was also frozen out. His exclusion was coordinated with the late 1960s relocation of medical cytogenetics from the pathology to the genetics department.

Cytogenetics developed in Toronto in a disjointed fashion. Initially supported by grants awarded to both the Departments of Genetics and Pathology, it consolidated within the latter department under Pat Conen's leadership. From the first, however, this situation was seen to be anomalous.[67] In recommending change for the Genetics Department in the fall of 1964, AL Chute made clear the need to "combine cytogenetics and the other aspects of genetic study in one area under one Director." [68]

As Chute submitted his recommendations, cytogenetics was also coming into view for a different reason. Because of Conen's failure to succeed in a grants

competitions, and because of the negative reviews of his applications, it was decided to have cytogenetics subjected to external review.[69] Margery Shaw and Klaus Patau of the University of Michigan and the University of Wisconsin, respectively, submitted their report in February of 1965. It was damning.[70]

Conen was doing very unsophisticated work, they said, and his work lacked clear aims and coherent organization. He was doing "too many different things to do everything well."[71] In particular, his reports of specific anomalies did not, it was argued, warrant the attention he gave them in the literature. Conen was advised to select one among his diverse research interests and pursue that exclusively.[72]

Yet Shaw and Patau were careful to place their criticism in context. They pointed out that

> further progress in human cytogenetics still depends to a considerable degree on a continued collection of cases. Their usefulness is not necessarily impaired if they are found by haphazard sampling of a suitable population of patients rather than in the course of a well-thought-out survey. If the cytological and clinical analyses are competently done and carefully described, their value would suffer little if the interpretation should lack sophistication. Interesting observations have been made in Dr Conen's cytogenetics laboratory, and we do not doubt that this work will continue to be useful if not outstanding.

Moreover, Shaw and Patau saw Conen's lack of mastery of the field as standard. There was a "shortage of technically competent workers in this field and even among the technically competent a degree of amateurism is the rule rather than the exception. In regard to genetic knowledge, clear thinking, and originality, Dr Conen is probably about average. In regard to technical skill, the work done in his laboratory is undoubtedly above

average." Given the desirability of the hospital having a cytogenetic research laboratory, Conen was to be judged by prevailing standards. Shaw and Patau concluded by agreeing with the most generous of the three anonymous reviewers that "This sort of non-specific screening program has some value in turning up new anomalies" and that such work should thus continue.

The mid-1960s witnessed the slow termination of the discovery phase in medical cytogenetics. Those who saw themselves as leading the field were increasingly embarrassed by the amateurishness of case reports, even as they acknowledged their continued value.[73] Pat Conen's interest was resolutely morphological, rather than functional.[74] Indeed, much of the work conducted by Toronto or London-based or Toronto-trained workers was of this kind. Yet by the latter-half of the 1960s, workers like Irene Uchida were shifting from such clinically-oriented work towards locus-studies, where cytogenetic evidence was used to aid in gene mapping. Conen made no such moves.

In fall 1969, the Cytogenetics laboratory was put under Margaret Thompson's supervision, as acting head of the Division of Genetics.[75] This reorganization was in recognition of the desirability of placing cytogenetics within the Department of Genetics (when established), physically and administratively, and overcoming the accidents of Toronto history which had seen this service develop within Pathology. The memo that outlined this administrative change took care to thank Conen for his role in pioneering medical cytogenetics – developing the first hospital cytogenetics laboratory in Canada. The memo noted that the change did not reflect negatively on his capacities, and

encouraged his future interest in the field.[76] Yet his continued work in the area would be conducted without formal affiliation with the geneticists at Sick Kids.

By the time Siminovitch arrived as Chief Geneticist at Sick Kids, the hospital-based workers had already completed considerable reorganization. They had brought medical cytogenetics under the auspices of genetics and established a strong research focus in genetic-metabolic disease with clear links to Siminovitch's cell biology team. Upon his arrival, Siminovitch was able to support further development along these lines. When the new Department of Genetics was initiated, under Siminovitch's direction, the re-organization of cytogenetics was completed. Pat Conen was not cross-appointed, and new cytogenetics capacity was recruited. Ron Worton, who had completed his Ph.D. at the University of Toronto in Siminovitch's Department of Medical Biophysics, became the research cytogeneticist at Sick Kids.[77] Siminovitch also supported the research focus in genetic-metabolic disease, through institutional recognition of the interdisciplinary research programs at the hospital.[78] He chaired the search committee to find the coordinator for the research program in "genetic metabolic disease," and strongly supported the appointment of Andrew Sass-Kortsak.[79] In the fall of 1971, in a brief submitted by the hospital to achieve funding from the provincial health insurance program, the program in genetic metabolic disease was identified as a major area of research: "A Major thrust of the Department of Genetics is predicated on the idea that development of knowledge about the biochemical basis of genetic disease is one of the

most important problems in paediatric medicine, and part of our program will therefore be centered on this area."[80]

Pat Conen shared with Edward Reed the ignominy of being frozen out of the political community of medical genetics, even as these individuals remained technically relevant to the field. Siminovitch's efforts to co-ordinate medical genetics in Toronto across the hospital and the university, in the first-half of the 1970s, illuminate what it was about their interests that were not appropriate to the emerging field. Moreover, Siminovitch's efforts in this period illuminate both how parallel and how divergent were the visions of medical genetics held by the university and hospital workers who *were* incorporated into the new department.

Making the New Department of Medical Genetics: Merging Sick Kids and Cell Biology

Within a few short years of his appointment as Chief Geneticist and Department Head at the Hospital for Sick Children, Siminovitch's dual location facilitated efforts to amalgamate the hospital and university departments into a single Department of Medical Genetics. The merger was more than a name-change and institutional reshuffling, however. This next step in the reorganization of medical genetics in Toronto completed the transformation of the meaning of the field. By incorporating the medically-oriented human geneticists at the hospital with the more genetically-oriented members of the Cell

Biology group, medical genetics was reproduced as a discipline without species distinctions and with a re-ordered hierarchy of knowledge. The parameters of the re-ordering were not, however, without contest.

Siminovitch's proposal for a merged Department was externally reviewed. Charles Scriver, a medical geneticist of the old dispensation from Montreal conducted a site visit and received comments from involved participants. His impression was favorable.[81] Scriver's commentary confirms the fact that this merger was by no means a conquest of the old-order medical geneticists. Louis Siminovitch was not, Charles Scriver noted in his report, a "'medical geneticist' in the true sense of the word."[82] But Scriver was particularly enthused by Siminovitch's interest in his field: "Could anyone not welcome the desire of a group of "basic scientists" to become more involved in the broader issues of medicine?" he asked rhetorically.[83]

The merger that Siminovitch advanced in the early 1970s reflected the changing status of genetics within both biological research and medical research. The merger incorporated the genetically-oriented workers within the Cell Biology Group, downgraded the significance of Microbiology from an independent to an auxiliary discipline, and divested responsibility for Immunology. This reshuffling reflected the sense that genetics was an increasingly important, and fundable discipline in the medical sciences.[84] It also laid claim to the applicability of 'basic' genetics research in clinical medicine. The merger was, as Siminovitch put it, a "vertical integration" of "basic" and "clinical" interests.[85]

In advancing the claim that genetic science was inherently 'applicable' to health, Siminovitch was not alone. As he noted in his "Proposal to Create a Department of Medical Genetics," "the Medical Research Council has recently recognized the importance of medical genetics by specifically indicating that genetics would have a high priority for the creation of Medical Research Council Groups."[86] And, as Mark Pearson, one of the younger members of the Cell Biology Department put it, in his letter to Scriver advocating the merger, "There is an increasing overlap between basic and clinical genetics. Graduate students trained in basic molecular genetics in my laboratory are attracted to the problems of genetic regulation in higher organisms, especially those related to human disease."[87]

Yet the merger did more than enhance the attractiveness of 'basic' genetics in the eyes of funders and students. In producing this integration and conceiving it as vertical the merger also polarized the field internally. Ironically, though the new medical genetics was presented as erasing the 'basic' and 'clinical' divide through the medium of 'applicability,' it was actually generating it. While the basic geneticists were extant, having pursued their constitution in the years of the Cell Biology group, the clinical geneticists were a new entity. Moreover, this new entity implied a rather radical re-shaping of the formerly medical (read human) geneticists as simply 'clinical geneticists' – a beast of a different and lower order. Such a re-shaping suggested the removal of some of the preoccupations of human genetics from the medical genetics department, namely most population genetics, while emphasizing a capacity in which the Sick Kids group was actually weak: clinical practice. Charles Scriver, in his review of Siminovitch's

proposal, had noted the absence of many skills among the faculty of the proposed Department. Among these weaknesses were clinical genetics, human biochemical genetics and human population genetics.[88]

Though Siminovitch supported research programs at Sick Kids which recognized the research interests of the old order medical geneticists – notably the genetic-metabolic disease group – he tended to ignore this dimension of their work in his statements on departmental policy. He did not identify the medical geneticists as involved in 'real' research, but rather as the "clinically-oriented group," even as he acknowledged the weakness there. "Although our Department is concerned with service and clinical aspects of genetics," he wrote in reflecting upon Scriver's basically positive review, "the present staff includes only four who are medically trained." Meanwhile the research strengths Siminovitch acknowledged were those developed in the old Department of Medical Cell Biology: molecular biology and somatic cell genetics.[89]

Though providing a rather inaccurate description of the department, then, Siminovitch continued to conceive of the new Department of Medical Genetics as having an internal hierarchy between basic and clinical genetics. In seeking recognition as a Graduate Department at the University, Siminovitch argued that, "Although important problems in microbial genetics remain to be solved, the focus of activity is currently shifting to the study of the genetics of somatic cells and their viruses on the one hand, and to clinical genetics on the other (antenatal diagnosis, biochemical detection of inborn errors, screening programs for heterozygotes and counselling, cytogenetics, drug sensitivities)."[90]

Yet Siminovitch's interpretation did not go entirely uncontested. In writing their response to the Scriver report, two hospital-based medical geneticists, Margaret Thompson and the recently-appointed Ronald Worton, presented a somewhat different picture. Without contesting the hierarchy of knowledge between basic and applied research, their discussion sought to preserve a space for human genetics *as* basic research. They characterized the merged department as involving both "'basic' molecular genetics" and "'basic' human genetics." Implicitly disagreeing with the sentiment that no research was conducted at the hospital, they pointed to the existence of rather different roles for the two heretofore separate units: notably, "an implicit obligation to focus research on areas more or less directly related to child health" at the hospital.[91]

Struggles over the design of teaching programs at the graduate and undergraduate level revealed the efforts of the hospital-based medical geneticists to produce a definition of the term 'medical genetics' that left room for their continued research relevance. Responding to a memo which had suggested that members of the new department would not know the difference between clinical and human genetics, Margaret Thompson soberly offered a set of definitions.[92] Clinical genetics, she argued, "is patient-oriented and clinician-oriented. Its emphasis is on the role of genetics in disease, and it requires some background in clinical medicine." Human genetics by contrast is "concerned with genetic variation in man in its broad aspects. This field deals with normal as well as abnormal variation. It includes such topics as cytogenetics, transmission genetics, population genetics, and evolutionary genetics, with emphasis on principles rather than on clinical genetics." Medical genetics, Thompson offered, "has a somewhat broader

meaning....It involves application of genetics to the understanding of normal and abnormal human biology, but does not imply, as the others do, that the organism of study is necessarily man. Thus it includes such fields as molecular and mammalian genetics in so far as these fields relate to improving understanding of human biology." The conclusions of such a set of definitions were, Thompson proposed, quite clear. While clinical genetics was taught to physicians, medical or human genetics was the proper subject for graduate education within the department.[93]

In presenting this definition, Thompson was not resisting change. On the contrary, this definition exemplified her embrace of change, as she was defining a discipline she had not actually been trained in. In general, those old-order medical geneticists included in the reorganized department were seeking to re-define themselves in relation to changing definitions of medical genetics.

The definition being advocated by Thompson was emerging in the 1970s – in part through the efforts of professional self-development at the national level. Nancy Simpson, also a student of Ford Walker, was using a similar definition in her work in the 1970s. In 1974, as she negotiated her impending relocation to Queen's, Simpson argued for naming the Division she was to head medical genetics rather than human genetics "because the general consensus of opinion across the country is that Human Genetics restricts such a division to the study of humans whereas one might want at some time along the way to do studies on animals and our primary interest is in genetics as it relates to medicine."[94]

This new definition of medical genetics being proposed by the old-order medical geneticists was welcoming of the basic geneticists in embracing their interest in non-human organisms. Yet Thompson and her colleagues were still preserving space for workers whose primary research organism was the human animal. In doing so, they contested the primacy of basic genetic knowledge. In the fall, Thompson and Diane Cox produced a "Statement on Graduate Training in Medical Genetics" that made such an argument explicit and garnered the ire of at least one non-hospital faculty member. At this time, graduate teaching for the Department of Medical Genetics was organized through Siminovitch's old Department of Medical Biophysics – the application for a separate graduate program within Medical Genetics had been stalled. Thompson and Cox argued that this way of organizing graduate training in human genetics was "seriously inadequate." Their concerns dealt chiefly with the dominance of the basic school, and the inadequacy of specific attention to questions of human genetics. Because of an undue focus on "areas of limited importance to genetics," and the weakness of staff in certain areas of human genetics, as had been identified in the Scriver report, graduates from this program were indistinguishable from Medical Biophysicists, and were unable to take their place in the medical genetics field after graduation.

Thompson's and Cox's conclusions were highly critical.

> Some years ago, the University of Toronto was training far more human and medical geneticists than now, with far fewer resources. Several of its graduates [Thompson and Cox among them] are in leading positions in medical genetics in Canada and elsewhere. In our years as a Department of Medical Genetics we have trained virtually no students (perhaps one) who can be expected to work as medical or

> human geneticists. It is urgent to re-examine our graduate program in light of its very serious problems and the need for medical geneticists.[95]

Thompson's and Cox's comments elicited a strong response from Paul Sadowski, a researcher based at the university. Their suggestion that the existing training program was weakened by focusing on problems "of limited importance to genetics" which Sadowski understood as "DNA replication, packaging, maturation and recombination, RNA transcription and control of gene expression, [and] physical studies of macromolecules" was taken to betray "an extremely narrow view of genetics." Moreover, the suggestion, made by Thompson and Cox, that a graduate program in human genetics could not be housed within the Department of Medical Biophysics because of its strict requirements was met with the rejoinder "Who could possibly dispute that a human geneticist should have some background in mathematics and biochemistry?" While conceding that "we may not now be training medical geneticists," Sadowski added that, "it is by no means clear to me what phenotype of the final product called a "medical or human geneticist" should be."[96]

Clarifying the 'phenotype' of the medical geneticist was a contested process. For his part, Siminovitch worked to emphasize the basic school as the chief research effort within medical genetics, though he also provided support to those research programs within the hospital, such as genetic metabolic disease, which preserved a research role for human genetics while proving amenable to collaboration with the basic approach.[97] The university workers classified human genetics research as applied and/or clinical work, and correspondingly downgraded its presumed capacity to produce scientific knowledge.

But the old order medical geneticists also participated in the redefinition of their field over the course of the 1970s. Without contesting the fact of hierarchies of knowledge, Thompson and her colleagues sought to remake themselves as collaborators in work which incorporated basic research questions, and preserve space for themselves as producers of high status knowledge. They insisted upon including themselves *as* medical geneticists, resisting their downgrading to the non-researcher class of 'clinical geneticist.' But at the same time, they conceded the reality of that new category. In redefining medical genetics, then, they sought to preserve space for basic research on the human organism, while conceding that the superiority of this field as a research enterprise lay in encompassing the organisms that were the preserve of the basic geneticists.

Conclusion

The 'new' medical genetics reflected a distinct way of constructing knowledge production that had powerful effects. This was a framing of medical genetics that maximally reduced the old medical genetics tradition – one that was primarily concerned with the human animal as a distinct species for which related but separable research questions applied. The consequence of this vertical integration of and polarization into 'basic' and 'clinical' spheres, and the corollary minimization of human genetics, was to produce a department, and a research trajectory, that downplayed the priority of specifically human-order knowledge, made the human animal a less likely source of

scientific knowledge, and made all knowledge on the genetics of non-human organisms appear inherently applicable to the human animal

Noreen Rudd, one of the clinical geneticists appointed to Sick Kids under the new dispensation, identified some of the structural ways in which research on the human meaning of genetic disease was lost.[98] "Today," she wrote in 1974, "diagnosis of genetic diseases is academic. We know nothing of the molecular basis, the genetic mechanism or the natural history of the disease, all things which we are supposed to relay to families during genetic counselling." But having identified three lacunae, she focused on only one, advocating for data collection and analysis "following the natural history and reproductive history of these families" so that information on rare genetic diseases was not lost. "This should be given careful consideration in the funding of a service," she noted. "It is not a fundable research project."[99] Ironically, in Toronto at this time, Donald Stewart, a pediatrician and not a geneticist, was conducting the follow-up study of children born with sex chromosome anomalies, producing precisely this kind of knowledge, but with minimal interest from the geneticists.

Endnotes: Chapter 5

[1] N Ford Walker and JM Naylor, "Human Genetics," *Canadian Journal of Genetics and Cytology*, 3 (1961), 79.
[2] Margaret Thompson, Memorandum to Members of the Department of Medical Genetics, June 11, 1975 (UofT, A83-0007/009, File: HSC).
[3] Harry Marks, in his study of the production of a scientific clinical praxis in twentieth-century America, argues that unlike most historians of science and medicine who study "groups bound by professional training and circumstance," his study is different. "This is not a history of clinical pharmacology or of biostatistics," he writes, "....Rather, the therapeutic reformers discussed here constitute a *political* community, a group joined by their belief in the power of science to unite both medical researchers and practitioners *despite* obvious differences of training and circumstance." Like Harry Marks I am studying a *political* community, yet members of this community shared a group identity based, to some extent, on 'professional training and circumstance.' Unlike Harry Marks, then, I do not presume that the fact of professional identity diminishes the historical contingency or political contours of group constitution. Harry Marks, *The Progress of Experiment: Science and Therapeutic Reform in the United States, 1900-1990*, (Cambridge University Press, 1997), 2-3, emphasis in original.
[4] Ken MacTaggart, "Major Research Centre: Hospital for Sick Children Building to be Opened January 15th for Inspection," *Toronto Globe and Mail*, January 3, 1951 (OA, MS755, Reel 125).
[5] Ron Kenyon, "Co-ordinate all Research to Treat Sick Children: Doctor Predicts Improved Results," *Toronto Telegram*, December 1, 1953 (OA, MS755, Reel 132)
[6] Minutes for the Committee on Research, Jan 26, 1954 (HSC, CRM, Vol. 1953-1959)
[7] *Sixth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1959, 8 (HSC).
[8] Dr Farmer, attachment to the Minutes of the Committee on Research, April 6, 1960 (HSC, CRM, Vol2 1960-1966)
[9] Minutes of the Committee on Research, April 6, 1960 (HSC, CRM, Vol2 1960-1966).
[10] Dr Rhodes, attachment to the Minutes of the Committee on Research, April 6, 1960 (HSC, CRM, Vol2 1960-1966).
[11] Minutes for the Committee on Research, Feb 24, 1960 (HSC, CRM, Vol. 2, 1960-1966). This had been discussed in the late 1950s, when the desire was articulated for "University recognition of the Research Institute as a training centre for students seeking higher degrees." *Fifth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1958, 11 (HSC). This was again an area of active consideration in the mid-1960s, the Research Institute wanted to be considered a separate department within the Faculty of Graduate Studies for the purposes of graduate instruction, yet it met some resistance, see: Minutes for the Committee on Research, November 3, 1965; Jan 5, 1966; May 25, 1966; June 29, 1966 (HSC, CRM, Vol. 2, 1960-1966)
[12] The Board refused the proposed reorganization which would have returned to a pre-RI situation, as was essentially being proposed in 1960. See for example, Minutes of the Committee on Research, November 15, 1961 (HSC, CRM. Vol. 1960-1966).
[13] Minutes of the Committee on Research, April 23, 1968 (HSC, CRM, Vol. 1967-1973). For the plans, see for example: Minutes of the Committee on Research, October 13, 1967 (HSC, CRM, Vol. 1967-1973); Sass-Kortsak, Plans for Further Development and Expansion of Research Activities in the Department of Paediatrics, December 1967, attached to Minutes of the Committee on Research, December 13, 1967 (HSC, CRM, Vol. 1967-1973).
[14] Space problems continued to plague the genetics Department. This has everything to do with the emphasis on research. In the summer of 1975 Siminovitch drafted a report on the Department of Genetics at HSC. There had been a miscalculation about the amount of space needed strictly to meet the service obligations of the Department, and there were the unforeseen demands associated with the amniocentesis program. But these service space needs had research implications, as even clinical geneticists were expected to have research interests and thus required research space. More importantly, space was needed for "our present young active investigators to develop properly" which involved space for their needs and

for students and post-doctorals.: "The Hospital for Sick Children, Department of Genetics," [Siminovitch], July 1, 1975 [update on the status of the Genetics Department], (UofT, B79-0051/007, File: Hospital for Sick Children: Department of Genetics).

[15] In the mid-1960s, reorganization involved encouraging more collaboration between the clinical and research arms of the hospital. See: further plans for reorganization where the Director argued that "'esprit de corps' and the research 'education' of clinicians are not necessarily compatible with the ... objective [of getting research done] and someone must decide which is most important to this Institution. On this decision will eventually hinge all the others.": Minutes of the Committee on Research, January 22, 1964 (HSC, CRM. Vol. 1960-1966). In April of 1965, the same Director was emphasizing things rather differently, arguing that it is "axiomatic that The Research Institute will be of little value to The Hospital for Sick Children unless it is as closely associated with every aspect of patient care as possible." To that end he recommended joint appointments in the Institute and to the Hospital staff and also paying the salary on a pro rata basis depending on commitments in each sphere. See: Hartfort, Memorandum for Research Committee Meeting, April 7, 1965, attached to Minutes of Committee on Research, April 7, 1965 (HSC, CRM, Vol. 1960-1966).

[16] "The introduction of prepaid, governmental-sponsored, medical care," the Minutes pointed out, "is facilitating the latter (available time).": Minutes of the Committee on Research, October 13, 1967 (HSC, CRM, Vol. 1967-1973)

[17] Minutes of the Committee on Research, October 13, 1967 (HSC, CRM, Vol. 1967-1973)

[18] Minutes of the Committee on Research, May 27, 1970 (HSC, CRM, Vol. 1967-1973)

[19] "While no definite decision could be reached due to the uncertainty of the retirement of Dr Walker, it was unanimously agreed that it would be most desirable to have Dr Fraser on the staff of the Institute." Offers were made but Fraser turned them down Minutes of the Committee on Research, January 7, 1959; May 20, 1959 (HSC, CRM. Vol. 1953-1959)

[20] Minutes of the Committee on Research, June 10, 1959 (HSC, CRM. Vol. 1953-1959)

[21] Minutes of the Committee on Research, December 19, 1959 (HSC, CRM. Vol. 1953-1959)

[22] Chute, "Report Re Department of Genetics," September 1964, attached to Minutes of the Committee on Research, September 2, 1964; see also: Minutes of the Committee on Research, June 29, 1960 (HSC, CRM. Vol. 1960-1966).

[23] He did make efforts to address medical questions and participated in medically-oriented research, however. See his effort to make blood group genetics seem relevant to medicine in: TE Reed, "Why are there Blood Groups?" *University of Toronto Medical Journal*, 39:6 (April 1962), 243-247.

[24] Minutes of the Committee on Research, November 15, 1961 (HSC, CRM. Vol. 1960-1966).

[25] Minutes of the Committee on Research, February 7, 1962; June 6, 1962; September 12, 1962 (HSC, CRM. Vol. 1960-1966).

[26] Minutes of the Committee on Research, October 10, 1962 (HSC, CRM. Vol. 1960-1966). Reed paid some attention to the issue, apparently preparing a memo outlining his views on the future of the Department of Genetics at the RI, but his memo is not available. Minutes of the Committee on Research, October 24, 1962 (HSC, CRM. Vol. 1960-1966).

[27] Minutes of the Committee on Research, November 14, 1962; February 6, 1963 (HSC, CRM. Vol. 1960-1966).

[28] AL Chute, "Report Re Department of Genetics," September 1964, attached to Minutes of the Committee on Research, September 2, 1964 (HSC, CRM. Vol. 1960-1966).

[29] Minutes of the Committee on Research, June 13, 1963 (HSC, CRM. Vol. 1960-1966). The lack of space caused significant problems, and the committee, confirming the "importance of a genetics department to this Research Institute" even suggested that outside space be rented if necessary. More space was needed for Reed's work and for future work, and even Margaret Thompson's request for an office was refused as part of the overall space problem in this department. Minutes of the Committee on Research, September 4, 1963; October 2, 1963; December 18, 1963 (HSC, CRM. Vol. 1960-1966). Thompson, found herself working at Princess Margaret Hospital because of the shortage of space at Sick Kids.

[30] AL Chute, "Report Re Department of Genetics," September 1964, attached to Minutes of the Committee on Research, September 2, 1964 (HSC, CRM. Vol. 1960-1966).

[31] *Ibid.*
[32] Chute argued that this reorganization should "combine cytogenetics and the other aspects of genetic study in one area under one Director." *Ibid.*
[33] In discussing the difficulty of finding an adequate person, Chute cited Clarke Fraser and Irene Uchida. *Ibid.*
[34] Committee on Genetics, Report, December 11, 1964, attached to Minutes of Committee on Research, Feb 3, 1965 (HSC, CRM, Vol. 1960-1966).
[35] This report was then sent on the Committee on Research. Memo, to DJ Maybee, from Secretary, Medical Advisory Committee, Jan 19, 1965, attached to Minutes of Committee on Research, Feb 3, 1965 (HSC, CRM, Vol. 1960-1966).
[36] Reed was to transfer all of his work from the hospital to the university as chair of this committee, but I don't know what transpired. Committee on Genetics Report, December 11, 1964, attached to Minutes of Committee on Research, Feb 3, 1965 (HSC, CRM, Vol. 1960-1966).
[37] On the Flexnerian reforms see: AB McKillop, *Matters of Mind: The University in Ontario, 1791-1951*, (Toronto: University of Toronto Press, 1994), 347-361.
[38] Claude Bissell, *Halfway up Parnassus: A Personal Account of the University of Toronto, 1932-1971* (Toronto: University of Toronto Press, 1974), 104, 92.
[39] *Ibid.*, 105, 106.
[40] Similar developments took place at the University of Western Ontario. This school had a far less auspicious record of interwar reform along Flexnerian lines, see: McKillop, *Matters of Mind*, 355-56. Yet after the war, the medical school developed a clear commitment to medical research. This commitment was personified in the appointment of Bertram Collip, of insulin fame, as Dean of the Faculty of Medicine, from 1947 through 1961. Dr G Edward Hall served a Dean for a short period before Collip, and before he was appointed as the university's president. Hall was a clear advocate of research. On Collip see: Alison Li, J.B. Collip and the Making of Medical Research in Canada, Ph.D. thesis, University of Toronto, 1993. Moreover, like Toronto, in the mid-1960s, Western finally implemented a plan (first muted in the early post-war years) to develop a new medical sciences building and a university hospital on campus. Murray Barr, *A Century of Medicine at Western: A Centennial History of the Faculty of Medicine, University of Western Ontario* (London: University of Western Ontario, 1977).
[41] Report by Dr Connell, October 28, 1965 (UofT, A83-0007/001, File C)
[42] Lily Kay, *The Molecular Vision of Life: Caltech, the Rockefeller Foundation, and the rise of the new biology* (New York: Oxford University Press, 1993), 4, 5.
[43] Lou Siminovitch, letter to Dr George Connell, Department of Biochemistry, University of Toronto, Jan 13, 1965 (UofT, A83-0007/001, File C).
[44] *Ibid.*, Siminovitch had very strong feelings about research. It should, he argued, take precedence over teaching in the sense that good teaching would emerge from good research. He was also a very strong proponent of multidisciplinary research. His remarks about genetics are in this vein. See: Siminovitch, Activities of the Ontario Cancer institute from 1958 to 1968, Cooperation – Key to Success in Modern Medicine, (UofT, A83-0007/004, File: OCI – 10 year report).
[45] *Canadian Medical Research Survey and Outlook*, A Report to the Medical Research Council of Canada, MRC Report #2, September 1968, Section 7, Medical Genetics. It is apparent in the "tentative lecture schedule for genetics" produced by Margaret Thompson, c. 1966. This lecture schedule was produced in response to a request dated Dec 10, 1965; thus it was likely produced in early 1966. All of the topic proposed, together with the laboratory subjects, involve human material and human processes; population genetics and behavioral genetics are included. See: Reports of Working Parties Re Curriculum, Section 2, Drs Thompson, Macpherson and Wardlaw, pp. 3-5 (UofT, A83-0007/002, File: Cell Biology-Teaching). And is clear in the summary of "current research by academic staff" for 1968/69 at the Department of Zoology – the historic home of genetics at the university. For a scientist like Siminovitch, committed to a molecular orientation for genetics, the overview of genetics projects listed here, would have confirmed his cynicism had he seen it. Among the human geneticists were Alex Bell, Margaret Thompson and TE Reed. They were engaged respectively on research in: nuclear sex chromatin survey in Toronto newborns; genetics of muscular dystrophy and other childhood disorders, and in dermatoglyphics in childhood

malformation syndromes; population genetics and the anthropological and clinical aspects of human population genetics. See: Department of Zoology, University of Toronto, Current Research by Academic Staff, 1968-1969 (UofT, A74-0022/054, File: Dept of Zoology).

[46] EA Sellers, Associate Dean, Faculty of Medicine, letter offering appointment to Louis Siminovitch, Oct 21, 1966, (UofT, A83-0007/004, File: no name)

[47] *Ibid.*,

[48] Siminovitch used the term "multidisciplinary" but his usage was closer to what is generally understood as interdisciplinary – that is, breaking down and moving across disciplines rather than simply involving more than one. He described multidisciplinary research as "problem or system oriented." See: Siminovitch, Activities of the Ontario Cancer Institute from 1958 to 1968 (UofT, A83-0007/004, File: OCI –10 yr. report)

[49] Siminovitch, Brief Outlining Need for a New Department of Medical Cell Biology," N.D. c. 1968/69 (UofT, A83-0007/002, File: No File).

[50] Siminovitch, letter to DS Rickert, Donner Foundation, Jan 13, 1969 (UofT, A83-0007/005, File: Dr Chute)

[51] He also sat on the Committee to find a head of a new Department of Immunology. John Law, letter to Siminovitch, Nov 9, 1966, asking him to be on the search committee (UofT, A83-0007/005, File: Hospital for Sick Children, Toronto)

[52] John Law, chairman of the HSC, letter to a candidate, Dr Fudenburg, California, April 18, 1968 (UofT, A83-0007/005, File: Hospital for Sick Children, Toronto). In the late 1960s the university seems to have been experiencing some financial distress and though the HSC search committee wanted to be able to offer a new Medical Geneticist a clear sense of their relationship to and authority within the university, they could not do so. Though Siminovitch supported the idea of the creation of a separate department of Medical Genetics, from his Department of Cell Biology, there was no willingness on the part of the Dean to make such financial commitments. Siminovitch, letter to John Law, Oct 2, 1969 (UofT, A83-0007/005, File: no File).

[53] Minutes of the Committee on Research, October 13, 1967 (HSC, CRM, Vol. 1967-1973)

[54] The appointment was initially for 2 years and Siminovitch was to give 20% of his time to the hospital. Minutes of the Committee on Research, September 30, 1970 (HSC, CRM, Vol. 1967-1973)

[55] See Margaret Thompson's Curriculum Vitae, October 1971, attached to: MW Thompson and M Buchwald, "Genetic Studies of Cultured Human Somatic Cells," MRC Grant Application, November 9, 1971 (UT, A79-0061/005, File 44).

[56] I know of no direct links, but Alex Bell cited some of Siminovitch's unpublished data in a joint publication with DG Baker, which suggests some link, if only indirect: AG Bell and DG Baker, "Irradiation-induced chromosome aberrations in normal human leukocytes in culture," *Canadian Journal of Genetics and Cytology*, 4 (1962), 340-51. There were also links between Siminovitch and one of the "pioneers of human cytogenetics in Toronto," as Ford Walker called him, Rothfels, see: KH Rothfels and L Siminovitch, "An Air-Drying Technique for Flattening Human Chromosomes in Mammalian Cells Grown In Vitro," *Stain Technology*, 33 (1957), 73-77.

[57] See; XY Hu, et al, "Duplicational mutation at the Duchenne muscular dystrophy locus: its frequency, distribution, origins and phenotype-genotype correlation," *American Journal of Human Genetics*, 46:4 (1990), 682-95; EF Gillard, et al, "Molecular and phenotypic analysis of patients with deletions within the deletion-rich region of the Duchenne muscular dystrophy (DMD) gene," *American Journal of Human Genetics*, 45:4 (1989), 507-20; RG Worton and MW Thompson, "Genetics of Duchenne muscular dystrophy," *Annual Review of Genetics*, 22 (1988), 601-29.

[58] Sass-Kortsak, Plans for Further Development and Expansion of Research Activities in the Department of Paediatrics, December 1967, attached to Minutes of the Committee on Research, December 13, 1967 (HSC, CRM, Vol. 1967-1973)

[59] *Ibid.*

[60] *Ibid.*

[61] The venture involved Sass-Kortsak, Margaret Thompson, Sanford Jackson and others. This was seen as an area of great promise: "as a major diagnostic tool in the future. It may even extend to diagnosis in fetal

life by testing of amnion cells. It would seem to us that, by entering this field now, we could gain a priority that would establish our Hospital as a reference centre for the diagnosis of metabolic disease." Proposal to Initiate studies into the use of fibroblast cultures as a medium for study of metabolic reactions in inherited metabolic diseases," attached to Minutes of the Committee on Research, November 27, 1968 (HSC, CRM, Vol. 1967-1973)

[62] Curriculum Vitae of Manuel Buchwald, December 1969, enclosed in Memorandum Re: New Appointments in Genetics, attached to the Minutes of the Committee on Research, May 27, 1970 (HSC, CRM, Vol. 1967-1973)

[63] Memorandum Re: New Appointments in Genetics, attached to the Minutes of the Committee on Research, May 27, 1970 (HSC, CRM, Vol. 1967-1973). See also: MW Thompson and M Buchwald, "Genetic Studies of Cultured Human Somatic Cells," MRC Grant Application, November 9, 1971 (UT, A79-0061/005, File 44).

[64] Sass-Kortsak, Plans for Further Development and Expansion of Research Activities in the Department of Paediatrics, December 1967, attached to Minutes of the Committee on Research, December 13, 1967 (HSC, CRM, Vol. 1967-1973)

[65] Memo to Committee on Research, from Director, RI, September 20, 1967, attached to Minutes of the Committee on research, September 27, 1967 (HSC, CRM, Vol. 1967-1973)

[66] Minutes of the Committee on Research, June 29, 1966; September 7, 1966; October 26, 1966 (HSC, CRM, Vol. 2 1960-1966)

[67] By early in 1961 there were moves afoot to amalgamate the various chromosome studies that were occurring in the Departments of Genetics and Pathology. Minutes of the Committee on Research, Feb 1, 1961; March 1, 1961 (HSC, CRM, Vol. 1960-1966)

[68] AL Chute, "Report Re Department of Genetics," September 1964, attached to Minutes of the Committee on Research, September 2, 1964 (HSC, CRM. Vol. 1960-1966).

[69] Minutes of the Committee on Research, September 2, 1964 (HSC, CRM. Vol. 1960-1966).

[70] M Shaw and K Patau, Report, Cytogenetics, Jan 11, 1965 attached to Minutes of Committee on Research, Feb 3, 1965 (HSC, CRM, Vol. 1960-1966).

[71] Patau and Shaw noted that he was pursuing research on muscular dystrophy, cytogenetics, electron microscopy and lung pathology. *Ibid.*

[72] Bayzar Erkman, Conen's assistant, was seen as having more potential, particularly for her work on uncultured tumor cells; it was suggested that an investment in her further training would not be wasted. *Ibid.*

[73] Yet even as they despised the amateurishness of Conen's approach, the commentary of Patau and Shaw and the three anonymous reviewers also demonstrated their conviction that human-order knowledge was still "leading edge" in medical cytogenetic research. Of value was research which identified cytogenetic status in tumor cells, and new clinical anomalies, and made available information about the relationships between clinical effects and cytogenetic status. *Ibid.*

[74] This focus continued. In 1968, when the joint proposal to "initiate studies in the use of fibroblast cultures as a medium for study of metabolic reactions in inherited metabolic disease," was submitted to the research committee, the authors distinguished their work from superficially similar efforts by Pat Conen. Conen had "already made application for grants to support research into some metabolic diseases using Fibroblast tissue cultures. He is primarily interested," they added, "in those diseases which can be demonstrated by morphological changes in the fibroblasts, particularly by the accumulation of metachromatic staining granules." "Proposal to Initiate studies into the use of fibroblast cultures as a medium for study of metabolic reactions in inherited metabolic diseases," attached to Minutes of the Committee on Research, November 27, 1968 (HSC, CRM, Vol. 1967-1973)

[75] Siminovitch was aware of this.

[76] Memo from Dr WL Donohue to Margaret Thompson, September 16, 1969 (UofT, A83-0007/005, File: No File)

[77] Ron Worton became the research cytogeneticist at HSC. He had done his Ph.D. at the University of Toronto in the Department of Medical Biophysics, and thus likely knew Siminovitch. Graduating with a Ph.D. in 1969 with a dissertation on "Physical Characterization of Hemopoietic Stem Cells," he went on to

do post-doctoral work in the US on "Biochemical studies of gene regulation in Drosophila melanogaster," and "Studies with human chromosome variants." He was appointed to Sick Kids in September 1971 and identified his research as concerning the "structure and function of chromosomes." See the curriculum vitae of Ron Worton and his Terms of Appointment in (UT, A83-0007/003, File: Staff CVs).

[78] Another research focus that was approved and with which Siminovitch was closely associated, was "developmental biology." Review of Status – Research Committee, Minutes of the Executive of the Research Advisory Committee, Dec 20, 1972 (HSC, CRM, Vol. 1967-1973).

[79] Minutes of the Executive of the Research Advisory Committee, February 14, 1973 (HSC, CRM, Vol. 1967-1973); Siminovitch, letter to Dr Aser Rothstein, Director, RI, Dec 14, 1973 (UofT, A83-0007/005, File: Dr Sass-Kortsak); Minutes of the Executive of the Research Advisory Committee, December 19, 1973 (HSC, CRM, Vol. 1967-1973).

[80] Hospital for Sick Children, Toronto, Genetics Program [draft of brief submitted to OHSIP], revised October 27, 1971 (UofT, B79-0051/010), File: Ministry task force [also Box 5, File: OHC- Task Force on Genetics])

[81] Charles Scriver, "Appendix. Report to the Executive Committee of the Faculty of Medicine, 1972, submitted to Dean Connell, Nov 28, 1972 after a site visit and review of the proposal (UofT, A83-0007/002, File: Dept Genetics, UofT, next staff mtg.). On the overlap between basic and clinical genetics see: Mark Pearson, letter to Charles Scriver, Nov 16, 1972 (UofT, A83-0007/002, File: Dept Genetics, UofT, next staff mtg.).

[82] He added that, "this is not the time for the trade union approach to problem solving." Charles Scriver, "Appendix. Report to the Executive Committee of the Faculty of Medicine, 1972, submitted to Dean Connell, Nov 28, 1972 (UofT, A83-0007/002, File: Dept Genetics, UofT, next staff mtg.).

[83] Charles Scriver, "Appendix. Report to the Executive Committee of the Faculty of Medicine, 1972, submitted to Dean Connell, Nov 28, 1972 (UofT, A83-0007/002, File: Dept Genetics, UofT, next staff mtg.).

[84] See: Siminovitch, "Proposal to Create a Department of Medical Genetics (UofT, A83-0007/002, File: Medical Genetics, Grad Dept, UofT.

[85] Genetics was seen to erase the basic/clinical divide. *Ibid.*

[86] *Ibid.*

[87] Mark Pearson, letter to Charles Scriver, November 16, 1972 (UofT, A83-0007/002, File: Dept Genetics, UofT, next staff mtg.)

[88] Charles Scriver, "Appendix. Report to the Executive Committee of the Faculty of Medicine, 1972, submitted to Dean Connell, Nov 28, 1972 (UofT, A83-0007/002, File: Dept Genetics, UofT, next staff mtg.).

[89] Siminovitch, Department of Medical Genetics, N.D. (UofT, A83-0007/002, File: Medical Genetics. Grad Dept. UofT) In a revised version of this piece, Siminovitch put it differently: "Although one of the major responsibilities of our department lies in the service and clinical aspects of genetics, we are short of members who are practicing clinicians. This weakens the efficiency of our total program." Siminovitch, Department of Medical Genetics, Future Development of Staff, August 1973 (UofT, A83-0007/002, File: Faculty of Medicine, Budget Ctte, L Siminovitch)

[90] "Outline – Application for a Graduate Department of Medical Genetics," January 22, 1974 (UofT, A83-0007/004, File: No Name).

[91] MW Thompson and RG Worton, "Department of Medical Genetics, Position Paper," N.D. c. 1972 (UofT, A83-0007/002, File: Dept Genetics, UofT, next staff mtg.).

[92] In a memo on the topic of graduate teaching Noreen Rudd stated that "There was some discussion regarding the title of the course, i.e. clinical versus human genetics. Some individuals felt that many members of our department would not appreciate the difference between these two courses." See: Minutes of Staff Meeting, June 20, 1975 (UofT, A83-0007/004, File: No Name).

[93] Margaret Thompson, Memorandum to Members of the Department of Medical Genetics, June 11, 1975 (UofT, A83-0007/009, File: HSC).

[94] Nancy Simpson, letter to Michael Partington, Jan 23, 1974, attached to Simpson and Partington, letter to Mahon, June 6, 1974 (UT, B79-0051/10, File: Ministry Task Force)

[95] Margaret Thompson and Diane Wilson Cox, "Statement on Graduate Training in Medical Genetics," November 20, 1975 (UofT, AS83-0007/004, File: No name).

[96] Paul Sadowski, "A few thoughts on the statement on Graduate Training in Medical Genetics," November 26, 1975 (UofT, AS83-0007/004, File: No name). Siminovitch recognized the distinctiveness of the medical genetics group at the hospital, and the tensions that arose from merging the hospital and university Departments of Medical Genetics. "[T]he intellectual and research interests of the members of the University Department of Medical Genetics, housed in the Medical Sciences Building, are quite different from some of those at the Hospital," he wrote, "and thus problems arise continuously in trying to reconcile these groups in respect to departmental objectives." While he felt that because of his position, as head of both Departments, he was able to "keep the interests of both in mind," he added that "this may not be so in the future." Siminovitch advocated that his replacement be "a clinically-trained person with strong research interests." "The Hospital for Sick Children, Department of Genetics," [Siminovitch], July 1, 1975 [update on the status of the Genetics Department], (UofT, B79-0051/007, File: Hospital for Sick Children: Department of Genetics).

[97] Submitting a report in the summer of 1975 Siminovitch argued that there had "excellent progress" in research since 2 ½ years ago when research had been "our weakest area." Siminovitch, "The Hospital for Sick Children, Department of Genetics," July 1, 1975 [update on the status of the Genetics Department], (UofT, B79-0051/007, File: Hospital for Sick Children: Department of Genetics).

[98] Rudd did her pediatric residency at Sick Kids from 1966 through 1968, but there is no indication of her involvement with the Research Institute and thus genetics at this time. After a period in the US, she was appointed as staff physician and geneticist at Sick Kids, and as a clinical teacher in the university Faculty of Medicine, in 1971. See her CV (UT, A83-0007, Box 3, File: Staff CVs.

[99] Rudd made these comments to Siminovitch for the benefit of the provincial Task Force on Genetic Services that he led. Noreen Rudd, letter to Siminovitch, November 12, 1974 (UofT, A83-0007/009, File; HSC), emphasis in original.

Chapter 6

Making Genetic Medicine: Managing the Growing Burden of Genetic Disease

Introduction

Over the latter-half of the twentieth century, genetics has become of increasing relevance to medicine. This growing importance is due, the advocates of genetic medicine suggest, to the "obvious change in importance of genetic factors in disease."[1] With medical and public health triumphs in the control of exogenous factors in disease causation in the 20th century, so the argument goes, attention has turned to endogenous factors.

But more is at work in the growing importance of genetic medicine since the Second World War than this simple narrative allows.[2] In the first instance, it is by no means established that human geneticists conceded the irrelevance of their model of disease causation in the period of the ascendance of the infectious disease paradigm. Constitutional medicine in general, and Toronto's indigenous tradition in particular, paid close attention to susceptibilities, tendencies and predispositions – all of which were seen to play a role in infectious disease. Moreover, many complex diseases – such as pyloric stenosis and congenital heart disease – were credible objects of genetical inquiry for

members of the Ford Walker school in the 1940s and 1950s. The indigenous tradition constructed a human genetic science with broad etiological parameters, and blurred distinctions between genetical and congenital, which asserted a large domain for genetic medicine. This research tradition sought ways to make sense of illness that referenced more than single genetic agents in systems of simple causation.

Moreover, even as the indigenous tradition passed from favor, the blurring between genetical and congenital did not cease to be of use to the Toronto workers. On the contrary, with the rise of a more exacting model of genetical causation, such blurring became a systematic and deliberate slippage and was of *enhanced* value. Though their explanatory frameworks became narrower, medical geneticists in Toronto continued to assert a broader competence for a wide range of conditions. Alongside purely genetic disease, medical geneticists laid claim to congenital malformations as instances of gene-environment interaction. Acknowledging the uncertainty of genetic cause in these cases, Toronto workers nonetheless sought to interpret and manage these phenomena. The significance of genetic disease in an age of antibiotics was bolstered, then, by accounting practices which included complex, congenital phenomena within the purview of genetic medicine, even as the discussions of what were "genetic" conditions became more classically construed.

Expansive readings of the relevance of human genetic expertise derived from more than just the accounting practices of medical geneticists, however. The value of genetic medicine was also manifested in the applied work performed. Heredity counseling, the enduring practice of human geneticists, offered to help 'avoid the birth of

a defective child.' So while Mendelian ratios were relevant, genetic counselors also made extensive use of empirical risks of congenital malformation. Howard Valentine, a London, Ontario-based physician who specialized in medical cytogenetics in the 1960s under Murray Barr's tutelage, and ran the follow-up of the London newborn trial, concluded from such traditions that the term "genetic counselling" was inappropriate. He advocated a shift to the language of "reproductive counselling" to better describe the scope of actual practice.[3] But in the early 1970s when Valentine advocated this change, medical geneticists were consolidating an opposite strategy: encompassing the wide range of 'reproductive' concerns under the auspices of genetic practice.

In the 1970s, medical geneticists worked to systematically organize their profession and its practices. Workers in Toronto and throughout the country sought to increase the general population's access to extant practices such as genetic counseling, and newer practices such as population screening and prenatal diagnosis. These applied efforts were gathered together under the auspices of a new clinical category – "genetic services" – and medical geneticists coordinated themselves as the self-regulating profession in that domain. The slippage between congenital and genetical which operated through such practices as prenatal diagnosis was institutionalized in the process of professional co-ordination.

Finally, the growing importance of genetic medicine cannot be attributed solely to the expansive practical or professional domain. We miss a significant piece of the picture if we miss the rhetorical flourishes which accompanied and enhanced the growth of medical genetics in this period. Indeed, discussions of the decline in infectious disease

were accompanied by discussions of the growing *burden* of genetic disease.[4] If the argument about the decline in infectious diseases suggested that relative rates of genetic and infectious diseases were changing, the burden of genetic disease rhetoric suggested, more boldly, that genetic diseases were growing – because of medical miracles, human breeding, and, in the atomic age, an enhanced and threatening "load" of mutations.

This chapter investigates the rhetorical, institutional and professional work of medical geneticists, principally those in Toronto, in advancing the place of genetic medicine from the 1950s through the 1970s. I try to answer the question "What is the utility of genetics for medicine?" by assessing the historically contingent scope and significance of 'genetics' and 'utility.'

The Burden *of Hereditary Disease*

In 1955, an article in Canada's national newsmagazine asked rhetorically: "Are we Breeding a Nation of Invalids?" "Canadians," the author wrote, "are spending a staggering $373 millions a year on medical services." Moreover, they were doing so "[i]n an antiseptic age of medical miracles, when vaccines, vitamins and penicillin have become household words." "There are fewer than fifteen million of us," Doris McCubbin continued. "But probably more than two million are chronically ill and disabled." The causes of this seeming paradox of increased spending and decreased health were clear.

"[W]e've played hob with the old law of survival of the fittest .... We have made it possible for many people who would have died fifty years ago to survive and have children."[5]

McCubbin devoted extensive space in her article to a discussion of some of the approximately 500 hereditary diseases that were then known. Her catalogue encompassed those "severe hereditary diseases" which were "easy enough to detect because they are passed directly from parents to children," and included: a "tendency" to develop cataracts; Bright's disease, Parkinson's disease, and infantile glaucoma.[6] McCubbin also pointed to some of the less well-defined hereditary ills, which included tendencies to diabetes, cleft palate and harelip, and the recessive conditions, where the "diseases [were] passed on by carriers of hidden genes" and were "far less easy to detect and control." Among these were pernicious anemia, epilepsy, amaurotic idiocy (Tay Sachs), tendencies toward tuberculosis, rheumatic fever, pneumonia and some forms of arterial heart disease. Heredity was especially important in mental disease, and McCubbin headlined that section of her article with the warning that "Now More Morons Marry."[7]

McCubbin's sense of heredity included a host of tendencies and implicated many common congenital conditions and even infectious diseases.[8] This expansive interpretation of hereditary disease was also presented by members of the Ford Walker school in the 1950s, whose work was featured in the press. Ford Walker's "chief research project," in 1950 was reported by the media to be "the study of hereditary factors in polio."[9] In this decade, the indigenous tradition continued to support an expansive

interpretation of the utility of genetics for medicine through an expansive reading of the range of diseases amenable to genetical investigation.

Even as members of the Ford Walker school were motivated by biochemical research to address narrower models of genetical causation, the press continued to highlight the breadth of the indigenous tradition. The discovery by Ford Walker and Oliver Smithies of inherited haptoglobins was reported in 1955 and was said to make paternity tests "much more accurate." Meanwhile, "another Canadian," Irene Uchida, who had announced her findings at the same international conference, was reported as disclosing "that palm-reading may show whether a child has been born with a heart defect." While Ford Walker's and Smithies' work suggested that "Inheritance of the protein type seems to follow exactly the same laws of genetics as does inheritance of red-cell types," Uchida defended herself against the charge of "palmistry." Elaborating on what I have dubbed the Mongol method, Uchida argued that "It is a scientific finding of peculiar patterns in the palms of some children known to have congenital heart defects. It follows earlier discovery," she added, "that certain patterns on the fingers, palms and soles often indicate idiocy."[10]

In the same year, the twin method also gained press attention. "Four hundred twins from the Toronto area are going to visit the Hospital for Sick Children," a 1955 article declared "in a study by the Research Institute aimed at eliminating possible errors in determining fraternal and identical twins."[11] Correct diagnoses were "crucial in much research on hereditary aspects of disease," the article added, "since only identical twins inherit the same combination of genes." Ford Walker was cited as saying that "The whole

question of hereditary aspects of disease, particularly mental disease, is a complicated one." Research at Sick Kids on these questions suggested that in terms of cleft lips and palates, "genes for hare-lips don't always show." Identical twins might be discordant for this feature, but "the unaffected twin may later give birth to an affected child."[12] Uchida's study of congenital heart disease again came into view. While her work suggested that the condition was not inherited, and that prenatal developmental upsets played a leading role, she was "trying to find out why a definite pattern of inheritance shows up in some families with the disease yet this is not true of the twins studied."[13]

The breadth of genetic disease imagined by members of the Ford Walker school was not exclusive to the Toronto community. In the summer of 1958, when the International Congress of Genetics held its 10th annual meeting in Montreal, Canadian newspaper readers got a sense of the diversity of genetic science. There were announcements of the "major breakthroughs in fundamental research in the field of genetics." This research "done on bacteria and viruses" which demonstrated that "genes are the basic structure determining the functions and forms of life," meant that "We're beginning to understand what makes life tick on a much more basic level."[14] Meanwhile, Denmark's "unique registry" was also highlighted. This registry attempted to catalogue all Danes with hereditary disease, together with their relatives. In addition to collecting family genealogies, and assessing identical and fraternal twins, the registry sought to distinguish between diseases that were "entirely due to heredity and those where the

tendency to get the disease is only passed from one generation to another as in tuberculosis."[15]

The indigenous tradition in Toronto, and the research traditions of some other workers elsewhere, supported an expansive reading of the burden of genetic disease.[16] In the 1950s, this expansive reading was further enhanced by the conviction that the burden was growing through more than the reproduction of a wide range of heritable disease.

"An eminent American geneticist named H.J. Muller," Dorris McCubbin wrote in her pessimistic report, "has sounded a further warning note in this dark picture. Muller is worried about that strange and unexplainable process in human evolution known as mutation .... Muller believes that a backlog of defective heredity is being built up and passed on to future generations." [17] In making this point, McCubbin was popularizing the first Presidential Address to the American Society of Human Genetics, given by Muller in 1949: "Our Load of Mutations."[18]

Muller, as Diane Paul has argued, was a lifelong eugenicist.[19] Muller's pessimistic interpretation of mutations and their role in evolution was christened the "classical" position by his nemesis, Theodosius Dobzhansky, in what would come to be known in the population genetics community as the classical-balance controversy.[20] Muller's pessimism about the negative implications of mutations was evident also in his, and his allies', interventions in debates about the perils of atom bomb testing.[21] But while the classical position was especially supportive of the burden narrative, the balance position was not much used to deflate the argument about the burden of genetic disease.[22] More to the point, the advocates of the balance position shared with their classical opponents

support for the eugenic control of what seemed to be obviously harmful mutations.[23] Ultimately, as Paul has argued, Muller was successful in having the language of genetic "load" – with all that such a term implied – established within scientific and popular discourse.[24] In the realm of human infirmity, the idea of genetic load supported an expansive reading of the value of genetic medicine.

By the mid-1950s, with 'fallout' becoming a household word in the face of above-ground nuclear testing, popular concern over radiation hazards was heightened.[25] Popular Canadian accounts highlighted mutation hazards: "radiation from current atomic tests to which people are generally exposed is enough to cause genetic alterations in thousands of future babies," was the warning conveyed by "a prominent California Institute of Technology Scientist." "From a humanitarian point of view," the scientist intoned ominously, "any increase in the number of individuals that are defective either mentally of physically is not to be lightly dismissed."[26] Canada's federal Minister of Health and Welfare, Paul Martin, insisted that "no immediate or longterm harmful effects will result despite a slight but noticeable increase of radioactivity in the world."[27] But the peril was reiterated. For workers at the Chalk River research facilities of the Canadian Atomic Energy Commission, this peril suggested the need to "Discourage Chalk River Weddings."[28] And it meant that "about 35,000 defective children will be born to future generations of Canadians as a result of the radioactivity from nuclear tests to date..."[29]

Toronto-trained workers, notably Irene Uchida, Elizabeth Curtis and Diane Wilson Cox, added their own research to the chorus of concern in the early 1960s.[30] From her new position in the Department of Medical Genetics at the Children's Hospital in

Manitoba, Irene Uchida, with Elizabeth Curtis, published a study which suggested "A Possible Association Between Maternal Radiation and Mongolism."[31] The press reported that "A Winnipeg researcher thinks she has found a connection between pre-pregnancy radiation and the birth of mongoloid children."[32] Wilson Cox also used medical records of exposure to X-rays to suggest the possibility of genetic damage from radiation.[33]

By the 1960s, narratives of genetic causation frequently highlighted more mechanical genetic processes. The press reported on those workers outside the human genetics tradition who were seeking to tackle human disease with genetic tools. Cancer was a notable focus of such work, and viral research and research on DNA was featured.[34] Meanwhile, among human genetics workers, single gene effects attached to metabolic abnormalities and chromosomal anomalies emerged as centrally important. A newspaper article which featured research on mental retardation, reported that "Science has pretty well debunked the Jukes and Kallikuks [sic] theory of inherited retardation."[35]

Ford Walker articulated these emphases in 1961, when she addressed members of the Academy of Medicine in Hamilton about the "gene theory related to retardation." Reporting on the "recent discovery of the role of chromosomes in mental retardation," she noted that "mongolism – a type of mental retardation – could be explained due to an excess of genes. Albinism, however, had the normal amount of chromosomes in each cell, but one gene (governing the color of skin, eyes and hair) was recessive and did not perform its proper function."[36] While still at Sick Kids in 1962, Nancy Simpson was featured in a discussion of diabetes, a disease she had studied for her doctoral

dissertation. Rather than highlighting the complexity of hereditary processes in such common diseases, this report suggested that even complex diseases would observe simple genetic laws.[37]

As discussions of genetic causation in disease became more mechanistic in this period, narratives of burden continued. Cancer, described as a complex molecular process involving DNA, "is the penalty for the evolution of man, animal and plant into complex forms of life," according to a report on research presented at the 1962 Canadian Cancer Conference.[38] But in the 1960s, paralleling the attention to more discrete mechanisms, commentators were increasingly likely to produce numerical estimates of the burden. "Between 300 and 400 diseases are the result of errors inherited from parents, many of whom did not suffer the illnesses themselves," Dr William Donohue, the Chief Pathologist at Sick Kids, argued in a seminar he conducted for the Ontario Association of Pathologists on "inborn errors of metabolism." These illnesses were especially important, Donohue noted, "because modern medicine was keeping many such persons alive to an age when they marry and increase the population bearing the inherited conditions."[39]

At its Annual Meeting in 1960, the Genetics Society of Canada joined the chorus of those concerned about "the levels and effects of radiation from fallout and other sources." A four-person Committee on Radiation Biology was appointed which convened a meeting to determine the Canadian "research needs" in this area.[40] As a member of this committee, Ford Walker co-authored a report on the "Human Genetics" component of the meeting, and outlined the kinds of projects that were being, and could be, conducted in

Canada.[41] She and her co-author cited a 1958 WHO study on the "Effects of Atomic Radiation," and identified two basic concerns about the "burden" of genetic disease which genetic research should answer: "(1) What is the "load" of hereditary diseases and handicaps in human populations, and (2) What fraction of this load is maintained in the population by repeated mutations of natural origin?" As a partial answer to the first question Ford and her co-author cited data which indicated that "about four children out of every hundred born will be severely affected at some time in their lives by conditions that are largely or in part determined by genetic factors (and also that about 25 per cent of hospital beds and institutional spaces are occupied by these individuals)."[42]

While a post-doctoral fellow teaching the short course in medical genetics in Bar Harbor, Maine in the mid-1960s, Margaret Thompson frequently advanced estimates of the burden of genetic disease. She castigated doctors for their ignorance of basic genetics arguing that "Estimates are that 6 percent of all births are defective in some important way, and the incidence of such tragedies is constantly growing."[43] Thompson suggested that the growth of knowledge about the role of genes in disease, whether in single gene disorders, chromosomal anomalies or "conditions caused by multiple factors only partly inherited, such as diabetes or heart disease and many of the congenital malformations" should encourage attention to genetics by public health workers. "It is estimated that 6 percent of all children will suffer at some time during life from a disorder partly or wholly genetic in origin," she said.[44]

Genetic disease, Thompson argued, was increasing by comparison with the "conquest" of infectious disease.[45] Drawing on a tradition of blurring across genetical and

congenital conditions, Thompson argued that "Hereditary diseases are becoming an increasingly serious health problem."

> Sixty out of every 1,000 children born today are burdened by some significant congenital defect. About 25 per cent of hospital beds are occupied by persons whose illness stems from a congenital condition. In Ontario this totals 12,000 beds. Fifty years ago, 80 per cent of childhood deaths were caused by infectious diseases and two per cent by diseases of known genetic origin. Today, only one per cent of deaths come from infectious diseases and 12 per cent from ailments of known genetic origin.[46]

Managing the Burden: Heredity Counseling in Toronto

Though McCubbin's analysis of the burden of genetic disease had identified "deep national problems," she advocated no particular solution. Indeed, she noted that "Most of the plans to solve the problem of hereditary diseases ... are as explosive as a barrel of TNT, for they invariably include some measure of birth control, planned parenthood and sterilization." But McCubbin did identify one limited way in which this problem was being addressed.[47] She cited an earlier article in the same magazine which had featured the profession of heredity counseling.[48]

In this article, McCubbin's colleague, Sydney Katz, constructed a familiar argument about the dilemma of modern medicine:

> Modern medicine, it can be argued from a eugenical point of view, is ... weakening the human race. Miracle drugs and new surgical techniques have all but abolished nature's law of the "survival of the fittest." The weak and the unfit,

> who in previous times might have died, now live and reproduce. Often their children are either defective or carry black genes.[49]

But where McCubbin had been indecisive about solutions, Katz was enthusiastic. His article highlighted a "new profession" – heredity counseling – and his article featured one of only ten members of this "most exclusive professional group in North America" – Norma Ford Walker.[50] In this article, Ford Walker was cited as acknowledging the growing burden of genetic disease, and the diverse array of conditions encompassed by that category. She recommended heredity counseling as a credible way for individual couples to manage this burden.

The practice of heredity counseling emerged out of a "reform eugenic" impulse, Daniel Kevles has argued. In the 1940s, in the United States and Britain, a small number of "heredity clinics" opened in Universities and hospitals.[51] But where mainline eugenics had enjoined compulsion in the management of reproduction to address the apparent failure of natural selection, heredity counseling put a voluntarist twist on the reproductive solution.[52]

In Toronto, Ford Walker began her enduring association with the Hospital for Sick Children in 1940. Though we have few records of her work in this period, it is likely that she provided some counseling advice on genetic questions.[53] For by the early 1950s, she was an acknowledged member of the select fraternity.[54] In his Presidential Address to the American Society of Human Genetics in September 1951, Lee Dice of the Heredity Clinic at the University of Michigan described those "few places in North America where persons can go for advice about their heredity." Among those mentioned was "The

Department of Genetics of the Hospital for Sick Children in Toronto" which operated "an heredity clinic under the direction of Norma Ford Walker."[55] The following year, when Dice chaired a panel discussion on "genetic counseling" at the Fifth Annual Meeting of the American Society of Human Genetics, one of those "persons who are experienced in giving counsel" whom he asked to present their opinions was Ford Walker.[56]

Lee Dice's Presidential Address articulated clear reform eugenics hopes for heredity clinics.[57] Echoing the warnings made by Muller in his Presidential speech to the Society in 1949, about the danger of "deterioration of the world's stock of human genes through the accumulation of harmful mutations," Dice noted the "repugnant" nature of many methods for containing the menace, such as "destroying those individuals who exhibit the trait" or compulsorily segregating or sterilizing them. The solution for a "democracy such as ours," Dice argued, was the Heredity Clinic, which functioned through the "cooperation of the people in a program for voluntary limitation of the reproduction of inherited defects."[58]

Ford Walker's stance on mainline eugenics was similar to that of her heredity counselor colleagues.[59] Though she was not an active participant in the public debates over eugenics in the inter-war or war-time years, many of her colleagues in the Dionne project had taken a public stand against the claims of mainline eugenics.[60] In general, eugenic commentary was infrequent in her work and in that of her students. Moreover, Ford Walker took an interest in medical phenomena, and was far from exclusively interested in questions of intelligence and social character – trademark concerns of mainline eugenicists. Finally, unlike many emerging human geneticists, Ford Walker did

not publish in explicitly eugenic journals.[61] Indeed, Ford Walker presented herself in many press accounts as a liberal thinker. Adoption, she was cited as stating, was as good an option as childbirth for having a healthy child – "on the whole our genes are pretty much the same," Ford Walker argued.[62] She also, and repeatedly, addressed the issue of racism and inter-racial intermarriage. "As a geneticist," she was quoted as saying in the 1954 article, "I regard the color of skin as unimportant."[63]

In the 1950s, when Lee Dice and his colleagues were working through the American Society of Human Genetics to advance genetic counseling, Ford Walker provided rare public commentary on eugenics. In the 1954 article by Sydney Katz, she expressed her distaste for the eugenic sterilization program in Alberta, and noted that "the Nazis in Germany misused sterilization and gave it a bad name." She indicated her disbelief in the simple inheritance of capacity, noting that "many outstanding men have arisen from 'poor' stock....'From shirt sleeves to shirt sleeves every third generation' is an old wives tale which has stood the test of time," she was quoted as saying.

Diane Paul has argued that the term eugenics did not assume its status as a pejorative in professional circles until the 1960s.[64] Thus, Ford Walker did not shy away from indicating her support for the broader social goals of eugenics, even in the mid-1950s. "The heredity counselor," the 1954 article stated, "has a deep interest in eugenics – improving the vigor of the human race." Ford Walker was cited as being in agreement with the argument made by "many geneticists" that the "spectacular succes[ses]" in improving animal stock have not been matched by similar efforts with human beings.[65]

Through heredity counseling, human geneticists advanced a non-coercive approach to the management of human reproduction.[66] Ford Walker saw her role as helping people "avoid the tragedy of a defective child." But this was to be done through advice alone: "My job is to give information," she said. "Not force my ideas on anyone."[67] And in discussing cases where the "client takes long chances after getting advice and, as a result, has a defective child," Ford Walker expressed confidence that "the advice has still been of value. "If you expect a blow you can roll with it," she says. It's the unexpected blow that causes trouble.""[68] Ford Walker, it was reported, was "reluctant to advocate a change [to reproductive practices] through compulsory measures. "It's a free country," she says, "People should be allowed to have children if they want to.""[69]

Yet though formally voluntarist, heredity counseling worked to produce and enforce conformity. As Molly Ladd Taylor has argued, this was a voluntary and individualistic eugenics that dispensed with the older strategy of enjoining members of the middle classes to observe their *duty* toward the race – a strategy which had clearly failed by the late 1930s. Instead, heredity counseling worked to foster middle class *desire*. Ladd Taylor suggests that its chief advocates, in particular Sheldon Reed in the United States, promoted a narrative of large, happy families of "normal" children which saw little place for divorce, disability or childlessness.[70]

Heredity counselors presumed the inherent value of the knowledge they conveyed. As Sydney Katz described Ford Walker: "She knows the kind of children you'll have." A 1965 article, written with Margaret Thompson's aid, put it similarly:

"[G]eneticists can't answer the question, "Will my baby be normal?" Geneticists will never hold all the answers. It will never be possible to predict, or avoid, all births of defective children. But genetic knowledge, wisely applied, can prevent much of the present burden of hereditary disease.[71] Contrary to retrospective commentary on the early years of heredity counseling this information, and the work of the heredity counselor, was understood as useful.[72] Providing information to couples and individuals about their Mendelian risks, or their statistical risk where no genetic mechanisms were known, enabled people to govern their lives and reproduction with full knowledge. Even where such information could not 'prevent' genetic disease, it was said to help 'clear the air' for parents, by neutralizing the shame and blame of a child with a genetic anomaly.[73]

Heredity counselors also presumed the shared desire of lay-persons for this knowledge, and the shared understanding of its 'appropriate' use. Though framed by Ford Walker as a service *for* individuals, individuals were seen to be served through their pursuit of the goals identified by Ford Walker.[74] And complaints were sometimes voiced by counselors when parents did not take appropriate steps in light of "advice."[75]

In 1973, as prenatal diagnosis was emerging into public visibility and practical availability, an article reporting on a panel discussion in Toronto addressing the "moral, social and ethical issues of genetics" highlighted these tensions:

> An obstetrician believes some families whose unborn child has been diagnosed as being genetically defective should be advised to have an abortion. A pediatrician believes the facts should be laid before the parents and the decision left to the parents, with good counselling supplied if necessary. A nurse wonders who should take the responsibility if a family cannot make an intelligent decision. And a geneticist says lab technicians become upset if they have spent a great deal of

time assessing abnormal chromosomes and then find out the mother will not have an abortion.[76]

The expectations of normative conduct that were held by heredity counselors, were specifically gendered. As Molly Ladd Taylor has argued, the "happy families" that were produced through genetic counseling as the objects of desire, observed rigidly defined gender roles – gender roles which were seen to observe the dictates of evolutionary biology.[77]

Heredity counselors drew on genetics as a way to contest older narratives of female blame.[78] Norma Ford Walker presented Mendelian processes as particularly useful for countering "myths about human heredity," most of which, as Katz's 1954 article pointed out, "stress the importance of what happens to the mother during pregnancy." For Ford Walker then, genetics offered a response to the ancient thesis of maternal impressions, that a "harelip" was the result of a pregnant woman seeing a rabbit, or a red birthmark from a mother's consumption of strawberries.[79]

Though Ford Walker likely exaggerated the relevance of the thesis of maternal impressions,[80] the expectation of maternal responsibility was general. Commenting in 1951 on a couple whose child was born with Tay Sachs, Ford Walker noted that the mother initiated contact, as was usual, since the woman "was blamed for the defective child."[81] Mendelian genetics allowed Ford Walker to stress to a couple that "You are equally responsible for the child. You both carry recessive genes."[82] Once Trisomy 21 was demonstrated as the cause of Mongolism, Ford Walker expressed enthusiasm in 1959 that "The genetic explanation of the non-separation (or non-disjunction) of the

chromosomes will now prevent the sense of guilt or shame which has been felt in many families to whom a mongoloid child has been born, and should instead give comfort and peace of mind."[83]

But if the thesis of maternal impressions was dismissed as "black magic," the gendering of blame was maintained in scientific discourse.[84] Doris McCubbin had highlighted the role of the "emancipation of women" in upsetting the "balance of nature" and producing the growing burden of genetic disease. "Geneticists now know that the number of defective children rises sharply in women over thirty," McCubbin wrote. "Here then is another dilemma of the streamlined century: marriage and childbearing is being postponed to a point where it is dangerous to the nation's health."[85]

Women's reproductive lives were seen as profoundly affected by genetic disease and by the normative codes which prescribed appropriate behavior in these cases. Ford Walker encouraged men to 'pick their mate' for "broad hips, large limbs, big feet, a high IQ and a serious nature" rather than "sexual charm." Though abjuring directive counseling in most instances, "Early motherhood" was described as "one of the few subjects on which Dr Walker will give definite advice."[86] Like Ford Walker, Margaret Thompson also recommended that women have their children while younger.[87] But as an individual who had sat as the genetics expert on the Alberta Eugenics Board in the early 1960s, Thompson was less prone to circumspection.[88]

"Is battering a baby," Thompson asked rhetorically at the National Conference on Maternal and Child Health in 1967, "any worse than thoughtlessly conceiving an infant with a 25 per cent risk of a severe genetic disease?"[89] Thompson frequently repeated a

story of four women faced with the fact of Duchenne Muscular Dystrophy in their families. This story made clear the normative expectations of women's conduct. It also made clear how non-obvious was the task self-regulating one's reproduction to guard against the burden of genetic disease.[90]

> Two of them were urged to have their daughters undergo a chemical test that would reveal whether they too were carriers. One became angry, saying that a positive result of such a test would "blight" her daughter's life in the community. The other said simply that she and her daughter did not have time for the test. Yet if the daughters had carried the trait they could pass it on lethally to any boy infants they bore. One of the other two women carriers of the dystrophy trait responded to the suggestion that she might want to consider limiting her family by saying that she did not know why she should, as it was not her fault that she carried the deadly gene. The fourth case, however, was what genetic counselors hope for, she [Thompson] said. Informed that the wife carried the dystrophy trait the couple decided that the children they wanted so badly should come by adoption.[91]

The practice of heredity counseling was presented as gender-neutral – affecting 'parents' for example. At the same time, discussions made clear the disproportionate responsibility of women in managing this emerging practice. Women were construed as the usual and best sources of knowledge about the family and thus heredity: "Women," Ford Walker was reported as saying, "are the [heredity] counselors best friends. "They have a natural bent for remembering births, marriages, deaths, operations, sicknesses and abortions.""[92] Moreover, women were seen as profoundly affected by the imperatives of genetic 'quality control.'

In Ford Walker's and Thompson's commentaries, women's disproportionate responsibility for providing care within the confines of the nuclear family emerged

uncontested. Indeed, genetic counseling made sense of these social relations – it was advanced as a partial solution which sustained such gender roles in the face of their actual un-manageability. In discussing a case in 1951, Ford Walker noted that "The mother in this case was very glad to have the genetics of the defect explained to her and to be encouraged to limit her family." The family was poor and from an "isolated part of Newfoundland." They had "two normal and two affected children and the care of the affected children was a very great burden," Ford Walker added.[93]

In an article on heredity counseling in 1965 in *Chatelaine*, featuring Margaret Thompson, the extent to which women's lives and life decisions were regulated by genetic disease was highlighted. "Susan, a teen-ager preparing for her future, went to a genetic counseling clinic recently," we are told. "She wanted to know if she was a carrier of the hemophilia that affected her brother. The answer could help her decide whether to concentrate on a career; or marry and not have children; or marry and have her own children; or adopt them."[94]

Yet though commenting on such restrictive opportunities for women, Norma Ford Walker and Margaret Thompson were, as women scientists of their generation, living examples of broader horizons. Ford Walker used her gender to validate her role as a heredity counselor, to support the developing practice of genetic counseling and to re-produce women as the chief objects of such practices.

In his 1954 article on heredity counseling, Sydney Katz, though speaking primarily about Norma Ford Walker, described the heredity counselor as "a man to whom couples, worried by some physical flaw in their family background, can go with the

question: "Can we have a normal and healthy child?"" Against this male bias, Ford Walker was reported in the same article as arguing that "Heredity counseling is a natural field for a woman. It's normal for her to be interested in babies, families and health."[95] At the International Congress of Genetics in 1958, Ford Walker repeated her claim that "The field of human genetics is one in which women have an edge over men. "Probably because a woman can get so much closer to a family when developing a pedigree," ... [pointing out that] the wife usually knows more about her husband's family history than he does himself."[96] Irene Uchida, still working at the Hospital for Sick Children, was described in this article as assisting with the genetic counseling and agreeing that "it is almost an advantage to be a woman "because we often find it easier to talk to the parents and get the family history.""[97]

Indeed, the gender of Toronto's genetic counselors was deployed as a resource – rendering the service more palatable to patients. Ford Walker was presented to readers in Katz's article as a sympathetic "handsome sixty-year old University of Toronto professor who heads the genetics department of Toronto's Hospital for Sick Children." [98] Ford Walker was careful to present herself as a compassionate woman. In describing her style in the 1952 panel discussion on genetic counseling, Ford Walker argued that she "would not bluntly tell" the parents of their one-in-four chance of the repetition of a fatal disease in each further child, and, she would "refer to the condition as Tay-Sachs disease, this term being much more acceptable to parents, lacking as it does the stigmata [sic] suggested by amaurotic idiocy."[99] In being "friendly" and caring, Ford Walker was using a widely available cultural script of the female practitioner. Such a script may have made

Ford Walker, Irene Uchida and Margaret Thompson – Ph.D.-trained scientists all – more comfortable in a clinical context. It may also have made the potentially disturbing process of investigating risk of disease in families less threatening for members of the public, and thus encouraged the growth of this practical service.[100]

In being a woman, in producing a research school populated by women who also practiced as genetic counselors, and in insisting that women were the most appropriate practitioners of genetic counseling, Ford Walker was unlike many of her North American colleagues. Yet in advocating for women's place as heredity counselors, and as the chief objects of heredity counseling practice, Ford Walker reproduced the gender roles that Molly Ladd Taylor suggests were mandated by American advocates of the practice, even while creating opportunities for some women.

Managing the Burden: Practical Work in the Hospital

The members of the Ford Walker school built a presence within the hospital as practical workers, capable of providing some service to patients – particularly through heredity counseling. While conventional human genetics skills with pedigree analysis and statistical risk assessment were resources for this work, Ford Walker and her students and colleagues also drew on indigenous skills and traditions. The preponderance of women in the Ford Walker school was, as we have seen, pressed as an advantage in performing such sensitive work. Moreover, the methods emphasized by the indigenous tradition were

also of practical value. Indeed, the picture of Norma Ford Walker at work that accompanied Sydney Katz's 1954 article on heredity counseling showed her analyzing the feet of one of a pair of twins. "By comparing footprints," the caption read, "Dr Norma Walker can tell if twins Frances and Mary MacLeod are identical."[101]

The research of the Ford Walker school with twins and the Mongol served as an entrée into the world of applied genetics by supporting diagnostic protocols in suspected cases. Some of Ford Walker's more enduring contributions to the literature were her standardized protocols for 'objective' diagnosis of twins and Mongols.[102] By the 1950s, the use of dermatoglyphics in diagnosing Mongols was of considerable importance at Sick Kids. Indeed, as Irene Uchida and a co-author noted in their study of cardiac malformations in Mongols, "almost every mongoloid baby in Toronto was seen," being referred primarily for the confirmatory dermatoglyphic test for mongolism and for consequent medical or genetic counseling.[103] Diagnostic efforts were so great that the Ontario Association for Retarded Children funded a 'special service' at Sick Kids. Between 1956 and 1959 this service provided dermatoglyphic diagnosis and some counseling for approximately 359 cases of suspected Mongolism.[104]

The research capacities of the Ford Walker school provided a resource for applied efforts. Likewise, the practice of genetic counseling served as an important justification for the school's research work. In seeking funds for a research project in harelip and cleft palate in the summer of 1950, Ford Walker made the connection to genetic counseling explicit: "Both harelip and cleft palate," she argued, "are crippling anomalies which handicap the affected individual to such an extent that families are anxious to have

accurate information regarding the factor of inheritance."[105] Ongoing studies of cleft lip and palate continued to have clear genetic counseling dimensions throughout the 1950s. By 1959, when the collection of pedigree data for this study came to a close, Ford Walker reported that "Part of the data from this material will be combined with a similar sample of patients collected at the Montreal Children's Hospital to give reliable risk figures for the genetic counseling of these anomalies.[106]

The connections between research and applied practice were more than technical and rhetorical, however. They also existed at the level of finances, for genetic counseling was funded primarily as research, into the 1970s. Commenting on the genetic counseling facilities available in North America, Lee Dice listed the "heredity clinic under the direction of Norma Ford Walker" operated by the Department of Genetics at Sick Kids and "supported by a research grant."[107]

Though the geneticists had a practical capacity in clinical medicine, this capacity derived from research concerns and strayed far from traditional treatment protocols. Emphasizing this stance, Ford Walker argued that dermatoglyphic diagnosis of mongolism was especially useful for helping "to convince parents that the disturbance of growth in their defective mongoloid child began at least five to six months before birth; that it was not due to any accident of birth or illness in infancy and that the damage is so extensive that treatment is probably of little avail."[108]

This detachment from traditional clinical concerns of treatment or management would change slowly. It was aided, in the 1950s, by biochemical workers who brought to the geneticists a new commitment to, and enthusiasm for, medical treatment of genetic

disease. Though produced by non-geneticists, then, the biochemists' enthusiasm for clinical management and treatment fed the growth of medical genetics.[109]

Managing the Burden: Beginning to Treat

In 1959, as Hubert Soltan drafted his Doctoral dissertation, he reiterated Ford Walker's sense that treatment was foreign to the geneticists. The genetical side of the problem of Duchenne Muscular Dystrophy, Soltan argued, was "not directly concerned with the search for a cure, [though it] is basic to an understanding of the disease."[110] Medical genetics possessed the applied capacity of heredity counseling, but the relationship of this practice to clinical service was unclear. Indeed, this practice was derided as insufficient by the more clinically minded. As a 1968 editorial in the *Canadian Medical Association Journal* put it, genetic counseling would at best only reduce future generations of the afflicted but it would not solve the problems of those with us today.[111] Biochemical analyses promised to take genetic study beyond such stalemates.

Even as Soltan conceded the general irrelevance of human genetics for clinical medicine, he gestured toward a new capacity, one which disputed Ford Walker's pessimism. Biochemical analysis of muscular dystrophy encouraged a "modern" and optimistic view of the place of genetics within medicine, he argued. Soltan referenced the British worker, Julia Bell, as a representative of an "older view of a fixed hereditarily determined state." Bell was cited as having argued in 1943 that "The untiring efforts of

the medical profession can do little to alleviate the condition once it has been allowed to rise; indeed, they cannot be expected to do so any more than they can be expected to turn a blue eye into a brown one." But this older, and pessimistic, view of medicine's capacity to deal with genetically-related disease was being displaced, Soltan suggested, "with the more modern one that an inherited defect is the result of failure in a specific enzymatic reaction determined by altered genes. It may be compensated for, if only we have definitive knowledge of the site and type of defect."[112] "[C]hanging concepts in medicine," Soltan argued, "are bound to result in a new emphasis: the emphasis on genetics as applied to human ailments."[113]

This 'new emphasis' was made possible in Toronto by the work of the biochemists at Sick Kids on genetic metabolic disease. Unlike the geneticists, whose applied practice involved genetic counseling, the analysis of metabolic conditions by the biochemists was tied to a treatment imperative. Andrew Sass-Kortsak's interest in galactosemia, for example, was exclusively clinical. He sought to bring the issue to clinical attention – arguing that the disease, "a congenital familial inborn error of metabolism" likely due to a specific gene, was "commoner than we think" and required careful diagnosis if treatment were to be possible. In this effort, involving publications in the *Canadian Medical Association Journal*, Sass-Kortsak encouraged the involvement of others on staff at the HSC and the Research Institute, including Ford Walker.[114]

Sass-Kortsak's work on Wilson's disease through the Research Institute also had a therapeutic component. In the metabolic unit, therapeutic trials were undertaken with various de-coppering agents.[115] Similarly, Donald Fraser's work on rickets that were

resistant to treatment with vitamins had both a research and a therapeutic orientation.[116] In Fraser's view, genetically determined forms of the disease were becoming more important in the face of what he thought to be the world-wide control of forms of rickets that resulted from vitamin deficiency. "Biochemical genetics," he suggested, was making a "tremendous contribution ... to the understanding and successful management of inborn errors of metabolism."[117]

The most successful episode of management that emerged from these metabolic concerns involved phenylketonuria. This condition arose from an inherited inability to metabolize phenylalanine, which therefore accumulates after birth in developing tissues causing severe neurological damage. In the late-1950s, technical developments in the screening of, and treatment for, PKU were imported into Toronto by biochemical workers at Sick Kids. This work was taken up with great energy by a non-geneticist, Michael Partington. Yet the strategies for PKU management in Ontario and Canada that emerged, in part through Partington's efforts, were of great consequence for medical genetics. The PKU episode was and remains one of the classic models of successful genetic medicine today.[118] It was a model of medicine that conformed with the models of treatment and cure promoted by modern medicine, and in that, it was profoundly unlike the model of care promoted by genetic counseling: reproductive management. Yet it worked to support further incursions of genetics into medicine, and it also encouraged the budding enthusiasm in the 1950s for a model of classical genetics that – in its radical simplicity – seemed wildly successful.

In the fall of 1958, a newspaper report announced "Help for Retarded: Baby Girl Responding to Treatment for Unusual Mental Deficiency." This report highlighted work underway through Sick Kids' Research Institute in the treatment of PKU using a special diet. This was, the article suggested, one of the recently recognized "biochemical diseases." "Both parents," the article explained, "play a part in the transmission of the disorder, but the metabolic abnormalities do not occur until after birth because of the mother's ability during pregnancy to utilize the foetus's excess phenylalanine."[119]

By the late 1950s research from other centers was providing convincing evidence that PKU could be controlled through the administration of a synthetic diet. Efforts to deal with the inherited metabolic disorder were taken up in Toronto by the biochemists and these efforts were soon led by Michael Partington, a young MD with a Ph.D. in Pathology who worked as a research fellow in neurology at the Hospital for Sick Children from 1959 through 1961.[120] Partington took on, as one of his duties, management of PKU patients on observation at the HSC.[121] He soon began working to publicize the issue among medical practitioners.[122]

Partington was not disinterested in the tools of reproductive management. He advocated the potential of biochemistry to aid in carrier detection of parents liable to have children with PKU [123] in order to "improve the accuracy and value of eugenic advice."[124] But Partington also pursued work that would facilitate treatment. He sought to define the clinical signs that might be detected by alert physicians in time to initiate treatment and he attempted to aid in the case finding process by surveying affected families in

Ontario.[125] It was this latter clinical strategy that was of greatest interest to the medical profession.

In 1960, the Canadian College of General Practice initiated a voluntary campaign among practitioners to detect infants with PKU. By this time, the College had learned from Partington that "the clinical picture is not characteristic enough to permit a diagnosis by itself".[126] PKU, it appeared, was a condition for which there were not adequate predictive signs. If the clinician was to be guided solely by symptoms, the pathological consequences of the disease would already have taken effect, and once in effect they could not be reversed. The College thus requested that its membership test all infants, regardless of symptoms. They sent out kits for urine testing, and publicized the campaign in the *Canadian Medical Association Journal*.[127] In advocating the attention of clinicians to this rare condition, the College argued "that recent evidence strongly suggests that treatment by a diet low in phenylalanine – from the first weeks of life – will prevent the appearance of mental deficiency."[128] State screening programs soon began to replace the relatively ad hoc efforts of medical and disease group associations. In Ontario a program was initiated in 1965 (though the province had been involved in a PKU program to provide financial assistance for the diets since 1963).[129]

The success of the PKU program was good news for the growth of genetics in medical research and practice. The provincial advisory committee which helped to establish and oversee the province-wide program in PKU screening soon anticipated further growth in screening for genetic metabolic diseases, arguing that "consideration is now being given to widening the program to cover other errors of metabolism for which

effective treatment is available and where the practicability and specificity of the screening procedure have been established."[130]

At Sick Kids, the successes of PKU advanced efforts to develop a coherent research program in genetic-metabolic disease in the latter-half of the 1960s. Sass-Kortsak noted in a 1967 report on a "Genetic, Biochemical and Paediatric Center for the Study of Inborn Errors of Metabolism" that "With increasingly effective control of infections by preventive measures and the use of antibiotics, our attention must be turned towards the degenerative diseases and towards metabolic diseases."[131] Sass-Kortsak also affirmed the disinterest of the geneticists in treatment: "In this endeavour," he noted, "the paediatricians' main aim is to understand the disease in order to diagnose and treat the patient. The geneticist will be primarily engaged in a study of the mode of inheritance, linkage studies, detection of heterozygotes, etc. The biochemist will primarily use this type of condition as an experiment of nature to help him to better understand metabolic mechanisms.[132]

The emergence of a treatment capacity for a genetic disease, though not promoted by geneticists, made genetic medicine more attractive. The fact that this treatment success addressed what seemed to be a particularly intractable problem, added to the enthusiasm. Genetic medicine provided "New Hope for Mentally Retarded," as one article headline put it.[133] Ford Walker also emphasized the more intangible benefits of this new approach, drawing on both biochemical and cytogenetic enthusiasms. Addressing the Academy of Medicine in Hamilton, Ontario, in 1961 Ford Walker argued that "Many parents were now reassured that it was through no fault of their own that one or more of their children

were mentally retarded."[134] In 1959, the Director of Sick Kids Research Institute cited PKU in support of the pursuit of this promising new area of research. Directing his plea to the Chairman and Board of Trustees, the Director wrote:

> it would seem that with the unusual facilities available in your Institute, it should be possible to undertake, in association with the Department of Genetics, a study of the possibility that the mental defects which are known to persist in some families from one generation to another could quite readily, as with the case of phenylketonuria, be an example of the persistence of gene-carried metabolic abnormalities which may produce their manifestations either sooner or later during the individual's life, and may quite possibly be the determining factors producing various types of mental and emotional derangement requiring institutional care in later life.[135]

In 1969, when assessing the value of the provincial PKU program, the committee emphasized the value of the recent "appreciation that some types of retardation can be prevented if they are recognized and treated early in life."[136]

Managing the Burden: Growing Needs and Growing Practices

In the late 1960s, Canadian medical geneticists confidently predicted more growth in the scope and significance of their activities. Diseases with a genetic cause were growing, genetic counseling was a valuable resource, and new practical interventions, including treatment, had or were emerging.

"Improvement of medical and surgical procedures has resulted in a gradual control of those diseases attributable to infections and nutritional deficiencies," wrote one

of Ford Walker's ex-students, James Miller, in advocating more attention to genetic disease in the mid-1960s.[137] "Concomitantly, there has been an increase in the prevalence of chronic long-term illnesses, a large proportion of which are genetically determined."[138]

Miller and his colleagues Margaret Thompson, Hubert Soltan and Clarke Fraser, the leader of the Montreal group of medical geneticists, emphasized the value of genetic counseling in the management of genetic disease.[139] Clarke Fraser put the matter bluntly in 1968: "Genetic counselling is about the only acceptable eugenic measure we now have available to restrict the increase of undesirable genes in the population. Should we not use it as much as we can?"[140] Hubert Soltan, in 1972, argued that: "Many people in the Western World, satisfied that their personal problems of "quantity" and spacing of offspring have been solved ... are turning their attention more intensely than formerly to the "quality" of their offspring." More cautious than Fraser, Soltan also warned that the expectations "often far exceed what the medical profession can deliver."[141]

These workers agreed that genetic counseling addressed not simply chromosomal or clearly genetic disease, it included "malformation[s]" – a range of more common conditions which were "multifactorial," or "seem to be determined not by genes at a single locus but by many genes with small additive effects."[142]

James Miller had tried, in mid-decade, to estimate the population burden of those diseases which fell within the genetic counselor's purview. But too little was known about the "scope and nature of the problem," Miller argued. Still, what data were available confirmed the significance and the shifting demography of genetic disease.[143]

Data from British Columbia suggested that "at any one time approximately 50% of the beds are occupied by children whose illnesses are solely, or partially, of genetic origin."[144] Miller advocated more research to better determine the "load of genetically determined disease" in populations. In the early 1970s, medical geneticists produced more exact calculations, to confirm the practical value of their work, and the need for its expansion.[145]

Charles Scriver and his Montreal colleagues, on behalf of a loosely organized "Committee for Improvement of Hereditary Disease Management,"[146] which he had spearheaded in the early 1970s, published an important study which estimated the "frequency of genetic disease and congenital malformation among patients in a pediatric hospital." Merging these two distinct categories in their final publication, they reported their results as demonstrating:

> that 30% of the admissions to our pediatric hospital reflect abnormal gene-environment interaction. This number represents some 4000 families in need of physicians with specific skills in diagnosis, counselling and management of their genetically allied problems.[147]

Moreover, the authors expressed concern "about a major deficiency" revealed by their survey: "In the period of observation," they wrote, "no more than 300 families received any type of formal counselling about the genetic component of their child's illness." Physician comprehension of the scope of the problem would have to increase. So too would the "available resources for genetic counselling."[148]

The broad range of "genetically allied problems" that medical geneticists sought to manage, and the corollary changes in the demography of disease burden which seemed to be self-evident, encouraged medical geneticists in the belief that their services were increasingly relevant. By the 1970s, new investigative practices like carrier screening and prenatal diagnosis expanded the populations 'at risk,' and provided still more possibilities for growth.

Carrier testing promised "to remove much of the uncertainty from genetic counselling," Thompson argued.[149] It also, as Soltan pointed out, created "a new category of concerned persons, which will grow in importance in the years ahead."[150] "Amniocentesis (if it can be done early enough and safely enough)," Fraser argued in the late 1960s, "will allow early diagnosis of sex, of chromosomal aberrations, and (in tissue culture) of certain inborn errors of metabolism."[151] In the early 1970s, when Hubert Soltan summarized the state of genetic counseling in Ontario, he could be more definite. The "classical" techniques of investigation which were "performed on the patient or relatives who have actually been born," had been "augmented by the development and acceptability of techniques which result in a direct study of cells or fluids produced by a foetus."[152]

Workers in Toronto and London, Ontario were among the first to pursue these new possibilities in Canada. London workers, arguing that "A fear of a deformed or mentally retarded child is a concern of most women some time during pregnancy," began to use amniocentesis for prenatal diagnosis in the fall of 1969. In Toronto, workers at both Sick Kids and Toronto General Hospital collaborated in developing an "Amniotic

Fluid Study Group" in the summer of 1971. Arguing that "The contribution of genetic factors to human disease is becoming increasingly evident," they started to perform the test by the fall of that year. By the summer of 1973, when both centers reported their results to the annual meeting of the Society of Obstetricians and Gynecologists of Canada, the London group had performed 100 tests and the Toronto team had performed 59.[153]

"The most common indication [for amniocentesis]," the London group noted, "was maternal age ... and next was a previous trisomy-21 infant."[154] Down's syndrome, then, was the chief object of attention for prenatal diagnosis in both Canadian centers.[155] To this cytogenetic focus, the Toronto workers added attention to single gene disorders which manifested themselves in biochemically detectable ways – drawing on the tradition of research in the genetic-metabolic diseases. Toronto workers were quick to pursue carrier screening and prenatal diagnosis of such diseases as Tay Sachs, in Toronto's Jewish community, and to explore the prospects of screening and prenatal diagnosis for Duchenne Muscular Dystrophy and Cystic Fibrosis.[156] But while the focus of prenatal diagnosis was clearly on strictly 'genetic' disease at first, the program had more expansive potential. The Toronto group soon coordinated its work with radiographers from Mount Sinai Hospital who performed ultrasound, initially for placental localization, but increasingly to detect fetal abnormalities. They also made use of a fetoscope, to visualize the fetus and reveal disorders not apparent through cytogenetic or biochemical tests.

Geneticists and cytogeneticists were involved in this work, but a larger team of workers was necessarily involved, as the Toronto group emphasized: "In our opinion, the field of antenatal genetic diagnosis is a good example where interdisciplinary cooperation is not only advisable but essential."[157] But it was the medical geneticists who assumed leadership in coordinating and regulating these activities on a national scale, and in making sense of them as elements in a new category of clinical practice: genetic services.

Managing the Burden: Managing the Profession

In the 1970s, a comparatively small group of workers in Canada, a majority of them linked to Toronto either by training or employment,[158] utilized available institutions to address issues in genetic medicine. They worked to increase the availability of genetic services throughout the country, to institute protocols for the conduct of these services, and to establish self-governing professional organizations. They were supported in this by the recently clarified institutional situation of medical genetics in Toronto, and by the chief administrator in that department, Louis Siminovitch. Siminovitch was a new convert to the concerns of practical medical genetics, but his administrative capacities and connections were put to good effect in this decade.

Administrative interventions were propelled, in part, by popular interest in genetics. Popular interest was heightened in the 1970s because of the expanding availability of genetic counseling, genetic screening and prenatal diagnosis, and the

controversial nature of these practices, particularly the latter. It was also due to the association of some of these developing services with more speculative activities: the increasingly publicized attempts to achieve *in vitro* ("test tube") fertilization, hypothetical capacities in "genetic engineering" and debates over recombinant DNA, which were especially fervent in the U.S. In the lay and the scientific imagination these issues all touched on the domain of genetics. Such an expansive reading built on a history of systemic blurring, and worked to confirm the merits of professional authority among medical geneticists and their more experimental colleagues.

The issues that achieved some prominence in the 1970s had not gone un-noticed in previous decades. In the early days of enthusiasm about medical cytogenetics, for example, a neurologist at Sick Kids was moved to comment that "There is hope that some day man may be able to alter the genetic structure..."[159] More prominently, Nobel laureate Francis Crick, who was in Toronto to receive an award from the Gairdner Foundation in 1962, argued that "Human control of the hereditary mechanism will be achieved eventually."[160] The early 1960s also witnessed publicity on the debates within the medical community about the propriety of human experimentation in "test tube baby" research.[161]

Prenatal diagnosis was the subject of press attention years before it was pursued. A team of Montreal researchers at McGill University, which included Clarke Fraser, were reported to have been awarded $20,000 from the federal government in 1959 to track "clues that seem to indicate abnormal births are signalled by changes in a mother's

blood."[162] In a related fashion, the popular discussion of David Carr's research on chromosome anomalies in abortuses highlighted the possibility that "research could eventually lead to discoveries that would help the human body cast off unborn, abnormal children."[163] But it was not until the late 1960s, coincident with the 1969 liberalization of the abortion law, that there was significant press attention to a possibility which had been technically apparent since 1966: that "Specific types of mental retardation, such as mongolism, are now possible to detect in unborn babies."[164]

In the 1970s, press attention was more systematic – often addressing a range of 'genetic' concerns as a related package, and thus dramatizing the social significance of genetic medicine. Lydia Dotto, a journalist who wrote extensively on genetic issues in the 1970s, did a series of articles on the topic in the summer of 1972. This series discussed both the pragmatic dangers of genetic services and the far-fetched possibilities in genetic engineering. Dotto highlighted the genetic services then becoming available in Toronto – amniocentesis[165] and screening for Tay-Sachs; she noted the existence of concerns surrounding abortion, the possibility of coercion[166] and the slippery slope.[167] But the dilemmas posed by existing genetic services were only the beginning of Dotto's exploration. The dilemmas extended to the possibility "not only of correcting genetic defects, but of engineering people to possess certain characteristics." This might include, scientists warned, "curing socially unacceptable behaviour."[168] There were also the possibilities of test tube fertilizations, surrogate motherhood, the artificial womb, cloning and genetic surgery of both the corrective and engineering persuasions.[169] As the author

of an article in a national newsmagazine put it "The new science of genetics is both a burden and a boon to any responsible young couple planning a family."[170]

Perhaps unsurprisingly, geneticists who commented publicly in the 1970s accepted that this breadth of issues fell within their ambit.[171] Louis Siminovitch was deeply interested and engaged, and committed to discussion and debate.[172] He took the broad range of concerns into the elite-based policy-making forum of the Ontario Council of Health, as a member of the Health Research Committee. The Council accepted and published his recommendations in 1973 as, *Social Implication of Developments in Biomedical Sciences*.[173] The document cited three main issues related to the potential for "genetic manipulation in man":

> 1. The use of nuclear transplantation to produce multiple copies of identical organisms (cloning);
> 2. The potential genetic manipulation associated with procedures for fertilisation and early development *in vitro*, and reimplantation *in utero*;
> 3. The diagnosis of genetic disease prenatally by biochemical or cytogenetic analysis of amniotic cells sampled early in pregnancy and grown *in vitro* (amniocentesis).[174]

Of these three, two were still areas of speculation. While noting the complexity of the speculative issues,[175] Siminovitch focused most attention on the one activity already in the realm of scientific fact rather than science fiction – amniocentesis. By the mid-1970s, the public consciousness was awakened to another element in the debate over genetic science: recombinant DNA. New kinds of hazards – specifically biohazards – were added to the list of possible dangers attached to genetic science. In some discussions, a narrow conceptualization of biohazards came to dominate the debate over genetics. But, in many

contexts, a broad debate over genetics continued, one that merged practices currently underway with practices that might never develop.[176] Sitting as a member of a United Church Commission on Genetic Engineering in the mid-1970s, Siminovitch expanded his list to make more explicit the issues surrounding genetic screening, and the remote possibility of "genetic engineering," or "cloning," in humans.[177]

The breadth of concern with the human implications of genetics that Siminovitch corroborated in his popular and policy-setting endeavors encouraged and validated efforts at professional self-regulation. Siminovitch served as the chair of a Committee to Canada's Medical Research Council which followed the American lead in pursuing controls on recombinant DNA research which were self-administered and facilitative, rather than legislated and restrictive.[178] Siminovitch also worked with his new colleagues, the old-order medical geneticists, to manage the issues which stemmed from practical applications in genetic medicine.

Working through such institutions as the Genetics Society of Canada, the Medical Research Council, and in Ontario, the Ontario Council of Health, medical geneticists and their allies facilitated the expansion of services, while producing structures of self-regulation to manage the conduct of these services. Professional self-regulation addressed both popular and practitioner interest in the orderly management of these new and potentially threatening capacities. While these organizational initiatives were unprecedented, they drew on and institutionalized enduring interpretations and practices.

At the 1970 meeting of the Genetics Society of Canada (GSC) – a Society whose membership was primarily composed of non-human geneticists – a motion was passed in favor of genetic counseling services. The motion read: "I favour urging the provision of more adequate genetic counselling facilities in Canada according to the need." This membership support permitted the GSC Committee on Genetics as it Relates to Social Problems to "establish a study to investigate the status of genetic counselling services in Canada."[179]

The GSC committee was chaired by James Miller, a Vancouver-based medical geneticist who had done his Master's degree in Toronto under Ford Walker and his Ph.D. in Montreal, at Canada's other major center for medical genetics. The committee's membership included two other human geneticists, John Hamerton of Manitoba (a cytogeneticist émigré from Britain) and Diane Wilson Cox of Toronto. Formally, it also included two non-human geneticists.[180] But more important than these two official members in terms of influence were the two informal participants, Louis Siminovitch and Margaret Thompson of Toronto, who frequently attended and advised the meetings.

Armed with the mandate of the Society, this group turned its attention to the proliferating array of social issues that seemed attached to genetic science in the early 1970s – seeking to exert professional control.[181] Miller was interested in addressing the issue of the "manipulation of human germ cells."[182] Others demurred. "In my opinion," Diane Wilson Cox wrote, "the Committee on Genetics as it Relates to Social Problems should apply itself to problems where there is a high probability of influence in planning and policy."[183] Convinced by this argument, the group decided that issues of

amniocentesis and genetic counseling, and related questions of accreditation and funding, were of sufficient importance, and sufficiently amenable to professional self-regulation, to warrant attention.

When the GSC Committee identified these priorities, the policy relevance of prenatal diagnosis was already clear. John Hamerton, one of the members of the GSC Committee, had succeeded in having the MRC establish a Working Group on Prenatal Diagnosis of Genetic Disease in the fall of 1971. Chaired by Hamerton, and including the GSC committee chair, James Miller, and frequent attendee, Louis Siminovitch,[184] the Committee was to "keep a watching brief on research developments in Canada and elsewhere and to do what it can to co-ordinate Canadian efforts in this field."[185]

The chief task of the MRC Working Group would prove to be a national trial of amniocentesis of genetic disease, one that paralleled the similar national trials of PND in Britain and the U.S.[186] The Working Group established a registry, run by Nancy Simpson at Queen's, which gathered data from participating centers across the country on the safety and efficacy of prenatal diagnosis using amniocentesis. It reported in 1976,[187] that "Amniocentesis for the diagnosis of certain classes of genetic disease can now be considered to be safe, accurate and reliable when carried out at about 16 weeks' gestation, monitored by ultrasound and performed by an obstetrician trained to carry out the procedure.[188] Nancy Simpson and her co-authors from the MRC Committee added that PND should be carried out "in a major health sciences centre."[189]

While some attention had been paid to the possibilities of prenatal diagnosis since at least the late 1950s, and while some centers had begun to experiment with amniocentesis for PND by the turn of the decade, this trial established prenatal diagnosis in Canada. Through participation, the trial institutionalized capacity in all of Canada's medical schools.[190] It created the incentive, and provided technical and some financial support to those medical geneticists and their obstetrician allies who were interested in developing the service.

Moreover, the overlap in membership between the MRC and GSC committee facilitated the creation of a set of guidelines for practice which established professional standards for conduct, and thus confirmed the respectability of the procedure. John Hamerton, Chair of the MRC working Group, but concurrently member of the GSC Committee, drafted these guidelines.[191] They were promulgated in 1974 and publicly attributed to a joint committee of the Genetics Society of Canada, the Canadian Pediatric Society and the Society of Obstetricians and Gynecologists of Canada. Amniocentesis, the guidelines said, "followed by appropriate counselling is becoming standard medical practice in genetic high risk pregnancies for the diagnosis of genetic disease."[192] When the Working Group on PND published their final report, the existence of these guidelines were a validating resource: the final report stated that the "Canadian guidelines for genetic amniocentesis were adhered to."[193]

The guidelines confirmed the standardized system that had been institutionalized in participating centers during the trial: a team approach, with the team including professional expertise that would be available only in major university-affiliated

hospitals, a referral system, a counseling context that was largely non-directive,[194] procedural consistency, and a set of predictable indications.[195]

The guidelines had been advocated as a means to set limits on the use of prenatal diagnosis. In March 1973, Margaret Thompson "stressed" to the GSC committee "that there were dangers in emphasizing the role of amniocentesis in a genetic service program. It is obvious that already this service involves a considerable amount of work for very little yield, i.e., most of the pregnancies which are monitored will have [sic] a normal fetus." Thompson noted that the demands were not, at present unreasonable, but given the likelihood of increased demand "it may very well be that this procedure will consume an incredible amount of space and time in the very near future." She recommended two things: "a cost-benefit analysis of this procedure at the earliest possible date"; and, "some tightening up of criteria" for which she recommended a joint statement from the GSC and SOGC. She reported to the committee that Hamerton would prepare a statement and discuss it with the president of the SOGC.[196]

Yet while Thompson and her colleagues may have wished to avoid over-emphasizing the merits of prenatal diagnosis in addressing the burden of genetic disease, the GSC guidelines also encouraged growth. The indications listed by the guidelines established a set of limits that were more putative than real. Given the restricted use of antenatal diagnosis by Canadian women at this date, the limits served as a set of targets that required substantial growth in infrastructure if they were to be met.[197]

The systemic slippage between genetical and congenital disease also encouraged growth. While chromosomal and genetic-metabolic indications were the focus of the

initial study, amniotic fluid was soon being assessed for alpha-fetoprotein (AFP) in various centers to diagnose neural-tube defects. The first report from the MRC Working Group, while enthusiastic about the "high accuracy and reliability ... in diagnosing both chromosomal abnormalities and biochemical disease" cautioned that there were "clear limitations to the use of AFP values in amniotic fluid.... Future work," they argued, "is therefore needed."[198] In less than three years, the members of the MRC committee were able to report on an extension of the initial collaborative study, which confirmed that "antenatal diagnosis of open neural tube defects is being carried out effectively in Canada .... This suggests," they wrote, "that the AFP concentration should be measured in any sample of amniotic fluid collected for other reasons."[199]

When the GSC Committee identified its list of items worthy of professional attention, it had included genetic counseling alongside amniocentesis. The 1971 GSC survey had confirmed that genetic counseling was being provided in centers affiliated with all 13 of Canada's medical schools. But though fairly well established, problems with this service were considerable and included such issues as under-utilization, excess demand, competition, lack of co-ordination, and financial stringencies. James Miller stressed that accreditation was a favored option as a way to "straighten out certain existing confusions in the financing of genetic councelling [sic] units.[200]

By the 1970s, though medical genetics was achieving increasing success, it was beginning to face structural problems. Heredity counseling had emerged in Toronto through research practices and research funding. Pioneered as a discipline by Ph.D.s it

was not a medical specialty and had no ready access to clinical payment or governance systems. The usual solutions were unavailable: even where billing categories were established for such work within existing fee-for-service medical schemes, some of the "counsellors," not being MDs, were not in a position to bill.[201]

Members of the GSC committee represented, for the most part, the old-order medical geneticists. Fee-for-service funding, or accreditation by the Royal College of Physicians which was the usual venue for a medical specialty, implied that only clinicians could practice. The committee thus advocated some combination of "a new organization dealing specifically with genetic counselling" with "provincial governments establishing recognized centers responsible to Health Services in each province" – in other words, block funding.[202] This model allowed the old-order workers, largely Ph.D. trained, to continue their primary identity as researchers – an identity staunchly defended by the old-order medical genetics during the restructuring of medical genetics in Toronto in the 1970s – while retaining a practical and applied role within the hospital that had been an enduring part of medical genetics practice.

Not all agreed with this approach, especially those new-order medical geneticists content with a largely clinical orientation. As James Miller put it in reporting on the survey of genetic counseling in Canada, "there is a great deal of strong feeling about the matter of accreditation."[203] Allen Gardner, an MD who headed the new cytogenetics program at Toronto General Hospital, advocated for funding and accrediting medical genetics as a *medical* specialty. It should be accredited, he argued, by the Royal College of Physicians and Surgeons of Canada, and this would allow funding by OHIP along

standard lines. "I see no reason," he wrote, "to drastically disrupt present patterns of medical practice in order to provide genetic services." Under this scheme, Ph.D. medical geneticists became peripheral. Gardner identified them with the nurses, technologists, social workers and secretaries as "paramedical personnel" whose presence would oblige the availability of an additional budget from which to pay salaries.[204]

Clarke Fraser, informal head of the Montreal community of medical geneticists collaborated with Margaret Thompson and the GSC committee to resolve the issue of national accreditation in accordance with the model preferred by the old-order medical geneticists. Fraser organized a national meeting, held in the summer of 1973 and informally piggy-backed onto the AGM of the ever-supportive Genetics Society of Canada. This meeting produced a mandate in support of "genetic counselling as a legitimate health service which should receive adequate payment for services,"[205] and reached agreement on accreditation on a group basis (of centers rather than individuals). A national steering committee of four persons was struck, led by Margaret Thompson, and with considerable overlap with existing committees.[206] Thompson coordinated a meeting for the fall of 1974, involving "senior medical geneticists"[207] who were "representatives of the 15 or so centers in Canada where genetic counselling in relation to children's diseases is a recognized activity."[208] In 1975, a national self-regulating professional body, the Canadian College of Medical Geneticists, was announced.[209] Yet while important, professional self-regulation would prove hollow if medical geneticists could not serve as the primary discipline in coordinating the disparate array of activities involved in the practical work of genetic medicine. In Ontario, by the early

1970s, much of the work done on behalf of genetic medicine could be billed for independently – namely cytogenetic, biochemical, obstetrical and radiological services. Yet there were no billing categories for counseling and dermatoglyphics. Moreover, medical genetic personnel – unless they were MDs – could not submit the bills.[210] In Toronto, many of these un-billed-for practices were financed through research grants or line-items in the hospital budget.[211]

Such funding questions would have to be addressed at the provincial level and early in the decade, relatively ad hoc efforts were made to achieve new structures of financial support. The Toronto workers submitted a brief to the provincial insurance body, OHSIP, in the fall of 1971 to argue for program rather than fee for service funding.[212] But more formal efforts were soon pursued. The 1973 meeting which had stimulated the creation of the College had addressed the full range of issues in the organization of genetic medicine, including "accreditation, payment and recognition of genetic services."[213] Hubert Soltan had agreed, as a result of the 1973 gathering, to "convene a meeting of Ontario genetic counsellors ... to consider especially the problems of funding and accessibility of services." A provincial organization, the Association of Genetic Counsellors of Ontario, was the result.[214] Meanwhile, James Miller, as President of the Genetic Society of Canada, and Diane Wilson Cox, representing the Committee on Genetics as it Relates to Social Problems, were emboldened by the 1973 meeting to lobby provincial ministries of health. In a letter sent to the various Ministers they advocated for the development of accredited genetic counseling services. "Because of the financial and social benefits of genetic counselling," they argued, "we believe such counselling should

be financed as part of medical care. Centres to be financed should be accredited; co-ordination and extension of work of each centre should make the services accessible to all."[215] The response from the Minister in Ontario indicated the existence of some discussions with the Ontario Medical Association (OMA) "to determine the best method to follow for the future."[216] Yet from the perspective of the medical geneticists, the OMA, which represented medical practitioners and preferred fee-for-service financing systems, was not in a position to address their concerns.

Louis Siminovitch was kept informed of these professional efforts by Margaret Thompson. Arguing that such strategies, while important, would not "provide us with comprehensive effective mechanisms to handle these problems" and that "the Government has to play a significant role in this area," Siminovitch lobbied the Ontario Council of Health for a Task Force.[217] The Task Force was duly established in September of 1974, with Siminovitch as the chairman.[218] It drew on material produced by the old-order medical geneticists to define its approach – namely, the "Canadian guidelines for antenatal diagnosis of genetic disease: a joint statement," and the Recommendations taken from the brief of the Association of Genetic Counsellors of Ontario.[219] The results of the Task Force, which were well received by the Council, recommended a coherent system of genetic services in Ontario: well funded, with consistent procedures, and regionalized through university-based centers. Its recommendations, published in 1976, served as a benchmark for further development. It proposed a model of block funded, regional, university-based centers with multidisciplinary teams; and, it established a commitment to population-access to services that were defined as necessary.[220]

Reflecting the breadth of practices that seemed increasingly relevant to genetic medicine, the Task Force identified itself, in 1976, as the "Task Force on Genetic Services"[221] But this was a new way of framing the practical work of medical geneticists, for when the Task Force was initiated, in 1974, it had been called the "Task Force on Genetic Counselling Services" and its scope was identified as "Genetic Counselling and Dermatoglyphic Services in Ontario Hospitals."[222]

While engaging in professional co-ordination, then, medical geneticists were concurrently engaged in re-defining their practices, to make sense of the growing array of applied work that was within their professional purview. This involved, in the first instance, the use of the term 'genetic services.' But it also involved redefining the meaning of genetic counseling.

The term 'genetic counseling' had been used by the Toronto workers to describe a range of practical work performed by the medical geneticist. It was not solely restricted to the communication of genetic information, but included the work done to support the production and validation of diagnoses and risk estimates. In seeking funds to support the meeting which would establish the new College, Thompson and Miller wrote that "The term "genetic counselling" commonly used to describe the aspects of human genetics related to service, is not to be construed merely as counselling; rather, it includes validation of the diagnosis, genetic work-up (including laboratory services), estimation of risk, communication of risk to the family, and follow-up."[223] By defining genetic counseling in this way, medical geneticists made sense of their demand for block funding, so that the disparate practices of varied disciplines were subsumed under their

professional auspices. As this demand was met, however, the need for such an improbably expansive definition was reduced. Moreover, the new term 'genetic services' – especially in light of the expansion of practices under the auspices of genetic medicine – did a better job of describing the practical work of the medical geneticist.

Clarke Fraser played a central role in establishing a new definition of genetic counseling. He chaired a meeting sponsored by the US National Genetics Foundation in 1972 to develop a new definition.[224] Genetic counseling was defined as "a communication process dealing with the human problems associated with the occurrence, or the risk of occurrence, of a genetic disorder in a family." The affected individual or family was to be helped to "comprehend the medical facts"; appreciate the role of heredity in the disorder; "understand the alternatives for dealing with the risk"; choose the appropriate course of action; and, make the best possible adjustment.[225] This new definition was promulgated formally and informally in Canada.

Medical geneticists might practice genetic counseling, but they were more than genetic counselors. The scope of their work – as the burden of genetic disease – was correspondingly larger. Fraser had invited "genetic counsellors" to a meeting on "genetic counselling" in the summer of 1973 to initiate the formal work to build a national accrediting body for medical geneticists.[226] But when the national meeting was held in the fall of 1974, it was called the "National Conference on Standardization of Medical Genetics Services."[227]

Endnotes: Chapter 6

[1] Elizabeth Ives, "Genetics and Genetic Counselling," *Canadian Journal of Public Health*, 57:11 (Nov 1966), 518. See also James Miller, "Human Genetics in Public Health Research and Programming," *Canadian Journal of Public Health*, 57:1 (January 1966); Nancy Simpson, "Experiences of a Genetic Counselling Clinic in Kingston, Ontario," *Canadian Journal of Public Health*, 66 (Sept/Oct 1975), 375-383.

[2] For a nuanced discussion of the "health transition," see: Allan Brandt; "Behavior, Disease, and Health in the Twentieth-Century United States: The Moral Valence of Individual Risk," in Allan Brandt and Paul Rozin, eds. *Morality and Health*, (New York and London: Routledge, 1997).

[3] GH Valentine, "Reproductive Counselling Services," *Canadian Medical Association Journal*, 106 (April 8, 1972), 757.

[4] Narratives of hereditary disease and their burdens have a long history; they are not exclusive to the post-war years. They are visible in the 19th century see: Charles Rosenberg, "Heredity, Disease and Social Thought," *No Other Gods: on Science and American Social Thought* (Baltimore: Johns Hopkins University Press, 1976); Carlos Lopes-Beltran, "Forging Heredity" From Metaphor to Cause, a Reification Story," *Studies in the History and Philosophy of Science*, 25:2 (1994), 211-235.

[5] Doris McCubbin, "Are we Breeding a Nation of Invalids?" *Maclean 's Magazine*, April 2, 1955, 14, 15.

[6] *Ibid.*, 15.

[7] *Ibid.*, 15, 93.

[8] McCubbin cited such authorities as Tage Kemp, a Professor of human genetics in Copenhagen and Director of the Danish registry of hereditary disease, and Franz Kallman a hereditarian psychiatrist attached to the New York State Psychiatric Institute of Columbia University. She may also have had some knowledge of the Toronto community, since she cited an article in an earlier issue of *Maclean's* which featured Ford Walker.

[9] "But she continues some study in dental heredity and in dermatoglyphics – the fingerprint side," the article continued: "Multiple births study material for Geneticist," *Globe and Mail*, February 27, 1950 (UT, A73 0026, 105, 61). Meanwhile more strictly genetic diseases were not necessarily highlighted as such. The Muscular Dystrophy Association of Canada, appealing in 1955 for funds in its second year of operation, featured as one of the five projects such funds were supporting a study directed by Ford Walker on "the possible hereditary aspects of the disease." Samuel Campbell, "Always Fatal Disease Hits 10,000: Canadians Seek Research Help," *Toronto Star*, November 11, 1955. (OA, MS 755, Reel 140).

[10] Alton Slakeslee, "Two Toronto Scientists Find New Blood Types," *Toronto Telegram*, September 7, 1955. Uchida's study was highlighted in two separate reports: "Toronto Doctor Says Palms Key to Heart Defects," *Toronto Globe and Mail*, September 7, 1955; and also in the *Toronto Star* (OA, MS 755, Reel 140).

[11] "Will Test 400 Pairs of Twins to Avoid "Identical" Errors," *Toronto Star*, September 28, 1955 (OA, MS 755, Reel 140).

[12] A later article reported on the Cleft Palate Research and Treatment Centre at Sick Kids, with which Ford Walker was involved. It reported that "The experience at this clinic has confirmed previous findings that heredity is a factor in 32% of the cases ...": Ben Rose, "Foundation Backed Clinic Aids Hundreds with Cleft Palates," *Toronto Star*, September 26, 1956 (OA, MS 755, Reel 145)

[13] "Will Test 400 Pairs of Twins to Avoid "Identical" Errors," *Toronto Star*, September 28, 1955 (OA, MS 755, Reel 140).

[14] "Geneticists Discuss Notable Advances," *Globe and Mail*, August 22, 1958 (OA, MS 755, Reel 155).

[15] This article also noted that "One practical aspect of the Copenhagen file is that a doctor can consult it to decide how he should advise an improved patients in respect to whether he should have children and what are the chances of the disease being passed on." "Danes Delving into Heredity," *Toronto Telegram*, August 21, 1958 (OA, MS 755, Reel 155).

[16] Of course, this narrative was not without challengers. "Noted Montreal neuro-surgeon," Wilder Penfield, was cited as denying that epilepsy was "any more a hereditary disease than many other maladies," and

should not generally factor into decisions about marriage. "Epilepsy not Found Hereditary," *Globe and Mail*, December 7, 1957 (OA, MS 755, Reel 150). One doctor, lecturing in Hamilton, Ontario in 1956, was quoted as arguing that "People who are afraid that the new medical science is going to produce a race of weaklings and misfits can stop worrying." Discussing the decline in the infant mortality rate in the previous decades, he argued: "Heredity isn't such a big factor as some people think .... Good care, both before and after birth, is much more important." Kingsley Brown, "Future Misfits Denied," *Hamilton Spectator*, June 6, 1956 (OA, MS 755, Reel 145)

[17] McCubbin, "Are we Breeding a Nation of Invalids?" 93-94. For another article reporting the warnings of an "internationally famous geneticist," see: Editorial, "Survival of the Sickest Growing Problem for Man," *Orillia Daily Packet and Times*, August 14, 1961 (OA, MS 755, Reel 192). While genetic medicine was not the only benefactor of narratives on the conquest of infection, it made a special claim to importance in the era of mutagenic danger. At Sick Kids, research on metabolic disease, before it was narrated as "genetic metabolic" disease, was promoted as necessary because of the conquest of infection. See, for example: Minutes of the Committee on Research, September 15, 1954 (HSC, CRM, Vol. 1953-1959).

[18] Diane Paul, ""Our Load of Mutations" Revisited," *Journal of the History of Biology*, 20:3 (Fall 1987).

[19] *Ibid.* See also Michael Dietrich, "The Origins of the Neutral Theory of Evolution," *Journal of the History of Biology*, 27:1 (Spring 1994), 28

[20] Muller was convinced that genetic variations are usually fitness decreasing and would be reduced through the action of natural selection except for the restraints imposed by civilization. He advocated artificial means to reduce the ever-increasing "loads" of harmful variations. Dobzhansky, made the contrary argument – that heterozygous and not homozygous genotypes were fitter, and that evolution acted to maintain, not decrease, genetic variation in populations. To artificially reduce genetic variability could be disastrous. Yet this reasoning did not make Dobzhansky a non-eugenicist, John Beatty has argued; rather it implied a different kind of eugenic program, based on the maximization of a different set of genotypes. John Beatty, "Weighing the Risks: Stalemate in the Classical/Balance Controversy," *Journal of the History of Biology*, 20:3 (Fall 1987), 302. See also Dietrich, "The Origins of the Neutral Theory."

[21] As Beatty has argued, the balance position, by contrast, could be used to support contrary social policy implications with respect to radiation, and debate between the two camps was intensified by these political differences. Beatty, "Weighing the Risks."

[22] Diane Paul, "Eugenics and the Left," in Diane Paul, *The Politics of Heredity: Essays on Eugenics, Biomedicine and the Nature-Nurture Debate*, (Albany, NY: State University of New York Press, 1998). Those who warned against wholesale restrictions on breeding because of the unknown benefits of the alleles involved in these diseases in a heterozygous state were drawing on a balance argument, however. See: Elizabeth Ives, "Genetics and Genetic Counselling," *Canadian Journal of Public Health*, 57:11 (Nov 1966), 518. See also James Miller, "Human Genetics in Public Health Research and Programming," *Canadian Journal of Public Health*, 57:1 (January 1966), 516.

[23] Dobzhansky opposed general variation-reducing strategies, Beatty argues, but "he explicitly recommended eugenic measures to control the frequency of specific mutations responsible for traits like retinoblastoma.": John Beatty, "Weighing the Risks," 306 footnote 79

[24] Paul, ""Our Load of Mutations" Revisited."

[25] John Beatty, "Genetics in the Atomic Age: The Atomic Bomb Casualty Commission, 1947-1956," in K Benson, J Maienschein and R Rainger, *The Expansion of American Biology* (New Brunswick NJ: Rutgers University Press, 1991), 296-7; Michael Dietrich, "The Origins of the Neutral Theory," 30

[26] AH Sturtevant was featured in this report: "Brooding Biologist Sees Atom Peril for Babies," *Toronto Globe and Mail*, January 12, 1955 (OA, MS 755, Reel 139). For more articles of this kind see: "A Doctor Vs Scientists," *Guelph Mercury*, January 31, 1958 (OA, MS 755, Reel 155).

[27] "World Level of Radioactivity Harmless: Martin," *Globe and Mail*, February 16, 1956 (OA, MS 755, Reel 145)

[28] "Discourage Chalk River Weddings, Fear Radiation Effect on Children, Genetic Peril of A-Blast seen Grave," *Globe and Mail*, August 16, 1955. See also: "Doctors Seek More News on A-Dangers," *Globe and Mail*, August 17, 1955 (OA, MS 755, Reel 139). For more on Chalk River see the series of articles in the *Globe and Mail*: "Chalk River Labs Study Radiation," March 16, 1957; "Invisible but Deadly Atomic

Radiation Cuts Human Life Expectancy," March 18, 1957; "Constant Safeguard Needed to Protect Workers," March 19, 1957 (OA, MS 755, Reel 150)

[29] George Noorfhof, "The Grim Facts about Increasing Radioactive Fallout: 35,000 Defective Children Canada's Future Legacy?" *Toronto Star* March 26, 1959, (OA, Reel 163). Muller, who abjured compulsion, expressed enthusiasm for reproductive control in the interests of the genetic health of the population. In his much cited comments at the International Congress of Genetics in Montreal in 1958, he argued that "People are going to have to do a better job of picking their mates or the world will fill up with misfits." Phyllis Griffiths, "He Hits Love at First Sight," *Toronto Telegram* August 26, 1958; Muller suggested that "eventually more consideration may be given to the quality of future generations of men than to the feeling of parents known to be of an inferior strain in deciding whether to have children." Fred Poland, ""Selective Breeding" Acceptance to Grow US Geneticist Says," *Montreal Star* August 26, 1958; "Can't rely on Whims of Parents," *Globe and Mail*, August 26, 1958, (OA, Reel 155)

[30] This research was well integrated into the community of North American human genetics workers. Irene Uchida and Elizabeth Curtis thanked James Crow for "statistical analysis of the data and for his help in preparing this paper." And James Neel and William Schull paid them the complement of a refutation. Diane Wilson Cox's relations with Neel and Schull were happier. It was them she thanked for "reading the manuscript and making helpful suggestions." Irene Uchida and Elizabeth Curtis, "A Possible Association Between Maternal Radiation and Mongolism," *Lancet*, 2 (October 14, 1961), 850. Citing their own work with the survivors of Hiroshima and Nagasaki in the Atomic Bomb Casualty Commission, they noted the discrepancy of their much larger data set with that of Uchida and Curtis. WJ Schull and JV Neel, "Maternal Radiation and Mongolism," *Lancet*, 1 (March 10, 1962), 537-8. Wilson Cox also thanked Canadian researchers like Clarke Fraser, Howard Newcombe, TE Reed. Nancy Simpson and Norma Ford Walker. Diane Wilson Cox, "An Investigation of Possible Genetic Damage in the Offspring of Women receiving Multiple Diagnostic Pelvic X Rays," *American Journal of Human Genetics*, 16:2 (June 1964), 228-9.

[31] Uchida and Curtis, "A Possible Association," 848-50.

[32] Doug Smith, "Winnipeg Researcher Links X-Ray, Mongolism," *Winnipeg Free Press*, October 17, 1961 (OA, MS 755, Reel 192)

[33] Diane Wilson Cox (nee Diane Wilson), was a Master's student of Ford Walker. She began her study on the inheritance of congenital dislocation of the hip – then shifted her attention toward the more engaging question of the genetic effects of radiation, taking advantage of the records of extensive exposure to diagnostic X-rays amongst children treated for the condition at Sick Kids. Wilson Cox's findings were not statistically significant: "It is not possible to conclude with certainty from this study that genetic damage from multiple diagnostic X-rays has been detected." Yet, the data did point in this direction and she argued that, "Any possible decrease in the [X-ray] dose received is desirable, both for the individual and for the population as a whole." Diane Wilson, "An Investigation of Possible Genetic and Somatic Damage From Multiple Pelvic X-rays to Individuals with Congenital Dislocation of the Hip," University of Toronto, MA Thesis, 1961, 74. (UT. T79 0107, File 54). She was equally equivocal in her published article but did insist on the possibility of genetic damage from radiation and argued, in conclusion, that "In the final assessment of genetic damage from radiation, it must be remembered that only a small amount of the total genetic damage would be expected to appear in the first generation offspring, since most autosomal recessive mutations would be unexpressed." Diane Wilson Cox, "An Investigation of Possible Genetic Damage in the Offspring of Women receiving Multiple Diagnostic Pelvic X Rays," *American Journal of Human Genetics*, 16:2 (June 1964), 228.

[34] Joan Hollobon, "Signposts of the Future in Medical Research," *Globe and Mail*, January 5, 1962 (OA, MS 755, Reel 205); Ron Poulton and Ken MacTaggart, "Cancer Drama: Lid Lifted off Secret of Life," *Daily Colonist*, April 17, 1962 (OA, MS 755, Reel 205); Joan Hollobon, "An Elegance of Design Behind the Jargon," *Toronto Globe and Mail*, June 14, 1962 (OA, MS 755, Reel 205). These studies did not emerge from communities of medical geneticists, but from more basic workers. Studies from human geneticists, notably Madge Thurlow Macklin, might continue to feature tendencies: "Cancer Can Be Inherited – Toronto MD," [reporting on Madge Macklin], *Toronto Telegram*, March 1, 1961; "Inherited Cancer only 'A Tendency'," *Toronto Telegram*, March 2, 1961 (OA, MS 755, Reel 192)

[35] "Retardation Ranges and Causes Examined," *Welland Evening Tribune*," March 24, 1960 (OA, MS 755, Reel 191).
[36] 'Geneticist Tells Role of Genes in Retardation: Theory is Bottom of Radiation Study." *Hamilton Spectator*, February 22, 1961 (OA, MS 755, Reel 192). Ford Walker, cited as a "eugenist at Sick Children's Hospital," reported on a Toronto study which confirmed that Mongolism "is caused by an extra chromosome appearing during conception." She also identified "The main trend today ... where abnormal internally produced chemicals affect the function of the brain and where correction of this can produce control of the mental retardation of the child." "Retardation Ranges and Causes Examined," *Welland Evening Tribune*, March 24, 1960 (OA, MS 755, Reel 191).
[37] "Diabetic Research Project," *Cornwall Standard Freeholder*, March 24, 1962 (OA, MS 755, Reel 205). This is evident in Simpson's research too, see: Nancy Simpson, "Multifactorial inheritance: a possible hypothesis for Diabetes," *Diabetes*, 13 (1964), 462. A report on the research of the Sick Kids workers Nancy Simpson, Diane Wilson Cox and Andrew Sass-Kortsak on Wilson's disease, highlighted the careful pursuit of a family group in Virginia, from whom "copious notes and blood samples" were taken. This disease "which appears to be an inherited inability of dispose of copper accumulation in the body" was reported to likely be due to a "recessive gene from both parents who may be only carriers of the disease.": "Researchers Find Clue in Virginia," *Globe and Mail*, July 23, 1962 (OA, MS 755, Reel 205). See also a report on CF research at HSC, that "Its precise cause is unknown. The accepted medical view is that the disease begins in the unborn infant as a result of its inheriting the same kind of special gene from each parent. It is the conjunction of the two recessive genes, one from each parent, that produces the CF-prone child." Stasia Evasuk, "Mother's Tears Tell of Daughter's Tragedy: She has only three years," *Toronto Telegram*, May 27, 1961 (OA, MS 755, Reel 192). Reporting on Boston doctor's efforts to detect carriers: Nelson Skuce, "Top Authority Here: Race to Crack 'CF' Mystery," *Ottawa Journal*, October 23, 1961 (OA, MS 755, Reel 192).
[38] Joan Hollobon, "Burden of Humans: Cancer Called Evolution Penalty," *Globe and Mail*, June 12, 1962 (OA, MS 755, Reel 205). See also an article on hemophilia which noted that "Medical research has found means of treating haemophilia victims so they live long enough to have children thereby tending to spread the disease through inheritance.": "Rare Disease, Haemophilia, Said Spreading," *Hamilton Spectator*, June 20, 1962 (OA, MS 755, Reel 205)
[39] "Inherited Diseases Hitting More People," *Toronto Telegram*, October 20, 1962 (OA, MS 755, Reel 205)
[40] HB Newcombe, Chairman, "Biological Effects of Radiation: Report of a Committee of the Genetics Society of Canada on the Needs for Research in Radiation Biology," *Canadian Journal of Genetics and Cytology*, 3 (1961), 61.
[41] N Ford Walker and JM Naylor, "Human Genetics," *Canadian Journal of Genetics and Cytology*, 3 (1961), 78.
[42] *Ibid.*, 79. Wilson in her MA cites Newcombe, 1960 as supporting the statement that "Of all births, 2.5 to 4 per cent are seriously affected by hereditary disease." Diane Wilson, "An Investigation of Possible Genetic and Somatic Damage," 26. (UT. T79 0107, File 54). Howard Newcombe, a population geneticist working for the Atomic Energy Commission of Canada, advocated for and worked to develop registries, notably one in BC, that enabled better estimates to be developed. See: "Data on Births Deaths Valuable in Diseases," *Globe and Mail*, June 6, 1962 (OA, MS 755, Reel 205); "Child Deformity Deaths Rising," [newspaper unknown], June 2, 1965 (OA, MS 755, Reel 311).
[43] "MDs Ignorant of genetics, Toronto Scientist claims," *Toronto Globe and Mail*, August 11, 1965, (OA, Reel 250).
[44] Joan Hollobon, " Cites Vital Role of Genetics in Public Health," *Globe and Mail* March 23, 1967, (OA, Reel 298).
[45] See for example: Ives, "Genetics and Genetic Counselling," 518. See also Miller, "Human Genetics in Public Health Research and Programming"; Margaret Thompson, "Genetic Counseling in Clinical Pediatrics," *Clinical Pediatrics*, 6:4 (April 1967). Genetic medicine was not invariably associated with these narratives about the "paradox" of modern medicine. See, for example: Kingsley Brown, "Future Misfits Denied," *Hamilton Spectator* (June 6, 1956), OA, Reel 145; Editorial, "A Paradox of Progress,"

Peterborough Examiner (September 13, 1958), OA, Reel 155; NJ Berrill, "Abnormal Babies Should Not be Encouraged to Live," *Saturday Night* (December 6, 1958).

[46] Sidney Katz, "This medical detective gives odds on your chances of a normal child," *Toronto Daily Star* Nov 24, 1967, (OA, Reel 299). This 80% may be 60% the microfilm copy is hard to read. FC Fraser put the issue more frankly: "Whenever a baby is born deformed or develops a disease not obviously environmental in origin, the physician is likely to be asked what caused the trouble." In seeking to answer this question the issue of further births would emerge. "This," Fraser suggested, "is where genetic counselling starts." FC Fraser, "Genetic Counselling and the Physician," *Canadian Medical Association Journal*, 99:19 (Nov 16, 1968), 927

[47] She complained that "a large section of the country can't even get advice on heredity. There are only two doctors [in Toronto and Montreal] who specialize in the field, and counsel the public on a regular basis."

[48] McCubbin, "Are we Breeding a Nation of Invalids?" 94.

[49] Sidney Katz, "She knows the kind of Children you'll have," *Maclean's Magazine* (December 1, 1954), 85.

[50] *Ibid.*, 32.

[51] Daniel Kevles, *In the Name of Eugenics: Genetics and the Uses of Human Heredity*, revised edition, (Cambridge, Mass., London: Harvard University Press, 1985, 1995, 1997), 253. The rise of an individualistic eugenics fits Hamilton Cravens' interpretation of the shift from a group to an individualist ethos in the 1950s. See: Hamilton Cravens, "The Case of the Manufactured Morons: Science and Social Policy in Two Eras, 1934-1966," in H Cravens et al, eds. *Technical Knowledge in American Culture: Science, Technology and Medicine Since the Early 1800s*, (Tuscaloosa and London: The University of Alabama Press, 1996).

[52] Not all reproductive management was advocated by geneticists or for genetic reasons: See the article reporting advocacy by a physician of abortion in cases of Rubella infection during pregnancy: to avert "the family catastrophe" of abnormal children. "Doctor Favors Abortion in Some Cases," *Toronto Telegram*, May 12, 1956 (OA, MS 755, Reel 145) The current of fear facilitated enthusiasm for more than just medical genetics and heredity counseling. Both compulsory and voluntarist means for restricting the reproduction of the "unfit" were recommended. While many commentaries on abortion, especially in the early 1950s, did not mention defect as grounds for the procedure, by the latter half of the 1950s commentaries increasingly did recommend abortion on grounds of defect, often mentioning genetic defect explicitly: Joan Finnigan, "Should Canada Change its Abortion Law?" *Chatelaine*, August 1959. Dr Elizabeth Bagshaw, physician at the Hamilton birth control clinic from its inception in the 1930s was cited as arguing that "We know the country needs lots of people. But we need the right kind of people: "Only Family Planning Clinic Starts Evening Sessions Here Next Month," *Hamilton Spectator* September 28, 1959, (OA, Reel 163).

[53] In the summer of 1944, Ford Walker reported on the case of a large kindred which included two siblings with phenylketonuria resident at the Ontario Hospital in Orillia. She attempted to provide information about the status of three first cousins of these two affected children by looking in detail at the family history. This was a plea for the production and retention of good medical records by Canadian hospitals. Moreover, this project demonstrates some of the non-familial functions of heredity counseling: the review was not undertaken for the children or their parents, but likely for the Children's Agency that was caring for these wards of the state, in the interests of assessing their suitability for adoption. Norma Ford, "The Value of Clinical Records in Medical Research," *The Canadian Hospital*, 21 (1944), 33. Genetic knowledge seems to have been used to this end quite frequently. Two of the cases that Valentine followed-up from the Sergovitch study of newborns were adopted and Valentine was clear that the genetic status of these "chosen" children should be made available to their prospective adoptive parents.

[54] "Heredity counselors belong to the most exclusive professional group in North America," Katz noted. "There are only ten of them."" Katz, "She knows the kind of Children you'll have," 32.

[55] Lee R. Dice, "Heredity Clinics: Their Value for Public Service and for Research," presidential address to the American Society of Human Genetics, September 11, 1951, *American Journal of Human Genetics*, 4: (March 1952), 9, 10. The clinic in Toronto was one of only 8 facilities in North America that Dice discussed, and one of 2 in Canada. Dice also made mention of a "recently organized" Department of

Medical Genetics in the Children's Memorial Hospital of Montreal which was under the direction of F Clarke Fraser.

[56] "Statement by Norma Ford Walker," in Lee R Dice, "A Panel Discussion: Genetic Counseling," *American Journal of Human Genetics*, 4 (1952), 336.

[57] Kevles argues that this Clinic, which opened in 1940, was probably the first in America. In making this argument, Kevles contradicts Dice who ceded this honor to the Eugenics Record Office. Dice, "Heredity Clinics: Their Value for Public Service and for Research," 9.

[58] Dice, "Heredity Clinics: Their Value for Public Service and for Research," 2.

[59] Ford Walker was not above hereditarian polemics. In a 1929 talk, for example, she presented "As an outstanding example of heredity ... the famous chart of two American families, the Max Jukes who never did one outstanding deed for the welfare of the nation and who through jails and asylums cost the state $1,250,000 and the Jonathon Edwards family who were all professors, lawyers and of whom no-one was every known to have been convicted of crime. Of this family Sir Vincent Massey is a descendant." "Heredity Topic initial Victoria Health Lecture: Dr Norma Ford compares topic to fortune telling as matter of chance," *Varsity*, December 10, 1929 (UT, A73 0026, 105, 61). Yet though asserting the "pronounced inheritance factor" in such phenomena as taste reactions, Ford Walker did not permit heredity to dictate social relations. While heredity might explain why "junior doesn't like spinach," it would not relieve "junior" of his obligations. "Children shouldn't be allowed to become picky or finicky," Ford Walker argued. "We've all got to live together. They can learn to adjust themselves quite easily," she added. "Junior OK Though He Dislikes Spinach: Merely Matter of Heredity Dr Norma Walker [sic] says; PTC is Guide; Don't Allow Children to become "Picky" of "Finicky," she warns," *Star*, May 21, 1936. (UT, A73 0026, 105, 61).

[60] In none of the clippings which record Ford Walker's many public talks on nature and occasionally heredity is the word "eugenics" ever present. See especially: "Zonta Hears Dr N Ford Talk About Human facts: Explains some reasons for eye colors; left handedness; Subject Heredity; Gryllo Blatta Discoverer has many Attainments, Much Charm," *Mail*, Jan 9, 1936; "Junior OK Though He Dislikes Spinach: Merely Matter of Heredity Dr Norma Walker [sic] says; PTC is Guide; Don't Allow Children to become "Picky" of "Finicky," she warns," *Star*, May 21, 1936 (UT, A73 0026, 105, 61).

[61] Norma Ford did publish in the *Journal of Heredity* which was run by the American Breeders Association, an organization with a strong eugenic history, but this was as close as she came to a eugenics journal, of which there were many. In this seeming aversion to such journals, Ford Walker was unlike her closest competitor for the designation of "pioneer" of medical genetics in Canada. In Montreal, the prolific F Clarke Fraser, began the work of building a major medical genetics center in 1945. One of his major areas of interest was genetic counseling and he published not infrequently in eugenics journals on this and other topics.

[62] Zoe Bieler, "Woman Geneticist Declares: More Mixed Marriage Pacts Held Big Factor for World Peace," *Montreal Star* (August 23, 1958). (OA, Reel 155). She was not, however, a wholehearted enthusiast of "artificial insemination" in cases of "childless marriage." Yet her concern was not with "illegitimacy" but with the thoroughly modern problem of management – the number of children born per donor and the difficulty of tracing family pedigrees in the face of donor anonymity. By contrast see: Charles Neville, "Is it Adultery?" *Maclean's Magazine* (February 15, 1949), 9, 42-44

[63] Indeed, Ford Walker encouraged "interbreeding": "New combinations produce better stock," she stated. Katz, " She Knows the Kind of Children," 79. At the International Congress of Genetics in Montreal in 1958, Ford Walker joined with other delegates in approving of racially mixed marriages: "If we are ever going to have peace and happiness on earth we must have more mixed racial marriages," she said.: Zoe Bieler, "Woman Geneticist Declares: More Mixed Marriage Pacts Held Big Factor for World Peace," *Montreal Star* August 23, 1958. Delegates to the Congress appear to have debated the issue in their concluding session: "Racial Intermarriage: No Incompatibility Geneticist Claims," *Montreal Star*, August 27, 1958, (OA, Reel 155). Together with Oliver Smithies, Ford Walker argued in 1959 against the segregation by race of blood in blood banks – in effect, arguing against the racist use to which a technology she had helped develop could be put. Ford Walker was cited as an "advocate of mixed racial marriages" who said it would be ridiculous to think that mixing could cause color changes in future offspring. Smithies

was cited as arguing that the "slight medical benefit" of such discrimination couldn't outweigh the "sociological harm" of such a protocol. At a meeting in Chicago, a doctor argued that racial transfusions would be better if made on the same race. Though the policy of both the Canadian and US Red Cross was not to segregate there was apparently a state law in Louisiana prohibiting inter-racial transfusions except in an emergency. This commentary was widely cited in Canadian papers, see: "MDs Here Hit Racial Transfusion Idea," *Toronto Telegram*, (Nov 12, 1959); "Advises Blood Donor of Same Racial Stock," *Globe and Mail* (November 12, 1959); "Doctors Split on Racial Blood," *Toronto Star* (Nov 12, 1959), (OA, Reel, 164). On racial debates over blood banking see Keith Wailoo, *Drawing Blood: Technology and Disease Identity in Twentieth Century Medicine* (Baltimore: Johns Hopkins University Press, 1997), 149-150.

[64] Diane Paul, *Controlling Human Heredity: 1865 to the Present*, (New Jersey: Humanities Press, 1995).

[65] Katz, "She knows the kind of children you'll have," 32, 79, 84-5.

[66] Some individuals continued to press for more coercive restraints. See: "Hopeless to Get Feeble-Minded into Orillia Hospital, Doctor States," *Globe and Mail*, May 6, 1949 (OA, MS 755, Reel 117); "Bar Children to Defectives," *Toronto Telegram*," May 31, 1949 (OA, MS 755, Reel 117); Ron Kenyon, "Sterilize Ontario Unfit? Alberta and 27 States Find Practice Pays," *Toronto Telegram*, May 5, 1950 (OA, MS 755, Reel 121); "Obstetrician's View: World May Need Birth Control," *Toronto Star*, March 17, 1960 (OA, MS 755, Reel 177); "Women's Institute asks for Sterilization of Low Mentality Women," *St Catherine's Standard*, May 26, 1961 (OA, MS 755, Reel 192); "MD Urges: Baby Bonus to Health Parents," *Toronto Telegram*, Nov 17, 1961 (OA, MS 755, Reel 192); "These Men Should be Sterilized," *Toronto Telegram*, January 9, 1965 (OA, MS 755, Reel 311); Editorial, "Sterilization for Defectives?" *Toronto Star*, October 4, 1965 (OA, MS 755, Reel 311; "Dennison Sees Need for Selective Breeding," *Globe and Mail*, February 24, 1967 (OA, MS 755, Reel 298); Birth Control Pills for Diabetics?" *Hamilton Spectator*, March 16, 1967 (OA, MS 755, Reel 298). Robert McClure, who was then Moderator of the United Church of Canada, caused a flurry of mostly negative publicity when he suggested compulsory sterilization. See: "McClure's Sterilization Said 'Extraordinary, Nonsense,'" *Toronto Daily Star*, April 29, 1969; Editorial, "To Set the Battle Rolling," *Globe and Mail*, April 30, 1969 (OA, MS 755, Reel 361)

[67] Katz, "She knows the kind of children you'll have," 32, 79, 84-5.

[68] *Ibid.*, 84.

[69] *Ibid.*

[70] Molly Ladd Taylor, "Eugenics and the Baby Boom," paper presented at, Women, Science and Health in Post-War North America: Comparative Canadian-American Perspectives, March 5, 1999, York University.

[71] Knowledge of genetics promised to be of value for individuals and for the public's health: "Today [1965] geneticists can't answer the question, "Will my baby be normal?" Geneticists will never hold all the answers. It will never be possible to predict, or avoid, all births of defective children. But genetic knowledge, wisely applied, can prevent much of the present burden of hereditary disease. Dr Margaret Thompson as told to Shirley Mair, "Should you have a baby?" *Chatelaine* (February 1965), 60.

[72] Paul notes that these clinics were of limited efficacy and points to their limited client populations to support such an argument. While this seems a valid analysis in retrospect, and by comparison with their later growth, it diminishes the value that was seen to exist in such work as the time. See: Diane Paul, *Controlling Human Heredity*, 128; Diane Paul, "Eugenic Origins of Medical Genetics," in Diane Paul, *The Politics of Heredity: Essays on Eugenics, Biomedicine and the Nature-Nurture Debate*, (Albany, NY: State University of New York Press, 1998), 143.

[73] The first heredity counseling clients introduced in Katz's article arrived in Ford Walker's office "numbed by the news that their first child was born an idiot." "If this is what God thinks of our marriage," the wife was reported to have said, "we should get a divorce." Ford Walker's investigation demonstrated that the parents were "equally responsible for the child..." Some years later, after adopting a child, the wife told Ford Walker that she had "cleared the air for us. Our marriage is getting along fine." Katz, "She knows the kind of Children you'll have," 79, 32.

[74] Diane Paul, *Controlling Human Heredity*, 127; Diane Paul, "Eugenic Origins of Medical Genetics," 145-6.

[75] "Families found unwilling to admit genetic defects," *Globe and Mail*, April 8, 1965 (OA, MS 755, Reel 311).
[76] Leone Kirkwood, "If an abnormal fetus not aborted, lab technicians upset, MD says," *Globe and Mail*, Nov 16, 1973 (OA, MS 755, Reel 534). The "MD" cited here was actually Margaret Thompson.
[77] Ladd Taylor, "Eugenics and the Baby Boom."
[78] Ladd Taylor suggests that Sheldon Reed often told stories of genetic counseling where his role involved sheltering the women from blame. Ladd Taylor, "Eugenics and the Baby Boom."
[79] Yet though contesting older simplisms, much of the information provided about Mendelism was of an amateurish variety. In describing the phenomenon of dominance, Katz wrote that "the prominent nose gene dominates the rather moderately shaped nose." Katz, "She knows the kind of children," 79.
[80] Charles Rosenberg notes that this thesis was not supported by "cautious physicians" even in the first half of the 19th century: "Heredity, Disease and Social Thought," *No Other Gods*, 27.
[81] "Statement by Norma Ford Walker," in Lee R Dice, "A Panel Discussion: Genetic Counseling," *American Journal of Human Genetics*, 4 (1952), 337.
[82] Katz, "She knows the kind of Children," 32.
[83] Norma Ford Walker, "Mongolism and the Recent Break-Through," Second Conference on Mental Retardation, Canadian Association of Retarded Children, 1959 (Roeher).
[84] The thesis of maternal impressions was described as part of the "black magic school of genetic study." Katz, "She knows the kind of Children," 79.
[85] McCubbin, "Are we Breeding a Nation of Invalids?" 94.
[86] Katz, "She knows the kind of Children," 83. For more of Ford Walker's comments about non-directiveness see also: Zoe Bieler, "Woman Geneticist Declares: More Mixed Marriage Pacts Held Big Factor for World Peace," *Montreal Star* (August 23, 1958). (OA, Reel 155).
[87] Sidney Katz, "This medical detective gives odds on your chances of a normal child," *Toronto Daily Star*, Nov 24, 1967 (OA, MS 755, Reel 299)
[88] On Margaret Thompson's work as a heredity counselor in Alberta see: Margaret W Thompson, "A New Heredity Counseling Service in Western Canada," *Eugenics Quarterly*, 6:3 (September 1959), 167-170; Joan Hollobon," Cites Vital Role of Genetics in Public Health," *Globe and Mail*, March 23, 1967, (OA, Reel 298); Dr Margaret Thompson as told to Shirley Mair, "Should you have a baby?" *Chatelaine* (February 1965); Sidney Katz, "This medical detective gives odds on your chances of a normal child," *Toronto Daily Star* Nov 24, 1967, (OA, Reel 299); Dr Margaret Thompson, "Who will your baby look like?" *Chatelaine* May 1969; James Thompson and Margaret Thompson, *Genetics in Medicine* (Philadelphia and London: WB Saunders Company, 1966). Interviewed for the hospital newsletter while serving as Acting Director of the Department of Genetics, she described her work in genetic counseling as "forecasting the probability of parents transmitting hereditary diseases to their children.": "Meet the Staff: Dr Margaret Thompson, Acting Director, Department of Genetics," *Paediatric Patter* [newsletter of the HSC], April 1968 (HSC).
[89] Joan Hollobon, " Cites Vital Role of Genetics in Public Health," *Globe and Mail* March 23, 1967, (OA, Reel 298).
[90] That this absence of self-regulation was common is attested to also by Hubert Soltan's Ph.D. dissertation on DMD. He noted that the average family size in DMD families, "must lead to the conclusion that eugenic considerations have not entered into the planning of these families – families which are acutely aware of the nature and prognosis of Duchenne muscular dystrophy." Hubert Soltan, "Some Genetical Aspects of the Duchenne Form of Muscular Dystrophy," University of Toronto, Ph.D. thesis, 1959, 125, 145. A "London Letter" in the *Canadian Medical Association Journal* which reported on a study of the effectiveness of the UK's first genetic counseling clinic noted that "It is astonishing that so many of the high-risk couples were undeterred from further procreation, and so many of the low-risk were deterred.": "Effectiveness of Genetic Counselling Clinics," *Canadian Medical Association Journal*, 104 (May 22, 1971), 882.
[91] "MDs Ignorant of genetics, Toronto Scientist claims," *Toronto Globe and Mail*, August 11, 1965, (OA, Reel 250). Thompson repeated this discussion of resistance in a more academic publication. She wrote that "Many parents refuse carrier detection tests because, "I'd just as soon not know." One mother of our acquaintance does not want her daughter tested to learn whether she is a carrier of Duchenne muscular

dystrophy because "if news got around, it could blight her chances of marriage."": Margaret Thompson, "Genetic Counseling in Clinical Pediatrics: What to do with Inquiries about Heritable Disorders," *Clinical Pediatrics*, 6:4 (April 1967), 207

[92] Katz, "She knows the kind of Children you'll have," 82.

[93] "Statement by Norma Ford Walker," 337.

[94] Thompson as told to Mair, "Should you have a baby?" 60.

[95] Katz, "She knows the kind of Children you'll have," 32, 79.

[96] Zoe Bieler, "Woman Geneticist Declares: More Mixed Marriage Pacts Held Big Factor for World Peace," *Montreal Star* (August 23, 1958). (OA, Reel 155)

[97] *Ibid.*

[98] Katz, "She knows the kind of Children you'll have," 32.

[99] "Statement by Norma Ford Walker," 336.

[100] Charles Davenport shared the faith that women, because of "female tactfulness" were appropriate for assessing heredity and the Eugenics Record Office's field workers were mostly women. See: Amy Sue Bix, "Experiences and Voices of Eugenics Field-Workers: 'Women's Work' in Biology," *Social Studies of Science*, 27 (1997), 636, 649; Diane Paul, *Controlling Human Heredity*, 54-57. In North America today, there is a feminized profession of 'genetic counselor' (about 93% women in Canada and the US are women). Predictably, it is also a devalued, "service" profession, with Master's level training and little involvement in "medical research." Ford Walker was not prescient, however: the medical science profession she was describing and the "allied health profession" that exists today are profoundly different, and there are still old-order medical geneticists with Ph.D.s and many with MDs who also conduct genetic counseling. Dorothy Wertz, "Is there a "Women's Ethic" in Genetics: A 37-Nation Survey of Providers," *Journal of the American Medical Women's Association*, 52:1 (Winter 1997), 34.

[101] Bieler, "Woman Geneticist Declares.". A 1958 article which noted that "Many parents and potential parents come to the Hospital for Sick Children in Toronto seeking advice on whether it would be wise to have children considering their genetic background," also remarked that "Dr Walker is particularly interested in doing research on twins and mongolian imbecile children. She believes that genetic factors are involved in the incidence of Mongolian children more than is commonly supposed."

[102] Norma F. Walker, "Determination of the Zygosity of Twins," *Acta Genetica Statistica Medica*, 7 (1957), 33-38. Norma Ford Walker, "The use of dermal configurations in the diagnosis of Mongolism," *Journal of Pediatrics*, 50 (Jan-June, 1957), 19-26; Norma Ford Walker, "The use of dermal configurations in the diagnosis of Mongolism," *Pediatric Clinics of North America*, (May 1958), 531-543.

[103] Richard D Rowe and Irene Uchida, "Cardiac Malformation in Mongolism: A Prospective Study of 184 Mongoloid Children," Final Report to the National Health Grants Program, April 17, 1961 (OA, RG 10-22, NHGP, Box 18, File 199)

[104] *Sixth Annual Report of the Research Institute*, Jan 1 to December 31, 1959, 44 (HSC).

[105] AB LeMesurier and NF Walker, "Incidence and Etiology of Harelip and Cleft Palate," Application for a Public Health Research Grant, NHGP, May 31, 1950 (OA, RG 10-22, Box 1, File 9).

[106] *Sixth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1959, 43 (HSC).

[107] Dice, "Heredity Clinics: Their Value for Public Service and for Research," 10.

[108] NF Walker, "The Use of Dermal Configurations in the Diagnosis of Mongolism," *Journal of Pediatrics*, 50 (Jan-June 1957), 26. This comment was repeated in a very similar article published in 1958: NF Walker, "The Use of Dermal Configurations in the Diagnosis of Mongolism," *Pediatric Clinics of North America*, (May 1958), 541-2.

[109] The enthusiasm attached to biochemistry is especially apparent in one article in the hospital newsletter in 1961: "The Department of Genetics is well known for its continued investigation of twins and for the diagnosis and study of mongoloid retarded children, as well as for a number of special researches, including cleft lip and palate, congenital dislocation of the hip, and more recent chromosomal studies. Branching out into association with biochemical and metabolic studies, genetics demonstrates that it is a vigorously growing science in which important developments are taking place." "Meet the Staff: Norma Ford Walker, and Department of Genetics," *Paediatric Patter*, January 1961 (HSC).

[110] Soltan, "Some Genetical Aspects of the Duchenne Form of Muscular Dystrophy," Ph.D. thesis, 2.

[111] Editorial, "Genetic disease," *Canadian Medical Association Journal*, 98 (Feb 24, 1968), 414-416.
[112] Soltan, "Some Genetical Aspects of the Duchenne Form of Muscular Dystrophy," Ph.D. thesis, 13-14.
[113] *Ibid.*, 1-2.
[114] Harry Bain, Drummond Bowden, Lawrence Chute, Sanford Jackson, Andrew Sass-Kortsak and Norma Ford Walker, "Galactosaemia: Commoner than we think?" *Canadian Medical Association Journal*, 76 (Feb 15, 1957), 278; Andrew Sass-Kortsak, "Galactosaemia," Editorial, *Canadian Medical Association Journal*, 74 (May 1, 1956), 738.
[115] *Fifth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1958, 17 (HSC).
[116] Therapeutic efforts are reported in the annual report and in publications: *Fifth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1958, 23 (HSC); D Fraser and RB Salter, "Diagnosis and Management of Various Types of Rickets," *Pediatric Clinics of North America*, (May 1958), 417-441.
[117] In making this argument, Fraser echoed prevalent beliefs. The Research Institute argued that Pediatric research was justified for its attention to new problems. Of decreased urgency were problems of survival in childhood due to infections and birth injury. Growing in significance were problems arising in "the intranatal and immediate post-natal periods – and with congenital anomalies." Donald Fraser, Clinical Manifestations of Genetic Aberrations of Calcium and Phosphorus Metabolism," *Journal of the American Medical Association*, 176:4 (April 29, 1961) presented in 1959, 113.
[118] Diane Paul, in *The Politics of Heredity*.
[119] David Spurgeon, "Help for Retarded: Baby Girl Responding to Treatment for Unusual Mental Deficiency," *Globe and Mail*, November 28, 1958 (OA, MS 755, Reel 155).
[120] Partington recalled that his work with the PKU clinic located him next door to Norma Ford Walker. He wrote later that her "infectious enthusiasm for medical genetics nearly had ... [him] taking yet another two years of fellowship training, this time in genetics." Margaret Thompson, Nancy Simpson and Michael Partington, "Norma Ford Walker," in HC Soltan, ed., *Medical Genetics in Canada: Evolution of a Hybrid Discipline, Essays on the Early History*, (University of Western Ontario, Regional Medical Genetics Centre, 1992), 31-2.
[121] Michael Partington and Nancy Simpson, "Kingston (Queen's University) and Eastern Ontario: regional development," in Soltan ed., *Medical Genetics in Canada*, 51-2.
[122] *Sixth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1959, 34 (HSC). While at Sick Kids, Partington used funds for a research grant from the National Health Grants Program to undertake various investigations of phenylketonurics and "resulted in the establishment of a clinic for the diagnosis and treatment of phenylketonuria." Final Report, Phenylketonuria, Brain Damage in Children, received Nov 12, 1964 (OA, RG 10-22, Box 90, File: 1490). The medical profession was not alone in doing such work. Since 1958, the Canadian Association for the Mentally Retarded, and the affiliated Ontario branch, had been publicizing the disease.
[123] M Partington, "Brain Damage in Children," Progress report to the NHGP, received Oct 13, 1960 (OA, RG 10-22, NHGP, Box 90, File 1489). "Phenylalanine load tests have been performed on some 26 parents and 50 other relatives of phenylketonuric patients in an attempt to detect the heterozygote."
[124] MW Partington, "Observations of Phenylketonuria in Ontario," *Canadian Medical Association Journal*, 84:18 (May 6, 1961), 991. The interest in the potential of carrier detection was clearly quite strong in initial efforts to deal with PKU through dietary management and before it became conceivable to co-ordinate clinical and state efforts in such a massive way. See, for example: Wallace Grant, "Impressions from the Ninth International Conference of Paediatrics and the First International Medical Conference on Mental Retardation – July 1959," 2nd Conference on Mental Retardation, CARC, 1959 (Roeher).
[125] Partington's research on PKU was funded by the National Health Grants program (maternal and child health grant), (OA, RG 10-22, NHGP, Box 90, Files 1489-1490). Michael Partington, "The early symptoms of phenylketonuria," *Pediatrics*, 27 (March 1961), 465-73; MW Partington, "Observations of Phenylketonuria in Ontario," *Canadian Medical Association Journal*, 84:18 (May 6, 1961), 985-991.
[126] WB Fraser, "A Case Finding Campaign on Phenylketonuria," *Canadian Medical Association Journal*, 83 (Nov 19, 1960), 1119.
[127] *Ibid.*, 1118-9.
[128] *Ibid.*, 1118.

[129] PKU Advisory Committee to the Maternal and Child Health Service, Ontario Department of Health," "The Newborn Phenylketonuria Screening Program in Ontario," *CMAJ*, 101:4 (August 23, 1969), 185-90.
[130] *Ibid.*, 189.
[131] Andrew Sass-Kortsak, Plans for Further Development and Expansion of Research Activities in the Department of Paediatrics, December 1967, attached to Minutes of the Committee on Research, December 13, 1967 (HSC, CRM, Vol. 1967-1973). Soltan made a similar argument in his introduction that attention was shifting from infectious to hereditary diseases as the "ravages of the majority of these [infectious] diseases are finally controlled." "[C]hanging concepts in medicine," he argued, "are bound to result in a new emphasis: the emphasis on genetics as applied to human ailments." Soltan, "Some Genetical Aspects of the Duchenne Form of Muscular Dystrophy," Ph.D. thesis, 1-2.
[132] Sass-Kortsak, Plans for Further Development and Expansion.
[133] Pat McNenly, "Toronto Dramatic Research Progress: New Hope for Mentally Retarded," *Toronto Daily Star*, May 13, 1960 (OA, MS 755, Reel 177). For the Canadian Association for Retarded Children, which started up in the late 1950s with great hopes of biomedical research, it confirmed that "biochemistry offered the greatest promise of preventive measures.": "Look to Biochemistry: Study of Retardation is on a National Scale," *Globe and Mail*, January 15, 1960 (OA, MS 755, Reel 177); "Two Halifax Doctors working on cure for mental retardation," *Halifax Chronicle*, May 26, 1961 (OA, MS 755, Reel 192). "Retardation Research Breaking New Ground," *Globe and Mail*, March 29, 1962 (OA, MS 755, Reel 205); Ken MacTaggart, "Shiny-eyed David Saved from Mental Darkness," *Toronto Telegram*, December 24, 1960 (OA, MS 755, Reel 177)' Bruce Levett, "Mentally retarded child born every 25 minutes in Canada," *Windsor Star*, August 6, 1961 (OA, MS 755, Reel 192); Marilyn Anderson, "PKU can ruin lives...Simple test can detect tragic disease," *Niagara Falls Review*, May 31, 1965 (OA, MS 755, Reel 251).
[134] "Geneticists Tells Role of Gene in Retardation: Theory is Bottom of Radiation Study," *Hamilton Spectator*, February 22, 1961 (OA, MS 755, Reel 192). See also: "Hope to Treat Incurable Mongolism as Result of Newest Research Work," *London Free Press*, February 23, 1961 (OA, MS 755, Reel 192) – this article features the work of the Barr school.
[135] *Fifth Annual Report of the Research Institute*, Jan 1 to Dec 31, 1958, 7 (HSC).
[136] PKU Advisory Committee to the Maternal and Child Health Service, 185. For information on state programs in Canada as of the mid-1970s see: JC Haworth, JR Miller and CR Scriver, "Screening, counselling and treatment of hereditary metabolic disease; a survey of resources in Canada," *Canadian Medical Association Journal*, 111 (Nov 16, 1974), 1147-1153.
[137] Miller presented this paper at the annual meeting of the Canadian Public Health Association in 1965 and it was reprinted from the Proceedings of a Symposium on Human Genetics and Public Health held in Minneapolis, Minnesota in 1964.
[138] James Miller, "Human Genetics in Public Health Research and Programming," *Canadian Journal of Public Health*, 57 (January 1966), 1.
[139] *Ibid.*, 3. Margaret Thompson, " Genetic Counseling in Clinical Pediatrics: What to do with Inquiries about Heritable Disorders," *Clinical Pediatrics*, 6:4 (April 1967)
[140] FC Fraser, "Genetic Counselling and the Physician," *Canadian Medical Association Journal*, 99 (Nov 16, 1968), 932
[141] Hubert Soltan, "Genetic Counselling in Ontario," *Ontario Medical Review* (June 1972), 337.
[142] *Ibid.*, 338; Fraser, "Genetic Counselling and the Physician," 928; Thompson, "Genetic Counseling in Clinical Pediatrics," 203.
[143] Miller, "Human Genetics in Public Health Research and Programming," 2,3,4. Miller cited the much-publicized figures of CO Carter from the Great Ormond Street Hospital for Sick Children: "In 1914, two thirds of all deaths were attributable to environmental factors such as tuberculosis, pneumonia and infections of various sorts, and only 16% were attributable to causes which might be termed genetic or partly genetic. In 1954, only about 15% were classified as environmental, while over one-third were in the wholly or partly genetic class..." Elizabeth Ives also cited this data and emphasized "the increasing importance of genetic factors in disease." Elizabeth Ives, "Genetics and Genetic Counselling," *Canadian Journal of Public Health*, 57 (Nov 1966), 514.
[144] Miller, "Human Genetics in Public Health Research and Programming," 2.

[145] See also: Nancy Simpson, "Experiences of a Genetic Counselling Clinic in Kingston, Ontario," *Canadian Journal of Public Health*, 66 (Sept/Oct 1975).
[146] On this committee see: Lili De Grandpre, "Project aids genetic disease patients," *Canadian Medical Association Journal*, 108 (May 19, 1973), 1320-1; Committee for Improvement of Hereditary Disease Management, "Management of Maple syrup urine disease in Canada," *Canadian Medical Association Journal*, 115 (Nov 20, 1976), 1005-13; JC Haworth et al, "Screening, counselling and treatment of hereditary metabolic disease; a survey of resources in Canada," *Canadian Medical Association Journal*, 111 (Nov 16, 1974), 1147-53.
[147] Charles Scriver et al, "The Frequency of Genetic Disease and Congenital Malformation among Patients in a Pediatric Hospital," *Canadian Medical Association Journal*, 108 (May 5, 1973), 1111.
[148] *Ibid.*, 1114.
[149] Thompson, " Genetic Counseling in Clinical Pediatrics," 206. Fraser also discussed "New techniques ... for detecting recessive genes in the heterozygote." FC Fraser, "Genetic Counselling and the Physician," *Canadian Medical Association Journal*, 99 (Nov 16, 1968), 928.
[150] Hubert Soltan, "Genetic Counselling in Ontario," *Ontario Medical Review* (June 1972), 338.
[151] Fraser, "Genetic Counselling and the Physician," 928
[152] Soltan, "Genetic Counselling in Ontario," 339.
[153] For the London group see: HH Allen et al, "Infants undergoing antenatal genetic diagnosis: a preliminary report," *American Journal of Obstetrics and Gynecology*, 118 (Feb 1974), 310-3. For the Toronto group see: TA Doran et al, "The antenatal diagnosis of genetic disease," *American Journal of Obstetrics and Gynecology*, 118 (Feb 1974), 314-21
[154] Allen et al, "Infants undergoing antenatal genetic diagnosis: a preliminary report," 312
[155] 49 of 73 cases reported by the Toronto group were performed for late maternal age or previous down's syndrome child. Doran et al, "The antenatal diagnosis of genetic disease," 316. See also: Maggie Siggins, "Mongolism test in unborn babies," *Toronto Telegram*, February 25, 1969 (OA, MS 755, Reel 361).
[156] On Tay Sachs see: "Chemical Link in Mental Illness," *What's New*, HSC Newsletter, 2:8 August 1970 (HSC); "Killer disease may be prevented," *What's New*, HSC Newsletter, 5:1 (Jan 1972); JA Lowden et al, "Screening for carriers of Tay-Sachs disease: a community project," *Canadian Medical Association Journal*, 111 (August 1974), 229-33; JA Lowden, et al, "Antenatal Diagnosis of sphingolipid and mucopolysaccharide storage diseases," *Canadian Medical Association Journal*, 113 (Sept 20, 1975), 507-511; JA Lowden, "Role of the physician in screening for carriers of Tay-Sachs disease," *Canadian Medical Association Journal*, 119, (Sept 23, 1978), 575-8. On CF see: "HSC Launches war on Cystic Fibrosis," *What's New*: HSC Newsletter, 6:8 (October 1973); G Forstner, et al, "Cystic Fibrosis: present status and future prospects in detection of patients and carriers," *Canadian Medical Association Journal*, 113 (Sept 20, 1975), 550-6. On DMD see: Elaine Hutton and Margaret Thompson, "Carrier detection and genetic counselling in Duchenne muscular dystrophy: A follow-up study," *Canadian Medical Association Journal*, 115 (Oct 23, 1976), 749-42.
[157] Doran et al, "The antenatal diagnosis of genetic disease," 319. See also: Robbie Salter, "Amniocentesis: whereby a family of specialists detects some genetic diseases before birth," *University of Toronto Bulletin*, April 23, 1976, 4-5.
[158] One could quibble with this statement, but it is accurate in spirit if not in the final accounting. Of those fully or partially involved in organizational machinations, I count Nancy Simpson, James Miller, Margaret Thompson, Diane Wilson Cox, Hubert Soltan and Louis Siminovitch on the Toronto side. On the non-Toronto side I count Louis Dallaire, Charles Scriver, Clarke Fraser (James Miller, who took his Ph.D. in Montreal, can also be categorized here), all of Montreal, and John Hamerton of Manitoba. There were also some obligatory non-human geneticists technically involved with the GSC committee but who do not seem to have been particularly active: Hans Stich and G Subden.
[159] He made this comment with after a discussion of Pat Conen's research. Pat McNenly, "Toronto Dramatic Research progress: New Hope for Mentally Retarded," *Toronto Daily Star*, May 13, 1960 (OA, MS 755, Reel 177).

[160] "MDs May Soon Solve Inherited Disease," *Toronto Star*, November 23, 1962; see also: "British Biophysicist Foresees Human Gene Control," *Globe and Mail*, November 23, 1962 (OA, MS 755, Reel 205)

[161] "Test Tube Baby Splits Canada MDs," *Toronto Telegram*, January 23, 1961; "Some Doctors OK Test Tube Baby Research," *Toronto Daily Star*, January 23, 1961 (OA, MS 755, Reel 191).

[162] "Seek Prenatal Clues," *Toronto Star*, January 26, 1959 (OA, MS 755, Reel 163)

[163] "UWO Medical Research Awarded Associateship," *London Free Press*, March 11, 1967 (OA, MS 755, Reel 298)

[164] Maggie Siggins, "Mongolism Test in Unborn Babies," *Toronto Telegram*, February 25, 1969 (OA, MS 755, Reel 361). Amniocentesis was discussed at the Annual Meeting of the Society of Obstetricians and Gynecologists in 1969: Lou Lee, "Can determine condition of fetus: Doctors Study fluid around unborn baby," *Globe and Mail*, June 14, 1969 (OA, MS 755, Reel 361)

[165] Amniocentesis aroused considerable commentary. Mollie Gillen, "Is your unborn baby normal?" *Chatelaine*, January 1972. See also: "New medical tests raise touchy issues," *Hamilton Spectator*, Jan 24, 1973, OA, Reel 533. Siminovitch was one who pointed out the "Pandora's box of problems". While the advantages in terms of the prevention of disease and preservation of resources were clear, Siminovitch wondered whether society might come to view those born with detectable disabilities in a different light -- as not warranting social support, or as being inappropriate. "Ability to spot a defective fetus creates a new dilemma on abortions, doctor says," *Toronto Star*, Jan 25, 1973, (OA, Reel 533). See also: Joan Hollobon, "Scientists foresees 'his' and 'hers' punchcards recording gene defects," *Globe and Mail* Jan 25, 1973, (OA, Reel 533). Though the need for social involvement in decision-making was most pressing in the field of amniocentesis -- then in practice and expanding -- other genetic developments which might become available, such as test tube babies that could be grown outside the womb, cloning, or genetic manipulation, might become available. Siminovitch called for the involvement of a wide segment of society in developing guidelines for the use of such a tool. Neil Morris, "Guideline help sought on use of genetic tool," *London Free Press*, Jan 25, 1973, (OA, Reel 533). Siminovitch recommended a public advisory body to deal with these questions. Glennis Zilm, "Genetic advances may present ethical and social questions," *Ottawa Citizen*, June 5, 1973, (OA, Reel 534). This article was distributed by CP and was widely published around the country. See also: Naomi Mallovy, "Your Child's Health: How can we tell what they will inherit?" *Chatelaine*, October 1973, 132

[166] Some commentaries took a decidedly sinister tone. Dr. Bentley H Glass, retiring president of the American Association for the Advancement of Science was quoted in the early 1970s for his statements that "in the foreseeable future no parents will have the right to burden society with a malformed or mentally incompetent child." ML Chazottes, "If your children could inherit cancer, should you have children?" *Maclean's Magazine*, March 1971, 67, 68. Racist views were prevalent. Nobel Laureate William Shockley, inventor of the transistor propounded the view that blacks have lower intelligence than whites, due to their genetic inferiority: Lydia Dotto, "Genetic engineering: science versus morals," *Globe and Mail* July 22, 1972, 28. David Suzuki pointed to the statement of the president of the CMA, in the summer of 1971, that educated, higher income groups are restricting their family size and therefore being outbred by lower-class groups, and that recipients of welfare should be sterilized: David Suzuki, "Genetics: will this science save us or kill us?" *Canada and the World*, Feb. 1972, 15. See: "Force birth control on welfare people doctors' leader says," *Toronto Star*, June 9, 1971, (OA, Reel 459).

[167] She cited David Suzuki as pointing out that "The dilemma always sets in when one starts to concern himself with the borderline inherited defects." Lydia Dotto, "The search for the disabling gene," *Globe and Mail*, July 20, 1972.

[168] Lydia Dotto, "Some geneticists predict an end to certain disease, the regeneration of useless limbs," *Globe and Mail*, July 24, 1972, 11. In 1974, it was clear only that "Advances in genetics have brought great potential benefits and also possible hazards, both demanding ethical decisions." These advances included such things as carrier detection, amniocentesis, treatment of genetic biochemical disease and the long-term effect on the gene pool, genetic engineering, cloning, surrogacy. Joan Hollobon, "Facing the decisions that medical science has forced upon us," *Science Forum*, February 1974, 18-19. On IVF see also: "Frank

Sartwell, "Test-Tube Babies: Moral Issues must be faced says suppressed report," *Toronto Star*, July 29, 1974, C3.

[169] Lydia Dotto, "If the baby is born from a test tube would average parent feel same family love?" *Globe and Mail* July 21, 1972, 10. As Dotto noted, these issues were too important to be left exclusively in the hands of scientists. James Watson was cited as pointing out that "This matter is far too important to be left in the hands of the scientific and medical communities." David Suzuki, Canada's iconoclast public scientist concurred. Lydia Dotto, "Genetic engineering: science versus morals," *Globe and Mail*, July 22, 1972, 28

[170] ML Chazottes, "If your children could inherit cancer, should you have children?" *Maclean's Magazine*, March 1971, 67, 68

[171] David Suzuki, still one of Canada's chief commentators on science and society issues, gained much of his media exposure during debates over genetic science in the 1970s. As a fairly renowned *Drosophila* geneticist at UBC he was particularly well equipped to comment. But though a "basic" scientist, he too saw the issue as encompassing such capacities as prenatal diagnosis, cloning, and eugenics. Unlike most scientists, however, Suzuki saw the issues in genetics as having much to do with powerful cultural beliefs. As a child, he and his family had been interned, along with other Japanese Canadians; Suzuki consistently raised the issue of his "Japanese genes" and the power of racist sentiment in biology. The breadth of his analysis consistently extended into the influence of social and cultural standards. Alexander Ross, "Could this man manufacture 3,000,000 Trudeaus?" *Maclean's Magazine*, March 1971. This article is cited extensively in: Marq de Villiers, "Science is beginning to promise ageless, beautiful people," *Toronto Telegram*, May 1, 1971, (OA, Reel 459). See also: David Suzuki, "Genetics: will this science save us or kill us?" *Canada and the World*, Feb. 1972. See also the series by Lydia Dotto, *Globe and Mail*, July 20-24, 1972. David Suzuki, "Viewpoint: Science vs. politics in Boston," *Science Forum*, Vol. 53, October 1976, 16. See also: David Suzuki, "Viewpoint: Why I believe in the public's good sense," *Science Forum*, October 1977; David Suzuki, "Citizen Involvement in Science," *Science Forum*, July-August 1978; Patrick Best, "Scientists 'misguided', David Suzuki draws a bead on his peers," *Ottawa Citizen*, Feb. 22, 1978, 9. David Suzuki, "Viewpoint: A personal statement of principle," *Science Forum*, August 1977, 13. See also an interview with Suzuki in: "Genetic engineering," *Financial Post*, June 10, 1978, 38.

[172] Siminovitch was one of the two individuals who created *Science Forum* in the late 1960s, precisely because a forum for discussion about scientific issues was much needed in Canada. Work on its development began in 1967, and the first issue was published in 1968. See: (UT, LS, 3, Science Forum, Science Forum - Editorial Board). His private correspondence with a US scientist, who would prove to be one of the more vocal critics of recombinant DNA research, suggests that by the fall of 1972 Siminovitch had identified the diverse range of concerns over developments in genetics that he would speak to for the remainder of the decade. See correspondence with Robert Sinsheimer, Nov. 1972, (UT, MG, 6, Dr. L Siminovitch). Siminovitch's correspondent, Robert Sinsheimer, Chairman of the Division of Biology at the California Institute of Technology became one of the most cogent scientific critics of rDNA research in the US. See: Dr. Robert Sinsheimer, "Troubled dawn for genetic engineering," *New Scientist*, 68, October 16, 1975, in: James Watson and John Tooze, *The DNA Story: A Documentary History of Gene Cloning*, (San Francisco: WH Freeman and Co, 1981), 52-55.

[173] Report to the Ontario Council of Health, 1973. See also: (UT, LS, 8, Ontario Task Force on Health Research requirements). Siminovitch then published the same document in at least two other places: L Siminovitch, "Genetic manipulation: now is the time to consider controls," *Science Forum*, 6:7-11, June 1973; L Siminovitch, "Genetic manipulation: now is the time to consider controls," *Canadian Nurse* 69, 11: 30-4, Nov. 1973

[174] *Social implications of developments in Biomedical Sciences*, Report to the Ontario Council of Health, 1973, 6.

[175] While the possibility of *in vitro* fertilization offered promise to "women with blocked oviducts who desire their own children" it also posed challenges, such as the safety of the procedure, the morality of such experimentation in "man", the use of resources in the context of "overpopulation", and the potential for "genetic manipulation in man" that access to the developing blastocyst would provide. Genetic manipulation was already possible in bacteria, Siminovitch noted, and experimentation continued with great fervor in this area and might eventually be applicable in humans. Siminovitch did not discuss any of

the dangers as they would come to be articulated in the orthodox rDNA debate. Instead, he noted the promise with respect to disease and warned of what he considered to be remote dangers with respect to providing "man with the prerogatives of designing his own heredity, rather than using the present lottery system of chance mating." *Social implications of developments in Biomedical Sciences*, Report to the Ontario Council of Health, 1973, 7, 8.

[176] Some articles addressed rDNA almost exclusively: Thomas Land, "Scientists frightened about genetic engineering success," *Financial Post*, Nov. 16, 1974, 14. This article merely reported on international events. "Genesis part II: from a handful of dust, man creates life," *Maclean's Magazine*, February 23, 1976. Carl Edgar Law, "Keeping the demon in the bottle," *Financial Post*, October 14, 1978, 35; Michael Enright, "Things best left alone?" *Maclean's Magazine*, December 27, 1976, 27. For articles which integrated the discussions see: Constance Mungall, "Genetic engineering, how much should we accept?" *Chatelaine*, September 1975; Charles White, "Genetic engineering: It's not nice to fool with mother nature," *Canada and the World*, October 1977; Charles White, "Genetics: Carbon copy society," *Canada and the World*, November 1977; Sheila Gormley, "Genetic Science can now determine the whole future of heredity," *Toronto Life*, February 1978; Patrick Best, "Scientists 'misguided', David Suzuki draws a bead on his peers," *Ottawa Citizen*, Feb. 22, 1978, 9; "Cloning: has man's reach exceeded his grasp?" *Maclean's Magazine*, April 3, 1978. Some articles continued debates about some medical genetic practices - especially amnio -- with little reference to new developments in genetics, and without rDNA entering into it. See: Robbie Salter, "Amniocentesis: whereby a family of specialists detects some genetic disease before birth," *University of Toronto Bulletin*, April 23, 1976. See also: Frank Appleton, "Brave new genetics," *Globe and Mail* weekend *Magazine*, August 14, 1976; Sheila Gormley, "Genetic Science can now determine the whole future of heredity," *Toronto Life*, February 1978; Ben Rose, "Diagnosing defects in the unborn," *Science Forum*, Jan-Feb. 1979. And some continue with the debates about genetic advances, without reference to rDNA. See: "Cloning: has man's reach exceeded his grasp?" *Maclean's Magazine*, April 3, 1978.

[177] On the UCC Commission see: correspondence, Ray to Siminovitch, Oct. 11, 1974, (UT, MG, 3, United Church). For Siminovitch's assessment of the issues for this Commission, see: L Siminovitch, "Status of Information on Possible Impact of Genetic Advance on Man." Feb. 10, 1975, 7, (UT, MG, 3, United Church). In the ensuing discussion about Siminovitch's paper, it became clear that the concept of "genetic engineering" was contested. Both Siminovitch's definition of genetic engineering as "the manipulation of genetic material" and the list of issues to be discussed alongside it were challenged. A broad definition including "methods of transmitting life, artificial insemination, artificial fertilization (*in vitro*), artificial implantation in the uterus, ectogenesis and cloning" was presented as an alternate. Siminovitch argued that, in fact, the term "genetic engineering" was problematic and not used by the "scientific community". In the end, commissioners agreed to add two items to Siminovitch's list -- artificial insemination and population genetics. UCC Commission on genetic engineering, "Record of Proceedings," March 21, 21, 1975, 2, (UT, MG, 3, United Church).

[178] Susan Wright has argued that, the debate notwithstanding, the American system of controls was ultimately engineered to generate self-regulation by those research granting councils which were most interested in facilitating the work of researchers. Susan Wright, *Molecular Politics: Developing American and British Regulatory Policy for Genetic Engineering, 1972-1982*, (Chicago and London: University of Chicago Press, 1994). The Canadian climate in relation to rDNA was a pale reflection of the American debate, where legislative oversight was seriously entertained. The federal government was eager to hand responsibility for this matter to the MRC – to treat this as a bureaucratic rather than a political concern. For more information on the rDNA debate see: Fiona Miller, "The Recombinant DNA Controversy: Managing the Challenge to Medical Genetics in Ontario," unpublished MS, presented to the Canadian Society for the History of Medicine, the Learned Societies, Memorial University, St. John's, Newfoundland, June 6, 1997.

[179] "Report of Genetic Counselling Services in Canada, 1971," prepared by the Committee on Genetics as it relates to Social Problems, *Genetics Society of Canada Bulletin*, Vol. 3:3, Jan 1972, 21, (UT, A83 0007, Box 5, File: Genetics Society).

[180] Hans Stich and G Subden

[181] One of the non-human geneticists made an effort to have the committee "consider topics ... other than those which directly relate to human genetics." Indeed, Stich argued that developments in the fields of agriculture and fish biology were socially relevant and thus were potentially human problems which should be considered by the committee. Jim Miller, memo to members of the GSC ctte, Feb. 1, 1973, (UT, MG, 4, Amniocentesis).
[182] But it was seen not to be "of great urgency since no work in this area is going on in Canada to our knowledge." James Miller, memo to members of the GSC ctte, Feb. 1, 1973, (UT, MG, 4, Amniocentesis).
[183] D Cox, letter to Jim Miller, Jan 30, 1973, (UT, MG, 4, Amniocentesis).
[184] Louis Dallaire of Montreal was also a member of the MRC committee and Nancy Simpson became deeply involved with its primary activity, the development of a registry.
[185] John Hamerton, "The Medical Research Council Working Group on Prenatal Diagnosis of Genetic Disease," *Prenatal Diagnosis Newsletter*, MRC, Montreal, 1:1 (June 1972), 2. This objective required a number of corollary institutional developments: a central registry for the data gathered on amniocentesis; prenatal diagnosis of genetic disease by the participating centers across the country; and, a newsletter, the *Prenatal Diagnosis Newsletter*. The first issue was published in June 1972; the last issue in December 1976. The newsletter was edited by Dr. Louis Dallaire, Section, Génétique Médicale Hôpital Sainte-Justine, Montreal, and one of the members of the Working Group. The newsletter served to disseminate information from and to participating centers. A number of subsidiary developments were also undertaken at this time: a central cell strain registry which would "accumulate and disseminate information on the cell culture banks being maintained in laboratories across Canada..."; and, sponsored by the Quebec government, a Repository for Mutant Human Cell Lines in Montreal. John Hamerton, "The Medical Research Council Working Group on Prenatal Diagnosis of Genetic Disease," *Prenatal Diagnosis Newsletter*, MRC, Montreal, 1:1, (June 1972), 2. Hy Goldman, "The Repository for Mutant Human Cell Strains," *Prenatal Diagnosis Newsletter*, MRC, Montreal, 1:1, (June 1972), 5-7. The repository actually stored human cell strains; the registry merely compiled information about the availability of human cell strains in labs throughout Canada.
[186] On the American trial see: Charles Lowe, "The National Amniocentesis Registry," In BH Cohen, et al, eds., *Genetic Issues in Public Health and Medicine* (Springfield, Ill.: Charles Thomas, 1978).
[187] The final report was first presented at the Annual meeting of the Society of Obstetricians and Gynecologists of Canada in June 1976 and was published in the *Canadian Medical Association Journal* soon thereafter: Louis Dallaire, Editorial: "Intégration du diagnostic prénatal des maladies génétiques a la pratique médicale," *Canadian Medical Association Journal*, 115, (October 23, 1976), 713-714; Nancy Simpson et al, "Prenatal diagnosis of a genetic disease in Canada: report of a collaborative study," *Canadian Medical Association Journal*, 115, (October 23, 1976), 739-748. The MRC also published it as a monograph: *Diagnosis of Genetic Disease by Amniocentesis During the Second Trimester of Pregnancy. A Canadian Study*, Report #5, MRC, Ottawa, 1977
[188] Nancy Simpson et al, "Prenatal diagnosis of genetic disease in Canada," 745.
[189] *Ibid.*, 739. "The Canadian Registry for Prenatal Diagnosis of Genetic Disease, Preliminary Report," *Prenatal Diagnosis Newsletter*, 5:1, (June 1976), 2. The efforts made to publicize the results of the MRC Working Group study were quite extensive, see: correspondence, Hamerton to Whetham, April 22, 1976, minutes of mtg., November 17, 18, 1975, (UT, LS, 8, Working group on prenatal diagnosis).
[190] London, Ontario was excluded from the MRC study for lack of accuracy in their data. But their capacity was already established, as we have seen, and they were in active conversation with and sought to comply with the national standards. Toronto was represented twice, at HSC and TGH, to bring the total to 13 centers. The other centers were Victoria, Vancouver, Edmonton, Calgary, Edmonton, Saskatoon, Winnipeg, Hamilton, Kingston, Ottawa, Montreal, Halifax.
[191] Guidelines for the delivery of antenatal diagnosis of genetic disease in Canada, draft prepared by the GSC, sub-committee on social responsibility in Science (Members: Miller, Wilson Cox, Subden, Hamerton; Invited: Siminovitch, Doran, Thompson), attached to Memo from Hamerton to Miller, Cox, Subden, Siminovitch, Thompson and Doran, May 25, 1973 (UT, A83-0007/004, Amniocentesis).
[192] "Canadian guidelines for antenatal diagnosis of genetic disease: a joint statement," *Canadian Medical Association Journal*, V111, July 20, 1974, 180

[193] Simpson et al, "Prenatal diagnosis of genetic disease in Canada," 740

[194] The guidelines did not specifically mention the need for non-directiveness in counseling, though the language implies an "informed decision-making" model. The key exception concerns the willingness of the "parents" to consider abortion in the event of the finding of a serious and untreatable genetic disease. The guidelines recommend that "Both parents' views on therapeutic abortion should be ascertained before amniocentesis and the tests should not be undertaken where (in the face of serious genetic disease untreatable *in utero*) the parents are unalterably opposed to abortion." "Canadian guidelines for antenatal diagnosis of genetic disease: a joint statement," 183. This proviso seems to have been common, see also: JA Lowden, et al, "Antenatal diagnosis of sphingolipid and mucopolysaccharide storage diseases," *Canadian Medical Association Journal*, 113, (Sept. 20, 1975), 507-8. One highly critical letter to the editor which followed on the publication of the MRC PND study suggested that the "aim is to kill those affected by disease." Simpson responded that they advised neither amniocentesis nor abortion, "we attempt to inform the families of their risks and available options and help them make a decision...": MJ Newman; Nancy Simpson, "To the Editor," *Canadian Medical Association Journal*, 116 (Jan 26, 1977), 134.

[195] After their publication, James Miller with another Vancouver colleague wrote in their support while admitting to no involvement in their drafting. RB Lowry and JR Miller, Correspondence: "Amniocentesis and prenatal diagnosis in medical practice," *Canadian Medical Association Journal*, 111, (October 5, 1974), 633

[196] Minutes of GSC ctte mtg, March 8, 1973, attached to: Jim Miller, memo to members of GSC ctte, March 14, 1973 (UofT, A83-0007/004, File: Amniocentesis)

[197] The report of the MRC Working Group study of antenatal diagnosis drew attention to the fact that "amniocentesis is used by only a small proportion of the female population at risk..." Moreover, they noted that, even at this low level, "the laboratory facilities and personnel are working at a maximum level consistent with reliability, safety and speed. Thus if the availability of the test is to be extended, an extension of the laboratory facilities will also be needed.": Simpson et al, "Prenatal diagnosis of genetic disease in Canada," 745, 758.

[198] Simpson et al, "Prenatal diagnosis of genetic disease in Canada," 745.

[199] Nancy Simpson, et al, "Antenatal diagnosis of neural tube defects in Canada: extension of a collaborative study," *Canadian Medical Association Journal* 120 (March 17, 1979), 653.

[200] "Report of Genetic Counselling Services in Canada, 1971," prepared by the Committee on Genetics as it relates to Social Problems, *Genetics Society of Canada Bulletin*, 3:3, Jan 1972, 22, (UT, A83 0007, Box 5, File: Genetics Society).

[201] Rudd memo (early 1970s) that OHSIP will not pay for genetic consultation; indeed, hospital not being reimbursed for any clinical work done in genetics department; Rudd negotiating with OMA for acceptance of proposed fee schedule for genetic counseling (p 6, notes, UofT, Dept medical genetics)

[202] Minutes of GSC ctte mtg, March 8, 1973, attached to: Jim Miller, memo to members of GSC ctte, March 14, 1973 (UofT, A83-0007/004, File: Amniocentesis). These issues continue to be relevant to medical geneticists in Canada today. And the trend now is toward only MDs having clinical contact. This has to do with issues of malpractice insurance – Ph.D. medical geneticists are not covered by the medical protective association, and with accrediting bodies with the clout to regulate the conduct of their membership – which the CCMG does not have, unlike the College. Conversation of the author with Dr Ron Carter, Vice President, Canadian College of Medical Geneticists, June 3, 1999, Ottawa.

[203] "Report of Genetic Counselling Services in Canada, 1971."

[204] H Allen Gardner, Submission to the Task Force on Genetic Services, attached to Gardner, letter to Siminovitch, December 10, 1974 (UofT, B79-0051/005, File: OCH – Task Force on Genetics).

[205] In the form letter sent to potentially interested participants, Fraser argued that the GSC survey of 1971 had revealed problems that were unlikely to be resolved quickly "unless there is some effort by genetic counsellors." The one-day meeting at York University was to attend to issues of "accreditation, payment and recognition of genetic services." Form letter from Clarke Fraser attached to: Jim Miller, memo to members of GSC ctte, March 14, 1973 (UofT, A83-0007/004, File: Amniocentesis). Minutes of GSC ctte mtg, March 8, 1973, attached to: Jim Miller, memo to members of GSC ctte, March 14, 1973 (UofT, A83-0007/004, File: Amniocentesis). To this end, Jim Miller prepared a statement on genetic counseling for the

GSC. Draft, Statement by the Committee on Genetics as it Relates to Social Problems of the Genetics Society of Canada, on Genetic Counselling, attached to: Jim Miller, memo to members of GSC ctte, March 14, 1973 (UofT, A83-0007/004, File: Amniocentesis). "The purpose of the meeting was to begin to develop a policy with respect to the proper recognition of genetic counselling as a health care service"; it was attended by observers from the federal and Ontario provincial departments of health. Jim Miller, memo to members of GSC ctte, March 14, 1973; attached form letter from Clarke Fraser (UofT, A83-0007/004, File: Amniocentesis). Mixed in with the development of institutional structures was a co-ordination of issues. At the same GSC meeting (May 16-17) at York University around which a national steering committee on genetic services was established (May 15), a discussion on the implications of advances in genetics was hosted (May 18). What unites these events, is both a set of issues and a cast of characters. Speaking at the symposium were Louis Siminovitch and James Miller; joining them from the lay community, were Dr. EJ Reed of Trinity College, University of Toronto, and Prof. H Krever, Faculty of Law, UWO. See: (UT, MG, 5, Genetics Society).

[206] The other members were Louis Dallaire, Elizabeth Ives, and James Miller. Thompson kept Siminovitch updated, see: "Progress report on Accreditation and Funding of Genetic Counselling and Genetics Services," Margaret Thompson to Louis Siminovitch, July 4, 1973, (UT, MG, 4, [No name of file]). This steering committee then took on the task of developing recommendations for an accreditation body. See correspondence in: "Progress report on Accreditation and Funding of Genetic Counselling and Genetics Services, to Louis Siminovitch, July 4, 1973, (UT, MG, 4, [No name of file]). One meeting of the steering committee was held in Saskatoon on June 29, 1973

[207] Margaret Thompson, letter to Dr WS Mahon, Senior Medical Consultant, Ontario Ministry of Health, August 1, 1974 (UofT, B79-0051/010, File: Ministry Task Force). The applications went in under James Miller's name as the Foundation did not make internal grants.

[208] Margaret Thompson, Memorandum to Members of the National Conference on Standardization of Medical Genetics Services, November 6, 1974 (UT, A83-0007/009, File: HSC)

[209] James Miller, "Canadian College of Medical Geneticists," *Canadian Medical Association Journal*, V113, Sept. 6, 1975.

[210] Hospital for Sick Children, Toronto, Genetics Program [draft of brief submitted to OHSIP], revised October 27, 1971 (UofT, B79-0051/010), File: Ministry task force [also Box 5, File: OHC- Task Force on Genetics])

[211] Margaret Thompson argued for "having the service component of medical genetics, which we are currently funding partly from research sources, recognized as a health care service and funded accordingly," doing this required some new accounting strategies, as the costs of service and research had always been "closely integrated." Carrier testing, for example, and many biochemical tests in amniocentesis were funded through research grants. Dermatoglyphics were paid for through the hospital budget, which funded a technician "Department of Genetics, HSC, Memorandum for Task Force on Genetic Counselling," attached to: Margaret Thompson, letter to Dr WS Mahon, Senior Medical Consultant, Ontario Ministry of Health, August 1, 1974 (UofT, B79-0051/010, File: Ministry Task Force)

[212] Hospital for Sick Children, Toronto, Genetics Program [draft of brief submitted to OHSIP], revised October 27, 1971 (UofT, B79-0051/010), File: Ministry task force [also Box 5, File: OHC- Task Force on Genetics])

[213] Form letter from Clarke Fraser attached to: Jim Miller, memo to members of GSC ctte, March 14, 1973 (UofT, A83-0007/004, File: Amniocentesis).

[214] Hubert Soltan to Margaret Thompson, June 20, 1973 attached to: "Progress report on Accreditation and Funding of Genetic Counselling and Genetics Services, Margaret Thompson to Louis Siminovitch, July 4, 1973 (UT, MG, 4, [No name of file]). There was a meeting in April 1974 at the HSC of Ontario genetic counselors; it was co-chaired by Hubert Soltan and Nancy Simpson. Correspondence, Agenda of meeting, April 24, 1974, UT, LS, 5, OCH-Task Force on Genetics (2). Out of these efforts emerged the Association of Genetic Counsellors of Ontario.

[215] Letter to Dr. Potter, from Diane Cox and James Miller, November 6, 1973, (UT, LS, 5, OCH Task Force on Genetics (2)).

[216] Letter to Diane Cox and James Miller from Dr. Potter, Dec. 7, 1973, (UT, LS, 5, OCH Task Force on Genetics (2))
[217] See correspondence in: "Progress report on Accreditation and Funding of Genetic Counselling and Genetics Services, to Louis Siminovitch, July 4, 1973; attached letter, Siminovitch to Dr. KC Charron, July 4, 1973, (UT, MG, 4, [No name of file]).
[218] Among the membership was TA Doran, A Sass-Kortsak, N Simpson, H Soltan and MW Thompson.
[219] *Genetic Services. A Report of the Ontario Council of Health*, 1976, Appendices 2 & 3 respectively.
[220] *Ibid.*, 6-8.
[221] *Ibid.*, 1976, 6-8.
[222] WS Mahon, Senior Medical Consultant for Task Force on Genetic Counselling Services, form letter to "Dear Doctor," May 6, 1974 (UT, B79-0051/10, File: Ministry Task Force)
[223] Grant application to HSC Foundation, July 2, 1974, (UT, LS, 4, OCH-Task force on genetics (2)).
[224] As Thompson and Miller wrote: "In an attempt to meet the increasing need for genetic services, the American Society of Human Genetics (to which most Canadian medical geneticists belong) and the National Genetics Foundation of the United States sponsored a small meeting in Washington in December, 1972. Dr F Clarke Fraser of McGill University chaired the meeting." "The Washington meeting," they added, "was concerned strictly with genetic counselling, but our proposal is to deal with the problem of the provision of medical genetic services in its full range rather than to concentrate on the genetic counselling aspect alone." Grant application to HSC Foundation, July 2, 1974, (UT, LS, 4, OCH-Task force on genetics (2)). Peggy Thompson attended this meeting and both she and Fraser were to report to the GSC Committee about it. Jim Miller, memo to members of the GSC ctte, Feb. 6, 1973, (UT, MG, 4, Amniocentesis); D Cox, letter to Jim Miller, Jan 30, 1973, UT, MG, 4, Amniocentesis. FC Fraser, "Genetic Counselling," *American Journal of Human Genetics*, 26 (1974), 637.
[225] Letter to Dr. Potter, from Diane Cox and James Miller, November 6, 1973, (UT, LS, 5, OCH Task Force on Genetics (2)). This letter blurs both old and new approaches – the definition is new, yet what is advocated for is funding for genetic counseling, meaning all genetic services. Nonetheless, this is the same as the definition provided by Fraser in: FC Fraser, "Genetic Counselling,", 637. It is also the same definition as was provided by the ASHG's Ad Hoc Committee on Genetic Counseling, which included Fraser, Thompson, Miller and American geneticists Charles Epstein, Barton Childs, Victor McKusick, Arno Motulsky, Marian Rivas, Margery Shaw and William Sly: "Genetic Counseling," *American Journal of Human Genetics*, 27 (1975), 240.
[226] Jim Miller, memo to members of GSC ctte, March 14, 1973; attached form letter from Clarke Fraser (UofT, A83-0007/004, File: Amniocentesis)
[227] Margaret Thompson, Memorandum to Members of the National Conference on Standardization of Medical Genetics Services, November 6, 1974 (UT, A83-0007/009, File: HSC)

Conclusion

As the tenure of Canada's Medical Research Council (MRC) Working Group on Prenatal Diagnosis drew to a close, its membership began to advocate for its continuation in some form. Louis Siminovitch took particular responsibility for this, drafting the section of recommendations to MRC dealing with "The Future of the Working Group."[1] There was a continued need, members argued, for a national coordinating body to foster further advancements in research and service in prenatal diagnosis. The national network of centers engaged in prenatal diagnosis was of inherent value – serving to maintain the stimulus on local centers to improve their efforts. Moreover, the continued presence of a national body addressed the tremendous public concern which surrounded genetic medicine. "The existence of a Working Group may allow," Siminovitch pointed out, "for some control on the ethical and moral aspects of prenatal diagnosis in Canada."[2]

Yet despite this plea, neither Canada's Medical Research Council nor Health Canada provided the funds to continue the Working Group. The Ontario Council of Health was also resistant to such demands. The Council had not created a Standing Committee to advise the Minister, as Siminovitch had recommended in his 1973 report on the *Social Implications of Developments in Biomedicine*.[3] Nor did the Council establish a "Standing Committee on Genetic Services" to advise the Minister of Health on policies, programs and funding, and to advise the centers on "all aspects of genetic services to be provided," as Siminovitch had suggested when chairing the Task Force on Genetics Services.[4] Yet the absence of such governmental supervisory bodies did not

detract considerably from the production and consolidation of genetic services in Canada and Ontario. In the 1970s, a small, but close-knit community of medical geneticists and their allies proved remarkably adept at expanding population access to services, establishing standards, and creating self-regulatory systems of oversight under the auspices of existing professional organizations.

Through such ad hoc organizing efforts, the old-order medical geneticists – trained as Ph.D. research scientists and concerned with the human animal – preserved their right to pursue applied human genetics within clinical environments, against the potential challenges of medical practitioners. In a similar vein, when the Department of Medical Genetics in Toronto was restructured to merge the 'basic' biologists from the university with the more practical, medical researchers at the hospital, the old-order medical geneticists preserved their identities as researchers, capable of producing fundamental knowledge.

The restructuring of the 1970s made organizational sense of the technical and epistemological changes which had been underway in Toronto since the 1950s. Those trained within Toronto's indigenous tradition, which developed in the 1930s and 1940s, had been interested in a broad etiological explanatory framework, encompassing environmental, hereditary and developmental influences. But this tradition of inquiry had passed over the course of the 1950s, in favor of an explanatory system emphasizing gene and chromosomal action. After the Second World War, Toronto's marginal research community, which had attended to human biology with an emphasis on heredity, merged with the broader currents of classical human genetic inquiry. Such changes were driven

by the opportunities for growth in an era of booming biomedicine,. and by the development of disciplinary coherence – symbolized by the founding of the American Society of Human Genetics in 1948. Through collaborations with biochemists, principally at Sick Kids, and the influence of a decidedly medical biochemical genetics, Toronto workers were re-made as classical human geneticists. By the 1970s, the old-order medical geneticists faced new epistemological challenges. With the consolidation of the 'new' biology, the human-animal as the primary source of research knowledge in medicine was challenged. Henceforth, medical geneticists would have to compete for explanatory relevance with other organisms, and frankly experimental methods.

Yet despite these changes and challenges, the old-order medical geneticists did not lose their expansive interpretation of genetic disease. In the 1950s, the Ford Walker school enjoyed medical relevance by attending to a diverse array of diseases whose causation was influenced by a range of developmental and environmental factors. Even after World War Two, as Toronto workers focused more narrowly on strictly genetic causation in their research, and the domain of formally genetic disease was correspondingly reduced, the scope of genetic medicine was not diminished. Instead, it was enhanced by the apparent growth, at least in relative terms, of the burden of genetic disease. In the post-war period, genetic disease was seen to grow through uncontrolled reproduction, mutation and the triumph of anti-bacterial medicine.

Where the indigenous tradition had blurred the lines between congenital and genetical conditions, expressing a disinterest in specifying whether diseases were strictly genetical or congenital, its more classical genetics descendant pursued a systemic

slippage, and many diseases which were clearly *not* explained by Mendelian models were retained within the orbit of genetic medicine. In the 1970s, when medical geneticists coordinated themselves professionally to better manage the expansive, and seemingly growing burden of genetic disease, the organization of genetic services institutionalized this highly productive slippage.

The contingent meanings of genetic disease which come into focus through the blurring and slippage between the categories of congenital and genetical disease were especially notable in the production of chromosomal anomalies. As medical cytogenetics swept the human genetics community in the 1960s, workers in both Toronto and London became active participants in the age of discovery. Researchers from these communities helped to make sense of medical cytogenetics by merging their local skills and metaphors with more generic cytological techniques.

By the late 1950s, Toronto workers were accepted members of the North American community of medical geneticists. They had divested themselves of the etiological presumptions of the indigenous tradition, yet they retained a metaphoric and technical attachment to the 'Mongol.' These skills and presumptions helped to make sense of medical cytogenetics in classical genetic terms, and to construct autosomal diseases as a coherent category which referenced Mongolism through dermal patterns and the rhetoric of severity.

On the eve of the 1960s, the London workers were only beginning to reorient themselves toward the human genetics community. Throughout the 1950s, Murray Barr

and his students and colleagues had used the sex chromatin as a tool of 'true sex' to interpret and manage the intersex. Though the formal meaning of the sex chromatin changed quite radically with the 1959 discoveries in medical cytogenetics, Barr's technical and metaphoric skills were still of use in the new era. Indeed, he and his students and colleagues used these traditions to help produce the sex chromosome anomalies as a coherent category of disease.

...

A project of this nature is necessarily only partial and suggestive. It seems appropriate, therefore, to provide comments about research which seems most needed in light of this study. First, the narrow focus of this project has allowed a detailed analysis that would not have been possible if the scope had been broadened. Yet it was not my intention to produce a story of developments that applied only in the communities under review. Nor does my focus on the Canadian context derive from any faith in the existence of distinct "national styles" in science across Canada's permeable border with the United States.[5] After all, it was the articulation of Ford Walker and her students with the American Society of Human Genetics after 1948 which allows us, ultimately, to call hers a school of human and medical genetics.

My study points to local institutional and conceptual changes in the organization of medical genetics and in the relations between human and basic genetics, and extends beyond the local to consider some of the national efforts at professional co-ordination

that occurred in the 1970s. I would like to argue that these local and national developments were part of the making of a decidedly North American medical genetics, and also that the changing meaning of medical genetics in Toronto points to broader shifts in North America in the relations between the human and medical sciences and biology generally. Yet establishing the generality of these transformations must await further research that looks more closely at US developments.

Second, this study gestures toward the significance of racial metaphors in making sense of disease. For Ford Walker, in the 1950s, genes that were associated with the development of disease were "black" – social distaste for persons with disease and disability was clearly paralleled with social fear of the racial 'other.'[6] Moreover, I point in this study to the symbolic authority of race in what was then called 'the Mongol.' The racialised otherness of the language of the Mongol supported the construction of this phenomenon as a disability of uncontested severity. For the Toronto workers, the ability to use the Mongol to symbolize severity supported efforts to expand their capacity to interpret and explain various diseases, and provided them with a practical task to be performed as a service in the hospital. In the 1960s, the symbolic authority of the Mongol was more generalized: in this decade, the severity of the still racialised condition of the Mongol supported the construction of categories of chromosome anomaly, with sex on one side (sex chromosomes) and severity on the other (autosomes).

Yet there is more to the social and metaphoric relations of race than this partial analysis reveals. While I discuss the structuring of the Toronto community by the social relations of gender, the racial contours of this community demand at least as close an

analysis. Throughout the period covered by my study, most researchers were 'white,' with the notable exception of Irene Uchida. The social relations of race helped to support the symbolic work of race, which used the racial 'other' as a sign of the lesser. At a minimum, a field dominated by 'whites' was less likely to harbor vocal critics of such symbolic content. In part, my failure to grapple with questions of race results from my inattention to human population genetics – where the racial identity of populations was of central importance. In Toronto, human population genetics mattered, but was not crucial in the production of medical genetics. The historiography of genetics suggests, however, that the detachment of human population genetics from medical genetics in Toronto was a local peculiarity and is not generalizable to the field. These questions demand fuller investigation.

Finally, this study focuses on the actions, efforts and interpretations of researchers and practitioners. While patients occupy these pages – their bodies and lives were, after all, the raw material for research – they do so as largely silent witnesses. Those in power – the researchers and practitioners – are presented as the primary actors in the dramas of intellectual and practical development. The agency of patients can be over-emphasized. They are, to use Adele Clarke's evocative phrase, only "implicated actors."[7] Yet the role of patients, of lay groups, and of non-medical professionals demands investigation. Such an investigation is especially important for histories of the post-World War Two period which, David Rothman suggests, has seen a radical transformation in the relations between doctor and patient.[8]

...

Throughout this dissertation, I have deliberately avoided addressing myself to the question of whether medical genetics was, or indeed is, a form of eugenics. In part this is because I hesitate to place such an onerous label on the individuals who form the subjects of this study without – for most of them – evidence of any formal allegiance. More to the point, if the label 'eugenist,' or even 'reform eugenist,' is stretched so far, it threatens to lose all explanatory value. It loses also, I fear, the ability to support the germane political concerns that are put forth in its name.

Diane Paul argues that the historical case concerning the links between eugenics and human and medical genetics is proven. She also points out that the demonstration of such historical links provides surprisingly little in the way of political guidance.[9] In part, debates about the links between eugenics and human and medical genetics are debates about hereditarianism. That genetic science is necessarily hereditarian is presumed by the assumption that the link between eugenic social goals and a hereditarian science would be politically regressive. If this study provides any political direction, then, it does so by pointing to the contingency of the meaning of genetic science.

There is optimism, I would like to think, in unearthing a research tradition in human biology that – though it did not survive growth and North American integration after World War Two – was less concerned with proving genetic causation than its more generic descendant. Analyses of human heredity might be as concerned with proving developmental and environmental as genetical influence, Toronto's indigenous tradition

suggests. Genetic science is a more contingent phenomenon than current emphases in genetic research would have us believe.

There is, of course, a paradox here. The indigenous tradition, in calling itself genetic in the 1950s, used the blurred boundaries between genetical and congenital that it still supported to assert an expansive value for *genetic* medicine. Optimism exists, then, in pointing to the contingency of this blurring, and the systemic slippage that followed it in the 1960s and 1970s. What would be the consequence for the "DNA mystique," I wonder, if prenatal diagnosis was *not* organized as a genetic service.[10]

Endnotes: Conclusion

[1] Correspondence, Louis Siminovitch to John Hamerton, Jan 12, 1976, (UT, LS, 8, Working group on prenatal diagnosis).
[2] Working group on prenatal diagnosis "Recommendations," (UT, LS, 8).
[3] *Social Implications of Developments in Biomedical Sciences*, A Report of the Ontario Council of Health, 1973, 4.
[4] *Genetic Services, A Report of the Ontario Council of Health*, 1976, 6.
[5] On national styles see: Mary Jo Nye, "National Styles? French and English Chemistry in the Nineteenth and Early Twentieth Centuries," *Osiris*, 8 (1993), 30-49.
[6] "Some genes carry disease and physical defects. Heredity counselors call them *black genes*." Sidney Katz, She knows the kind of children you'll have, *Maclean's Magazine*, 57 (December 1, 1954), 82, emphasis in original. That this was a racialist, rather than simply racist statement is evident in Ford Walker's repeated statements, in this article, about the merits of racial intermarriage, in the face of her client's and general social aversion: 79, 83.
[7] Adele Clarke and Theresa Montini, "The many faces of RU486: Tales of Situated Knowledges and Technological Contestations," *Science, Technology and Human Values*, 18:1 (Winter 1993), 42-78
[8] David Rothman, *Strangers at the Bedside: A History of How Law and Bioethics Transformed Medical Decision-Making* (Basic Books, 1991).
[9] Diane Paul, *Controlling Human Heredity: 1865 to the Present*, (New Jersey: Humanities Press, 1995), 134.
[10] Dorothy Nelkin, M Susan Lindee, *The DNA Mystique: The Gene as a Cultural Icon* (New York: Freeman, 1995).