Syncope, fainting, dizziness, weakness and palpitations occurring in the upright position are not uncommon complaints and are associated with a variety of disorders (Table 1). New tools and concepts have been developed, resulting in the emergence of new diagnoses, such as postural orthostatic tachycardia syndrome (POTS)\(^1\) and neurocardiogenic syncope,\(^2\) and new scales, such as the composite autonomic scoring scale\(^3\) and orthostatic intolerance grading by symptoms.\(^4\) Modern technology has allowed us to improve sensitivity in detecting dysautonomia. The head-upright tilt-table (HUT) test, over half a century old, has retained a central place in the investigation of syncope of unknown origin,\(^5-10\) orthostatic intolerance and dysautonomia.\(^11,12\) However, the test is of debatable value and has been the subject of many articles in the past 10 years. We review the physiologic basis of the HUT test, the method, patterns of response, indications and contraindications, and diagnostic validity.

**Physiologic basis**

On standing, about 300 to 800 mL of blood is forced downward to the abdominal area and lower extremities.\(^8,12\) Within seconds of this sudden decrease in venous return, pressure receptors in the heart, lungs, carotid sinus and aortic arch are activated and mediate an increase in sympathetic outflow. Through vasoconstriction of capacitance and arteriolar vessels and through increased heart output, a healthy subject is able to reach orthostatic stabilization in 60 seconds or less. This neurally mediated mechanism is the only one by which we can adapt to the first few minutes of an upright position, and it remains the most important afterward. Orthostatic stress and sympathetic activity have been shown to increase with the angle of HUT testing.\(^13-17\) Hemodynamic and hormonal data suggest that this stress is exerted mostly between 60° and 90°.\(^6,16\)

**Method**

Tilt-table testing examines the neurocardiovascular orthostatic response in a maximally controlled environment. With passive orthostasis, stress is maximized on the sympathetic system by blocking the influence of inferior limb musculoskeletal contractions that could increase venous return. The table angle, duration of tilting and addition of pharmacologic stimulation are all under the examiner’s control. The HUT test is a dedicated test in which the orthostatic challenge is much longer than can be allowed in an office setting, the controlled variables of the test maximize its value, and the partly automated setup enables the physician to pay more attention to the patient’s symptoms.

Tilt-table testing has 2 main phases. It begins with supine resting for at least 30 minutes. This phase has great importance because it allows stabilization of the cardiovascular system.
and may increase the sensitivity of the test. In the second phase the patient is tilted upright for 30 to 45 minutes, usually at an angle of 60° to 80°. At this angle near-maximal passive orthostatic stress is exerted. A third phase, in which the test is repeated with pharmacologic stimulation, is sometimes used in the investigation of unexplained syncope. Isoproterenol is the most common provocative agent; edrophonium, nitroglycerine, adenosine triphosphate, epinephrine and nitroprusside have also been used. During the entire procedure the blood pressure and heart rate are measured regularly with an automated device, at least every 3 minutes while the patient is tilted.

**Induced hemodynamic patterns**

Four patterns can be identified during HUT testing (Fig. 1). The normal response consists of an increase in heart rate of at least 10 beats/min, an elevation of diastolic pressure of about 10 mm Hg and little change in systolic pressure (Fig. 1A). Abnormal responses are POTS and orthostatic hypotension. The POTS pattern (Fig. 1B) consists of a sustained increase in heart rate of at least 30 beats/min or a sustained pulse rate of 120 beats/min. Orthostatic hypotension is defined as a reduction in systolic blood pressure of at least 20 mm Hg or a reduction in diastolic blood pressure of at least 10 mm Hg. Neurocardiogenic syncope (Fig. 1C) usually appears as a symptomatic and sudden drop in blood pressure, often after 10 minutes or more of HUT testing and frequently with simultaneous bradycardia. An immediate and continuing drop in systolic and diastolic pressure without a significant increase in heart rate signals the presence of dysautonomia (Fig. 1D). A psychogenic reaction relates to symptoms unrelated to changes in heart rate or blood pressure.

**Table 1: Principal causes of orthostatic symptoms**

<table>
<thead>
<tr>
<th>Orthostatic hypotension</th>
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<tbody>
<tr>
<td>Resulting from dysautonomia</td>
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<tr>
<td>Central (e.g., multiple system atrophy, Parkinson's disease)</td>
</tr>
<tr>
<td>Spinal (e.g., transverse myelitis, spinal tumors)</td>
</tr>
<tr>
<td>Peripheral (e.g., diabetic polyneuropathy, amyloidosis)</td>
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<tr>
<td>Resulting from vasovagal reactions</td>
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<tr>
<td>Induced (e.g., pain, carotid hypersensitivity)</td>
</tr>
<tr>
<td>Spontaneous: neurocardiogenic syncope</td>
</tr>
<tr>
<td>Resulting from cardiac malfunction</td>
</tr>
<tr>
<td>Pump failure (e.g., severe chronic heart failure, valvular dysfunction)</td>
</tr>
<tr>
<td>Arrhythmia (e.g., atrial fibrillation)</td>
</tr>
<tr>
<td>Resulting from absolute hypovolemia</td>
</tr>
<tr>
<td>Acute (e.g., hemorrhage, acute dehydration)</td>
</tr>
<tr>
<td>Chronic (e.g., adrenal insufficiency, salt-losing nephropathy)</td>
</tr>
<tr>
<td>Resulting from relative hypovolemia</td>
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<tr>
<td>Generalized vasodilation (e.g., sepsis, systemic mastocytosis)</td>
</tr>
<tr>
<td>Local venous pooling (e.g., severe venous insufficiency)</td>
</tr>
<tr>
<td>Resulting from extrinsic influences</td>
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<tr>
<td>Drugs (e.g., antihypertensive drugs, antiparkinsonian drugs)</td>
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<tr>
<td>Other (e.g., alcohol, heat)</td>
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<tr>
<td>Resulting from deconditioning (e.g., convalescent patients)</td>
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<tr>
<td>Postural orthostatic tachycardia syndrome</td>
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<tr>
<td>Psychogenic</td>
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</table>

**Indications**

HUT testing can be part of the investigation of any orthostatic symptom, especially in patients with no objective physical findings and no evidence of structural cardiovascular disease. Usually, it is part of the diagnostic algorithm of syncope or presyncope. The indications recommended by the American College of Cardiology are given in Table 2.

**Contraindications and adverse effects**

Contraindications to HUT testing are unstable cardio-

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vascular disease, pregnancy and patient refusal. Many laboratories recommend that men older than 45 years and women older than 55 years undergo stress testing before tilt-table testing and that women of childbearing age have a pregnancy test.8

HUT testing is generally safe, but there have been occasional reports of coronary vasospasm,22 chest pain,5 hypertension crisis1 and tachyarrhythmia.5,6 The most frequent adverse effects are hemodynamic changes, such as hypotension, tachycardia or bradycardia associated with orthostatic intolerance, presyncope or syncope. It is noteworthy that patients with neurocardiogenic syncope may rarely experience asystole (defined as ventricular pause of more than 5 seconds) or complete atrioventricular block during HUT testing. Lacroix and colleagues23 reported 10 asystolic reactions (6%) (average duration 12 seconds) among 179 patients investigated for neurocardiogenic syncope; 8 patients needed cardiopulmonary resuscitation for 20 to 30 seconds. Dhala and associates24 reported 19 asystolic reactions (9%) among 209 patients with suspected neurocardiogenic syncope and 3 asystolic responses (4%) among 75 healthy control subjects during HUT testing without pharmacologic stimulation. These subjects did not show a worse outcome than their nonasystolic counterparts during follow-up.24,25

Performance

We performed a MEDLINE search to identify studies of the reproducibility, sensitivity and specificity of HUT testing in adults using “orthostatic hypotension,” “neurally mediated syncope” and “syncope” as key words. Articles providing details about the HUT test and patient selection were included. We found many studies on the topic, but study methods and populations were quite heterogeneous.

Reproducibility

Reproducibility is an important characteristic of a diagnostic tool. From studies in which data on HUT testing were obtained on at least 2 occasions, with a known time interval,23,26–35 we calculated an average reproducibility of 81%. However, as Behzad and collaborators27 and other authors23,28 have highlighted, negative results are much more reproducible than positive ones (about 95% and 50% respectively).

The reproducibility of HUT testing depends strongly on population selection as it is increased in patients with severe and frequent orthostatic symptoms. Clustering of orthostatic symptoms in time also heavily impairs the reproducibility of any 2 diagnostic tests significantly apart in time.

Fig. 1: Responses to head-upright tilt-table testing. A: Normal response is characterized by absence of significant decrease in blood pressure (more than 20 mm Hg systolic or 10 mm Hg diastolic), absence of significant and sustained increase in heart rate (more than 30 beats/min) and absence of orthostatic symptoms. B: Postural orthostatic tachycardia syndrome (POTS) is characterized by significant and sustained increase in heart rate. C: Neurocardiogenic syncope is characterized by significant and sudden decrease in blood pressure, frequently associated with sudden bradycardia. D: Dysautonomic response is characterized by immediate, progressive and significant decrease in blood pressure, frequently without appropriate increase in heart rate.
Diagnostic validity

Age, severity of symptoms, type of symptoms, proportion of subjects with dysautonomia and selection of subjects can influence pretest disease prevalence. The lack of a gold standard for assessing the value of the HUT test is an important limitation; patients with dysautonomia are frequently identified by positive results of HUT testing.

Studies attempting to assess the validity of the HUT test as a diagnostic test have used a combination of questionnaire, physical examination and paraclinical tests (excluding HUT testing) as the gold standard for comparison purposes. Not surprisingly, estimates of sensitivity (number of subjects with positive findings on HUT testing divided by the total number of symptomatic subjects tested) are quite variable.

Studies assessing the ability of the HUT test to diagnose neurocardiogenic syncope averaged a sensitivity of 35% without pharmacologic stimulation and 57% with pharmacologic stimulation.2,27,31,36-43 Studies using HUT testing within the boundaries set by the American College of Cardiology guidelines6 averaged a sensitivity of 65%.31,38,48,53,58 It is noteworthy that the yield is not increased by repeating the test.27

The specificity (number of subjects with negative results divided by the number of healthy subjects tested) of the HUT test for neurocardiogenic syncope was 92% on average without pharmacologic stimulation22,34,37,56-58-71 and 81% with pharmacologic stimulation.30,51,53,55-58,62,63,67,69 Two investigations in which HUT testing was used within the boundaries set by the American College of Cardiology guidelines both yielded a specificity of 100%.31,58

Several investigations have established that abnormal results of tilt-table testing correlate with autonomic nervous system diseases7,26 and other tests of autonomic function.22-24,27 Axelrod and coworkers7 tilted 10 patients with familial dysautonomia at an angle of 90° for 5 minutes and had positive results in all cases. Ward and Kenny3 reported that 14 of 19 dysautonomic patients (74%) had orthostatic hypotension with a 70° tilt for 5 minutes. In the study by Khrubana and Nicholas27 73% of 39 dysautonomic subjects were correctly identified within 5 minutes at a 90° tilt. Grubb and colleagues29 identified patients with orthostatic intolerance and orthostatic tachycardia without full syncope (POTS) and studied HUT testing prospectively. A 45-minute 80° tilt resulted in a sensitivity of 100%.

Conclusion

Despite its limitations, the HUT test is useful in patients with a variety of clinical manifestations induced by orthostatism. It is most useful in documenting objective measures of orthostatic hypotension that cannot be obtained in a clinical setting.

Patients considered for HUT testing must be carefully selected to enhance diagnostic value. Abnormal hemodynamic response to the test in patients with clear clinical orthostatic symptoms is strong evidence for disease and should prompt changes in medical management, such as modification of lifestyle, use of compressive stockings or initiation of drug therapy.

Evaluation of treatment efficacy by serial HUT testing is still of unproven value. Despite the wide variability in orthostasis-related symptoms, the best indicator of treatment failure or success remains global evaluation of the symptoms experienced by the patient.

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