Orthostatic hypotension

Clinical experience with diagnostic tests[1]

Fetnat M. Fouad, M.D.
Robert C. Tarazi, M.D.
Emmanuel L. Bravo, M.D.

Orthostatic intolerance may be related to different causes. A combined investigative approach using a screening tilt test, blood volume determination, and hemodynamic evaluation has permitted classification of the disease into its different forms. A review of the authors' experience is summarized.

Index terms: Hypotension, orthostatic • Hemodynamics

Cleve Clin Q 52: 561–568, Winter 1985

Recurrent dizziness, weakness, and eventual loss of consciousness induced by standing are frightening symptoms, which usually trigger intensive investigations for possible cardiac cause, cerebral arterial disease, or a neurological lesion. If no obvious lesion is found, diagnosis is often thwarted by a lack of a clearly defined algorithm for a systematic approach to that common syndrome. The following outline is a review of our experience with patients referred because of recurrent symptoms varying from unsteadiness to graying of vision, and sudden syncope; in many, coronary or cerebral arteriography had been obtained by their physicians and showed no significant lesions.

Definition

Intolerance to orthostasis assumes many forms and may be related to different causes; in a few cases, manifestations are typical of some conditions and may help in the diagnosis of specific entities. It is important to determine at the outset whether the symptoms that develop on standing up

[1] Research Division, Clinical Science Department, The Cleveland Clinic Foundation. Submitted for publication June 1985; accepted Sept 1985. lp

0009-8787/85/04/0561/08/$3.00/0

are related to a fall in arterial pressure (orthostatic hypotension) or whether they are associated only with marked tachycardia and a narrowing of pulse pressure (excessive adrenergic stimulation). Separate from both these types are episodes of syncope that are associated with nausea and slowing of the pulse and take some time to clear up after fainting. These "vasovagal attacks" can occur in any position but are commonest in the upright posture.

The normal response to head-up tilt in our laboratory has been 119 ± 3 (standard error) to 116 ± 5 mm Hg for systolic blood pressure (SBP) and 74 ± 2 to 80 ± 3 mm Hg ($P < 0.05$) for diastolic blood pressure (DBP) in normal volunteers. In patients with documented autonomic insufficiency, these changes were 140 ± 7 to 81 ± 7 mm Hg ($P < 0.05$) and 77 ± 4 to 52 ± 5 mm Hg ($P < 0.05$), respectively. Therefore, orthostatic hypotension was defined by a fall of ≥30 mm Hg SBP and/or ≥10 mm Hg DBP[1]; more importance is attached to the fall in diastolic than to the systolic pressure because it is in marked contrast with the normal diastolic response to upright posture (standing).

Symptoms in orthostatic hypotension are notoriously variable from day to day or indeed within the same day; although always associated with the fall in pressure, the converse does not hold true and substantial falls in blood pressure may not always be symptomatic.

Pathophysiologic considerations

Cardiovascular adjustment to upright posture

There are relatively few instances in which diagnosis, localization of the lesion, and approach to therapy are as dependent on a thorough understanding of pathophysiology as is the case with orthostatic hypotension. The hemodynamic responses to upright posture have been studied extensively and are fairly well defined.[1–3] As one stands up, about 500 mL of blood is trapped in the distensible veins below the level of the heart; as a result, plasma is lost to the interstitial fluid[4] and venous return decreases. This peripheral relocation of intravascular volume and reduction in cardiac output would lead rapidly to severe hypotension and fainting were it not for potent activation of the sympathetic system by two separate routes: the first is the classical high pressure baroreceptor reflux and the second involves low pressure reflexes from the cardiopulmonary area whose importance has been appreciated only recently.[5–7] The diminished stretch of sensors in both the high- and low-pressure reflexogenic areas decreases their tonic inhibitory influence on the vasomotor center with consequent enhancement of sympathetic activity and repression of parasympathetic activity.

Classification of orthostatic intolerance

Intolerance to the upright posture can be classified according to the concomitant changes in arterial pressure and heart rate.

Marked tachycardia with normal or marked increase in diastolic pressure. These signs of marked sympathetic responsiveness to orthostasis (increased heart rate and possibly sweating) usually result from excessive stimulation of a functioning baroreceptor reflex induced by marked venous pooling or hypovolemia (idiopathic or diuretic induced). In both instances, the patient feels uncomfortable, with excessive palpitations and marked weakness. If prolonged, this excessive cardiac action may be followed by sudden slowing of the pulse, hypotension, and possibly fainting. This "secondary" vasovagal faint is thought to be related to stimulation of cardiac mechanoreceptors and is more likely to occur in cases of hypovolemia whether it is idiopathic or diuretic induced.[1]

Fall in both systolic and diastolic blood pressure (orthostatic hypotension) with no or normal increase in heart rate: The fall in arterial pressure on standing or head-up tilt has traditionally been subdivided into "sympathotonic" and "asympathotonic" types.[2] Although this approach helped substantially in our understanding of the syndrome when first introduced, a number of exceptions have blurred to some degree the sharp outline between the two types; moreover, more recent studies outlined a third type presumably caused by abnormal cardiogenic reflexes. We have therefore proposed a new classification that takes into account the advances of the past decade (*Table 1*).

Clinical syndromes

The range of neurohumoral responses to upright posture and diminished venous return has been recently reviewed.[1,8] The following discussion will therefore only highlight some aspects that are particularly relevant to clinical problems.

Autonomic failure

The basic characteristic of this type of orthostatic hypotension is the failure of increase in systemic vascular resistance despite the fall in cardiac output and arterial pressure.[1,9] Autonomic failure may occur because of lesions at different levels of the baroreceptor reflex arc. These include efferent pathway abnormalities as in diabetes mellitus and some forms of neuritis; central lesions, which are rare; and lesions of the efferent sympathetic and parasympathetic systems. Efferent lesions are the commonest. They are sometimes subclassified into central and peripheral types, the central type representing lesions in the autonomic tracts of the spinal cord (Shy-Drager) and the peripheral type representing a degeneration of postganglionic sympathetic fibers.[10]

More recently, we have come to appreciate fully the importance of a cardiac involvement in many of the neurogenic types of orthostatic hypotension. Both systolic performance and diastolic filling of the heart showed signs of impairment in patients with efferent adrenergic dysfunction. Stroke volume was reduced on head-up tilt more than could be accounted for by the fall in cardiopulmonary volume[11]; Fouad et al[12] recently reported a significant prolongation in left ventricle relaxation time in patients with efferent adrenergic dysfunction. Both observations are probably related to defective sympathetic support to the heart.

The cardiac aspects of autonomic failure can yield valuable clinical information. The marked reduction in stroke volume leads to a marked fall in systolic pressure on orthostasis particularly in older patients with less compliant large arteries. The change in stroke volume is also related to the response of heart rate to head-up tilt, and this has proved more complex than originally described.

A fixed heart rate has traditionally been viewed as a hallmark of autonomic failure.[13,14] This seemed to be supported from preliminary data in our laboratory; we used a noninvasive index to measure parasympathetic control of heart rate[15] in 4 patients with idiopathic orthostatic hypotension (*Table 2*). This index was markedly reduced in these patients compared to age-matched normal volunteers. However, more extensive laboratory experience with tilt test had shown that the change in heart rate during tilt varied from zero to +41 beats per minute. Similarly, the increase of heart rate in response to atropine varied from zero to +21 beats per minute. In general, orthostatic tachycardia is most prominent in autonomic dysfunction provoked by various drugs[1] and is least pronounced or completely absent in advanced organic autonomic patients with diabetic neuropathy.[14]

Table 1. Classification of orthostatic hypotension

Hypotension secondary to
- Failure of autonomic function
- Functional baroreceptor decompensation

Nonneurogenic hypotension consequent to hemodynamic stresses (reduced cardiac filling or impaired pumping efficiency)

Hypotension secondary to cardiogenic reflexes

Miscellaneous causes such as arteriolar diseases, adrenocortical insufficiency, arteriolar dilatation by vasodilators or by disturbances of acid-base balance

Table 2. An index (VHP) of parasympathetic control of heart rate in 4 patients with autonomic insufficiency

Patient no.	Age (yr)	BP (mm Hg)	HR (bpm)	VHP* (msec)
1	52	173/96	72	21 ± 2.4
2	55	116/96	71	12 ± 2.5
3	48	131/91	62	19 ± 1.0
4	52	186/103	82	14 ± 1.5

* X ± standard deviation, time interval for data analysis.
VHP = variation in heart period, *BP* = blood pressure, and *HR* = heart rate.

Functional baroreceptor decompensation

Central to the physiological adjustments to upright posture are the integrity of the reflex baroreceptor arc and the adequate responsiveness of the target organs to sympathetic activation. The integrity of the baroreflex arc is not, however, a qualitative characteristic, but rather a varying adjustable set that changes rather rapidly in response to exercise, sleep, many physiologic depressant drugs, and diurnal variations in autonomic neural tone. This variability in sensitivity of the baroreceptor reflex suggests that some patients could be functioning normally or at least asymptomatically at the fringe of baroreceptor compensation; under these conditions, the super-

A,B

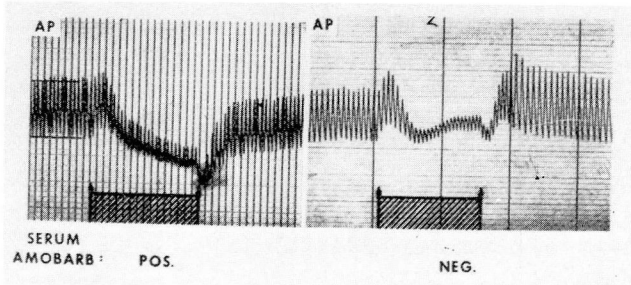

Fig. 1. **A.** Abnormal response to Valsalva maneuver (9-11-72). **B.** Response became normal when amobarbital was discontinued (9-14-72).

imposition of a functional and per se possibly slight depression of the baroreceptor reflex will precipitate significant symptomatic hypotension (*Fig. 1*). This occasional decompensation of the baroreceptors can help explain many clinical episodes of intermittent hypotension, orient investigations to identifying the provocative factors, and provide a rational basis for therapeutic advice.

Nonneurogenic hypotension

The vast majority of cases of nonneurogenic orthostatic hypotension result from inadequate cardiac filling either because of absolute or relative hypovolemia or because of some interference with venous return; others may be related to poor cardiac performance or to some obstruction to ventricular ejection. Diminished myocardial performance is not a common cause of orthostatic hypotension as distinct from hypotension at rest or following exercise. Patients with congestive heart failure are known to tolerate head-up tilt well, presumably because of their hypovolemia,[16] but orthostatic hypotension may become a problem after overtreatment with diuretics and converting enzyme inhibitors.[17] Severe aortic or pulmonary stenosis usually leads to exercise hypotension rather than an orthostatic fall in blood pressure.[18]

The consequence of interference with venous return is a reduction of cardiac output of such a magnitude that despite reflex stimulation of different compensatory mechanisms, arterial pressure falls. Broadly speaking, these cases form the group originally termed sympatheticotonic orthostatic hypotension.[2] The clinical signs of that sympathetic stimulation include pallor, sweating, and tachycardia; the latter, however, is inconsistent or could be obscured by medications, particularly β-adrenergic blockers.[19] The hemodynamic hallmark remains the marked increase in systemic vascular resistance attempting, but unable to compensate for the fall in cardiac output. The rise in systemic vascular resistance can at first maintain the diastolic pressure; the hemodynamic signs are then limited to a falling systolic pressure, narrow pulse pressure, and tachycardia. In patients with reduced aortic compliance, the fall in systolic pressure is exaggerated.[20] With further reduction in output, diastolic pressure also falls. This sequence of events must be differentiated from the "common faint" or vasovagal attack, in which situation (whether provoked by reduced venous return or intense emotional stimuli) total peripheral resistance and heart rate fall suddenly (*Fig. 2*). The fall in blood pressure is rapid and associated with signs and symptoms of increased vagal activity. The sudden vasodilation develops because of competing autonomic reflexes[21,22] and is not a preordained result of hemodynamic events. Although of neurogenic origin, this sudden hypotension is not due to autonomic failure but is more correctly related to activation of some depressor reflexes.

Vasodepressor cardiogenic reflexes

Early clinical experience with the common faint and more recently with the "pacemaker syndrome" has stressed the importance of differentiating cases of hypotension due to autonomic failure from those related to sudden activation of a depressor reflex. Broadly speaking, we could refer to "active" versus "passive" hypotension (active vasodilation or loss of vasomotor tone versus failure to respond to a drop in systemic flow). The diagnostic and therapeutic implications of the two are different.

The most common type of these hypotensions related to sudden vasodilation is the vasovagal or common faint. Most fainting spells occur when the subject is standing and are associated with a fall in arterial pressure. However, they may occur even in the supine position, particularly if provocative factors (emotional disturbances, pain, or sight of blood) are present. They are usually associated with signs of vagal activity (slowing pulse and nausea) and these symptoms clear slowly in contrast with those of progressive autonomic failure, which disappear as soon as the patient lies or falls down. The hemodynamic characteristic of the vasovagal syncope is a sudden fall in systemic resistance[21–25] caused by a

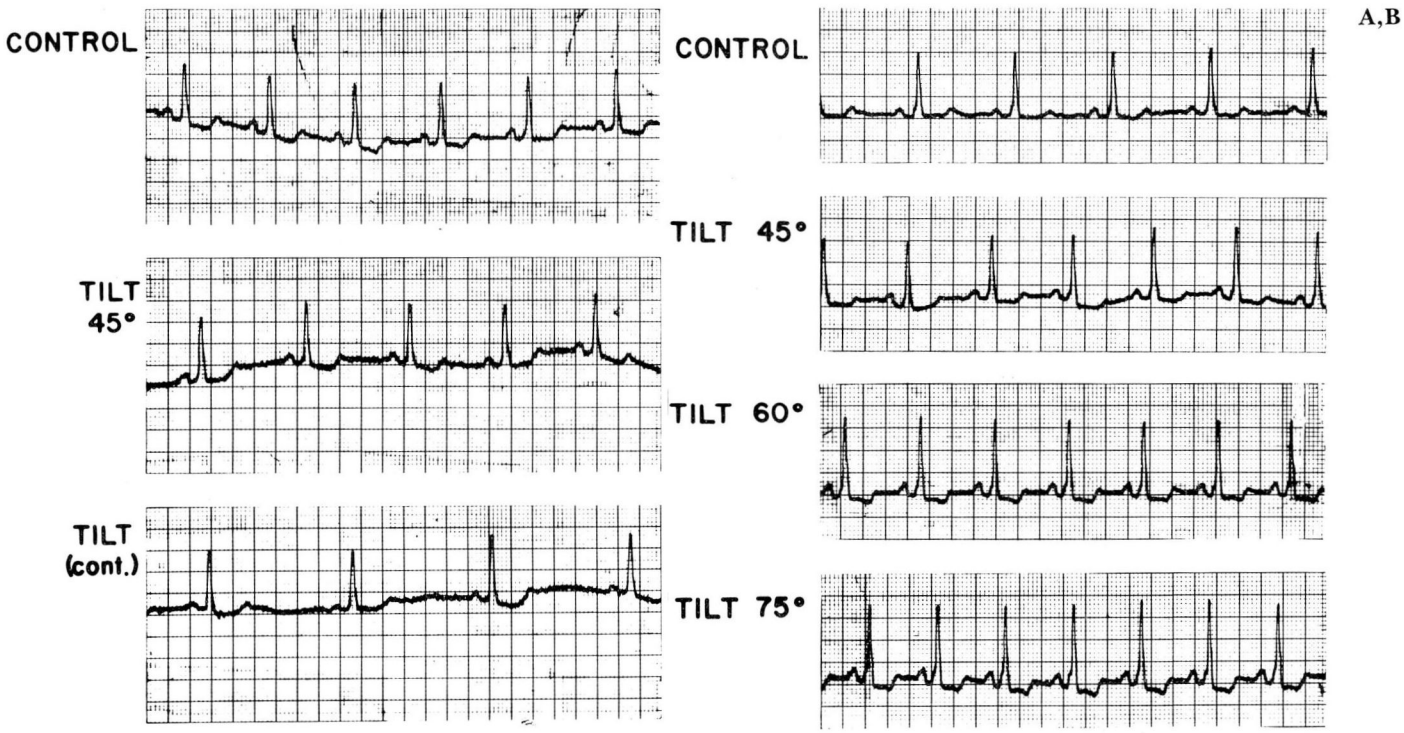

Fig. 2. **A.** Vasovagal response during head-up position (3-28-78).
B. Response of heart rate to tilt became normal when diuretic therapy was discontinued (5-3-78).

vasodepressor reflex initiated from ventricular mechanoreceptors activated by forceful contractions on a near-empty chamber.

Another example of hypotension related to a cardiogenic reflex is the "pacemaker syndrome."[7,26] Hypotension with light-headedness and near syncope can occur in patients during effective ventricular pacing. The mechanism underlying this fall in arterial pressure is not the simple reduction in cardiac output consequent on loss of atrial contraction[27]; a similar reduction in output could be easily compensated for by moderate vasoconstriction. The paradoxical lack of response of the peripheral resistance (which may indeed fall in some cases) was related temporally to the cannon waves in the atrial tracings (*Fig. 3*); this led to the suggestion that the abnormal resistance response was related to a reflex from distention of the atria.[7] In that respect, Kahl et al[28] found that inflation of a balloon in the left atrium led to a decrease in arterial pressure because the decrease in cardiac output was not compensated for by an increase in peripheral resistance. In contrast, similar decreases in output caused by occlusion of the superior vena cava led to fully compensatory increases in total peripheral resistance.

Localization of the lesion in autonomic dysfunction

The hallmark of autonomic insufficiency is an abnormal Valsalva test. The normal Valsalva response[29] has four components. Phase I is characterized by an initial rise in blood pressure associated with deep inspiration. Phase II represents the increase in intrathoracic pressure resulting in a reduction of venous return and consequent marked diminution of pulse pressure. During phase II, severe vasoconstriction occurs in a normal person, resulting in equilibration of the blood pressure at a low plateau with small pulse pressure. Phase III represents the restart of normal breathing with the initial filling of the pulmonary circulation leaving the systemic circulation empty, thus the arterial pressure falls dramatically. During phase IV, the cardiac output is distributed again to the systemic circulation, the latter being markedly vasoconstricted. The end result is an overshoot of systemic blood pressure, both systolic and diastolic. The changes

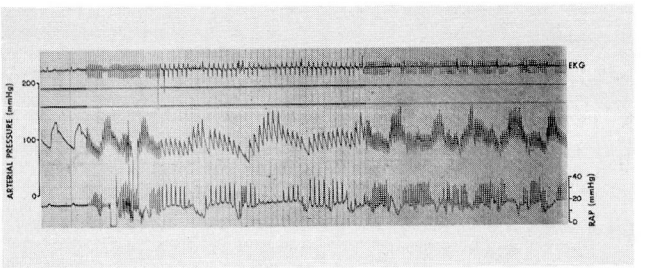

Fig. 3. Pacemaker syndrome. Blood pressure is lower when pacemaker is activated. These episodes are associated with cannon waves in right atrial pressure tracings.[6]

of heart rate during these phases have also been well described previously. The decrease of blood pressure during phase II is associated with tachycardia, while phase IV is associated with bradycardia; in both instances, the changes in heart rate are mediated via the arterial baroreceptors. In a patient with autonomic insufficiency, or in a patient with pharmacologic autonomic blockade (e.g., guanethidine), phase II is abnormal, i.e., the blood pressure continues to fall without reaching a plateau, and phase IV is abnormal, i.e., there is no overshoot of blood pressure. During these two phases, heart rate does not change significantly.[29] An attempt was made to quantitate these abnormalities by calculating the constriction and acceleration indexes[30]; however, this has not been proved.

Once autonomic insufficiency has been diagnosed, the next task is usually to localize the site of the abnormality along the baroreflex arc. Several tests have been devised for this purpose.

Cold pressor test[31]

In this test, the patient is asked to immerse his hand, up to the wrist, in ice-cold water for one minute. Somatic pain impulses are transferred through the spinothalamic tract to the hypothalamus. Efferent sympathetic impulses are directed to the heart and peripheral arterioles, producing tachycardia and an increase in total peripheral resistance (and blood pressure). A lesion in the efferent pathway of the baroreflex arc will prevent this response.

Hyperventilation[29]

Hyperventilation for 15 seconds results in hypocarbia and vasoconstriction of the brain stem vessels. The normal vasomotor centers sense this anoxia and induce vasodilation in response. A lesion in the vasomotor centers results in no change in blood pressure.

Baroreceptor sensitivity testing

These receptors are located in the aortic arch and the carotid sinus. According to the method of Gribbin et al,[32] a bolus of phenylephrine (25 to 50 μg) increases the blood pressure and results in a reflex slowing of the heart rate if the baroreceptors are sensitive. The sensitivity of the baroreceptors is quantitated by correlating the individual sytolic blood pressure with the subsequent R-R interval obtained from a simultaneous electrocardiographic tracing. Baroreceptor sensitivity was found to be blunted in a variety of conditions, notably old age, obesity, hypertension, uremia, and congestive heart failure.

Other tests

Other tests include the mental arithmetic and the reflex sweat test.[31] Efferent cardiac vagal fibers have been tested by examining the response of heart rate to atropine injection (0.03 mg/kg). Changes in heart rate in patients with idiopathic orthostatic hypotension are usually diminished compared to controls. Moreover, Fouad et al[15] adopted in man, a nonpharmacologic approach previously developed in dogs[33] for evaluation of vagal control of heart rate. The approach depends on the changes in R-R intervals, concomitant with respiration. Variation in heart periods was reduced in patients with autonomic insufficiency (*Table 2*). Finally, extra-adrenal stores of norepinephrine have been tested by injecting tyramine intravenously in three subsequent doses of 1, 2, and 3 mg. Because of the occasional extensive rise of blood pressure in some patients, 10 minutes are allowed between the individual injections after the blood pressure has returned to control level after each injection.[34] This test allowed the differentiation of two forms of autonomic insufficiency: the central type and the peripheral type.[10] The former was characterized by the presence of associated abnormalities of long tracts (pyramidal, extrapyramidal, or cerebellar) as well as marked increase in blood pressure and plasma norepinephrine in response to tyramine (sensitization hypersensitivity).

Summary

Orthostatic intolerance is not an uncommon

disorder. Its causes are multiple, but careful attention to clinical details and judicious use of selected tests to elucidate pathophysiologic mechanisms will allow accurate diagnosis in most cases. This will allow a rational choice of the therapeutic measures appropriate to the individual case.

Acknowledgment

We thank Mrs. Aldona Raulinaitis and Miss Tammie Lee for their help in preparing this manuscript.

Fetnat M. Fouad, M.D.
Research Division
Clinical Science Department
The Cleveland Clinic Foundation
9500 Euclid Ave.
Cleveland, OH 44106

References

1. Tarazi RC, Fouad FM. Circulatory dynamics in progressive autonomic failure. [In] Bannister R, ed. Autonomic Failure: A Textbook of Clinical Disorders of the Autonomic Nervous System. Oxford, Oxford Univ Press, 1983, pp 96–114.
2. Tarazi RC, Gifford RW Jr. Systemic arterial pressure. [In] Sodeman WA, Sodeman TM, eds. Sodeman's Pathologic Physiology: Mechanisms of Disease. 6th ed. Philadelphia, WB Saunders, 1979, pp 223–229.
3. Rushmer RF. Effects of posture. Part 1. Circulatory response to arising. [In] Cardiovascular Dynamics. 4th ed. Philadephia, WB Saunders, 1976, pp 363–384.
4. Tarazi RC, Melsher HJ, Dustan HP, Frohlich ED. Plasma volume changes with upright tilt: studies in hypertension and in syncope. J Appl Physiol 1970; **28:** 121–126.
5. Thorén PN, Noresson E, Ricksten SE. Resetting of cardiac C-fiber endings in the spontaneously hypertensive rat. Acta Physiol Scand 1979; **107:** 13–18.
6. Abboud FM, Mark AL. Cardiac baroreceptors in circulatory control in humans. [In] Hainsworth R, Kidd C, Linden RJ, eds. Cardiac Receptors. London, Cambridge Univ Press, 1979, pp 437–462.
7. Alicandri C, Fouad FM, Tarazi RC, Castle L, Morant V. Three cases of hypotension and syncope with ventricular pacing, possible role of atrial reflexes. Am J Cardiol 1978; **42:** 137–142.
8. Campese VM, Romoff M, Dequattro V, Massry SG. Relationship between plasma catecholamines, plasma renin activity, aldosterone, and arterial pressure during postural stress in normal subjects. J Lab Clin Med 1980; **95:** 927–933.
9. Stead EA Jr, Ebert RV. Postural hypotension: a disease of sympathetic nervous system. Arch Intern Med 1941; **67:** 546–562.
10. Ziegler MG, Lake CR, Kopin IJ. The sympathetic nervous system defect in primary orthostatic hypotension. N Engl J Med 1977; **296:** 293–297.
11. Magrini F, Ibrahim MM, Tarazi RC. Abnormalities of supine hemodynamics in idiopathic orthostatic hypotension. Cardiology 1976; **61**(suppl 1):125–135.
12. Fouad FM, El-Sanadi N, Hanson MR, MacIntyre WJ, Tarazi RC. Diastolic properties of the left ventricle in patients with autonomic dysfunction (abstr). Clin Res 1985; **33:** 185A.
13. Bradbury S, Eggleston C. Postural hypotension: a report of three cases. Am Heart J 1925; **1:** 73–86.
14. Ewing DJ, Campbell IW, Clarke BF. Assessment of cardiovascular effects in diabetic autonomic neuropathy and prognostic implications. Ann Intern Med 1980; **92:** 308–311.
15. Fouad FM, Tarazi RC, Ferrario CM, Fighaly S, Alicandri C. Assessment of parasympathetic control of heart rate by a noninvasive method. Am J Physiol 1984; **246:** H838–H842.
16. Abelmann WH, Fareeduddin K. Increased tolerance of orthostatic stress in patients with heart disease. Am J Cardiol 1969; **23:** 354–363.
17. Cody RJ Jr, Bravo EL, Fouad FM, Tarazi RC. Cardiovascular reflexes during long-term converting enzyme inhibition and sodium depletion. The response to tilt in hypertensive patients. Am J Med 1981; **71:** 422–426.
18. Weissler AM, Warren JV. Syncope, shock and sudden death. [In] Hurst JW, Logue RB, eds. The Heart, Arteries and Veins. New York, McGraw-Hill, 1966, p 356.
19. Garber AJ, Cryer PE, Santiago JV, Haymond MW, Pagliara AS, Kipnis DM. The role of adrenergic mechanisms in the substrate and hormonal responses to insulin-induced hypoglycemia in man. J Clin Invest 1976; **58:** 7–14.
20. Tarazi RC, Magrini F, Dustan HP. The role of aortic distensibility in hypertension. [In] Milliez P, Safar M, eds. Recent Advances in Hypertension. Reims, Boehringer Ingelheim, 1975, pp 133–142.
21. Bergenwald L, Freyschuss U, Sjöstrand T. The mechanism of orthostatic and haemorrhagic fainting. Scand J Clin Lab Invest 1977; **37:** 209–216.
22. Epstein SE, Stampfer M, Beiser GD. Role of the capacitance and resistance vessels in vasovagal syncope. Circulation 1968; **37:** 524–533.
23. Ruetz PP, Johnson SA, Callahan R, Meade RC, Smith JJ. Fainting: a review of its mechanisms and a study in blood donors. Medicine (Balt) 1967; **46:** 363–384.
24. Brigden W, Howarth S, Sharpey-Schafer EP. Postural changes in the peripheral blood flow of normal subjects with observations on vasovagal fainting reactions as a result of tilting, the lordotic posture, pregnancy and spinal anesthesia. Clin Sci 1950; **9:** 93–100.
25. Weissler AM, Warren JV, Estes EH Jr, McIntosh HD, Leonard JJ. Vasodepressor syncope: factors influencing cardiac output. Circulation 1957; **15:** 875–882.
26. Erbel R, Schweizer P, Fleischmann D, Meyer J. Contribution of atrial systole to cardiac performance. Hertz/Kreislauf 1977; **9:** 549–554. [Ger]
27. Braunwald E, Frahm CJ. Studies on Starling's law of the heart. IV. Observations on the hemodynamic functions of the left atrium in man. Circulation 1961; **24:** 633–642.
28. Kahl FR, Flint JF, Szidon JP. Influence of left atrial distention on renal vasomotor tone. Am J Physiol 1974; **226:** 240–246.
29. Sharpey-Schafer EP. Circulatory reflexes in chronic disease of the afferent nervous system. J Physiol 1956; **134:** 1–10.

30. Sharpey-Schafer EP. Effects of Valsalva's manoeuvre on the normal and failing circulation. Br Med J 1955; **19:** 693–695.
31. Ibrahim MM. Localization of lesion in patients with idiopathic orthostatic hypotension. Br Heart J 1975; **37:** 868–872.
32. Gribbin B, Pickering TG, Sleight P, Peto R. Effect of age and high blood pressure on baroreflex sensitivity in man. Circ Res 1971; **29:** 424–431.
33. Katona PG, Lipson D, Dauchot PJ. Opposing central and peripheral effects of atropine on parasympathetic cardiac control. Am J Physiol 1977; **232:** H146–H151.
34. Ibrahim MM, Tarazi RC, Shafer WH, Bravo EL, Dustan HP. Unusual tyramine responsiveness in idiopathic orthostatic hypotension. Med J Cairo Univ 1979; **47:** 49–55.

Commentary

Maurice R. Hanson, M.D., Department of Neurology, The Cleveland Clinic Foundation, comments: Of the many patients who present with complaints of syncope and presyncope, a small but important subset will do so because the systemic blood pressure falls to levels that fail to maintain adequate cerebral perfusion in the upright position. Most of these patients will prove to have hypovolemia, effects from drugs, poor conditioning, or peripheral nerve disease. A smaller percentage of patients will have no apparent cause and may be suspected of having idiopathic orthostatic hypotension (IOH). An even smaller percentage of these may have a multisystem neurologic disorder including Parkinsonian features, cerebellar dysfunction, and spasticity—referred to as the Shy-Drager syndrome—a progressive disease with a serious long-term prognosis.

Effective and appropriate treatment for orthostatic hypotension is dependent not only on a specific etiologic diagnosis, but in the case of IOH, on an anatomic diagnosis to determine what level(s) is impaired in the autonomic reflex arc, as is elegantly summarized here by Fouad et al.

In the past, therapeutic efforts to maintain normal blood pressure have been largely disappointing. The general strategies have consisted of increasing blood volume, stimulating the alpha adrenergic system, or both. Recently, the alpha adrenergic agonist (midodrine) has shown some promise. Recumbent hypertension remains a serious problem.

If the somatic neurologic disorder of Shy-Drager accompanies the orthostatic hypotension, treatment is more complex. For example, agents such as levodopa that are used to ameliorate the extrapyramidal symptoms may aggravate the hypotension. Hence, the management of IOH and its various subsets remain a complicated and challenging task.