RATIONAL TESTING

Postural hypotension

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This series of occasional articles provides an update on the best use of key diagnostic tests in the initial investigation of common or important clinical presentations. The series advisers are Steve Atkin, professor, head of department of academic endocrinology, diabetes, and metabolism, Hull York Medical School; and Eric Kilpatrick, honorary professor, department of clinical biochemistry, Hull Royal Infirmary, Hull York Medical School. To suggest a topic for this series, please email us at practice@bmj.com.

Postural hypotension can have various causes, and investigations include history taking, physical examination, and laboratory testing

A 70 year old man presents with recurrent lightheadedness for two to three weeks when getting up at night to pass urine. On questioning, he reports having occasional episodes of lightheadedness when standing for prolonged periods. Three months previously he had been started on the α adrenergic blocker alfuzosin 2.5 mg three times daily, after complaining of urinary frequency and a poor urinary stream; physical examination had found an enlarged prostate along with a value for prostate specific antigen within the normal range. His other medical history includes well controlled type 2 diabetes, for which he is taking metformin 500 mg three times daily and simvastatin 40 mg daily.

On physical examination, his blood pressure was 130/80 mm Hg (right arm supine) and 105/69 mm Hg (right arm standing) with the patient complaining of lightheadedness after standing up. His heart rate was a regular 88 beats/min supine and did not rise with standing. Physical examination was otherwise unremarkable.

Postural (also known as orthostatic) hypotension is an abnormal decrease in blood pressure—of at least 20 mm Hg systolic and 10 mm Hg diastolic—within three minutes of standing upright.[1] The prevalence of postural hypotension increases with age,[2] and among elderly people it ranges from 6% (in those who are healthy)[3] to 68% (in those in hospital geriatric wards).[4] In a prospective cohort study (n=33 346, 67.3% men, mean age 45.7 (standard deviation 7.4) years, and mean follow-up 22.7 (6.0) years) mortality and risk of a coronary event were significantly higher in those whose systolic blood pressure fell by ≥30 mm Hg (hazard ratio for mortality 1.6 (95% confidence interval 1.3 to 1.9, P<0.0001) and for risk of a coronary event 1.6 (1.2 to 2.1, P=0.001)); the study also found significantly higher mortality and risk of a coronary event in those whose diastolic blood pressure fell by ≥15 mm Hg (1.4 (1.1 to 1.9, P=0.024) and 1.7 (1.1 to 2.5, P=0.01)).[5] Patients often present with postural intolerance and recurrent falls, which are an important risk factor for hip fracture and head trauma.

LEARNING POINTS

- Postural hypotension is an abnormal fall in blood pressure—of at least 20 mm Hg systolic and 10 mm Hg diastolic—within three minutes of standing upright
- The commonest causes of postural hypotension are medications and conditions that cause hypovolaemia
- The patient's history is of particular importance and has a high diagnostic value
- Even after extensive evaluation, about a third of patients with persistent, consistent postural hypotension have no identified cause

What is the next investigation?

A detailed history and examination will be the next step. Measuring lying and standing blood pressures is the mainstay of evaluation.

History

The most common symptom is dizziness, often also described as lightheadedness, on standing, with or without gradual fading of consciousness.[6] Other associated symptoms include weakness, fatigue, lethargy, palpitations, sweating, and visual and hearing disturbances.[7] Hypoperfusion of the coronary circulation may aggravate angina pectoris and precipitate cardiac arrhythmias. Reduced sweating, symptoms related to gastroparesis, incontinence or urinary retention, constipation, erectile dysfunction, and ejaculatory dysfunction suggest that autonomic dysfunction is contributing to postural hypotension. In older patients symptoms of postural hypotension often arise after excessive nocturia or after a meal, and may worsen during exercise owing to autonomic dysfunction.

The patient's history is of particular importance and has a high diagnostic value. A medication history may indicate the cause of postural hypotension. If symptoms of postural hypotension are of acute onset ranging from days to weeks, the postural hypotension is probably secondary to fluid or blood loss or a medication effect. Even after extensive evaluation, about a third of patients with persistent, consistent postural hypotension have no identified cause.[8] The box outlines studies showing the role of medication, comorbities, sex, volume depletion, and autonomic disorders in postural hypotension.

Physical examination

The next step is to measure blood pressure and heart rate after 10 minutes of supine rest, repeated at three minutes after standing. If the patient cannot stand or is bedridden, a sitting measurement can be taken, but the sensitivity of the test may be reduced. Postural hypotension is considered clinically important if a reduction in blood pressure (≥20 mm Hg in systolic, ≥10 mm Hg in diastolic) is sustained at or beyond three minutes or the original symptoms are

Risk factors for postural hypotension

Medication

In a 1992 study conducted in elderly (aged 65 years or over) outpatients in general practice, current medication was found to be the most common risk factor for postural hypotension: diuretics (taken by 46% of almost 4000 study participants), sedatives (17%), centrally acting adrenergic blockers (15%), peripheral acting adrenergic blockers (10%), vasodilators (9%), β blockers (5%), and nitrates (5%).[9] Alcohol intake can cause postural hypotension.[9]

Comorbidities and sex

The same study found that additional risk factors included a history of heart failure (19%), varicose veins (25%), diabetes mellitus (14%), ongoing acute illness (10%), anaemia (2%), and Parkinson's disease (2%).[9] In another study, postural hypotension has been associated with increasing age, particularly in women, and with the presence of hypertension, antihypertensive treatment, diabetes, and current smoking in the general population.[5] In patients with diabetes, the presence of poor glycaemic control and hypertension are associated with an increased risk of postural hypotension, probably owing to autonomic dysfunction.[10]

Volume depletion

Hypovolaemia and intravascular fluid depletion can contribute to postural hypotension.[11 12] Common causes of fluid volume depletion include gastrointestinal losses (such as vomiting, diarrhoea, or gastrointestinal bleed) and skin losses owing to excessive sweating. Although rare in primary care setting, postural hypotension is one of the commonest presentations (12%) of Addison's disease.[13]

Autonomic disorders

Autonomic disorders are a rare cause of postural hypotension. The estimated prevalence of postural hypotension is 10% in diabetes, 37-58% in Parkinson's disease,[14 15] and rarely in other autonomic neuropathies.[16]

reproduced during active or passive standing.[17] The heart rate normally rises on standing, but an excessive rise (≥30 beats/min) is diagnostic of postural tachycardia syndrome, which suggests autonomic dysfunction. Lack of a rise in heart rate also suggests autonomic dysfunction or medication such as β blockers.[17]

Assessment of fluid volume status that finds dry mucosa, reduced skin turgor, delayed capillary refill, and low jugular venous pressure suggests dehydration.

In the evaluation of adults with suspected blood loss, the presence of postural dizziness has a sensitivity for moderate blood loss of only 22% (95% confidence interval 6% to 48%) but a much greater sensitivity for large blood loss of 97% (91% to 100%); the corresponding specificity is 98% (97% to 99%). Supine hypotension and tachycardia are often absent, even after as much as 1150 mL of blood loss (sensitivity 33% (21% to 47%) for supine hypotension).[18] In patients with vomiting, diarrhoea, or decreased oral intake, the presence of a dry axilla supports the diagnosis of hypovolaemia (positive likelihood ratio 2.8 (1.4 to 5.4)), and moist mucous membranes and a tongue without furrows argue against it (negative likelihood ratio 0.3 (0.1 to 0.6) for both findings).[18] In adults, the capillary refill time and poor skin turgor have no proved diagnostic value.[18]

Pallor suggests anaemia and blood loss. Murmurs or signs of congestive cardiac failure on cardiovascular examination suggest that structural or ischaemic heart disease is contributing to the postural hypotension.

A focused neurological examination will find any evidence of previous cerebral vascular disease, neuropathy, dementia, and movement disorders such as Parkinson's disease, which may coexist with postural hypotension. Any new neurological features, especially extrapyramidal signs, suggest a neurogenic cause of the postural hypotension and merits a specialist referral.

Postural hypotension may be suspected from the initial assessment if the patient has no features such as syncope that suggest alternative diagnosis and if the history is typical[19] (such as side effects of medication and conditions that can cause hypovolaemia through diarrhoea, vomiting, inadequate fluid intake, or haemorrhage).

Laboratory testing

In a patient who is anaemic—with or without a history of blood loss—a reduced haemoglobin concentration, reduced packed cell volume, and microcytic hypochromic anaemia suggest that the postural hypotension is likely to be caused by blood loss. An inappropriately raised urea concentration in relation to creatinine suggests dehydration that is caused by fluid or blood loss or diuretics and which results from the active reabsorption of urea in the proximal tubule. A raised white cell count and inflammatory markers suggest that intercurrent infection is causing postural hypotension. Hyponatraemia or hyperkalaemia may point towards hypocortisolaemia as the cause of the postural hypotension. A short Synacthen (tetracosactide) test with a peak cortisol concentration of ≥540 nmol/L 30 minutes after 250 µg of tetracosactide excludes Addison's disease.[20] Raised fasting glucose concentration (≥7 mmol/L) or a postprandial hyperglycaemia of ≥11.1 mmol/L with or without osmotic symptoms suggests diabetes,[21] which can cause autonomic dysfunction and postural hypotension.

Outcome

After the patient stopped taking alfuzosin following the first consultation, he still had postural symptoms. His symptoms of a bladder outlet obstruction did not worsen. At a return visit two weeks later, the blood pressure was 126/80 mm Hg (right arm supine) and 102/68 mm Hg (right arm standing) with a heart rate of 78 beats/min, which rose to 88 beats/min on standing. He had no pallor and clinically he was euvolaemic. Focused neurological examination showed tremor at rest. His full blood count and biochemical profile was normal. He was referred for neurological evaluation.

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10-MINUTE CONSULTATION

Chronic chilblains

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This is part of a series of occasional articles on common problems in primary care. The *BMJ* welcomes contributions from GPs.

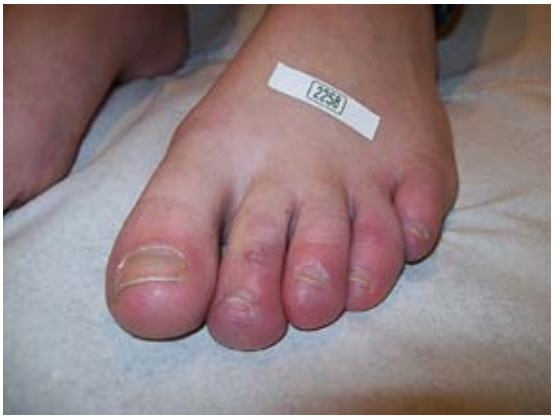
A woman visited her general practitioner in mid December with pain and reddish discoloration of her toes. Her symptoms had recurred every winter, but resolved completely in the summer. In previous years, she had had similar symptoms in her fingers.

What you should cover

Chronic chilblains are cold induced, painful or itching, red-blue lesions on the fingers, feet, ears, or thighs (figure).[1] The condition occurs throughout the world, more commonly in women than men. The average Dutch general practitioner reports four new cases a year (Continuous Morbidity Registration Nijmegen, the Netherlands; unpublished data). If patients consult a doctor at all, it will be their general practitioner.[2]

Symptoms usually start in early winter and vanish in spring, but often recur the next winter. Sometimes symptoms persist owing to continued exposure to cold, which is commonly associated with work conditions (cold storage work, for instance). Ulceration may also be present.

In clinical settings, chronic chilblains are associated with connective tissue disease, particularly systemic lupus erythematosus, but the evidence for this association is not substantial. Although up to a third of cases of chronic chilblains are reported to be diagnosed as chilblain lupus erythematosus, the proportion of patients with chilblains in a group with systemic lupus erythematosus did not differ from patients in the control group.[3] Persistence of lesions during the summer is probably associated with chilblain lupus erythematosus.[4] Case reports have linked the disorder to rare forms of vessel disease and rare conditions such as Sjögren syndrome and chronic myelomonocytic leukaemia. The presence of cryoproteins, cold agglutinins, and hereditary protein C and S deficiencies are not associated with chronic chilblains.[5]



What you should do

The main aim is to differentiate chronic chilblains from chilblain lupus erythematosus and other mimics.

Ask about the typical symptoms of chronic chilblains, particularly the specific pattern of the course: did the symptoms start when average temperatures drop below 10-15 degrees Celsius? Do the symptoms decline in spring? And does relapse occur in consecutive winters? Any family history of chilblains supports the diagnosis, because a hereditary factor may be involved in the onset of chronic chilblains.[2]

Persistent symptoms during the summer, a rash associated with discoid lupus erythematosus, photosensitivity, arthralgia, arthritis, oral ulcers, seizures, or psychosis suggest chilblain lupus erythematosus.[4]

Chronic chilblains are commonly confused with Raynaud's syndrome. If the patient reports a history of the characteristic paroxysmal and biphasic white, and later blue discoloration, after each exposure to cold, this will help to differentiate this syndrome from chronic chilblains.

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- Frequent exacerbations in chronic obstructive pulmonary disease (*BMJ* 2011;342:d1434)

Inspect the affected skin for red-blue lesions that are typical of the disorder. Such lesions are usually swollen and may be ulcerated.

Pulsation of the peripheral arteries should be normal; otherwise, peripheral vessel disease is a possibility.

For diabetic patients, the possibility of a diabetic foot should be considered, particularly if peripheral vessel disease or other ischaemic problems are present.

Additional tests are useful in some cases: If chilblain lupus erythematosus is suspected, a negative antinuclear antibody test makes systemic lupus erythematosus unlikely. Other laboratory investigations are not usually helpful. Skin biopsy does not usually help differentiate between chronic chilblains and its mimics.[1]

Various interventions have been suggested, including vitamin D_3 (which has no therapeutic effect[6]), nifedipine, and a corticosteroid cream. Our study of the patient's perspective shows that most patients visited a general practitioner, but were not given much useful information. Most patients tried a number of remedies without success.[2]

Simple advice for self management may be helpful (know that the disease is usually harmless and self limiting in spring, avoid exposure to cold, and wear adequate clothing).

The best evidence is provided by a randomised controlled trial of just 10 patients, which favoured nifedipine 60 mg/day over placebo.[7]

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STATISTICAL QUESTION
Screening tests: likelihood ratios

Answer *c* is the likelihood ratio for a positive test result on screening.

CASE REPORT
Jaundiced after a party

1 The diagnosis is most likely to be drug induced liver injury associated with MDMA consumption. However, a diagnosis of acute viral hepatitis should be excluded. Alcoholic hepatitis is unlikely with an ALT greater than 300 IU/L.

2 Drug induced liver injury is essentially a diagnosis of exclusion. Exclude other causes of acute liver dysfunction with tests for liver autoantibodies, copper, caeruloplasmin, ferritin, and viral immunology, which are normal in this condition. Hepatobiliary ultrasonography is often normal. A biopsy will show characteristic features of drug induced inflammation.

3 Drug induced liver injury is classified into three types—hepatocellular, cholestatic, and mixed—on the basis of biochemical features. Hepatocellular disease is often more severe, whereas patients with the cholestatic and mixed types are more likely to develop chronic disease.

4 Remove the precipitating agent and then provide supportive care with fluids. If liver failure develops, give prophylactic antibiotics and lactulose to prevent hepatic encephalopathy. This should allow the liver time to recover and liver function to normalise. Assess patients who continue to deteriorate for liver transplantation.

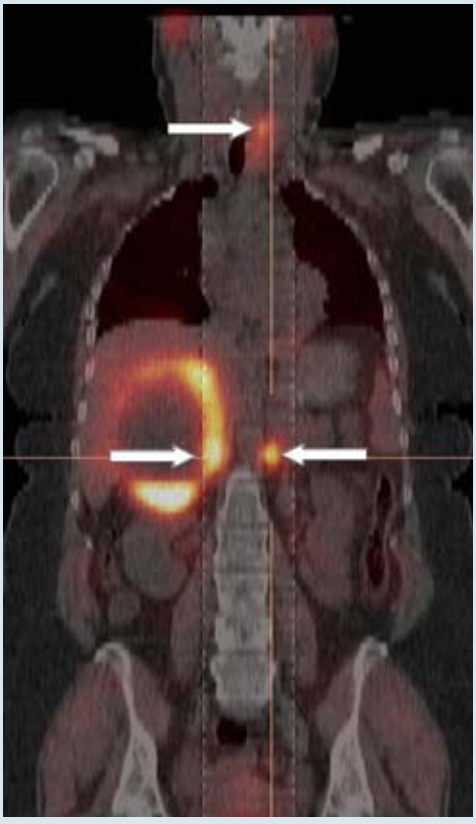
PICTURE QUIZ
A woman with episodic headaches, sweating, and palpitations

1 The ^{123}I-MIBG SPECT scan shows increased uptake of marker in the right upper abdomen and in the regions of the left adrenal gland and left thyroid lobe.

2 A thyroid nodule in someone with phaeochromocytoma should raise suspicion of medullary thyroid carcinoma as part of multiple endocrine neoplasia syndrome type 2 (MEN2).

3 Further investigations of the thyroid nodule include thyroid ultrasound, fine needle aspiration cytology, and serum calcitonin. Serum calcium and parathyroid hormone should also be checked because of the occurrence of primary hyperparathyroidism in MEN2.

4 The management of phaeochromocytoma includes α adrenoceptor blockade (with or without β adrenoceptor blockade), followed by surgical resection. Thyroid medullary carcinoma is treated with total thyroidectomy.



Coronal ^{123}I-MIBG SPECT fusion scan showing an increased uptake in the large right adrenal mass, in the left adrenal, and in the left lobe of the thyroid (arrows). The uptake in the region of the parotid glands is a normal finding