Investigation of the patient with night sweats

In this series, we present authoritative advice on the investigation of a common clinical problem, specially commissioned for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.

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Night sweats can be a benign symptom or a manifestation of serious illness. Diagnosis of the cause relies on a thorough history and examination, supplemented by step-wise investigations in selected patients. This article discusses the causes of night sweats and outlines a practical approach to diagnosis.

What causes night sweats?

Sweating is part of the body's temperature control mechanism and is mediated by the parasympathetic nervous system. It is activated normally under conditions of excessive heat production, such as raised external temperature, exercise, emotion or fever.

Abnormal sweating can occur in response to hormonal changes, altered temperature control or illness. It is often associated with flushing (warmth and redness of the face or trunk) and followed by cooling of the skin, which may be the reported symptom, described as chills or shivers (Table 1).

Sweating is more likely to be experienced at night due to covering the body with bedclothes and lying in bed, where the efficient cooling mechanism of evaporation is minimised. Also, body temperature normally exhibits diurnal variation, with higher levels occurring in the evening.

Night sweats are common: in one study they were reported by 41% of 2267 patients visiting a primary care physician.[1] A Google search of the term 'night sweats' yields over 1.5 million results.

Night sweats can be graded as mild, moderate or severe, as described in Table 2.

Common causes

Night sweats occur often in hot weather or when

IN SUMMARY

- **Night sweats are common; they can be a benign symptom or a manifestation of serious illness.**
- **Diagnosis of the cause of night sweats relies on a thorough history and examination, supplemented by step-wise investigations in selected patients.**
- **A serious underlying illness should be suspected when no obvious cause for night sweating is apparent from the history, the sweats are severe and cause drenching of sheets, they are persistent for more than one month, or they are associated with other systemic symptoms.**
- **Systemic symptoms to look for include fever of 38°C or more, suggestive of an infection, autoimmune disease, endocrine disorder or malignancy, and weight loss of at least 10% body weight within six months, suggestive of an endocrine disorder or malignancy.**
- **Most initial investigations of night sweats are used to detect nonspecific indicators of the presence of systemic disease.**
- **Further testing will depend on the patient's clinical features, duration of symptoms and results of preliminary tests.**

Table 1. Definitions

Fever
Oral temperature >37.2°C at 6 a.m.
(or >37.7°C at 4 p.m.)

Chills
Cooling of the skin secondary to sweating

Cold shivers
Increased skeletal muscle tone in response to cooling

Table 2. Grading of night sweats

Mild
Patient may have to turn over the pillow or remove a blanket

Moderate
Patient wakes up and needs to wash his or her face or the affected area

Severe
Patient needs to change clothing

people use a heater, electric blanket or warm bedding. They can also be due to stress or anxiety.

Physiological night sweats or hot sweats and flushes occur as common symptoms of oestrogen deficiency at menopause (Table 3). They can also occur occasionally with testosterone deficiency at male menopause (andropause).

Night sweats can be a symptom of a serious underlying illness, which should be suspected in the following cases:

- when no obvious cause is apparent from the history
- when the sweats are severe and cause drenching of the sheets resulting in awakening
- when they are persistent for more than one month
- when they are associated with other systemic symptoms (see below).

Symptoms suggestive of an underlying illness

Fever of 38°C or more suggests the presence of an infection, autoimmune disease, endocrine disorder or malignancy. Weight loss of at least 10% body weight within a period of six months is also suggestive of an endocrine disorder or malignancy.

The triad of fever, night sweats and weight loss are designated 'B' symptoms in the Ann Arbor staging system for lymphomas and are seen most often in patients with Hodgkin's lymphoma. However, this triad may occur also in patients with other malignancies, notably in the presence of hepatic metastases, or in those with endocrine disorders such as hyperthyroidism.

Hodgkin's lymphoma generally presents with cervical lymphadenopathy, whereas non-Hodgkin's lymphomas may present with systemic symptoms only, associated with occult para-aortic or hepatic involvement. Associated fever in Hodgkin's lymphoma is classically a form of relapsing fever called Pel-Ebstein fever, in which fevers lasting three to 10 days alternate with similar afebrile periods.

Symptoms of acute infection may be apparent or night sweats may be the only symptom of occult infection. A study of patients with infectious mononucleosis showed these patients had significantly more night sweats than did patients with other upper respiratory infections.[2]

Night sweats can also be the presenting symptom of chronic infections, such as tuberculosis, infective endocarditis or human immunodeficiency virus (HIV) infection.

Endocrine disorders associated with night sweats include hyperthyroidism (Figure), nocturnal hypoglycaemia occurring in patients with diabetes mellitus, and uncommon endocrine tumours, such as phaeochromocytoma or carcinoid syndrome.

Causes that are often unrecognised

Night sweats may be the reported symptom of other sleep disorders, such as obstructive sleep

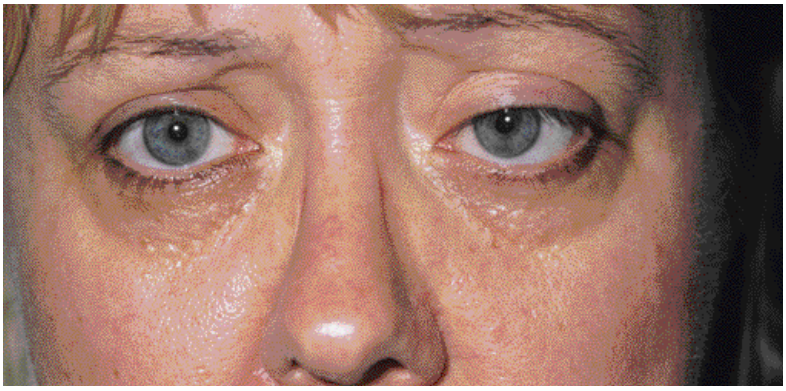
PHOTOLIBRARY

Figure. Hyperthyroidism, a common endocrine cause of night sweats.

Table 3. HOPE Study definition of hot flushes

Mild
Fleeting warm sensation without sweating; does not disrupt activity

Moderate
Warm sensation with sweating; does not disrupt activity

Severe
Hot sensation with sweating; disrupts activity

Table 4. Causes of night sweats

- Environmental – e.g. raised external temperature
- Hormonal – e.g. deficiency, excess, tumours
- Chemicals – e.g. medications, alcohol, foods
- Infection – e.g. infective endocarditis, infectious mononucleosis, HIV infection
- Malignancy – e.g. lymphoma
- Autoimmune disease – e.g. temporal arteritis
- Neurological disease – e.g. head injury, stroke, epilepsy, autonomic dysreflexia
- Idiopathic

apnoea[3] and nightmares, through restless movements, or gastro-oesophageal reflux,[4] through lung aspiration. They may also be the result of sympathetic overactivity, which occurs, for example, in congestive cardiac failure.

Medications can cause night sweats – for example, through a rebound effect of the antipyretics paracetamol and aspirin, the neurological side effects of antidepressants, or vasodilatation from antihypertensives, nicotinic acid and sildenafil. Hormonal therapy for cancer can also be associated with this troublesome side effect. Examples include tamoxifen used for breast cancer and nonsteroidal antiandrogens, such as bicalutamide, or gonadotrophin-releasing hormone analogues, such as leuprorelin acetate, used for prostate cancer.

Nonprescription drugs, such as alcohol, can also cause night sweats, as can hot or spicy foods.

Uncommon causes

Night sweats may be a symptom of autoimmune diseases, including temporal arteritis.[5] They may also occur in several neurological conditions, such as head injury, stroke, epilepsy, autonomic neuropathy and autonomic dysreflexia.

Occasionally idiopathic hyperhidrosis (excessive sweating) occurs.

Table 4 summarises the main causes of night sweats.

How are night sweats investigated?

Most initial investigations of night sweats are used to detect nonspecific indicators of the presence of systemic disease (Table 5).[6]

- A full blood count may show anaemia of chronic disease, a neutrophil leucocytosis related to bacterial infection, atypical lymphocytes in infectious mononucleosis, or lymphopenia in lymphomas and HIV infection.
- A very high erythrocyte sedimentation rate (ESR over 100 mm/hour) is characteristic of chronic infection, an autoimmune disease or disseminated malignancy.
- An elevated C-reactive protein (CRP) level has similar utility to the ESR in the investigation of night sweats. The level can rise within six hours of acute inflammation and levels over 100 mg/L are more suggestive of bacterial than viral infection.[7]
- General chemistry testing may direct further investigations to a particular organ, such as the liver, and a raised serum lactic dehydrogenase (LD) concentration is a tumour marker for lymphoma.

Table 5. Investigation of night sweats

Initial tests
- Full blood count
- Erythrocyte sedimentation rate
- Chemistry, including serum lactic dehydrogenase testing, C-reactive protein level measurement
- Serology for infectious mononucleosis
- Antinuclear antibody testing
- Thyroid function tests
- Chest x-ray

Selective tests
- Serology for HIV
- Mantoux test
- Cultures of urine and blood
- Sleep study
- Trial of therapy for GORD

Specialised tests
- Abdominal CT
- Gallium scanning
- Biopsy of enlarged lymph node, liver, skin, temporal arteries or bone marrow

Further testing will depend on the patient's clinical features, duration of symptoms and results of preliminary tests. In a sick patient with abnormal nonspecific blood results, further tests should be performed to look especially for evidence of ongoing infection. Such tests include:

- serology for infectious mononucleosis
- culture of urine
- blood cultures for infective endocarditis
- chest x-ray, looking for chronic lung infections, lymphomas or tuberculosis
- in at-risk populations, serology for HIV and a Mantoux test for tuberculosis can also be performed.

The longer the symptoms persist, the less likely that infection will be the cause. When symptoms last more than a few weeks and are not thought to be due to common physiological causes, thyroid function tests (TFT) should be performed

as well as antinuclear antibody (ANA) testing. In the presence of suggestive symptoms, a sleep study may be warranted, or a trial of treatment for gastro-oesophageal reflux disease (GORD) with an H_2-receptor antagonist or a proton pump inhibitor.

At this point most primary care physicians would choose to refer the patient for further investigation by a specialist general physician, haematologist, infectious diseases physician or rheumatologist. Further testing would be likely to include imaging studies, such as abdominal CT or gallium scanning, and biopsies of enlarged lymph nodes, or of the liver, skin, temporal arteries, muscle or bone marrow.

Conclusion

Night sweats are a common presenting symptom that challenges the clinician to distinguish between benign conditions and a large differential of possible underlying causes. MT

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