

Diagnosing Night Sweats

ANTHONY J. VIERA, LCDR, MC, USNR, Naval Hospital Jacksonville, Jacksonville, Florida
MICHAEL M. BOND, LT, MC, USNR, National Naval Medical Center, Bethesda, Maryland
SCOTT W. YATES, M.D., M.B.A., Dallas, Texas

Night sweats are a common outpatient complaint, yet literature on the subject is scarce. Tuberculosis and lymphoma are diseases in which night sweats are a dominant symptom, but these are infrequently found to be the cause of night sweats in modern practice. While these diseases remain important diagnostic considerations in patients with night sweats, other diagnoses to consider include human immunodeficiency virus, gastroesophageal reflux disease, obstructive sleep apnea, hyperthyroidism, hypoglycemia, and several less common diseases. Antihypertensives, antipyretics, other medications, and drugs of abuse such as alcohol and heroin may cause night sweats. Serious causes of night sweats can be excluded with a thorough history, physical examination, and directed laboratory and radiographic studies. If a history and physical do not reveal a possible diagnosis, physicians should consider a purified protein derivative, complete blood count, human immunodeficiency virus test, thyroid-stimulating hormone test, erythrocyte sedimentation rate evaluation, chest radiograph, and possibly chest and abdominal computed tomographic scans and bone marrow biopsy. (Am Fam Physician 2003;67:1019-24. Copyright © 2003 American Academy of Family Physicians.)

The symptom of night sweats is commonly encountered in clinical medicine, but there are no data regarding its actual frequency. Night sweats has been defined as drenching sweats that require the patient to change bedclothes.¹ This definition, however, probably does not describe the majority of patients who may complain of the symptom, and not all reports or studies cited through this article use this strict definition. The key words “night sweats” and “nocturnal hyperhidrosis” were used to search the MEDLINE literature from 1966 to July 2001, *Harrison's Principles of Internal Medicine*, 13th ed. CD-ROM, and the January 1999 *Physicians' Desk Reference* (PDR) Electronic Library CD-ROM. Abstracts for 338 citations in the MEDLINE literature were reviewed for articles, letters, and commentaries about diagnoses that had night sweats as a feature. There were 16 matches for night sweats in Harrison's and 11 pharmaceuticals with night sweats as a reported side effect in the PDR.

Evaluation

An extensive list of diagnostic considerations in patients with night sweats is provided

in *Table 1*.²⁻⁹ The history and physical examination are aimed at revealing associated symptoms that will narrow this broad differential diagnosis and guide additional studies. *Table 2* lists diagnostic actions to be considered based on findings from the history and physical.

HISTORY

Physicians should ask about fever, cough, and risk factors for tuberculosis (TB). In its pulmonary form, reactivation TB generally presents with cough in addition to the constitutional symptoms of weight loss and low-grade fever. Many patients experience night sweats several times per week. A history of (or risk factors for) human immunodeficiency virus (HIV) infection is important. The most common complaint with HIV infection is fever, with or without night sweats. This may be because of the virus or the result of HIV sequelae such as lymphoma or opportunistic infections.

Most patients with acquired immunodeficiency syndrome (AIDS)-related lymphoma have a history of fever, weight loss, and night sweats.¹⁰ AIDS-related infections might also cause night sweats, including *Mycobacterium*

A therapeutic trial of treatment for gastroesophageal reflux disease may relieve night sweats for patients who have an otherwise normal evaluation.

avium complex (MAC) infection and cytomegalovirus (CMV) syndromes. MAC infection in patients with HIV typically presents with fever, weight loss, and night sweats. It is a late complication of HIV infection that generally occurs in patients with CD4⁺ cell counts of less than 100 cells per mm³. TB also can be present in a patient infected with HIV. In this population, patients often present in the classic manner with cough, fever, and night sweats.

Sometimes, travel history is helpful in evaluating the potential for other infectious diseases. Persons with the chronic pulmonary form of histoplasmosis present similarly to those who have TB, with an increasing productive cough, weight loss, and night sweats.¹¹ Persons with coccidioidomycosis may present with cough, fever, and night sweats.¹² Risk factors for endocarditis also should be deter-

mined. The symptoms of infectious endocarditis are protean and include fever, chills, fatigue, sweats, and malaise. These night sweats may be related to nocturnal fever caused by transient bacteremia.

Low-grade fever that may be associated with night sweats is the most common systemic symptom of Hodgkin's disease. High fluctuating fevers accompanied by drenching night sweats (Pel-Ebstein fevers) may persist for several weeks with Hodgkin's disease. Night sweats may be the only presenting complaint for some patients. One study¹³ of patients with Hodgkin's disease who had sweating as their only symptom found a correlation with unperceived elevations in body temperature, or minor febrile pulses. Occasionally, patients with non-Hodgkin's lymphoma also may experience night sweats.

A history of recent upper respiratory infection may be significant because infectious mononucleosis (IM), usually caused by Epstein-Barr virus, may cause night sweats, particularly during the acute phase. In a study¹⁴ where the symptoms of IM were compared with other upper respiratory infections,

TABLE 1
Causes of Night Sweats

Malignancy	Endocrine	Other	Drugs (Table 3)
Lymphoma	Ovarian failure	Obstructive sleep apnea	Antipyretics (salicylates, acetaminophen)
Leukemia	Hyperthyroidism	Gastroesophageal reflux disease	Antihypertensives
Other neoplasm	Diabetes mellitus (nocturnal hypoglycemia)	Chronic fatigue syndrome	Phenothiazines
Infections	Endocrine tumors (pheochromocytoma, carcinoid tumor)	Granulomatous disease ⁵	Substances of abuse: alcohol, heroin
Human immunodeficiency virus	Orchiectomy ³	Chronic eosinophilic pneumonia	Over-bundling
Tuberculosis	Rheumatologic	Lymph node hyperplasia ⁶	Autonomic over-activity
<i>Mycobacterium avium</i> complex	Takayasu's arteritis	Diabetes insipidus ⁸	
Infectious mononucleosis	Temporal arteritis ⁴	Prinzmetal's angina ⁹	
Fungal infections (histoplasmosis, coccidioidomycosis)		Anxiety	
Lung abscess ²		Pregnancy ⁹	
Endocarditis			
Other infection			

Information from references 2 through 9.

night sweats were significantly more common in patients with IM.¹⁴ By the third week of illness, heterophile antibodies were positive in 90 percent of patients. If heterophile antibodies are not elevated, but the diagnosis is strongly suspected, IgM antibodies to Epstein-Barr virus viral capsid antigen (anti-VCA) may be measured, because they can be elevated for weeks to months after infection.

Women in the appropriate age range should be asked about symptoms of menopause, because patients with ovarian failure may experience hot flushes. Some women may experience a predominance of these during nocturnal hours.¹⁵ An elevated follicle-stimulating hormone test may be helpful in diagnosing menopause when the history is unclear.

Patients with diabetes experiencing nocturnal hypoglycemia may have night sweats without other hypoglycemic symptoms.¹⁶ This may be caused by missing a meal or performing unusually excessive exercise. Patients who are receiving large doses of evening insulin may be especially prone to nocturnal hypoglycemia.¹⁷ Risk factors for hypoglycemia may include tight diabetes control, renal insufficiency, polypharmacy, higher sulfonylurea or insulin doses, and advanced age.¹⁷

An association between gastroesophageal reflux disease (GERD) and night sweats has been suggested. Informal observations suggest that patients treated for GERD often have dramatic relief of their night sweats.¹⁸

Physicians should inquire about symptoms of hyperthyroidism, such as nervousness, palpitations, weight loss, and menstrual irregularity. The heat intolerance of hyperthyroidism may lead to night sweats, especially when combined with over-bundling or an overheated room.

Sleeping partners should be questioned about the patient's sleeping habits (snoring, apneic spells, and daytime sleepiness). Obstructive sleep apnea is a relatively common disorder affecting up to 4 percent of middle-aged men.¹⁹ It may be a common cause of heavy night sweats.²⁰

Antipyretic medications can sometimes cause night sweats because of a rebound effect.

TABLE 2
Evaluation of Night Sweats Based on Associated Symptoms or Signs

<i>Associated symptoms or signs</i>	<i>Action to consider</i>
Fever, TB exposure, HIV status or risk factors, cough, weight loss, immunocompromise	Purified protein derivative, chest radiograph, CBC, HIV test (CD4+ if known HIV positive), possibly blood cultures
Menopausal	Hormone replacement therapy (an elevated FSH test if uncertain based on history, helps confirm the diagnosis)
Firm lymphadenopathy in absence of current or recent infection	Lymph node biopsy
Recent upper respiratory tract infection	CBC; heterophile antibodies or anti-VCA evaluation
Diabetic	Rule out nocturnal hypoglycemia
Overweight; excessive daytime sleepiness, partner reports loud snoring and gasping during sleep, small oropharynx	Sleep study
Heartburn, indigestion	Trial of histamine H ₂ blocker
Heat intolerance, exophthalmos, tremor, other symptoms or signs of hyperthyroidism	Thyroid function test
Labile hypertension, paroxysms of headache or palpitations	Urine catecholamines or metanephrines measured in a 24-hour collection; if diagnosed, the tumor must be localized using radiologic imaging
Attacks of cyanotic flushing, watery diarrhea, wheezing, hypotension, or edema	High levels of urinary 5-hydroxyindoleacetic acid (5-HIAA) confirms diagnosis. Certain foods and medications may cause false-positive results (Table 3). Once diagnosed, the tumor must be localized using radiologic imaging.
Splinter hemorrhages, Janeway lesions, Osler's nodes, new heart murmur	Blood cultures including HACEK organisms, echocardiogram
No associated symptoms or signs	See Figure 1.

TB = tuberculosis; HIV = human immunodeficiency virus; CBC = complete blood count; FSH = follicle-stimulating hormone; VCA = viral capsid antigen; HACEK = Haemophilus species; Actinobacillus; Cardiobacterium; Eikenella; Kingella.

Alcohol use, particularly alcohol dependence, may cause night sweats.

Several medications may contribute to night sweats, but antipyretics are the most common. Acetaminophen and aspirin are cited as causes of night sweats. This is most likely a rebound effect as the antipyretic effects subside.⁹ Use of some antihypertensives, antidepressants, tamoxifen (Nolvadex), leuprolide (Lupron), and niacin are possibly causal as well.¹ Alcohol use, particularly alcohol dependence, also may cause night sweats. The PDR search revealed 11 pharmaceutical agents that were labeled as having night sweats as a side effect (Table 4).²¹

Directed inquiry of symptoms suggestive of myocardial ischemia, anxiety, depression, and rheumatologic diseases may be useful. While not specifically revealed in the searches, it is likely that any disease that results in autonomic overactivity (e.g., congestive heart failure via neurohumoral activation) may result in night sweats.

Carcinoid syndrome should be a consideration if the patient (usually in the sixth to eighth decade of life) has a history of attacks

TABLE 4
Drugs with the Labeled Side Effect of Night Sweats

Drug	Incidence
Donepezil (Aricept)	Infrequent
Indinavir (Crixivan)	Infrequent
Saquinavir (Fortovase, Invirase)	Less than 2 percent
Zalcitabine (Hivid)	Less than 1 percent
Cyclosporine (Neoral, Sandimmune)	Rare
Pegaspargase (Oncaspar)	1 to 5 percent
Rituximab (Rituxan)	Among most frequent
Interferon alfa-2a (Roferon)	8 percent
Daclizumab (Zenapax)	2 to 5 percent

Information from Physicians' desk reference. 53rd ed. Montvale, N.J.: Medical Economics, 1999.

of severe cyanotic flushing of the skin that lasts from minutes to days and is associated with other symptoms such as watery diarrhea, wheezing, hypotension, or edema. Symptoms are caused by a tumor that secretes serotonin and other biologically active substances.

The diagnosis of pheochromocytoma should be considered for patients with paroxysms of headache, palpitations, and sweating—especially in combination with hypertension. The paroxysms typically last from minutes to hours and may occur with varying frequency from once per month to multiple times in a 24-hour period.

PHYSICAL EXAMINATION

On physical examination, the patient's vital signs (particularly temperature and blood pressure) and body habitus should be noted. Lymphadenopathy or splenomegaly may prompt an evaluation for possible lymphoma or leukemia. Lymph nodes in either form of lymphoma are generally nontender and firm. Most patients with Hodgkin's lymphoma present with cervical lymphadenopathy, while those with non-Hodgkin's lymphoma present with peripheral lymphadenopathy. Biopsy is essential for diagnosis.

TABLE 3
Some Foods and Medications That May Interfere with 5-HIAA Test

Tomatoes	Acetaminophen	Mephenasin carbamate
Red plums	Caffeine	(some muscle relaxants)
Pineapple	Methocarbamol (Robaxin)	Phenacetin
Walnuts	Diazepam (Valium)	Aspirin*
Avocado	Glyceryl guaiacolate	Levodopa (Sinemet)*
Eggplant	(many cough medicines)	Phenothiazine*
Bananas		

5-HIAA = 5-hydroxyindoleacetic acid.

*—May cause false-negative result.

Evaluating Night Sweats

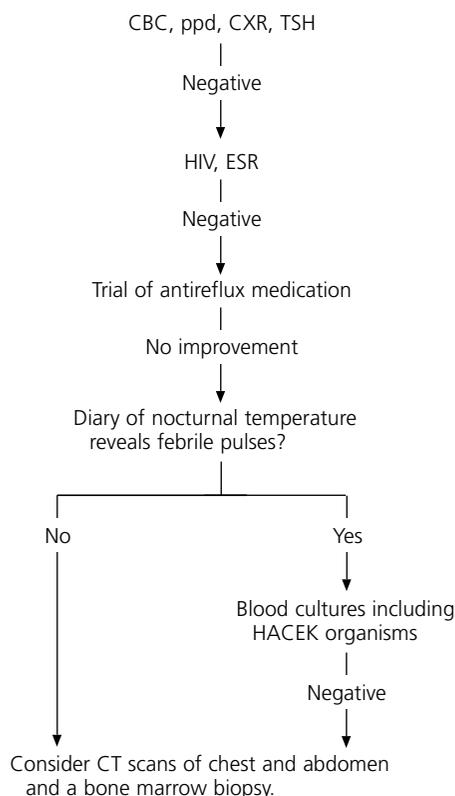


FIGURE 1. Evaluation of a patient with night sweats and no associated symptoms. (CBC = complete blood count; ppd = purified protein derivative; CXR = chest radiograph, TSH = thyroid-stimulating hormone; HIV = human immunodeficiency virus; ESR = erythrocyte sedimentation rate; HACEK = Haemophilus species, Actinobacillus, Cardiobacterium, Eikenella, Kingella; CT = computed tomographic)

Signs of immunocompromise may include cachexia or oral candidiasis. The oropharynx should be examined for redundant tissue consistent with the findings in obstructive sleep apnea. A fine hand tremor, exophthalmos, eyelid lag, or hyperreflexia suggests hyperthyroidism. An elevated blood pressure in association with night sweats may prompt an evaluation for pheochromocytoma. Signs of endocarditis such as splinter hemorrhages (dark red linear streaks under the nails), Janeway lesions (small, nodular hemorrhages on palms and soles), Osler's nodes (small, ten-

der nodules on finger or toe pads), and a heart murmur should be sought as well.

Evaluation When History and Physical Are Unrevealing

If the history and physical examination fail to reveal the possible etiology of the patient's symptoms, consider obtaining a complete blood count, purified protein derivative test, chest radiograph, and thyroid-stimulating hormone test. These tests are widely available, not particularly costly, and help rule out many of the potential diagnoses. An HIV test and erythrocyte sedimentation rate (ESR) evaluation may be added if necessary (*Figure 1*). The ESR evaluation helps rule out disorders that may cause night sweats but otherwise are relatively silent early in their course, such as endocarditis and Takayasu's arteritis.

An elevated ESR and positive blood cultures are present in more than 90 percent of cases of endocarditis. An echocardiogram also may assist in the evaluation of a patient with suspected endocarditis.

Takayasu's arteritis is a chronic inflammatory disease involving the aorta and its branches. Its cause is unknown. It also has been called pulseless disease because of the physical examination finding of diminished pulses in the upper extremities. A patient with Takayasu's arteritis may present with malaise, fever, night sweats, arthralgias, and weight loss months before vessel involvement is noted. An elevated ESR is a characteristic, but nonspecific laboratory finding. Diagnosis would be confirmed by aortography.

If the screening tests are normal and nocturnal GERD is suspected, a trial of antireflux measures may be considered. If the patient continues to complain of night sweats, a diary of the patient's temperature variations through the night may be helpful in revealing the presence or absence of febrile micropulses. Febrile pulses should reprompt a search for lymphoma or endocarditis. Blood cultures should be obtained to include cultures designated for the fastidious, gram-negative HACEK (Haemoph-

Blood cultures for fastidious, gram-negative organisms may be necessary if endocarditis is suspected and routine cultures do not grow bacteria.

ilus species, *Actinobacillus*, *Cardiobacterium*, *Eikenella*, and *Kingella*) organisms, which are not found with routine culture methods. Computed tomographic scans of the chest and abdomen, and a bone marrow biopsy to evaluate for silent neoplastic or granulomatous disease would complete the work-up.

If all studies are negative, the patient can be reassured that the night sweats are most likely benign (may be the result of over-bundling). The patient should be taught to do self lymph node examinations and report any changes noted in the absence of active infection. The patient should report development of any new symptoms and continue annual health examinations.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Navy medical department or the U.S. Navy at large.

The authors indicate that they do not have any conflicts of interest. Sources of funding: none reported.

The Authors

ANTHONY J. VIERA, LCDR, MC, USNR, is currently a staff family physician at Naval Hospital Jacksonville, Jacksonville, Fla. Dr. Viera received his medical degree from the Medical University of South Carolina, Charleston, and completed a family practice residency at Naval Hospital Jacksonville.

MICHAEL M. BOND, LT, MC, USNR, is currently a staff family physician at National Naval Medical Center, Bethesda, Md. Dr. Bond received a doctor of osteopathic medicine degree from Midwestern University—Chicago College of Osteopathic Medicine, Downers Grove, Ill. He completed a family practice residency at Naval Hospital Jacksonville.

SCOTT W. YATES, M.D., M.B.A., is currently in private practice in Dallas. Dr. Yates received his medical degree from the University of Texas Southwestern Medical School, Dallas, and completed residency training in internal medicine at the Methodist Hospital in Memphis, Tenn.

Address correspondence to Anthony J. Viera, LCDR, MC, USNR, Naval Hospital Jacksonville, Family Practice Department, 2080 Child St., Jacksonville, FL 32214-5005. Reprints are not available from the authors.

REFERENCES

1. Smetana GW. Diagnosis of night sweats. *JAMA* 1993;270:2502-3.
2. Levison ME. Pneumonia, including necrotizing pulmonary infections (lung abscess). In: Isselbacher KJ, ed. *Harrison's Principles of internal medicine*. 13th ed. New York: McGraw-Hill, 1994:1184-91.
3. Moore CB. Night sweats in prostatic cancer. *JAMA* 1969;208:155.
4. Morris GC, Thomas TP. Night sweats—presentation of an often forgotten diagnosis. *Br J Clin Pract* 1991;45:145.
5. Adlakha A, Kang E, Adlakha K, Ryu JH. Nonproductive cough, dyspnea, malaise, and night sweats in a 47-year-old woman. *Chest* 1996;109:1385-7.
6. McCluskey DR, Buckley MR, McCluggage WG. Night sweats and swollen glands. *Lancet* 1998;351:722.
7. Gordon DS. Night sweats: two other causes. *JAMA* 1994;271:1577.
8. Raff SB, Gershberg H. Night sweats. A dominant symptom in diabetes insipidus. *JAMA* 1975;234:1252-3.
9. Fred HL. Night sweats. *Hosp Pract* 1993;28:88.
10. Abouafia DM, Mitsuyasu RT. Neoplasms in the acquired immunodeficiency syndrome. In: Kelley WN, Schlossberg D, eds. *Textbook of internal medicine*. 3d ed. Philadelphia: Lippincott-Raven, 1997:1895-7.
11. Bennett JE. Histoplasmosis. In: Isselbacher KJ, ed. *Harrison's Principles of internal medicine*. 13th ed. New York: McGraw-Hill, 1994:856-7.
12. El-Ani AS, Elwood CM. A case of coccidioidomycosis with unique clinical features. *Arch Intern Med* 1978;138:1421-2.
13. Gobbi PG, Pieresca C, Ricciardi L, Vacchi S, Bertoloni D, Rossi A, et al. Night sweats in Hodgkin's disease. A manifestation of preceding minor febrile pulses. *Cancer* 1990;65:2074-7.
14. Lambore S, McSherry J, Kraus AS. Acute and chronic symptoms of mononucleosis. *J Fam Pract* 1991;33:33-7.
15. McAllister M. Menopause: providing comprehensive care for women in transition. *Lippincott's Prim Care Pract* 1998;2:256-70.
16. Gale EA, Tattersall RB. Unrecognised nocturnal hypoglycaemia in insulin-treated diabetics. *Lancet* 1979;1:1049-52.
17. Foster DW. Diabetes mellitus. In: Isselbacher KJ, ed. *Harrison's Principles of internal medicine*. 13th ed. New York: McGraw-Hill, 1994:1979-2000.
18. Reynolds WA. Are night sweats a sign of esophageal reflux? [Letter]. *J Clin Gastroenterol* 1989;11:590-1.
19. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 1993;328:1230-5.
20. Duhon DR. Night sweats: two other causes. *JAMA* 1994;271:1577.
21. Physicians' desk reference. 53rd ed. Montvale, N.J.: Medical Economics, 1999.