

CLINICAL REVIEW

Night Sweats: A Systematic Review of the Literature

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Background: Much of primary care involves helping patients manage symptoms. Nighttime sweating is a symptom linked to menopause, malignancies, autoimmune diseases, and infections. However, in primary care settings, night sweats are commonly reported by persons without these conditions.

Methods: We conducted a literature review, focusing on questions about definition, mechanisms, incidence/prevalence, measurement, clinical causes, evaluation, treatment, and prognosis. We limited our search to English language studies of adult humans published since 1966. Because studies of estrogen and androgen deficiency states had been reviewed by others, we excluded them. Search criteria were developed for each question. Publications meeting criteria were reviewed by the first 2 authors and consensus was reached through discussion.

Results: Prevalence estimates ranged from 10% among older primary care patients to 60% among women on an obstetrics inpatient unit. Life expectancy of primary care patients reporting night sweats did not appear to be reduced. Although many clinical causes have been suggested, most are not well supported. Algorithmic approaches to evaluation are not evidence-based. Alpha adrenergic blockers may reduce night sweats in patients taking serotonin reuptake inhibitors. Thalidomide and thioridazine may benefit some terminal cancer patients with night sweats.

Conclusions: The symptom, night sweats, appears to be nonspecific. Many questions about causation, evaluation, and management remain unanswered. (J Am Board Fam Med 2012;25:878–893.)

Keywords: Diaphoresis, Night Sweats, Symptom, Systematic Review, Thermoregulation

Bothersome symptoms, one fourth of which are chronic or recurrent, account for >50% of outpatient encounters.¹ At least one third to one half of these symptoms are never fully explained and others are particularly difficult to interpret. Included among these is the symptom, night sweats.

Patients' concerns about night sweats are fairly common. Ely² identified questions about the cause of night sweats as among the most frequent questions posed by patients for which he could find no evidence-based answer. In an effort to clarify what is currently known about night sweats, the authors

undertook a systematic review of the medical literature.

Methods

We searched the Medline database (Ovid Technologies) from 1966 through 2011 for all articles containing the Medical Subject Heading sweating combined with the text phrase night, which yielded 84 citations before applying the inclusion and exclusion criteria. We also searched using the text phrases night sweats and nocturnal diaphoresis. Text word searching was used because there are no Medical Subject Heading terms specifically addressing night sweats or nocturnal diaphoresis. We then limited our retrieval to English language and to studies categorized as adult and human, alone and in combination with category-specific terms (eg, specific diseases and conditions). We then excluded articles related to estrogen, menopause, perimenopause, and testosterone deficiency. This yielded 509 distinct citations. Reference lists from those publications provided additional citations.

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We also looked at the references provided in the section on night sweats authored by Smetana in Up-to-Date Version 19.6 (Up-To-Date, Inc), an electronic medical resource for clinicians and patients.³

To focus our search for information, we developed a set of 8 questions we believed to be of importance to clinicians and patients trying to understand and manage this symptom: (1) How have night sweats been defined? (2) What mechanisms could be responsible for night sweats? (3) What incidence, prevalence, and epidemiologic variables associated with night sweats are reported in population-based studies? (4) To what extent are subjective reports of night sweats associated with objectively measured night sweats, and how can discrepancies be explained? (5) What clinical conditions have been associated with night sweats? (6) How should patients bothered by night sweats be evaluated? (7) Aside from treatment of the underlying cause, how can night sweats be reduced/treated? (8) Are night sweats associated with adverse health outcomes?

More specific inclusion and exclusion criteria were then developed for several of the 8 focus questions. For question 3, we limited our review to studies that described a population defined by site rather than medical condition and that assessed all, or a random sample, of members. For factors associated with night sweats, studies were included if there was a comparison group and the researchers

used inferential statistics to compare the groups on variables associated with night sweats.

For question 5, we made a list of all the proposed clinical causes of night sweats found in review articles, online summaries, and book chapters. For each proposed condition we conducted searches of the English language literature using the name of the condition plus “night sweats.” We then only included cohort studies with a control group, case series of ≥ 10 individuals, or smaller case series when there was specific information about whether the night sweats resolved with treatment of the underlying condition. A number of studies involving patients with neoplasias were excluded because they grouped “B-type symptoms” (fever, night sweats, and weight loss) together.

The first 2 authors independently reviewed all relevant articles and then met to review and resolve any disagreements regarding their inclusion in the review. Finally, all authors met and reached consensus on final text and tabular content.

Results

How Have Night Sweats Been Defined?

The published definitions that we were able to locate are shown in Table 1. For the most part, definitions for night sweats appear to have been developed independently by these authors or passed down by word of mouth since they were rarely referenced. They vary primarily by their severity requirements with some authors proposing

Table 1. Published Definitions of Night Sweats

| Authors/Year | Purpose | Definition |
|--|-----------------------|--|
| Lister et al, 1989 ⁴⁷ | Clinical and research | “Recurrent drenching night sweats during the previous month” |
| Smetana, 1993 ⁵³ | Clinical | “Drenching sweats that require changing bed clothes” |
| Holtzclaw, 1996 ⁵⁴ | Clinical | “A nonspecific term that refers to heavy sweating during sleep” |
| Chambliss, 1999 ⁴⁴ | Clinical | “Unusual sweating that occurs only or mainly at night” |
| Mold et al, 2008 ³⁸ | Clinical | “Sweating excessively during the night during the past month” |
| Mold et al, 2002 ³⁷ | Research | “Sweating at night even when it is not excessively hot in your bedroom during the past month” |
| Lea and Aber, 1985 ⁵⁵ | Research | Mild: “no bathing or change of clothing required” Moderate: “sleep disturbed by need to arise and wash face or other affected body areas, but no clothing change” Severe: “both or clothing change required” |
| Quigley and Baines, 1997 ⁵⁶ | Research | Mild: “no change in bedclothes necessary; sweating only reported after specific questioning” Moderate: “no change of clothing necessary; washing of affected areas required; sweating volunteered by patients as a specific problem” Severe: “volunteered by patients as drenching sweats requiring a change of clothing or bed linen or both” |

subclassifying night sweats into mild, moderate, and severe. Some definitions specify a time interval, but none includes frequency criteria. Some require the absence of excessive daytime sweating, whereas one restricts nighttime sweating to sweating that occurs only during sleep. Patterns and locations of sweating (palmar/plantar, axillary, facial, truncal, diffuse, etc) are not specified. Most definitions exclude environmental factors such as room temperature or humidity. No published definition requires confirmation by an external observer or an objective test. None of the definitions requires that the symptom be bothersome to the individual or to others.

What Mechanisms Could Be Responsible for Night Sweats?

Regulation of sweating is complex, involving both thermoregulatory and nonthermoregulatory mechanisms. Despite a very large body of literature on physiological mechanisms related to sweating in humans,^{4–6} we found only a few studies examining mechanisms associated specifically with night sweats.^{7–9} Sweating helps to reduce core body temperature when it rises above certain limits or thresholds, called the thermoneutral zone (TNZ).¹⁰ Thermoregulatory defenses such as sweating are stimulated when threshold levels in core body temperatures trigger a hypothalamic response.¹¹ This can happen because of environmental heat exposure or decreased heat dissipation (eg, excessive clothing or bed coverings) or as a result of increased heat production (eg, excessive muscular activity). Release of inflammatory mediators during infections, autoimmune diseases, and malignancies can temporarily raise the TNZ, inducing chills and shivering that causes core body temperature to rise. Sweating occurs when the levels of these mediators and the TNZ return to normal.¹² Diurnal patterns of temperature elevation have been explained by nocturnal rise and fall of viral loads or bacteremic showers and periodic increases in interleukins (IL-1 α , IL-2, IL-4, IL-6) and tumor necrosis factor but no research was found to support this as a common mechanism responsible for night sweats.

Circadian variations influence sweating and other thermoregulatory responses during exercise^{13,14} and throughout the night with sweat thresholds lower in the morning than at any other time of day.¹⁵ Physical conditioning appears to reduce postexercise sweating thresholds, so sweating is promoted at somewhat

lower temperatures than expected.¹⁶ Whether this might put conditioned athletes at risk for night sweats has not been postulated in the literature; however, Kreider et al listed night sweats as one of the major symptoms of sports overtraining by prevalence in the literature.¹⁷ Empirical evidence shows that hypothalamic adjustments in thermoregulation occurs after 8 to 14 days of exercise in a hot environment.¹⁸

Acute and chronic anxiety states and physical conditioning can increase the responsiveness of sweat glands.^{5,19–21} Conditions that reduce the range (difference between lower and upper limits) of the TNZ can result in the need for more frequent adjustments and therefore more frequent sweating. This is believed by some to be a mechanism contributing to sweating during menopausal hot flashes.²²

Body temperature tends to fall slightly in the evening, and lower core temperature appears to facilitate sleep.²³ Depression is associated with loss of the usual reduction in core temperature that occurs in the evening and nighttime.^{24–30} One study found that depressed patients sweat more at night than control subjects but only during the 20 minutes just before the onset of rapid eye movement sleep.³¹ Sweating increases with increasing depths of nonrapid eye movement sleep. It is reduced during rapid eye movement sleep in the absence of emotionally charged dreams despite increases in brain glucose metabolism, increased temperature in many parts of the brain, increase skin sympathetic activity, and increased heart rate.^{31–36}

Nonthermoregulatory regulation of sweating could also be involved in some people who report night sweats. Sweating can result from a wide variety of medications that affect the sympathetic nervous system, the thermoregulatory center, or the sweat glands; and from sleep stage disturbances, autonomic nervous system disorders, medullary and spinal cord abnormalities, reductions in serum osmolality or abnormalities of osmoreceptor function, hypercapnia, and direct sweat gland stimulation by pressure, heat, trauma, or toxins.³ However, we could find no published studies beyond letters to the editor or single case studies linking any of these potential mechanisms to night sweats.

Some people who report night sweats may simply be more aware or concerned about nighttime sweating because they are awake for other reasons.

Table 2. Incidence and Prevalence of Night Sweats in Various Populations

| Authors/Year | Population (Country) | N | Prevalence and Incidence Estimates |
|--|--|------|---|
| Lea and Aber, 1985 ⁵⁵ | Hospital inpatients (US) | 174 | Prevalence: medicine: 33% Surgery: 33% Obstetrics: 60% Gynecology: 27% |
| Reynolds, 1989 ⁵⁷ | Consecutive patients seen in a gastroenterology practice* | 200 | Prevalence: 41% |
| Quigley and Baines, 1997 ⁵⁶ | Hospice inpatients patients, consecutive admissions (UK) | 100 | Prevalence: 16% overall 12% soaked bed clothes |
| Mold et al, 2002 ³⁷ | Primary care patients, consecutive visits (US) | 2267 | Prevalence: all: 41% Nighttime only: 23% 4–7 nights per week: 16% |
| Mold et al, 2004 ⁴⁰ | Primary care patients >65 years of age, recruited from billing records (US) | 795 | Prevalence: 10% |
| Mold et al, 2006 ³⁹ | Primary care patients, consecutive visits (US) | 363 | Prevalence: 34% 17% soaked bed clothes |
| Mold et al, 2008 ³⁸ | Consecutive patients undergoing polysomnography (US) | 282 | Prevalence: 28% |
| Mold and Lawler, 2010 ⁴⁶ | Consecutive patients >65 years of age enrolled in a primary care geriatric continuity clinic (US)* | 682 | Prevalence: 14% past year |
| Mold and Lawler, 2010 ⁴⁶ | Primary care patients >65 years of age, recruited from billing records (US) | 795 | Incidence (annual): 5% |
| Suwanprathes et al, 2010 ⁵⁸ | Random population sample, (Bangkok, Thailand)* | 4680 | Prevalence: 4.4% |

*Night sweats definition not provided in report.

Some individuals may be less tolerant of either sweat or its cooling effect or anxious about symptoms, like night sweats, that might indicate illness. One study, which reported an association between night sweats and sleep problems in men, supports this hypothesis.³⁷ Two studies reporting associations between subjective night sweats and awakening due to pain or a bitter taste also support it.^{38,39} In the 2004 study by Mold et al,⁴⁰ individuals who reported night sweats were also more likely to report many other symptoms about which they were queried. In a primary care population in South Korea in which the researchers used methods identical to those used in the 2002 study by Mold et al, researchers found a prevalence of only 21% compared with 41% in the US study, suggesting that either night sweats are less common in South Korea or that South Koreans are less likely to notice or be willing to report this symptom.⁴¹

What Incidence, Prevalence, and Epidemiologic Variables Associated with Night Sweats Are Reported in Population-based Studies?

In all the studies reviewed, individuals were asked specifically about night sweats and did not sponta-

neously report the symptom. In Table 2 we have listed the incidence and prevalence rates of night sweats reported in these populations. (The definitions used are listed in Table 1.) Table 3 lists variables found to be associated with the subjective report of night sweats in these population-based studies.

Prevalence estimates have varied from 10% in older patients recruited from primary care billing records to 41% in consecutive patients being seen in primary care or gastroenterology outpatient settings. The only incidence estimate (5%) was in the geriatric cohort recruited from primary care billing records.

To What Extent Are Subjective Reports of Night Sweats Associated with Objectively Measured Sweating?

We found no published studies addressing this question.

What Clinical Conditions Have Been Associated with Night Sweats?

Night sweats have been associated with a long list of clinical conditions.^{42–45} Table 4 lists all the

Table 3. Variables Associated with Night Sweats in Epidemiological Studies

| Authors/Year | Study Design | Analytic Method | Factors Associated with Night Sweats |
|----------------------------------|-----------------|---------------------|--|
| Lea and Aber, 1985 ⁵⁵ | Cross-sectional | χ^2 | Aspirin or acetaminophen use ($P < 0.05$) |
| Mold et al, 2002 ³⁷ | Cross-sectional | Logistic regression | All: panic attacks (OR, 4.8; 1.7–13.6)* Men: sleep problems (OR, 2.5; 1.7–3.8) Women: hot flashes (OR, 3.4; 1.1–10.0) Panic attacks (OR, 4.5; 1.2–16.7) |
| Mold et al, 2004 ⁴⁰ | Cross-sectional | Logistic regression | Age (OR, 0.94/year; 0.89–0.98) Fever (OR, 12.6; 6.6–24.1) Numbness hands/feet (OR, 3.3; 1.9–5.8) Muscle cramps (OR, 2.8; 1.5–5.2) Impaired vision–subjective (OR, 2.5; 1.4–4.3) Impaired hearing–subjective (OR, 1.8; 1.0–3.3) Symptoms of anxiety and stress ($P = 0.001$) Symptoms of dysphoria ($P = 0.001$) Pain and discomfort ($P < 0.0001$) |
| | | Cluster analysis | Daytime tiredness (OR, 2.0; 1.1–3.5) Waking with bitter taste (OR, 1.9; 1.2–3.2) Awakening with pain (OR, 1.9; 1.2–3.0) Legs jerk in sleep (OR, 1.8; 1.1–3.0) |
| Mold et al, 2006 ³⁹ | Cross-sectional | Logistic regression | Trouble breathing at night (OR, 2.8; 1.5–5.2) Awakened by aches and pains (OR, 3.2 (1.8–5.8) Epworth Sleepiness Scale (OR, 1.1 (1–1.1) |
| Mold et al, 2008 ³⁸ | Cross-sectional | Logistic regression | |

*ORs with 95% CIs.

CI, confidence interval; OR, odds ratio.

conditions for which we found data meeting our inclusion and exclusion criteria. In Table 5, we have listed the prevalence of night sweats among individuals in all the larger case series (≥ 10 cases) believing that comparing this information with the prevalence estimates from Table 2 might provide additional information regarding the strength of the associations between night sweats and specific medical conditions. Some series therefore appear in both Table 4 and Table 5.

Although mentioned in a least one review or book chapter, we could find no published studies meeting our inclusion criteria that support an association between night sweats and any of the following conditions: mixed connective tissue disease, polymyalgia rheumatica, polymyositis, dermatomyositis, Schnitzler syndrome, scleroderma, systemic lupus erythematosus, congestive heart failure, carcinoid syndrome, insulinoma, pheochromocytoma, brucellosis, dental abscess, lung abscess, fungal pneumonia, sinusitis, Castleman disease, oat cell carcinoma of the lung, renal cell carcinoma, reticulum cell carcinoma, splenic hamartoma, autonomic neuropathy, autonomic

dysreflexia, dysautonomia, anterior hypothalamic lesions, dorsolateral midbrain lesions, Hines-Bannick syndrome, multiple sclerosis, myasthenia gravis, Parkinson disease, pontine lesions, spinal cord transection, syringomyelia, bulimia, rickets, scurvy, alcoholism, anxiety, situational stress, night terrors, alcohol or benzodiazepine withdrawal, narcotic withdrawal, eosinophilic pneumonia, gout, immersion foot syndrome, Pink disease, or uremia. We also found no qualifying evidence for an association between night sweats and the following medications: anticholinergics, antipyretics, antitussives, antispasmodics, acetaminophen, β -blockers, decongestants, insulin, meperidine, nonsteroidal anti-inflammatory drugs, niacin, oral hypoglycemics, pilocarpine, salicylates, or γ -butyrolactone.

How Should Patients Bothered by Night Sweats Be Evaluated?

Several approaches to the evaluation of patients reporting night sweats have been proposed.^{3,42,43} However, no published studies have evaluated the accuracy or cost-effectiveness of specific night sweat evaluation protocols.

Table 4. Evidence Supporting Associations between Clinical Conditions and Elicited Subjective Night Sweats

| Clinical Disorder | | N | Comparative Data | Proportion with Night Sweats (if Comparison Group) or Proportion in Whom Night Sweats Resolved with Treatment |
|--------------------|--|------|------------------|--|
| Autoimmune | POEMS syndrome | 1 | No | Disorder treated, night sweats resolved ⁵⁹ |
| | Rheumatoid arthritis | 1 | No | Disorder treated, night sweats resolved ⁶⁰ |
| | Giant cell arteritis | 1 | No | Disorder treated, night sweats resolved ⁶¹ |
| Cardiovascular | Aortic dissection, chronic | 1 | No | Disorder treated, night sweats resolved ⁶² |
| | Nocturnal/Prinzmetal angina | 1 | No | Disorder treated, night sweats persisted ⁶³ |
| Endocrine | Diabetes insipidus | 1 | No | Disorder treated/night sweats resolved ⁶⁴ |
| | Hyperthyroidism | 1 | No | Disorder treated, night sweats resolved ⁶⁵ |
| GI | GERD | 12 | No | Disorder treated, night sweats resolved (100%) ⁵⁷ |
| Infectious disease | HIV | | | |
| | P24 Ag+, HIV– | 3816 | Yes | 5/58 (9%) |
| | P24 Ag–, HIV– | | | 38/3758 (1%) ⁶⁶ |
| | HIV-negative | 328 | Yes | 20/328 (6%) night sweats |
| | Acute HIV+ | | | 59/328 (18%) |
| | Chronic HIV+ | | | 39/328 (12%) ⁶⁷ |
| | HIV seroconverters | 110 | Yes | 18/22 (82%) night sweats |
| | Nonseroconverters | | | 6/88 (7%) ⁶⁸ |
| | IV drug users, HIV+ | 223 | Yes | 33/124 (27%) night sweats |
| | IV drug users, HIV– | | | 13/99 (13%) ⁶⁹ |
| | Hodgkin disease, HIV+ | 16 | Yes | 2/5 (40%) night sweats |
| | Hodgkin disease, HIV– | | | 3/11 (27%) ⁷⁰ |
| | HIV+ with persistent generalized lymphadenopathy | 88 | Yes | 12/38 (32%) night sweats |
| | HIV+ with lymphoma | | | 7/50 (14%) ⁷¹ |
| | TB patients, HIV+ | 158 | Yes | 24/48 (50%) |
| | TB patients, HIV– | | | 11/31 (35%) ⁷² |
| | HIV patients, TB+ | 899 | Yes | 15/44 (34%) night sweats |
| | | | | 108/855 (14%) ⁷³ |
| | HIV patients, TB– | 31 | No | 27/31 (87%) 4.8 episodes per week pretreatment; 1.6 episodes/week posttreatment ⁷⁴ |
| | HIV+, MAC | 25 | No | 21/25 (84%) had night sweats pretreatment; post treatment one of 25 (4%) had night sweats ⁷⁵ |
| | | 24 | No | 18/24 (75%) had night sweats pretreatment; posttreatment 6/24 (25%) had night sweats ⁷⁶ |
| | | 187 | No | 67/187 (36%) had night sweats pretreatment; posttreatment 40% had fewer night sweats when treated with 4 drugs; |
| | | 1748 | Yes | 70% had fewer when treated with 3 drugs ⁷⁷ |
| | HIV+, TB+ | | | 88/267 (33%) had HIV+ with TB+ |
| | HIV+, TB– | | | 191/1471 (13%) had HIV+ without TB |
| | HIV+, TB+ | | | 128/267 (48%) had night sweats past 24 hours |
| | HIV+, TB– | | | 368/1471 (25%) ⁷⁸ had night sweats past month |
| | Viral URI/Mononucleosis | 356 | Yes | Cohort matched on age, sex, date of diagnosis; night sweats more common in mononucleosis ($P = .000001$) ⁷⁹ |

Continued

Table 4. Continued

| Clinical Disorder | | N | Comparative Data | Proportion with Night Sweats (if Comparison Group) or Proportion in Whom Night Sweats Resolved with Treatment |
|----------------------------|---|------|------------------|--|
| | Tuberculosis | | | |
| | Hospitalized patients awaiting TB diagnosis (44 were TB-positive) | 101 | Yes | No significant difference in rate of night sweats between those with TB and those without TB ⁸⁰ |
| | Hospitalized patients in isolation awaiting diagnosis | 563 | Yes | 26/47 (55%) of TB patients reported night sweats; 141/516 (27%) of non-TB patients reported night sweats ^{52,81} |
| | Emergency department patients with sputum tested for TB | 145 | Yes | 13/28 (46%) with positive sputum reported night sweats; 29/113 (26%) with negative sputum reported night sweats ⁵¹ |
| | Hospitalized patients awaiting TB diagnosis | 101 | Yes | 44/100 were TB-positive; no association between reported night sweats and TB positivity ⁸⁰ |
| | Cysticercosis (<i>Coenurus</i>) | 1 | No | Case history; night sweats and lymphoma-like symptoms ceased with excision of larval cysts ⁸² |
| Medications | Antidepressants | | | |
| | Sertraline | 1 | No | Case history; night sweats resolved with discontinuation of sertraline suggest night sweats may be sign of "serotonin syndrome" ⁸³ |
| | Venlafaxine | 1 | | Case history; night sweats resolved when drug was discontinued ⁸⁴ |
| | Efavirenz | 1 | No | Case history; night sweats resolved with discontinuation of drug ⁸⁵ |
| Neoplastic and hematologic | Hemangioma, hepatic | 1 | No | Night sweats resolved when hemangioma removed ⁸⁶ |
| | Lymphoma | 85 | No | 4/14 (29%) with EBV Hodgkin disease had night sweats; in 75%, night sweats improved after treatment of disease ⁸⁷ |
| | Lymphadenopathy | 258 | Yes | 14/85 (17%) patients with TB had night sweats 24/98 (25%) patients with lymphoma had night sweats 5/17 (29%) patients with metastatic cancer had night sweats 0/6 (0%) of patients with sarcoidosis had night sweats 5.36 (14%) of patients with nonspecific reactive hyperplasia had night sweats ⁸⁸ |
| | Myelofibrosis | 24 | No | 21/24 (88%) night sweats improved >50% with JAK1 and JAK2 inhibitor treatment ⁸⁹ |
| Psychiatric/behavioral | Prostate cancer, inflammatory | 1 | No | Case study; treated, night sweats resolved ⁹⁰ |
| | Depression | | | |
| | HIV+ and depressed | 62 | Yes | 16/28 (57%) had night sweats |
| | HIV+ and not depressed | | | 7/34 (21%) ⁹¹ |
| | Night terrors | 1 | No | Case study, night sweats resolved with treatment for posttraumatic syndrome ⁹² |
| Sleep disturbance | Panic disorder | 175 | No | 26/175 (15%) of attacks occurred at night; 46/175 (26%) associated with sweating ⁹³ |
| | Obstructive sleep apnea | | | |
| | Snoring/daytime sleepiness | 4680 | Yes | 14/202 (14%) with snoring/sleepiness; 179/4478 (4%) with no snoring/sleepiness ⁵⁸ |
| | No snoring/sleepiness | | | |
| | Apnea-hypopnea index ≥ 15 | 282 | Yes | Subjective night sweats in 28/114 (25%) |
| | Apnea-hypopnea index <15 | | | Subjective night sweats in 50/167 (30%) ³⁸ |

GI, gastrointestinal; GERD, gastroesophageal reflux disease; IV, intravenous; TB, tuberculosis; URI, upper respiratory infection; EBV, Epstein-Barr virus; MAC, *Mycobacterium avium* complex.

Table 5. Prevalence of Subjective Night Sweats (Elicited) among Patients with Medical Conditions

| Condition | Prevalence in Specific Samples |
|---|--|
| Autoimmune diseases | |
| Polymorphic reticulosis | 7/34 (21%) ⁹⁴ |
| Endocrine diseases | |
| Diabetes mellitus | 14/22 (64%) with nocturnal hypoglycemia ⁹⁵ |
| Obesity, severe in residential treatment of obesity | 20/152 (13%) men; 47/234 (20%) women ⁹⁶ |
| Infectious diseases | |
| Adenovirus, immunocompromised | 4/15 (27%) ⁹⁷ |
| Endocarditis, <i>Cardiobacterium hominis</i> | 14/61 (24%) ⁹⁸ |
| HIV, acute | 5/58 (9%) of p24 Ag+/HIV− ⁶⁶ 7/20 (35%) ⁹⁹ 59/328 (18%) ⁶⁷ 88/151 (58%) ¹⁰⁰ |
| HIV, chronic | 18/22 (82%) ⁶⁸ 39/328 (12%) ⁶⁷ 19/49 (31%) ¹⁰¹ 126/899 (14%) ⁷³ 7/34 (21%) ⁹¹ 40/168 (24%) ¹⁰² 26/100 (26%) ¹⁰³ 62/109 (57%) ¹⁰⁴ 144/205 (70%) (average once/week) ¹⁰⁵ 18/176 (10%) with no AIDS-defining illnesses ⁵⁰ |
| HIV+, IV drug users | 33/124 (27%) ⁶⁹ |
| HIV+, generalized lymphadenopathy | 12/38 (32%) ⁷¹ |
| HIV+, <i>Mycobacterium avium</i> complex | 36/91 (40%) ¹⁰⁶ 27/31 (87%) ⁷⁴ 21/25 (84%) ⁷⁵ 18/24 (75%) ⁷⁶ 67/187 (36%) ⁷⁷ |
| HIV+, <i>Pneumocystis carinii</i> pneumonia | 46/99 (46%) ¹⁰⁷ |
| HIV+, pneumonia, bacterial | 22/94 (23%) ¹⁰⁷ |
| HIV+, tuberculosis | 66/85 (78%)* ¹⁰⁸ 306/899 (34%) ⁷³ With pleural effusion 54/65 (83%) ¹⁰⁹ 19/36 (53%) ¹⁰⁷ 24/48 (50%) ⁷² |
| Pneumonia, bacterial | 104/329 (32%) ¹¹⁰ |
| Tuberculosis | 22/40 (55%) ¹¹¹ Young adults 179/419 (43%), older adults 15/45 (33%) ¹¹² Young adults 34/73 (46%), older adults 17/72 (24%) ¹¹³ Young adults 48/88 (55%), older adults 9/50 (18%) ¹¹⁴ Young adults 14/29 (48%) ¹¹⁵ Older adults 2/35 (6%) ¹¹⁵ 12/17 (71%) ¹¹⁰ 24/98 (25%) TB patients presenting with lymphadenopathy ⁸⁸ 148/313 (48%) of TB outpatients ¹¹⁶ 11/31 (35%) of TB outpatients ⁷² |
| Tuberculosis, Beijing type | Young adults 14/29 (48%) Older adults 2/35 (6%) ¹¹⁵ |

Continued

Table 5. Continued

| Condition | Prevalence in Specific Samples |
|-------------------------------------|--|
| Tuberculosis | |
| Beijing | 308/880 (35%) |
| Non-Beijing type | 378/880 (43%) ¹¹⁷ |
| Beijing | 2/21 (10%) |
| Non-Beijing type | 7/20 (35%) ¹¹⁸ |
| Tuberculosis, extrapulmonary | 99/209 (48%) of patients with abdominal TB ¹¹⁹ |
| Medications | 28/54 (54%) with extrapulmonary TB ¹¹⁶ |
| Oblimersen sodium | 7/40 (18%) ¹²⁰ |
| Tacatuzumab | 2/12 (17%) ¹²¹ |
| Miscellaneous diseases | |
| Inflammatory pseudotumor | 2/25 (8%) ¹²² |
| Neoplastic and hematologic diseases | |
| Acute lymphocytic leukemia | 8/10 (80%) ¹²³ |
| Acute myelocytic leukemia | 8/22 (36%) ¹²³ |
| Lymphoma | 14/85 (17%) of those presenting with lymphadenopathy ⁸⁸ 7/50 (14%) with generalized lymphadenopathy ⁷¹ 3/10 (30%) lymphoma primary in liver ¹²⁴ 4/14 (29%) with EBV Hodgkin disease ⁸⁷ 5/12 (42%) with pancreatic lymphoma ⁸⁷ |
| Metastatic, mixed | 5/17 (29%) of those presenting with lymphadenopathy ⁸⁸ |
| Mesothelioma, peritoneal | 3/17 (18%) ¹²⁵ |
| Mixed, terminal | 12/77 (16%) admission to hospice 19/77 (25%) just before death ¹²⁶ |
| Myelofibrosis | 255/456 (56%) ¹²⁷ 8/22 (36%) ¹²⁸ 12/56 (21%) ¹²⁹ |
| Pancreatic cancer | 1/30 (3%) ¹³⁰ |
| Polycythemia vera | 198/405 (49%) ¹²⁷ |
| Prostate cancer, inflammatory | 7/12 (58%) ⁹⁰ |
| Thrombocytopenia, essential | 125/304 (41%) ¹²⁷ |
| Pulmonary diseases | |
| Eosinophilic pneumonia | 3/65 (5%) ¹³¹ |
| Sleep disorders | |
| Obstructive sleep apnea | 65/406 (16%) ¹³² |
| Toxic and metabolic diseases | |
| Silicone breast implants | 22/50 (44%) ¹³³ |

*Compilation of several case series.

EBV, Epstein-Barr virus; IV, intravenous; TB, tuberculosis.

Aside from Treatment of the Underlying Cause, How Can Night Sweats Be Ameliorated?

Few published studies have examined the question of symptomatic treatment of patients disturbed by frequent or severe night sweats, aside from the voluminous literature on postmenopausal night sweats and hot flushes. Those treatment approaches identified in our search are listed in Table 6.

Alpha adrenergic blockers may be effective in patients taking serotonin reuptake inhibitors. Nabilone, thalidomide, and thioridazine may be effective for

patients with terminal cancer, and etanercept may work in patient with myelofibrosis. However, these studies were too small and underpowered to yield reliable conclusions.

Is Nocturnal Sweating Associated with Adverse Health Outcomes?

Two population-based analyses were conducted comparing mortality rates in patients with and without night sweats.⁴⁶ Among one group of 842 primary care patients ≥ 65 years of age, 24% died

Table 6. Case Studies of Treatments Reported to Be Effective for Patients with Night Sweats

| Population | Treatment (Route of Administration Cited Only Where Provided) | Effectiveness |
|---|--|---|
| Patients with advanced cancer, referred for palliative care | Nabilone at 1 mg at bedtime or twice a day | 4/4 patients' night sweats improved (mean 5.75 points on the ESAS) ¹³⁴ |
| Patients with terminal cancer | Thalidomide at 100 mg at bedtime | 6 /7 patients improved an average of 4 points on a 5-point scale; recurred off of drug and improved again with reinstitution of drug ¹³⁵ |
| Patients with advanced local or metastatic cancer | Thioridazine at 10–30 mg at bedtime nightly | 15/17 patients reported improvement, poorly quantified ¹³⁶ |
| Patients with myelofibrosis | Etanercept at 25 mg subcutaneously twice weekly for up to 24 weeks | 6/8 (75%) improved with treatment ¹²⁸ |
| Patients treated for narcotic addiction with methadone | Desloratadine at 5 mg per day | 2/2 (100%) reported relief from night sweats within 1 day ¹³⁷ |
| Patients taking SSRIs | Mirtazapine at 15–60 mg per day | One case: dose-dependent reduction in night sweats ¹³⁸ |
| Patients taking SSRIs | Benztrapine at 0.5 mg at bedtime | One case: temporary relief from night sweats ⁸⁴ |
| Patients taking SSRIs | Terazosin at 1 mg per day to 2 mg at bedtime | Significant reduction in night sweats in 2/2 (100%), one after a day, the other after 4 weeks ¹³⁹ |
| Patients taking SSRIs | Terazosin | Significant reduction in night sweats in 20/20 (100%) ¹⁴⁰ |
| Patients taking SSRIs | Clonidine at 0.1 mg twice daily | One case: significant relief of night sweats after 3 week ¹³⁹ |

SSRIs, selective serotonin reuptake inhibitors; ESAS, Edmonton Symptom Assessment System (scored 0–10).

during the 8 years of follow-up. Night sweats persisted for >1 year in 50% of those who survived. No significant relationships were found between length of survival and history of night sweats in the month before enrollment after controlling for other predictors of mortality. The other analysis, described in the same journal article, involved 682 patients seen in a geriatrics clinic and followed for an average of 7 years. Again, there were no differences in survival between those who reported night sweats at time of the first visit and those who did not.

The occurrence of night sweats, as part of the so-called “B symptom complex,” has been considered a predictor of poor outcomes in patients with Hodgkin lymphoma,⁴⁷ yet when separated from the other B symptoms, weight loss and fever, the prognostic value of night sweats disappears.^{48,49} There is some evidence that in HIV-positive patients, the presence of night sweats is a weak predictor of earlier progression to AIDS.⁵⁰ However, this may simply reflect the presence of an undiagnosed AIDS-related condition.

Conclusions

Published definitions of night sweats vary primarily by required level of symptom severity. Lack of

standard definitions in literature hampers attempts to determine associations between night sweats and specific clinical conditions. We join the pleas of other clinicians for studies to include specific descriptors of how symptom-related information was obtained. Were symptoms volunteered, elicited, or were signs observed? Did descriptions include the duration, frequency, severity, and possibly the degree to which the symptom was bothersome to the patient or others? For night sweats and many other symptoms, it would be most helpful to know the incidence, prevalence, and duration in segments of the general population as well as those seen in clinical settings. There is a need to better understand stages in the natural history of a symptom: from onset to concern, to discussion with friends and family, to home-based remediation, to clinical presentation. Associations found in cross-sectional studies should be further examined in qualitative interviews, longitudinal cohorts, and considered in light of possible physiological mechanisms.

Mechanisms explaining patient-reported night sweats can be categorized as thermoregulatory, non-thermoregulatory, and increased awareness or vigilance. There is a lack of data on normal nocturnal sweating patterns for different age groups, sexes, and body locations. The accuracy of subjective reporting

of sweating has not yet been validated, although it likely to be greater when sweating is more frequent or severe. For more meaningful studies, patients should be asked to report immediately after objective recording periods as to whether they noticed their usual amount of sweating at the time of observation.

Although many causes of night sweats have been suggested in the literature, few have been firmly established. Clinical wisdom suggesting that tuberculosis causes night sweats appears to be valid in younger adults, those with extrapulmonary disease, and those who also have HIV/AIDS. However, the 2 studies that attempted to develop clinical prediction rules for tuberculosis, and included night sweats as an initial predictor, did not include the symptom in their final prediction models.^{51,52} The combination of HIV/AIDS and *Mycobacterium avium* complex appears most clearly to be associated with night sweats. The link between malignancies such as lymphoma and night sweats is less clear, and there is too little information available on which to base decisions about other medical conditions.

There has been little research on effectiveness of drugs to treat night sweats. Several small studies suggest that α adrenergic blocking agents may reduce night sweats in patients taking serotonin reuptake inhibitors, and the drugs thalidomide and thioridazine may benefit some terminal patients with cancer with night sweats. Anticholinergic agents are known to reduce sweating generally, and although no studies were found for this indication, these agents might be expected to reduce night sweats.

Most patients who report night sweats to their primary care clinicians probably do not have a serious disease causing the symptom. However, there is so little evidence regarding potential causes of night sweats that proposals or findings from any evaluation protocol must be viewed with extreme caution. Although it is reassuring that average life expectancy did not differ between those with night sweats and those without in 2 different studies of older primary care patients, very few of the patients in either study had night sweats that were severe.

This systematic review was conducted in search of published evidence to support the many assumptions of a symptom's clinical relevance. In the case of night sweats, we found very little evidence to support any sort of clinical recommendations. An additional intent of this article was to suggest a blueprint for reviewing and documenting research evidence about other symptoms. We have described the process and our

findings to inform future research on night sweats and to promote similar searches about other symptoms for which too little is known.

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