Hyperhidrosis: A Common Problem

Abstract

Focal hyperhidrosis is a disorder of idiopathic excessive sweating that typically affects the axillae, soles, palms, and face. This common problem may be associated with considerable physical, psychosocial, and occupational impairments. Current therapeutic strategies include topical aluminum salts, tap-water iontophoresis, oral anticholinergic agents, local surgical approaches, and sympathectomies. Although non-surgical treatment complications are typically transient, surgical adverse events may be permanent and significant. Considerable evidence suggests that botulinum toxin type A (BTX-A) injections into hyperhidrotic areas can considerably reduce focal sweating in multiple areas without major side effects. BTX-A has therefore shown promise as a potential replacement for more invasive treatments if topical options have failed.

Keywords: *hyperhidrosis, botulinum toxin, axilla*

Forum

Pre-test CME Quiz

Hyperhidrosis (HH) is characterized by sweating out of proportion with thermoregulatory requirements. Patients sweat excessively mostly in response to emotional and thermal stimuli, but also in response to other triggers (e.g., fine manual tasks, exercise) and even spontaneously.[1,2] Since no standardized definition of "excessive" sweating exists, clinicians typically define sweating as excessive or abnormal if it significantly interferes with daily life.

Clinical presentation

Hyperhidrosis is classified as either primary, also known as idiopathic, or secondary. The clinical presentation may be either focal or generalized. Primary hyperhidrosis most often presents as focal hyperhidrosis localized most commonly to the axillae, palms, feet or face.[3] Second-

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ary hyperhidrosis is usually generalized, however it can present in a localized, focal pattern. Secondary hyperhidrosis, as the name implies, is due to a variety of secondary causes, such as listed in Table 1.

Epidemiology and etiology

A survey of 150,000 households in the United States suggested that 2.8% of the population or 7.8 million people reported having unusual or excessive sweating, a figure comparable to psoriasis.[3,4,5] Although the condition affects males and females equally, females are more likely to seek medical attention for their symptoms. Nearly two-thirds of individuals with focal HH do not consult their physician regarding their condition,[3] presumably due to either social embarrassment or a lack of awareness that they are suffering from a treatable medical condition. As a result, the majority of individuals suffering from HH are undiagnosed and untreated. Primary focal HH most commonly affects individuals aged 25-64 years.[3] The average age of onset is 25 years, but it varies depending on the body area affected.[3,5,6] Palmar HH tends to begin in childhood and early adolescence,[5] while axillary HH tends to have a postpubertal onset.[3,5,6] The natural history of focal HH is uncertain, but some evidence suggests spontaneous regression over time, given the lower prevalence of the disorder among the elderly.[3,5]

The exact cause of focal hyperhidrosis is unknown, although sympathetic overstimulation of normal eccrine glands is the most likely etiology.[7] Interestingly, studies have shown an association between the sympathetic hyperactivity seen in hyperhidrosis with other autonomic disorders such as cardiac hyperexcitability. There is

Table 1: Differential Diagnosis of Generalized Hyperhidrosis

Drugs/Toxins
- Alcoholism
- Substance Abuse

Cardiovascular
- Heart failure
- Shock

Respiratory Failure

Neurologic
- Parkinson's disease
- Spinal cord injury
- Cerebrovascular accident

Endocrine
- Hyperthyroidism
- Diabetes Mellitus
- Pheochromocytoma
- Carcinoid syndrome
- Acromegaly
- Pregnancy
- Menopause

Infections

Malignancies
- Hodgkin's disease
- Myeloproliferative disorders

likely also a heritable component to this neurogenic overactivity, as 30 – 50% of patients have a positive family history.[8] The inheritance of focal HH is thought to be autosomal dominant with variable penetrance and expressivity.[9] Based on calculations of allelic probability, a child born to a parent with palmar HH has a 25% chance of also developing the disorder.[9]

Although there is evidence that age-related impairment in skin blood flow in response to passive heating may result in sweating irregularities in the elderly, studies that have attempted to separate the effects of chronological age from factors such as fitness level and the effects of chronic disease, have shown that thermal tolerance appears to be minimally compromised by age.[10,11] It remains unclear why HH appears not only to present in younger adults, but according to prevalence studies it abates or become less bothersome in older age.

Key Point

Hyperhidrosis or excessive sweating is very common (2.8% of the population) and usually begins in young adulthood

Impact on Quality of Life

Hyperhidrosis has a profound impact on social interactions and work related activities.[3,6-8,12,13] Routine social interactions such as holding hands, shaking hands or hugging become awkward. Patients report a sense of humiliation and embarrassment associated with soaked or stained clothing as well as perceived odours. Several studies have reported the majority of patients being less confident than they would like to be, many were frustrated and depressed, and most felt limited with respect to meeting people for the first time.[6-8,12,13] As one would expect, a great deal of time is invested in coping with this problem, with resulting negative consequences both socially and economically. Several studies using validated QOL measures suggest that HH is associated with impairments in QOL comparable to those associated with severe psoriasis or dermatitis/eczema as well as other severe chronic disease states such as end-stage renal disease, rheumatoid arthritis, and multiple sclerosis.[6,14,15]

Diagnosis and patient evaluation

A history focussing on location of excessive sweating, duration of the presentation, associated symptoms or comorbidities, family history, age of onset and any specific triggers allows one to differentiate primary from secondary hyperhidrosis.[16-19] The physical exam will be guided by any suggestion of secondary hyperhidrosis, and will also attempt to confirm the distribution of disease. Laboratory tests are uncommonly required if there is no suggestions of a secondary disorder on review of systems and the pattern is typical. A diagnosis of primary focal HH is most confidently made when excessive focal sweating occurs for greater than 6 months and is associated with 2 of

Table 2: Hyperhidrosis disease severity scale (HDSS)

My sweating is never noticeable and never interferes with my daily activities.	Score 1
My sweating is tolerable but sometimes interferes with my daily activities.	Score 2
My sweating is barely tolerable and frequently interferes with my daily activities.	Score 3
My sweating is intolerable and always interferes with my daily activities.	Score 4

the following 6 criteria:

- Bilateral and relatively symmetric distribution
- Impairment of daily activities
- Frequency of at least one episode per week
- Age of onset less than 25 years
- Positive family history
- Cessation of focal sweating during sleep

Measurement of Hyperhidrosis

Each evaluation should attempt to determine the volume of sweat production, the distribution of hyperhidrosis and the affect on quality of life. Gravimetric testing with filter paper measures the volume of sweat over a fixed period of time, but is impractical for clinical use. The starch iodine test provides a qualitative assessment of both volume of sweat production and extent of distribution. The area to be tested is dried and an iodine solution (1%–5%) is applied. After a few seconds, starch is sprinkled over this area. The starch and iodine interact in the presence of sweat to develop purplish sediment. This test is most helpful when delineating the area for treatment. (figures 1-3) To assess impact on QOL, various measures have been validated, such as the hyperhidrosis disease severity scale (HDSS).[16] (Table 2)

Key Point

Hyperhidrosis most commonly affects the axillae, hands, feet and face

Treatment of Options (table 3)

Topical treatments for hyperhidrosis

Although there are over 90 different compounds available, aluminum chloride hexahydrate is still considered the most effective topical agent.[7,19] It works through mechanical obstruction of the eccrine sweat gland pore. The main indication for aluminum chloride is for focal, mild axillary hyperhidrosis. Other topical products include glycopyrrolate, a topical anticholinergic product available as topical pads for mild cases of hyperhidrosis. The main limiting side effects of all of these products are skin irritation, lack of efficacy in moderate to severe axillary hyperhidrosis, and poor response on the palms and soles.

Systemic treatments for hyperhidrosis

Systemic anticholinergic drugs, such as glycopyrrolate, are the

Table 3: Treatments for Focal Hyperhidrosis

Treatment	Indication	Comments
Topical treatments	Axillary, facial, less commonly palmar and plantar hyperhidrosis	Short term action. Effective in mild cases. Major side effect is local irritation. Palms and soles less responsive.
Systemic treatments	Main role in generalized and compensatory hyperhidrosis	Limited efficacy due to anticholinergic side effects.
Iontophoresis	Palmar and plantar hyperhidrosis	Major limitation is the expense of the equipment and time consuming procedure.
Surgical sympathectomy	Hyperhidrosis unresponsive to topical or systemic treatment and botulinum toxin	Major limitation is possible surgical adverse events and an unacceptably high rate of compensatory hyperhidrosis.
Botulinum toxin injections	Axillary, palmar, plantar and facial hyperhidrosis	Safe, effective and well tolerated treatment with excellent patient satisfaction. Drug usually covered by third party insurance.

Key Point

Hyperhidrosis is rarely related to underlying medical conditions and typical cases do not require systemic investigations

primary oral agents available for treatment of hyperhidrosis. Unfortunately, at efficacious doses the side effects are generally not tolerable. Side effects consist of dry mouth, blurred vision, constipation, urinary retention, and palpitations. Other agents such as clonazepam, diltiazem, clonidine and non steroidal anti inflammatories have been reported to be useful in isolated cases.[7,19]

Iontophoresis

Iontophoresis is defined as the introduction of an ionized substance (usually tap water) through intact skin by means of an electrical current. It is most valuable for treatment of palmar and plantar hyperhidrosis, where efficacy can reach 90%.[7,18,19] Treatment is well tolerated, although dryness and irritation is common. The mechanism of action appears to be distal duct blockage. Iontophoresis machines are usually purchased by the individual (cost approximately $700 US) and can be easily taught to use at home. The main

Figure 1:

A Minor's iodine-starch test results in purple to black discoloration that delineates the area affected by excessive sweating. Figure shows the left axilla before starch iodine testing

disadvantage is the time consuming frequency of therapy which can be several times a week for 30–40 minutes each if both hands and feet are being treated.

Surgical treatments for hyperhidrosis

Surgery of the axillae to remove eccrine glands is reported, in uncontrolled trials, to have an efficacy in the range of 50%–90%.[7] Excision or curettage of the axillary vault can be complicated by infection, bleeding, delayed healing, flap necrosis, hyperhidrosis relapse and significant scarring.

Endoscopic thoracic sympathectomy (ETS) destroys the sympathetic ganglia by excision, ablation or clipping. Several studies validate the efficacy of ETS in palmar and axillary hyperhidrosis, however long term outcome studies have reported that patient satisfaction declines over time. The main complication with sympathectomy is compensatory sweating, which may occur in up to 96% of cases.[7] The compensatory sweating is generally mild, however has been reported to be severe in up to 40% of patients. In these situations, patients generally prefer their premorbid condition over the compensatory hyperhidrosis. Other less common side effects are Horner syndrome, neuralgia, pneumothorax and arrhythmia. More selective surgery has reported lower rates of compensatory hyperhidrosis. However, due to the still significant rates of compensatory sweating,

Key Point

The impact of HH on quality of life is easy to measure and essential in the management of patients

Figure 2:

The axilla immediately after iodine and starch have been applied

ETS surgery should be considered as a last resort.

Key Point

Topical non-prescription products should be tried first, but botulinum toxin injections are very effective for moderate to severe disease and are usually covered by third party health insurance

Botulinum toxin for hyperhidrosis

Botulinum toxin is produced by Clostridium botulinum and acts by inhibiting acetylcholine release at the neuromuscular junction, and thereby blocking the message that triggers eccrine sweat release. It is commonly used for moderate to severe disease or if mild cases do not respond to topical treatment. In Canada and the United States, the use of BTX-A in axillary hyperhidrosis is an approved medical indication and therefore the drug cost is commonly covered by third party insurance, making it a more affordable treatment option. Other botulinum preparations are being studied for use in hyperhidrosis, but are not approved in Canada or the US for this indication.

Botulinum toxin for Axillary hyperhidrosis

Several large randomized controlled clinical trials have documented Botulinum toxin (BTX) response rates to be very high, averaging over 90%.[16] BTX-A results in dramatic and statistically significant improvements in QOL measures such as emotional status, ability to participate in daily and social activities, productivity at work and number of clothing changes per day. BTX-A is a safe, well tolerated and highly efficacious treatment for axillary

Figure 3:

The colorimetric reaction that occurs in a patient with axillary hyperhidrosis and the locations of the greatest volume of sweating

hyperhidrosis in patients who have failed to respond to topical therapy. Typical starting doses are 50 units of BTX-A per axilla, although higher dosing may be required in some patients. Injections are usually intradermal, although subcutaneous placement may be equally effective and less painful. The mean duration of effect is 6–7 months.

Botulinum toxin for palmar and plantar hyperhidrosis

Two small, randomized, double-blind studies have evaluated the efficacy of botulinum toxin A in palmar hyperhidrosis and shown the overall response rate to be greater than 90%.[16] The main side effects were pain at the site of injection and transient minor weakness of intrinsic hand muscles lasting 2 to 5 weeks. Other studies have reported a minor weakness of finger grip in two thirds of patients, which lasts days to weeks. The duration of effect generally exceeded the length of the trials and is reported to be an average of 4 to 6 months. Although no randomized controlled trials have yet evaluated BTX-A for plantar hyperhidrosis, small case series and reports have demonstrated efficacy and improvement with dosages similar to those used in palmar studies with a similar duration of effect. Treatment usually consists of 100 units per palm or sole. Intradermal injection into the palm is painful, thus anesthesia is strongly

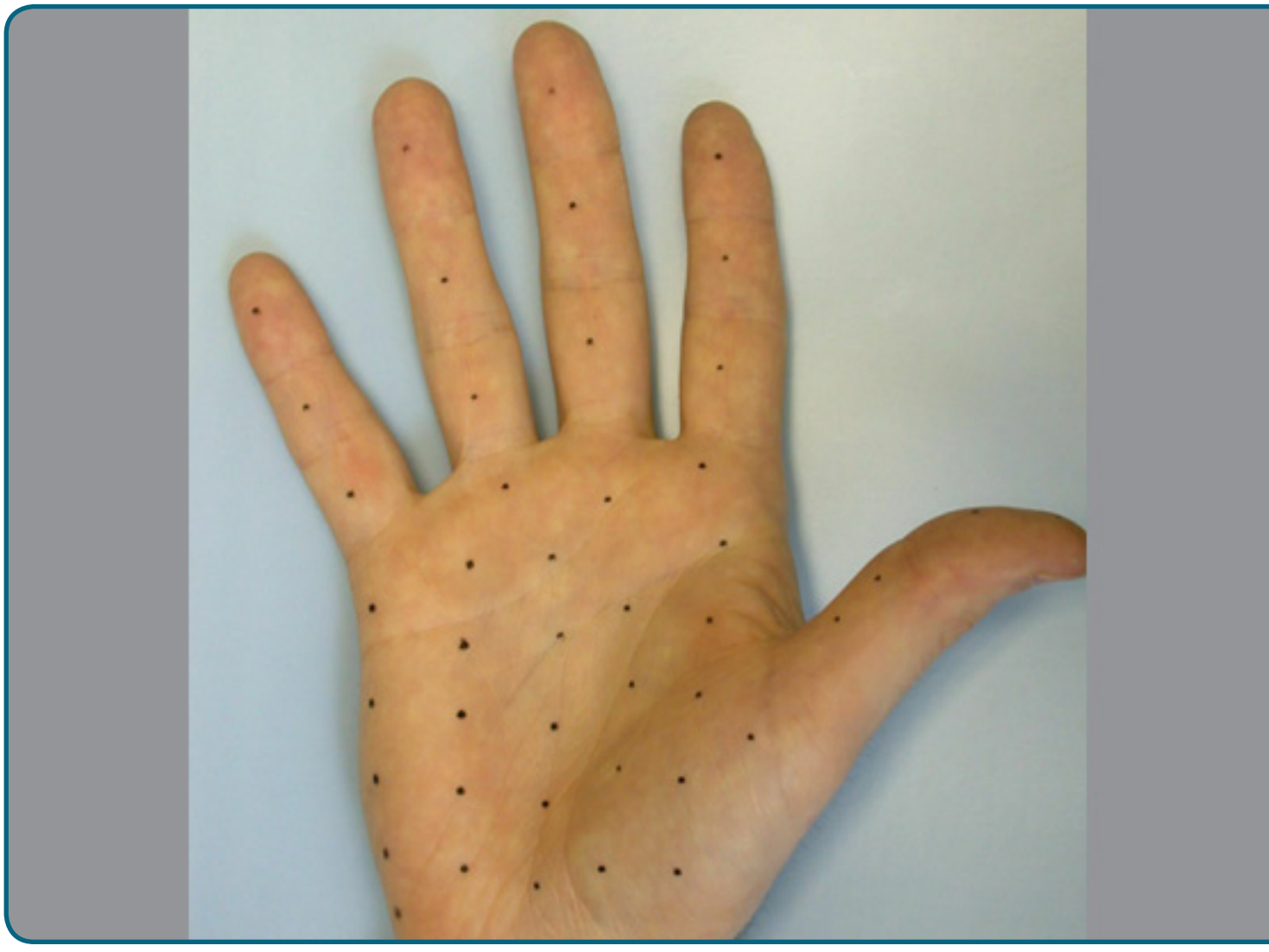

Figure 4:

The Palm Sites A representative map

recommended. Regional nerve blockade (median and ulnar nerves for the palms and posterior tibial and sural nerves for the soles) may be used, although success has been reported with Bier block and vibration. More recently, application of ice anesthesia has been shown to be practical and effective.[8] Topical anesthesia seems to be ineffective.

Botulinum toxin for facial hyperhidrosis

Facial hyperhidrosis can involve the upper lip, nasolabial folds, and malar regions, however the most commonly affected area is the forehead. Evidence is limited to case reports, but there are many reports in the literature with duration of effect in the range of 5–6 months. The main site of injection is a band along the hairline and extending into the temporal scalp. Frey's syndrome, or facial gustatory sweating after parotid surgery or trauma, is due to transection of the postganglionic sympathetic nerve fibres from the otic ganglion. Treatment of Frey's syndrome with BTX-A has produced clinically significant improvements in sweating and associated facial flushing, lasting up to 15 months.[20]

Treatment considerations with botulinum toxin

The main contraindications to

Summary of Key Points

Hyperhidrosis is very common (2.8% of the population) and usually begins in young adulthood

Hyperhidrosis most commonly affect the axillae, hands, feet and face

Hyperhidrosis is rarely related to underlying medical conditions and typical cases do not require systemic investigations

The impact of HH on quality of life is easy to measure and essential in the management of patients

Topical non-prescription products should be tried first, but botulinum toxin injections are very effective for moderate to severe disease and are usually covered by third party health insurance

Post-test

CME Quiz

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botulinum toxin therapy include neuromuscular disorders such as myasthenia gravis, pregnancy and lactation, organic causes of hyperhidrosis, and medications that may interfere with neuromuscular transmission.[7] Appropriate selection of patients is essential to ensure a satisfactory treatment response and avoid unnecessary frustrations.

Summary

Hyperhidrosis is a common and extremely distressing condition with a prevalence of 2.8% of the population. Effective treatment can dramatically improve a patient's quality of life and this underscores the challenge for physicians to diagnose and manage this condition.

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Clinical Pearls

Evidence of HH on clinical examination may be skin maceration, secondary infection, pigmentation, or foul smell in typical areas. Any suggestion of unexplained social embarrassment should prompt questions related to body habitus issues such as HH.

Cases unresponsive to topical over the counter preparations such as 20% aluminum chloride should be referred to a dermatologist for consideration of other therapies. If social anxiety is severe, co-referral to a mental health specialist may be beneficial.

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