TREATMENT OF HYPERHIDROSIS

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The primary function of the eccrine sweat glands is to assist in the maintenance of body temperature in response to heat exposure or exercise. Hyperhidrosis may be defined as sweating beyond what is necessary to maintain thermal regulation. It may be primary (idiopathic, essential) or secondary to a number of diseases and prescribed drugs. Hyperhidrosis can be localized or generalized. Regardless of the type or cause of the hyperhidrosis, it is frequently socially embarrassing and occupationaly disabling. Excess sweat on the hands may soil paper and art work, and make it virtually impossible to play many musical instruments. Careers in fields that require contact with paper, metal, and electrical components become unrealizable. Axillary and plantar hyperhidrosis may result in stains and damage to clothing and shoes. Generalized hyperhidrosis leaves affected individuals with wet clothing that may have to be changed a number of times each day.

Physiologically, sweating is a function of the sympathetic nervous system. A sweat control center located in the preoptic area and anterior hypothalamus contains neurons that are sensitive to changes in internal temperature and also cerebral cortical events. Sweat glands are innervated by sympathetic postganglionic fibers, but unlike ordinary sympathetic innervation the chemical mediator is acetylcholine. Sweating in response to thermal stimuli is generally acceptable and rarely a cause for complaint. Emotionally induced sweating tends to be localized to the palms, soles, and sometimes the forehead. Axillary sweating may be the result of both emotional and thermal stimuli.

The causes for generalized hyperhidrosis (Display Box 1) include a number of febrile illnesses, neoplastic and neurologic diseases, metabolic disorders, and drugs. The causes and conditions associated with localized hyperhidrosis include primary palmoplantar hyperhidrosis, unilateral circumscribed hyperhidrosis, hyperhidrosis associated with intrathoracic neoplasms, olfactory hyperhidrosis, gustatory hyperhidrosis, spinal cord injuries, and Frey's syndrome. Although primary or essential hyperhidrosis is the most common cause of palmoplantar hyperhidrosis it may also occur in some patients with Raynaud's disease, rheumatoid arthritis, erythromelalgia, nail patella syndrome, keratosis palmaris et plantaris with clindacytly, atrioventricular fistula, and cold injury. Whenever possible, the cause for hyperhidrosis should be identified, and if possible, treated.

Display Box 1. Hyperhidrosis—The Causes

Generalized
- Heat, humidity, and exercise
- Febrile diseases: acute and chronic infections, and neoplasia
- Metabolic: thyrotoxicosis, diabetes mellitus, hypoglycemia, gout, pheochromocytoma, hyperpituitarism, or menopause

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Primary or essential hyperhidrosis is a disorder that causes hyperhidrosis of the hands, feet, and sometimes the axillae. It is estimated that 0.6% to 1.0% of the population suffers from this problem. Primary hyperhidrosis may be inherited and in contrast to generalized hyperhidrosis usually has its time of onset in adolescence, but may begin in childhood and even infancy. It characteristically does not occur while sleeping. Primary hyperhidrosis is made worse by heat and emotional stimuli; however, it is important to note that although emotional stimuli are necessary for primary hyperhidrosis to occur in affected individuals, it is not a psychological disease but rather a physiologic disorder. It seems that in patients with primary hyperhidrosis, the hypothalamic sweat centers are more sensitive to emotional stimuli of cerebral origin than in ordinary people. The occasional onset of primary hyperhidrosis in the neonatal period is evidence that this is far more than an emotional disorder! A number of medical and surgical remedies are available for the treatment of hyperhidrosis (Display Box 2).

**Display Box 2. Treatment of Hyperhidrosis**

**Medical**

**Topical:**
- Antiperspirants: Drysol (aluminum hexahydrate in alcohol)
- 2% to 5% tannic acid solution
- 5% to 20% formalin solution
- 10% glutaraldehyde
- Anticholinergics

**Systemic:**
- Tranquilizers: Valium* (diazepam)
- Anticholinergics: Probanthine**
- (propantheline bromide), Robinul***
- (glycopyrrolate), Ditropan† (oxybutynin), or Cogentin†† (benztropine mesylate)

**NSAIDs:** indomethacin
- Calcium-channel-blockers: Cardizem†
- (diltiazem)
- Catapres††† (clonidine hydrochloride)
- Botulinum toxin

**Surgical**
- Sympathectomy
- Excision of axillary sweat glands
- Liposuction: Robinul

**Electrical**
- Iontophoresis

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* = Roche Pharmaceutical, Marati, Puerto Rico
** = Roberts Pharmaceuticals, Eatontown, NJ
*** = A. H. Robins Co., Richmond, VA
† = Hoechst Marion Roussel, Kansas City, MO
†† = Merck and Company Inc., West Point, PA
††† = Boehringer Ingelheim, Richfield, CT

**TOPICAL**

Aluminum chloride and tanning agents are sometimes effective in the control of localized hyperhidrosis.25 Although this mechanism has been disputed, aluminum chloride may decrease sweating by mechanically obstructing eccrine sweat gland pores. The atrophy of the secretory cells seen in eccrine sweat glands exposed to aluminum chloride may account for the reduced sweating that most people enjoy with the use of aluminum chloride–containing products. For most people with axillary hyperhidrosis, over the counter products are sufficient. For more severe sweating, aluminum chloride hexahydrate (20%) dissolved in anhydrous ethyl alcohol (Drysol, Person and Covey Inc., Glendale, CA) is frequently useful. The skin should be dry before application, because if moisture is present, irritating hydrochloric acid forms. Washing just before application should be avoided. The optimum way to use the product seems to be to apply it at bedtime to take advantage of the relative inactivity of sweat glands through the night and wash the product off first thing in the morning. Minor irritation can be relieved with the use of hydrocortisone cream. The product should be used nightly until an effect occurs, and then the interval between applications can be lengthened. Although occlusion with plastic wrap can be attempted if direct application is not effective, this is not only inconvenient, but results in increased irritation.

Glutaraldehyde, tannic acid, and formaldehyde may be useful to treat palmar and plantar hyperhidrosis, but their tendency to stain the skin and, in the case of formaldehyde solution, its sensitizing potential, limit their usefulness.17, 25
SYSTEMIC

For those patients whose hyperhidrosis is related to specific anxiety-producing events such as a speaking engagement, school dance, etc., the use of a drug such as diazepam may have an ameliorating effect. Systemic anticholinergics may be helpful, but unfortunately the dosages required to achieve reduced sweating also result in side effects including xerostomia, mydriasis, cycloplegia, and bowel and bladder dysfunction. Most patients with localized or generalized hyperhidrosis cannot tolerate them for long; however, the anticholinergic oxybutynin (Ditropan, Hoechst Marion Roussel, Kansas City, MO) has been found to be useful in the relatively rare syndrome of episodic hyperhidrosis with hypothermia. A second anticholinergic, benztrapine, was successfully used to treat hyperhidrosis in a patient with venlafaxine-induced excess sweating. Venlafaxine is an antidepressant that inhibits the reuptake of serotonin and norepinephrine. Sweating is said to occur in as many as 12% of all patients exposed to venlafaxine and other serotonin selective reuptake inhibitors (SSRIs). A nonsteroid antinflammatory agent, indomethacin, in a dose of 25 mg t.i.d. was prescribed for a patient with arthritis who coincidentally had lifelong idiopathic generalized hyperhidrosis. Quite unexpectedly she enjoyed a resolution of her lifelong hyperhidrosis. Although the mechanism for this beneficial effect is not clear, the information that prostaglandin E is found in increased amounts in the sweat of some patients with hyperhidrosis may offer an explanation. Influx of calcium from extracellular to intracellular space is necessary for the active secretion of sweat by eccrine sweat glands. This likely accounted for the improvement in palmar and plantar hyperhidrosis observed when a calcium channel blocker, diltiazem, was used to treat a family with palmar and plantar hyperhidrosis. Tricyclic antidepressants may cause excess sweating and yet one would expect the anticholinergic action of tricyclics should block sweating, not induce it. Clonidine, a centrally active α-adrenergic autoreceptor stimulant, has been found to be useful in the treatment of hyperhidrosis due to tricyclics as well as menopause. Oral propoxyphene hydrochloride (Darvon), a narcotic and weak ganglionic blocking agent, may have an ameliorating effect on hyperhidrosis in patients with autonomic dysreflexia. Autonomic dysreflexia is a syndrome of sympathetic hyperactivity due to bladder or bowel distension seen in some patients with spinal cord lesions at or above the sixth thoracic level (T6). Fluorocortisone acetate 0.3 mg daily may control sweating in quadriplegics in whom orthostatic hypotension precipitates a sympathetic discharge. The reader is cautioned that many of these reports of therapeutic efficacy are anecdotal and all of these systemic agents carry with them the risk of side effects.

AXILLARY HYPERHIDROSIS

Patients with axillary hyperhidrosis who are unresponsive to topical therapy benefit from surgical excision. The area of greatest sweating may be identified by draping a piece of simple tissue paper over the axilla. Sometimes this area is quite small, and simple excision with closure is sufficient to remedy the problem. Patients with moderate to severe hyperhidrosis may require a more extensive procedure with undermining and resection of all exposed sweat glands. In order to obtain good closure and avoid limitation of movement due to cicatricial contracture, Z-plasty and bat-shaped excisions and repairs can be employed. Alternative treatments for axillary hyperhidrosis include subcutaneous liposuction, botulinum toxin, iontophoresis, and sympathectomy.

SYMPATHECTOMY

Sympathectomy or upper thoracic (T2) ganglionectomy is frequently offered to patients with severe palmar hyperhidrosis. Lumbar sympathectomy is not usually employed for plantar hyperhidrosis because of the risk of sexual dysfunction. Although the efficacy of this procedure in the treatment of palmar hyperhidrosis is not in doubt, with success rates of 92% to 99%, the complications are significant. Among the complications are compensatory hyperhidrosis (increased sweating in some other area of the body), 24% to 100%; gustatory sweating (sweating usually of the face related to the eating of foods), permanent Horner’s syndrome, wound infection, hemothorax, intercostal neuralgia, and recurrence of hyperhidrosis. The advent of endoscopic sympathectomy has reduced the incidence of many complications. Compensatory hyperhidrosis is the most common complication and the major reason for patient dissatisfaction with the procedure. In a recent report on the com-
Complications experienced by 72 patients with palmar hyperhidrosis treated with transthoracic endoscopic sympathectomy, all patients except one complained of compensatory hyperhidrosis, with 41.7% complaining of moderate hyperhidrosis and 43.1% severe. In this study, 11 patients were not able to accept the consequences of compensatory hyperhidrosis, even though their palms had become dry postoperatively. Compensatory hyperhidrosis following sympathectomy can be far more life disrupting than palmar hyperhidrosis in that afflicted individuals may have to change sweat-soaked clothing five or six times per day. Moran states it quite succinctly:

Complications related to the surgical approach, such as Horner's syndrome, brachial plexus injuries, pneumothorax, and painful scars may occur, while following sympathectomy compensatory hyperhidrosis is usual and hyperhidrosis may recur.

**BOTULINUM TOXIN**

Botulinum toxin is a useful therapeutic agent for the treatment of a number of diseases related to muscular dystonia. This potent toxin has proven to be a highly effective remedy for the treatment of conditions previously recalcitrant in the fields of ophthalmology, otorhinolaryngology, pediatrics, gastroenterology, and urology. The cosmetic derenervation of muscles of facial expression using botulinum toxin has given dermatologists and plastic surgeons a new weapon against facial expression–induced wrinkles and lines. Side effects reported following the local injection of botulinum toxin have been few, and are usually related to undesired weakness in muscles adjacent to the treatment sites. Since botulinum toxin inhibits the release of acetylcholine not only at the neuromuscular junction, but also in postganglionic sympathetic fibers to sweat glands, it has been found to be useful to treat palmar and axillary hyperhidrosis. Responses have been as long as 1 year, but in most cases the effect begins to weaken in 4 months. Although effective, the clinical usefulness of this treatment is limited by the need for multiple and repetitive relatively painful injections, the cost of the botulinum toxin, and reports of weakness of the small muscles of the hands.

**IONTOPHORESIS**

By far, the simplest, safest, and most cost-effective remedy for palmar or plantar hyperhidrosis is iontophoresis, which is defined as the introduction of an ionized substance through intact skin by the application of a direct current. In 1936, Ichihashi used various solutions of atropine, histamine, and formaldehyde, and by iontophoresis demonstrated that sweating of the palms could be reduced. His work went relatively unnoticed until 1952 when Bouman and Gruenwald Lentzer published a report clearly demonstrating the efficacy of iontophoresis for the treatment of palmar and plantar hyperhidrosis in 113 patients. They demonstrated that the addition of an ionizable substance to the water was not necessary to obtain a therapeutic effect. Levit demonstrated a simple galvanic device that could be employed to relieve hyperhidrosis in 85% of affected patients. Although the exact mechanism by which iontophoresis relieves palmar or plantar hyperhidrosis is not known, it is thought to be due to poral plugging, because the effect is reversed by cellophane tape-stripping of the skin overlying eccrine sweat glands rendered euhidrotic by iontophoresis. For those patients who fail to respond to simple tap water iontophoresis, the addition of an anticholinergic directly to the tap water-filled treatment trays is frequently helpful. Although a number of devices are available for the administration of iontophoresis this author prefers the Fischer MD1a Galvanic unit (Fisher, Glendale, CA) and the technique employed is described in the Appendix section. Side effects from iontophoresis are few. Occasionally the palms become too dry and may become cracked or fissured, which may be relieved with the use of moisturizers or a reduction in the frequency of treatments. Erythema and less frequently vesiculation of the skin may follow treatments and can be treated if necessary with simple 1% hydrocortisone cream. Compensatory hyperhidrosis does not occur. Iontophoresis, when properly administered using effective devices, liberates the great majority of patients with palmar and plantar hyperhidrosis from the burden of their problem.

**SUMMARY**

The patient who complains of hyperhidrosis presents the physician with a diagnostic and therapeutic challenge. Patients who present with generalized hyperhidrosis are, in general, adults whose sweating occurs both during the waking and sleeping hours.
Such patients require a search for a cause that may sometimes be as simple as a drug that they are taking for some medical disorder. Occasionally a systemic illness may account for the onset of hyperhidrosis and a thorough exam and appropriate testing may be necessary to identify the cause. Most patients with primary or essential hyperhidrosis present in childhood or adolescence and have a problem localized to their hands and/or feet. They have a physiologic disorder not a psychiatric or endocrinologic disease. A number of systemic, topical, surgical, and electrical remedies are available for the treatment of hyperhidrosis. Patients with hyperhidrosis of the palm or soles deserve a trial of conservative therapy, iontophoresis in particular, before aggressive surgical techniques that carry with them the risk of lifelong troublesome side effects are offered.

References


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