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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 occupationally 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 clindactyly, 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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Sympathetic discharge: shock and syncope, intense pain, alcohol, and drug withdrawal
Neurologic: Riley-Day syndrome, irritative hypothalamic lesions
Drugs: propranolol, physostigmine, pilocarpine, tricyclic antidepressants, or venlafaxine

Localized
Heat
Olfactory
Gustatory: citric acid, coffee, chocolate, peanut butter, and spicy foods
Neurologic lesions
Primary or essential hyperhidrosis

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% glutaraldyde
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

* = Roche Pharmaceutical, Marati, Puerto Rico
** = Roberts Pharmaceuticals, Eatotown, NS
*** = A. H. Robins Co., Richmond, VA
† = Hoechrt 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, Hoechrt Marion Roussel, Kansas City, MO) has been found to be useful in the relatively rare syndrome of episodic hyperhidrosis with hypothermia.[21] A second anticholinergic, benztropine, was successfully used to treat hyperhidrosis in a patient with venlafaxine-induced excess sweating.[8] 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 antiinflammatory 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.[30] 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.[9] 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.[16] 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.[7] Oral propoxyphene hydrochloride (Darvon), a narcotic and weak ganglionic blocking agent, may have an ameliorating effect on hyperhidrosis in patients with autonomic dysreflexia.[29] 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). Fludrocortisone acetate 0.3 mg daily may control sweating in quadriplegics in whom orthostatic hypotension precipitates a sympathetic discharge.[18] 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.[14] Patients with moderate to severe hyperhidrosis may require a more extensive procedure with undermining and resection of all exposed sweat glands.[32] 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.[27] Alternative treatments for axillary hyperhidrosis include subcutaneous liposuction, botulinum toxin, iontophoresis, and sympathectomy.[2, 22, 26]

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.[3–6, 10, 13, 22, 23, 31] 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-

plications 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![4] 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[22] 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 denervation 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.[2, 24] 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.[24]

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.[15] 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.[1] 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.[19, 20] 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.[11, 12] 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.[28]

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

1. Bouman HD, Grunewald Lentzer EM: The treatment of hyperhidrosis of hands and feet with constant current. Am J Phys Med 31:158–169, 1952
2. Bushara KO, Park DM, Jones JC, et al: Botulinum toxin—a possible new treatment for axillary hyperhidrosis. Clin Exp Dermatol 21:276–278, 1996
3. Chen HJ, Shih DY, Fung ST: Transthoracic endoscopic sympathectomy in the treatment of palmar hyperhidrosis. Arch Surg 129:630–633, 1994
4. Chu D, Shi P, Wu C: Transthoracic endoscopic sympathectomy for treatment of hyperhidrosis palmaris. Kao Hsiung I Hseuh Ko Hseuh Tsa Chin 13:162–168, 1997
5. Drott C, Gothberg G, Claes G: Endoscopic transthoracic sympathectomy: An efficient and safe method for the treatment of hyperhidrosis. J Am Acad Dermatol 33:78–81, 1995
6. Edmondson RA, Banerjee AK, Rennie JA: Endoscopic thoracic sympathectomy in the treatment of hyperhidrosis. Ann Surg 215:289–293, 1992
7. Feder R: Clonidine treatment of excessive sweating. J Clin Psychiatry 56:1, 35, 1995
8. Garber A, Gregory R: Benztropine in the treatment of venlafaxine-induced sweating. J Clin Psychiatry 58:4176–4177, 1997
9. Goldyne ME: Indomethacin and hyperhidrosis. J Am Acad Dermatol 7:801, 1982
10. Gordon A, Zecmeister K, Collin J: The role of sympathectomy in surgical practice. Eur J Vasc Endovasc Surg 8:129–137, 1994
11. Gordon B, Maibach H: Eccrine anhidrosis due to glutaraldehyde, formaldehyde, and iontophoresis. J Invest Dermatol 53:436–439, 1969
12. Grice K, Sattar H, Baker H: Treatment of idiopathic hyperhidrosis with iontophoresis of tap water and poldine methosulphate. Br J Dermatol 86:72–78, 1972
13. Herbst F, Plas EG, Fugger R, et al: Endoscopic thoracic sympathectomy for primary hyperhidrosis of the upper limbs: A critical analysis and long-term results of 480 operations. Ann Surg 220:86–89, 1994
14. Hurley HJ, Shelley WB: A simple surgical approach to the management of axillary hyperhidrosis. JAMA 186:109, 1963
15. Ichihashi T: Effect of drugs on the sweat glands by catophoresis, and an effective method for suppression of local sweating: Observation on the effect of diaphoretics and adiaphoretics. J Orient Med 25:101–102, 1936
16. James WD, Schoomaker MC, Rodman MC: Emotional eccrine sweating. Arch Dermatol 123:925–929, 1987
17. Juhlin L, Hansson H: Topical glutaraldehyde for plantar hyperhidrosis. Br J Dermatol 97:327–330, 1968
18. Khurana RK: Orthostatic hypotension-induced autonomic dysreflexia. Neurology 37:1221–1224, 1987
19. Levit F: Simple device for the treatment of hyperhidrosis by iontophoresis. Arch Dermatol 98:505–507, 1968
20. Levit F: Treatment of hyperhidrosis by tap water iontophoresis. Cutis 26:192–194, 1980
21. LeWitt P: Hyperhidrosis and hypothermia responsive to oxybutynin. Neurology 38:506–507, 1988
22. Moran KT, Brady MP: Surgical management of primary hyperhidrosis. Br J Surg 78:279–283, 1991
23. Pillay PK, Thomas J, Mack P: Thoracoscopic ganglionectomy for hyperhidrosis. Stereotact Funct Neurosurg 63:198–202, 1994
24. Schnider P, Binder M, Auff E, et al: Double-blind trial of botulinum A toxin for treatment of focal hyperhidrosis of the palms. Br J Dermatol 136:548–552, 1997
25. Shelley WB, Laskas JJ, Satonove A: Effect of topical agents on plantar sweating. Archives of Dermatology and Syphilology 69:713–716, 1954
26. Shenaq SM, Spira M: Treatment of bilateral axillary hyperhidrosis by suction-assisted lipolysis technique. Ann Plast Surg 19:548–551, 1987
27. Stenquist B: Axillary hyperhidrosis: A simple surgical procedure. J Dermatol Surg Oncol 11:388–391, 1985
28. Stolman LP: The treatment of palmar hyperhidrosis by iontophoresis. Arch Derm 123:893–896, 1987
29. Tashjian EA, Richter KJ: The value of propoxyphene hydrocloride (Darvon) for the treatment of hyperhidrosis in the spinal cord injured patient: An anecdotal experience and case reports. Paraplegia 23:349–353, 1985
30. Tkach JR: Indomethacin treatment of generalized hyperhidrosis. J Am Acad Dermatol 6:545, 1982
31. Welch E, Geary J: Current status of thoracic dorsal sympathectomy. J Vasc Surg 1:202–214, 1984
32. West JR: Management of hyperhidrosis and bromhidrosis. Cutaneous Surgery, Philadelphia, WB Saunders, 1993, pp 699–707

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