peer-reviewed **CME**

Contributed by ***Antranik Benohanian***, MD, Dermatologist at CHUM, Assistant Professor of Clinical Medicine, Université de Montréal, Montreal, Quebec

French text published in ***LesCahiers de MedActuel***

Palmar hyperhidrosis:

A condition with unsuspected psychosocial and professional repercussions

learning objectives

- To understand the impact of hyperhidrosis on patients' quality-of-life and to offer the necessary psychological support.
- To be able to initiate a treatment tailored to meet the needs of each patient.
- To know other, more complex treatment options in case of failure.

key words

Palmar hyperhidrosis, aluminum chloride, botulinum toxin type A, anesthesia, nerve block.

Definition

The purpose of sweating is to assist with thermoregulation in order to maintain a stable body temperature of 37°C. Hyperhidrosis (HH) is defined as an amount of sweat that exceeds the volume necessary for thermoregulation.

Clinical case

A 33-year-old policeman consults his physician for a disabling case of palmar HH that has plagued him since childhood. Beyond the social embarrassment caused by his condition—when shaking hands, for example—the patient's profuse sweating is bothersome and exposes him to potential dangers when handling firearms, a common problem among soldiers with this same condition. His problem is exacerbated during the summer due to the intense heat and humidity. He is also suffering from plantar HH, but this bothers him less.

Differential diagnosis

The presence of droplets of sweat on the palms of both hands during the consultation is enough to confirm a diagnosis of palmar HH of idiopathic origin, given that the condition is bilateral and symmetrical. In asymmetrical cases, an underlying pathology should be ruled out (e.g., trauma, neurological etiology).

Clinical case revisited

The patient's palmar and plantar HH problem goes back to his childhood. The physical exam reveals nothing noteworthy, and the patient is still able to perform his duties as a policeman. Despite the potential for problems (e.g., warts, dyshidrosis, onychomycosis or other problems of the hands and/or feet), none are found. Table 1 lists conditions that may be triggered by HH.

Investigation

To make a diagnosis of HH, you should rely on the patient's history or careful observation of his skin or wet clothing at the affected site. Qualitative and quantitative sweat measurements are not usually necessary. The HH classification table lists the most common underlying pathologies.

Minor test

This test involves coating the area to be treated with iodine and then sprinkling it with corn starch. This test helps to delimit the hyperhidrotic areas that appear dark blue.

Prevalence

The HH rate is higher in children, adolescents and young adults. One epidemiological study on the prevalence of HH in the U.S. indicated an incidence rate of 2.8%. This is considerably higher than previous claims

of 0.5-1%. The condition affects men and women in the same proportion, although women consult more often. The U.S. study shows that 62% of subjects have never spoken about the condition to their doctor. According to this study, focal HH mainly affects the armpit (40%), and the hands and feet (40%); the condition is less common in the craniofacial area (10%) and groin. The vast majority of patients suffer in silence and refuse to speak with their doctor or loved ones because they are afraid of not being taken seriously. Some are told that it is a normal, albeit potentially harmful, physiological phenomenon that should be respected. It is true that in some cases the distinction between normal physiological sweating and pathological sweating is not always easy to make. As indicated in the testimonial on the previous page, palmar HH remains by far the type of hyperhidrosis with the greatest socio-professional impact.

Treatment

Antiperspirants and deodorants

Antiperspirants are designed to decrease the secretion of sweat by the eccrine and apocrine glands. The sweating process is blocked by creating a plug in the distal portion of the sweat gland duct (acrosyringium). The plug is essentially composed of aluminum-based salts. Deodorants are designed to diminish or suppress odor through the use of either an antimicrobial agent that fights odor or a perfume that masks it. The eccrine glands are generally active during the day and calm down during sleep. Antiperspirants containing aluminum salts should be applied at bedtime to avoid the potential irritation caused by the production of hydrochloric acid that forms when sweat meets aluminum salts.

Traditional treatment of focal HH

Anticholinergic agents

Unfortunately, the adverse effects caused by this group of drugs (e.g. oxybutynin [Ditropan], propantheline [Pro-Banthine]) are worse than the sweating itself. These effects include: tachycardia, dry mouth, decreased intestinal motility, and aggravation of certain conditions such as glaucoma, toxic erythema, seizure). Furthermore, these effects appear even before the sweating problem is controlled. Although these drugs have little place in the treatment of focal HH, some patients might benefit from them, at least in their topical form.

Table 1: Conditions triggered by palmar hyperhidrosis

Dermatits of the hands
Dyshidrosic eczema (pompholyx)
Contact dermatitis
Friction bubbles
Warts
Skiers' frostbite
Callosity
Ingrown nails
Trichomycosis axillaris
Erythrasma
Pitted keratolysis
Intertrigo
Tinea versicolore
Candidiasis
Tinea pedis
Onychomycosis
Recurrent bacterial infections

Source: Benohanian A. Antiperspirants and Deodorants. *Clin Dermatol* 2001;19:398-405.

Aluminum salts

Aluminum chlorhydrate is the most commonly used ingredient in over-the-counter antiperspirants. Its concentration is higher in antiperspirants than in deodorants. Aluminum choride is the most effective of the aluminum salts, followed by aluminum chlorhydrate in combination with zirconium and finally, aluminum chlorhydrate used alone. The disadvantage of aluminum chloride is that it is too acidic for general use and destroys several clothing fibres upon contact. It is easy to see why this product is not usually included in common antiperspirants.

Aluminum chloride hexahydrate in ethanol

This is sold in the form of a 20% alcohol solution in products such as Drysol. Aluminum chloride must be used in a particular way. The armpits, hands and feet must be washed and thoroughly dried. The aluminum chloride solution is applied with or without occlusion at bedtime because the glands are less active at this time. A cellophane sheet, gloves and plastic bags are used for the armpits, hands and feet respectively. The covering is kept on during the night. This process is repeated for two or three nights. The irritation caused by aluminum chloride in its alcoholic vehicle may pose a problem.

Aluminum chloride hexahydrate in 4% salicylic acid hydroalcoholic gel

This preparation, which can be compounded from Hydrosal Gel, was tried by the author for the first time in 1978 in a patient who was about to undergo armpit surgery for an HH problem that was resistant to Drysol under occlusion. His success was considerable; the surgery was cancelled and similar cases were referred by the same surgeon to attempt this formula.

The alcohol gel causes less irritation and dryness than the alcohol solution. Because the stratum corneum is more hydrated, the product is absorbed more effectively by the epidermis. Although aluminum chloride is soluble in water at 1:1, a 1:4 ratio is required for it to be soluble in ethanol. This property prevents aluminum chloride from reaching concentrations greater than 25% in ethanol. In the gel vehicle, aluminum chloride is dispersed in the form of microcrystals that can achieve supersatured concentrations as high as 55%. The presence of hydroxypropylcellulose in the gel helps the alumi-

num chloride reach these concentrations. The role of salicylic acid is to potentialize the permeability of aluminum chloride through the thick stratum corneum of the palms and soles of the feet, which is a difficult barrier to cross. This enables the aluminum chloride to gain access to the eccrine glands where its action is crucial. Moreover, salicylic acid has antiperspirant properties, which means that it works in synergy with aluminum chloride. This explains why Drysol, although effective against axillary HH, is less so or not at all against cases of palmoplantar HH. The cellophane occlusion is therefore not useful. The alcohol gel formulation is now recognized and recommended throughout the world for the initial treatment of focal HH before moving on to more radical or costly treatments.

Table 2: Classification of hyperhidrosis

Focale		Generalized	
Primary	Secondary	Primary	Secondary
Armpits, hands and feet are most common sites Forehead, scalp, groin and genital area are affected less often Eccrine glands are more active during the day and less so at night during sleep	Gustative HH is most common (Frey's syndrome)	Origin	Illness
		• Endocrine	• Pheochromocytoma • Thyrotoxicosis • Diabetes mellitus
		• Neoplasic	• Lymphoma • Leukemia • Kidney cancer
		• Neurological	• Carcinoid syndrome • Acromegaly
		• Biochemical	• Acetylcholinesterase inhibitors • Pesticides
		• Traumatic	• Autonomic dysreflexia • Post-traumatic syringomyelia
		• Various	• Anxiety • Hypoglycemia • Menopause
		• Night sweats	• Tuberculosis • Brucellosis

The commercial Hydrosal Gel contains 15% aluminum chloride. Higher concentrations can be compounded. The preparation of the aluminum chloride gel, salicylic acid or not, must be tailored to each patient taking into account their age, affected site, severity of the case, and the patient's tolerance. Local application of the preparation could be as infrequent as once a month. A container of this preparation costs about $30 and easily lasts one or two years if it is kept in the refrigerator. It should be noted that the preparation technique is laborious and requires a lot of patience and know-how on the part of the pharmacist. When successful, however, the results are very impressive.

In the vast majority of cases, simple solutions help resolve HH. The public is often unaware that these helpful solutions exist. Various treatment options are available based on age, affected site, severity of the case, and the patient's tolerance of treatments. Choose the most effective, least aggressive and most reasonably priced option. Expert pharmacists can concoct formulations that are adapted to the particular needs of each patient. For people who do not respond to aluminum salts, botulinum toxin type A (Botox) injections should be considered before opting for a surgical intervention such as exeresis of the axillary sweat glands or a sympathectomy.

Iontophoresis

Iontophoresis is an effective treatment for the hands and feet if there is enough time to perform it. It is generally poorly tolerated in the armpits because of irritation. The patient places the hands and feet to be treated into two basins filled with tap water through which travels a low-intensity galvanic current. The current's intensity is progressively increased to 20 mA or less depending on the patient's tolerance. A tingling sensation may occur. After 10 minutes, the intensity is gradually reduced to zero. The current is then reversed and brought gradually back up to 20 mA for an additional 10 minutes. Two to four weeks are required to achieve a result. The effect of iontophoresis can be potentialized by adding 1 or 2 mg of glycopyrrolate to the water in the basins.

Marketed iontophoresis devices are sold with detailed instructions about how they work and how to conduct an iontophoresis session.

These devices can be ordered with or without a prescription:

- Drionic: www.generalmedical.com
- i2m: www.i2m-labs.com
- Fischer: www.rafischer.com

Three sessions are recommended for the first week, followed by two

Clinical case revisited

The various stages of the topical treatment have proven ineffective in our patient (see treatment algorithm for palmoplantar HH), including supersaturated concentrations of aluminum chloride (55%) in a salicylic acid gel (6%). Iontophoreresis was discussed but excluded because of the time requirement (20-30 min/d). A thoracic sympathectomy was also discussed, but this was ruled out for the time being because of the risk of compensatory hyperhidrosis.

sessions the second week and three sessions for the next two weeks. The frequency of the sessions is then reduced to one session every 2-3 weeks and later to 1-2 per month. According to the manufacturer i2m, results appear as early as the fourth week. For more details, visit the Web site at www.i2m-labs.com.

Botulinum toxin for treatment of focal HH

Botulinum toxin (Botox) is now recognized as a safe and effective treatment for controlling focal HH and is indicated when 20% aluminum chloride hexahydrate proves ineffective or poorly tolerated.

This treatment was approved by Health Canada in September 2001 for use in the armpits. Most insurance companies cover this treatment for areas other than the armpits when it is warranted (www.sweatmanagement.ca).

Botox injections in hands and feet

When performing intradermic injections in the hands and feet, the major problem is the intense pain caused by the nerve endings present in the skin. This pain requires locoregional anesthesia because local anesthetics (e.g., EMLA cream under occlusion) have proven ineffective. The most commonly used method for relieving pain involves a nerve block followed by local intravenous anesthesia. Other methods have been reported (e.g., applying ice immediately after injection and cryoanalgesia with dichlorotetrafluoroethane), but performing injections into frozen tissue can be problematic.

Many physicians refuse to treat palmar HH with Botox because of the potential risks associated with the nerve block: damage to nerve structures, vessel punctures, diminished manual dexterity during the hours and days following the nerve block, and reactive hyperemia. The latter causes an increased tendency to bleed at injection sites, causing a considerable loss of rather costly injected Botox. As well, there is a risk of scarring when a nerve is constantly exposed to repeated needle-induced trauma.

Comments from patient who received Botox injections for palmar HH

"Since receiving Botox injections, my quality-of-life has improved considerably. Not only am I able to shake hands, my hands don't swell up anymore (they used to swell as soon as

Treatment algorithm for palmoplantar HH	
Mild	A. 30% aluminum chloride in salicylic acid gel B. 40% aluminum chloride in salicylic acid gel*†
Moderate	A. 55% aluminum chloride in 6% salicylic gel B. Iontophoresis (with/without 40-55% aluminum chloride in 6% salicylic acid gel) C. 100 unit Botox injections into the palm or 150 units into each sole D. 100 unit Botox injections into each palm or 150 units into each sole + 55% aluminum chloride in a 6% salicylic acid gel
Severe	A. 150 unit Botox injections per palm or 200 units per sole B. 150 unit Botox injections per palm or 200 units per sole + 55% aluminum chloride in a 6% salicylic acid gel C. Endoscopic transthoracic sympathectomy for palmar HH and lumbar sympathectomy for plantar HH

*** Preparation of 40% aluminum chloride in a salicylic acid gel:**

A supersaturated concentration of 40% aluminum chloride in a salicylic gel can be obtained using commercial Hydrosal Gel. The complementary quantity (32.5 g) of the active ingredient, finely ground, is partially dissolved with heat in an adequate solvent/cosolvent mixture. In addition, the appropriate mixture of gelling/thickening/anticristallising agents is dispersed in a test sample of 50 g of Hydrosal Gel (7.5 g $AlCl_3$, 6 H_2O). When shaken, the hot dispersion of the active ingredient is added to the previous mixture and both are blended (electric blender) until cool. The result is a clear, homogenous and consistent gel that is kept in the refrigerator.

† Recipe designed by Adom Boudjikanian, Ph D Pharm and Yetvart Paylan, B. Pharm (yetvart@hyperidrosis.com)

Advantage of aluminum chloride (15-55%) in salicylic acid gel (3-6%) adjusted to meet the needs of the patient

- As first-line treatment for axillary, inguinal, craniofacial, palmar and plantar HH.
- As a complementary treatment to iontophoresis and Botox injections when these fail to control focal HH when used alone.
- When used as a complementary treatment to Botox injections, the dose of the injections can be reduced and the interval between them can be increased. This reduces the potential risk of neutralizing antibodies forming that render Botox ineffective, as well as the cost.

they became moist). As well, most of my sweat-related problems have disappeared. Despite the warnings you gave me, I didn't experience any pain or restricted movement."

New on the horizon

As previously mentioned, the major obstacle to treating palmar HH with Botox is the intense pain caused by introducing a needle into the highly sensitive skin of the palms. A nerve block, which is most commonly used to fight pain, may cause complications. Needleless anesthesia is an alternative method that avoids the effects of a nerve block. In 2005, this method's principle was published in the *Journal of the American Academy of Dermatology* and details later appeared in an October 2006 "Special Report" in *Therapy*. The procedure can also be viewed on the site http://hyperhidrosis.ca. A paper on needleless anesthesia was presented at the Congrès de l'Association des dermatologistes du Québec in Saint-Sauveur in 2006.

Clinical case revisited

After receiving an explanation of the injection procedure, the chances of success (70%), and the risk of weakness following the injections (20%), the patient signed a consent form. He then received 100 units of Botox by direct injection with a needleless injector in his left hand only, given that the patient is right-handed. This precaution was taken in order to determine the patient's tolerance for treatment and susceptibility to muscular weakness, and to determine if 100 units was the appropriate dosage, without disturbing his professional activities or exposing him to danger. Unfortunately, the treatment did not provide the desired result.

On August 4, 2005, the patient received an additional Botox dose of 50 units in his left hand. This time, however, he received needleless anasthesia before being injected with Botox by a needle. Simultaneously, he also received 150 units of Botox in his right hand and experienced little or no muscular weakness afterwards. This time, the treatment was effective and its effect began to fade about six months later. Soon after the sweating began again, application of the 55% aluminum chloride gel with 6% salicylic acid was attempted; this approach proved to be effective and prolonged the remission. Thanks to the gel, the reinjection of Botox was put off until later and additional costs were avoided.

In addition to working alone in cases of less severe palmar HH, when combined with Botox, the gel helps avoid very high doses of Botox and prolongs the interval between injections, just as we saw with our policeman. Moreover, the gel helps prevent the formation of neutralizing antibodies that render Botox completely ineffective. Given that the patient suffers more during the summer season, it would be wise to plan Botox injections as needed as the summer approaches. His last visit took place on January 4, 2006, and he later reported by phone that everything was under control at the end of December, 2006, except that he needed to renew his prescription for the gel.

Impact of HH on quality-of-life

Focal HH is under-diagnosed and under-treated. It can cause a significant social, professional and psychological handicap, and devastate an individual's social and professional life. Despite intense information campaigns in the media in recent years, HH remains an unpopular subject in medicine and among a large number of physicians, as the following excerpts from a patient's testimonial reveal:

I have suffered from hyperhidrosis of the hands and feet since the age of 16. I am now 47. The horrible sogginess appears when it gets hot. I'm a veritable thermometer. As soon as the temperature hits 22ºC, my hands and feet begin to get moist and to sweat, and soon they are soaked with water. Sometimes they even drip. From a professional perspective, I would love to have studied but that would have meant flipping through books and writing; in the workplace I would have had to shake hands, so I had to bury that possibility. I had decided to suffer in silence with my handicap knowing that I would probably never be able to:

- walk comfortably hand-in-hand with my partner
- dance comfortably with my partner
- hold my child's hand
- hold a child in my arms without soaking his pyjamas
- play tennis, golf or cards
- wear open-toed shoes (swollen wet feet are slippery and dangerous)
- paint, knit, fix things around the house, etc.

In the winter of 2006, I was listening to a radio call-in show and heard a young woman with hyperhidrosis explain that she was doing much better thanks to the treatments she had received from a dermatologist. I took note of the doctor's name and made an appointment. I was very emotional as I explained to him how this problem had poisoned my life for 31 years. He assured me that he could treat me. He prescribed a gel that I had to apply every evening before bedtime for several months. I noticed an improvement after the very first application. After five days of application, my problem had largely disappeared. To prevent it from coming back, I do a gel treatment two days before and two days after a special event. On a very hot day about a month after my treatment, I felt the moistness returning and did a treatment. To stay comfortable, I have to apply the gel once every two weeks. How is it possible that no doctor was

able to refer me to a specialist who could treat me? I finally came to the conclusion that hyperhidrosis is still misunderstood by many physicians.

The doctor-patient relationship

It is absolutely essential to listen to your patient well and to understand his dilemma. My patients and the general public can access my Web site at www.hyperhidrosis.ca and contact me by e-mail at info@hyperhidrose.ca. They can get an overview of the problem and find hope once again.

Advice for patients

Instructions for using aluminum chloride for the treatment of sweating of the hands and/or feet.

1. At bedtime, wash and dry your hands and feet with a hair dryer (without heat) then apply a thin layer of gel on the palms of the hands or soles of the feet.
2. Initially, the gel should be applied every night. Six weeks of treatment are necessary to obtain tangible results on the hands. Sweating of the feet is controlled more quickly. Once the sweating is under control, the treatment frequency is adjusted to once a week or even less often. The optimal frequency for the application of the gel can vary from one person to the next and may be as rare as once a month. Some people prefer to use the gel every night for one or two weeks in order to achieve a remission that may last several months.
3. If the aluminum chloride content of the gel to be used on the hands and feet exceeds 30%, it is recommended that the gel be kept in the fridge and taken out one hour before use. It is also recommended that the gel be stirred with a sterile spatula before use.
4. These preparations are not intended for use in children unless recommended by a doctor.
5. The gel also rids the feet of the bad odor that often accompanies sweating.

Instructions for patients receiving Botox injections for palmar HH

Bruises may appear on the palms after the injections, but these will last only a few days. Muscular weakness in the hands may occur in about 20% of injected patients during the week following a Botox injection. On average, this lasts for two to three weeks and causes a loss of manual dexterity, especially at the tip of the fingers, potentially causing difficulties with:

- manipulating small buttons
- using eyebrow tweezers
- buckling a car seatbelt
- pinching and picking up small objects from a smooth surface
- closing a zipper
- rubbing a five dollar bill between the fingers to be sure there is only one
- sensitivity at the injection sites.

These effects usually disappear within 2-3 weeks and do not pose a problem for patients who need to undergo periodic treatments, such as once or twice a year, to keep their palmar HH under control.

The procedure can be seen on line at: www.hyperhidrosis.ca ■

references: 1. Lowe N, Campanati A, Bodokh I, et al. The place of botulinum toxin type A in the treatment of focal hyperhidrosis. ***Br J Dermatol*** 2004;151:1115-11122. 2. Benohanian A. Correspondence. The place of botulinum toxin type A in the treatment of focal hyperhidrosis. ***Br J Dermatol*** 2005;153:2:460-461. 3. Hornberger J, Grimes K, Naumann M et coll. Multi-Specialty Working Group on the Recognition, Diagnosis and Treatment of Primary Focal Hyperhidrosis. Recognition, diagnosis, and treatment of primary focal hyperhidrosis. ***J Am Acad*** Dermatol 2004;51(2):274-286. 4. Benohanian A. Needle-free anesthesia: a promising technique for the treatment of palmoplantar hyperhidrosis with botulinum toxin A. ***Therapy*** 2006; 3 (5):591-596. 5. www.hyperhidrose.ca 6. www.sweatmanagement.ca/ 7. www.botoxseveresweating.com/index.aspx 8. www.francehyperhidrose.org 9. www.abimelec.com/transpiration_excessive.html