Palmar Hyperhidrosis

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The sweating system of the human skin, a powerful thermoregulatory tool, consists mainly of two to four million eccrine sweat glands, first described by Purkinje in 1833. Diseases of the sweating system have been referenced in the literature for centuries, since the time of Hippocrates. However, hyperhidrosis does not appear in writing until more recent times. The French physiologist Claude Bernard suffered from a peculiar form of hyperhidrosis called gustatory hyperhidrosis (profuse sweating triggered during meals), and one of the characters in Charles Dickens's David Copperfield (Uriah) was described as having palmar hyperhidrosis. Like many other cases in the history of medicine, the benefits of a sympathectomy to treat hyperhidrosis were found serendipitously.

Physiology

Human skin contains two different types of sweat glands: the *eccrine* glands, which are involved in physiologic thermoregulation, open directly onto the skin, and are located throughout nearly the entire body surface; and the *apocrine* glands, which are only located in certain areas such as the axilla and perineum, secrete a viscous lipid-rich fluid through hair follicles, and are not involved in thermoregulation.

The eccrine glands respond to different local and central thermal stimuli. When central thermoreceptors detect an increase in body temperature, a sympathetic signal is triggered in the hypothalamus. Neurons from the hypothalamus descend via the autonomic bundle of the intermedio-lateral column of the spinal cord and merge with the preganglionic sympathetic neurons at every level of the thoracolumbar spine. The axons of the preganglionic neurons exit the spinal cord via the anterior roots and meet the postganglionic neurons located in the ganglia that form the paravertebral sympathetic chain. The postganglionic neurons that innervate the eccrine sweat glands are the only postganglionic neurons in the human body that release acetylcholine instead of epinephrine. In turn, the cell membrane of the cells of the eccrine glands has muscarinic receptors, which explains the use of muscarinic-antagonist anticholinergic drugs in the management of hyperhidrosis.

The technical definition of hyperhidrosis is "sweating that exceeds thermoregulatory needs" and it applies to all forms of hyperhidrosis. The first and most critical step in the evaluation of a patient with hyperhidrosis is to determine if it is a case of *primary* hyperhidrosis or *secondary* hyperhidrosis. Secondary hyperhidrosis is a manifestation of several medical conditions such as hypertension, hyperthyroidism, and lymphomas, among others, or can be a side effect of medications such as antidepressants and antivirals. Secondary hyperhidrosis is usually generalized and does not stop during sleeping hours. While most case of primary hyperhidrosis are typical and differ from secondary hyperhidrosis, a proper evaluation of the patient through a history and physical exam is mandatory to avoid a misdiagnosis.

Etiology

The etiology of primary hyperhidrosis is largely unknown. There is a strong clinical suspicion that there might be a genetic predisposition, since up to 30% of patients have at least one family member with the condition. Families with affected members in several generations have been studied and single nucleotide polymorphisms have been identified in chromosomes, 2, 14, and 16. It appears that the most common inheritance pattern is dominant, however, there is a complete lack of a mechanistic explanation.

Nevertheless, the clinical presentation of primary hyperhidrosis is so variable that the etiology is almost certainly multifactorial. Psychological factors may also play a role, if not in determining the onset of the disease, at least in determining its day-to-day manifestations. Since many patients have their onset in the early years of childhood, it is hard to

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believe this would be driven by a particular psychological issue. On the other hand, most patients experience worsening of their symptoms when they reach puberty, a time during which their social life starts to be affected by their condition. Whether this is true or is a simple perception, is also not clear.

An intrinsic autonomic dysregulation resulting in sympathetic overactivity is also a likely candidate to explain primary hyperhidrosis, but simple questions such as why is it focal and why there are no other manifestations of systemic autonomic dysfunction are still unanswered. Lastly, histological abnormalities, such as a higher number of ganglion cells, and enzymatic abnormalities such as a decrease in plasma nitric oxide levels, have been suggested as partial culprits for primary hyperhidrosis, but there is no obvious logical connection between those findings and the clinical manifestations of the disease.

Diagnosis

The diagnosis of primary focal hyperhidrosis is clinical and does not require any complementary tests. The history and the physical exam are enough to make the diagnosis and determine the severity of each case. Traditional studies such as the iodine-starch test are obsolete and do not add any valuable information.

Patients with primary focal hyperhidrosis typically have excessive sweating on their palms, soles, and/or axillae. The degree of sweating ranges from clammy skin in mild cases to constant literal dripping of sweat in more severe cases. Excessive sweating occurs regardless of ambient temperature, although heat tends to exacerbate it. Stressful situations also often make the sweating worse. Most patients have intermittent excessive sweating with some periods of relatively dry skin, and almost all patients have dry skin during sleep. There are unusual cases where excessive sweating affects other areas of the body such as the thighs, the buttocks, or the perineum. Furthermore, I have seen two patients with excessive sweating of the ventral aspect of a single forearm. These cases may be secondary to local eccrine gland hyperplasia, which has been described anecdotally in the literature.

Patients with primary focal hyperhidrosis are greatly affected by the condition, often at multiple levels. The excessive sweating of the palms makes it challenging to handle instruments, hold papers without ruining them, or properly use touch screens. Driving can be dangerous due to slipping on the steering wheel. Sports that involve holding a racquet, a bat, or a ball may be impossible to play efficiently. Last and just as important, the social life of patients with primary hyperhidrosis is severely impaired. From shaking hands to holding hands, to just interacting with peers in any way that involves contact can be so embarrassing that patients commonly withdraw from those situations. Patients with affected palms commonly wipe them constantly on their clothes or hold a cloth in their hands all the time. Patients with severely affected soles must use socks all the time. Patients with affected axillary regions usually have to change clothes several times a day and can only use dark-colored clothes.

There are other less common types of primary focal hyperhidrosis, which rarely affect children. One of them is facial hyperhidrosis, which is somewhat similar to the typical form of palmar hyperhidrosis but exclusively affects the face, forehead, and scalp. The other one is gustatory hyperhidrosis, which also involves excessive sweating and flushing of the face, but in response to the stimulus of taste.

Multidisciplinary Approach

Patients and families with primary focal hyperhidrosis often spend years without finding a reliable source of help, since general pediatricians are frequently unfamiliar with the condition or may not perceive it as a real disease. To provide the best possible care and the full range of management options to patients with hyperhidrosis, it is key that dermatologists, surgeons, pediatricians, cardiologists, and psychologists work together as a team. We feel a pediatrician should be part of the group to help rule out secondary hyperhidrosis in cases that are atypical or that cannot be easily evaluated by other specialists.

In patients who are potential surgical candidates, we obtain an EKG. A sympathectomy should not be offered to patients who have profound baseline sinus bradycardia or who have any type of arrhythmia. It is important that a cardiologist be part of the team to provide prompt follow-up when these or other abnormal findings are detected. Furthermore, the medical management of primary hyperhidrosis often involves medications that can have cardiovascular effects, so having a cardiologist familiar with the disease and its management is of great importance. Our team also includes a pediatric psychologist who evaluates every patient that is a potential surgical candidate. The goal of this is to make sure that they are mature enough to understand the implications of the elective procedure, that they participate actively in the decision to undergo a sympathectomy, and most importantly, to make sure that they do not have unrealistic expectations about how their social life is going to change after the operation.

Lastly, we meet with patients and their families twice before deciding about sympathectomy. During the first visit, in addition to the history and physical exam, the patient completes a quality-of-life questionnaire, the parents are given articles from the literature, and we discuss all the potential treatment options and their implications. When patients

become potential surgical candidates (either because they have failed or do not want to try medical options), we meet for a second time. During the second visit we discuss again every aspect of the operation, the patients meet with the psychologist, and if there are no contraindications, we proceed with the sympathectomy electively.

Medical Management

There are several medical options for patients with primary focal hyperhidrosis, and while they are remarkably diverse, they all have the common feature of not being a cure but an ongoing treatment. Since the pathophysiology of the disease is not understood, management modalities of the most extreme nature have been explored throughout history, from radiotherapy to antibiotics, from herbal medicines to acupuncture, just to mention a few. In the current era, the most common forms of medical management are:

1. *Topical antiperspirants*. This is the most common first-line form of therapy. These products are solutions of highly concentrated aluminum chloride hexahydrate, deposits of which block the outlets of the eccrine glands. The concentration varies from 10% in over-the-counter formulations to 20% in prescription-only formulations. Patients apply the solution over the affected areas at night. The area to which the product is applied needs to be covered with some type of plastic material such as gloves or plastic wrap, in order to avoid wiping it off with the clothes, sheets, or blankets. In the morning, the plastic cover is removed and the affected area is abundantly rinsed with water. The success rate of this form of therapy varies greatly. Common side effects include itchiness, irritation, and peeling of the skin, frequent reasons why patients abandon them.
2. *Iontophoresis*. The speculated mechanism through which iontophoresis can decrease the elimination of sweat is by temporarily blocking the outlets of the eccrine glands with salt deposits. The patient places the hands or the soles in a pan filled with tap water, to which a low-voltage 15–20 mA electrical current is applied. The affected areas need to be submerged for 20–30 min, two or three times per day, and after a few days of repeated sessions, the excessive sweating begins to decrease. At that time the patient can interrupt the daily sessions until the excessive sweating resumes, usually 2–4 weeks later. To increase the effectiveness, some will add antimuscarinic drugs to the water. Iontophoresis is contraindicated in patients with cardiac arrhythmias, pacemakers, skin lesions, seizure disorders, or any type of metallic implant. Common side effects include skin irritation and itchiness, paresthesias, numbness and tingling, among others. The success rate varies greatly in the literature. Regardless, it is generally not a very attractive option due to its time-consuming nature.
3. *Botulinum toxin*. Botulinum is the most powerful poisonous biological substances in nature. It is a neurotoxin that exerts its effect by blocking the release of acetylcholine from all neurons that use that neurotransmitter, which in humans includes: motor neurons, autonomic preganglionic neurons, parasympathetic postganglionic neurons, and cholinergic postganglionic sympathetic neurons, those that stimulate the eccrine glands being the only ones known. There are many medicinal uses of botulinum toxin, the oldest of which is the treatment of strabismus. Today the most common use, by far, is in cosmetology. For the management of hyperhidrosis, the toxin needs to be injected locally into the subcutaneous tissue of the affected area. Because the toxin does not spread, roughly every square centimeter of the affected area requires its own injection. This means that, for instance, a single palm of a teenager requires 50 or more injections. The effect of the toxin starts 24–48 h after the injection and lasts for about 12 weeks, after which the treatment needs to be repeated. Though effective and, for some patients an acceptable option, the injections are painful and followed by several days of swelling and local inflammation. This is rarely a sustainable management option in the pediatric population.
4. *Anticholinergics*. The use of acetylcholine in our nervous system is so ubiquitous that anticholinergic drugs have multiple applications in human medicine. The counterpart is that the side effects of these drugs spread over a wide range of organs and systems. For the management of primary hyperhidrosis there are several oral medications that can be used, the most common ones being glycopyrrolate and oxybutynin. These drugs are antagonists of the muscarinic receptors, and as such they block the input of the postganglionic sympathetic neurons on the eccrine glands. When taken orally, they have a half-life of about 3 h, so the effects last less than a full day. The most common way to use them is to take a dose in the morning prior to going to school or work and repeat the dose in the afternoon if the patient wants it. There is no lasting cumulative effect and so are taken as needed. As with the other medical options to treat primary hyperhidrosis, the success rate varies greatly and potential side effects are many and predictable, including headache, dizziness, dry mouth, dry eyes, constipation, urinary retention, and blurred vision. Blurred vision is due to the inability of the lens to accommodate, making activities like driving or operating machinery particularly dangerous. In our experience, approximately 25% of the patients are able to tolerate oral medications as a long-term treatment. The other 75% will abandon them due to the side effects, or due to

fear of long-term effects. There is a growing body of literature that suggests a link between anticholinergic drugs taken over prolonged periods of time and an increased risk of dementia. There are also commercially available wipes embedded with anticholinergic drugs that are used topically, theoretically avoiding significant systemic absorption.

Less common options include microwave ablation of sweat glands, antidepressants, surgical removal of the affected skin, and laser therapy, among others, none of which are approved for use in children.

Surgical Management

Surgical intervention is generally reserved for patients with primary palmar focal hyperhidrosis, which we believe is the only case for which surgery should be offered in children. Surgery for primary axillary or plantar hyperhidrosis (lumbar sympathectomy) should not be offered in the pediatric population because we believe the risks outweigh the benefits.

We offer a bilateral thoracoscopic sympathectomy to patients older than 8 years of age who have palmar focal hyperhidrosis (with or without other areas involved) and who have failed at least one form of medical therapy. Additionally, patients need to have a normal EKG and a favorable psychologic assessment. Patients without palmar hyperhidrosis or multifocal hyperhidrosis whose main concern is not the palmar sweating are not offered surgery. As regards the minimum age for surgery, we believe that while the operation can be done in younger patients, the quality of life is not critically affected by palmar hyperhidrosis during the first years of elementary school. This, however, should be discussed on a case-by-case basis.

Endoscopic sympathectomy was first performed in the 1930s. The principle of the operation is to interrupt sympathetic input to the eccrine glands of the palms. There are, however, multiple techniques described, each claiming to be the ideal one, but all focusing on the paravertebral sympathetic chain in the upper chest. Options include: dividing the sympathetic chain ("sympathotomy"), resecting a segment to include the involved ganglia ("sympathectomy"), clipping it, or chemically ablating it, any of which can be done at different levels. Clipping the chain has the theoretical benefit of being reversible, at least in the short term, and is not commonly used in children. Injecting the sympathetic chain with a local anesthetic is not used as definitive therapy but as a test to determine whether the operation might lead to excessive compensatory sweating, also generally not done in children.

Whether to perform sympathotomy or sympathectomy, and at what level, is a matter of the surgeon's preference—there is no definitive evidence to support one technique over another. It is clear the area that needs to be divided is below T2 and above T5. In general, a higher level of intervention is associated with a higher success rate, but also a higher incidence of compensatory sweating. Disrupting the sympathetic chain above T2 carries an unjustified risk of producing the Horner syndrome.

We perform bilateral sympathotomy at the level of T3. Patients are intubated with a double-lumen endotracheal tube for selective lung isolation and receive two large-bore peripheral IVs. No preoperative antibiotics are administered. Patients are placed in a supine position with the arms extended and the elbows flexed and well padded (Fig. 38.1). We prepare and drape the entire chest to have the option of a quick thoracotomy or sternotomy, in the unlikely event that it becomes necessary. We start on the right side, placing a 5-mm port posteriorly and a 3-mm port anteriorly in the axilla. A 4-mmHg CO_2 pneumothorax is used to collapse the lung. We identify the sympathetic chain, which runs along the vertebral bodies of the thoracic spine adjacent to the heads of the ribs. It is key to be familiar with the anatomy as the phrenic nerve and the vagus nerve look just like the sympathetic chain. Next, we identify and mark with cautery the third rib, and we confirm this with fluoroscopy, appending the images to the patient's electronic medical record (Fig. 38.2). We transect the sympathetic chain with monopolar cautery at the head of the third rib, making sure that the two ends retract far apart from each other. The entire surface of the head of the third rib is cauterized to ensure that there are no connecting fibers left. Additionally, we cauterize the third rib for a length of 2 in. to make sure that any potential bypassing fibers (nerve of Kuntz) are divided as well. Once this is completed, we allow the lung to expand and evacuate the CO_2 with a red-rubber catheter under a water-seal. We

Fig. 38.1 Patient position for the operation. The arms are extended, and the elbows are flexed and well padded. A double-lumen endotracheal tube is in place

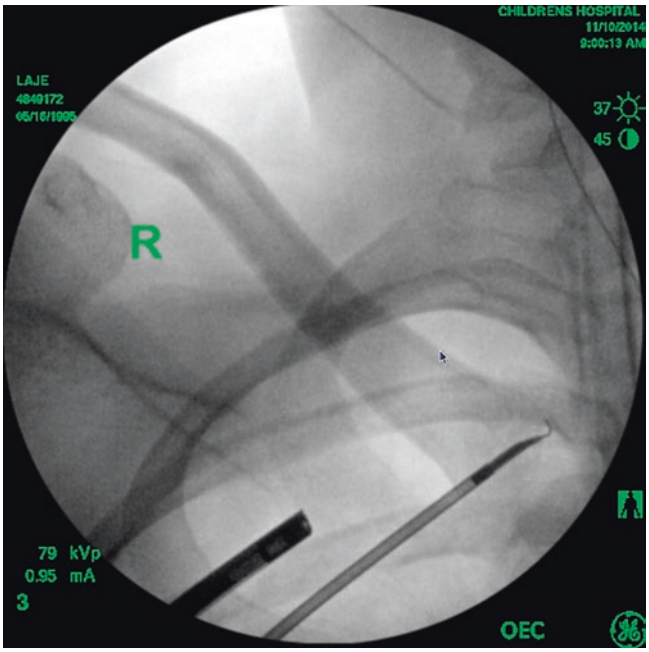

Fig. 38.2 Fluoroscopic identification of the third rib head on the right side

then repeat the procedure on the left side. The operation takes approximately 20–30 min per side. We leave no chest tube and admit all patients for overnight observation.

The risks of the operation are few but potentially significant and should not be minimized or dismissed. Major vascular and cardiac injuries have been described, as well as damage to the lung causing persistent air leaks. Occasionally one encounters branches of the azygous vein lying right on top or in the vicinity of the head of the third rib, in which case care must be taken to cauterize them appropriately. The careless manipulation of the sympathetic chain, by pulling too hard or by extending the cauterization too proximally can lead to temporary or even permanent Horner syndrome, which is an unacceptable complication.

Though not technically complications, there are a few potential known side effects of sympathectomy. The most relevant is *compensatory hyperhidrosis*. In practical terms, this is the postoperative development of excessive sweating on a body part that was not initially involved, mainly the thighs or the torso. The pathophysiology of this phenomenon is unknown and the diagnosis is not always easy given that most cases are mild. Interestingly, compensatory sweating can also be observed with medical treatment of primary focal hyperhidrosis. The incidence of this side effect is higher in adults than in children, although the actual numbers are unknown and vary substantially in the literature. The majority of the cases are not severe enough to require treatment. The only available treatment is anticholinergic. While in theory the sympathetic chain can be reconstructed with a nerve graft, such an approach has only been described anecdotally and the results are questionable. Compensatory sweating can develop from shortly after the operation to years later. Because of this, the nerve-blocking test (with a local anesthetic) has very low sensitivity and its risks are not justified. As regards the patients' perception of compensatory sweating, it is clear from the literature that a very low percentage of the patients who develop it regret having had the operation, since almost everyone prefers excessive sweating on the torso or thighs than on the hands. The most important aspect of compensatory sweating is to discuss its potential risk with the patient and the family before the operation, as many times as needed, so that they can make an informed decision. I cannot emphasize enough how careful we are in our practice in having multiple open and frank discussions with the patient and family about all the potential risks and side effects of surgery.

Outcomes

There is perhaps no operation in pediatric general surgery as rewarding as thoracoscopic sympathectomy. After years of suffering, patients wake up from the operation with their hands completely dry, and in essentially all cases the improvement in their quality of life is instantaneous. In our experience, the operation is 100% successful in controlling excessive sweating of the palms immediately after the operation, with only exceptional cases (<5%) recurring, typically in a milder form, years later. Almost all patients develop complete dryness of the palms—in fact, some need to use skin lotion to keep the skin comfortably moist. In our experience, about 30% of the patients who had excessive sweating of their feet and underarms (in addition to their hands), experience an improvement after the operation. This result is unpredictable, and we clearly explain to patients and parents that the operation is not intended for this purpose, but only for the hands. We see our patients in clinic 1 week after the operation for a wound check, and then we follow up by video-visit or by phone at 1 month, 6 months, 1 year, and yearly thereafter. At each visit, the patient completes a quality of life questionnaire. The overall satisfaction with the operation is very high (>95%).

Editor's Comments

Although it might be easy to callously dismiss palmar hyperhidrosis as trivial or merely a cosmetic concern, these patients are miserable and often desperate for relief. In severe cases, it is more than just a source of social embarrassment or teasing; writing or using a computer keyboard or phone can be extremely difficult, papers and clothes become ruined, and wearing gloves of any kind is impossible. It can be truly

debilitating. Nevertheless, given the risk of any surgical intervention, sympathectomy is probably best offered only after a thorough evaluation by a dedicated and experienced multidisciplinary team, after medical options have been tried and failed, and after the patient understands exactly what to expect.

In carefully selected patients, the thoracoscopic approach appears to be very safe and, in experienced hands, extremely effective. Complications such as Horner syndrome and organ or vascular injuries should be extremely rare. Sequelae such as compensatory sweating (usually on the torso), gustatory sweating (increased sweating during meals), and hands that are uncomfortably too dry are relatively common but generally well-tolerated. Regardless of side effects, the vast majority of patients are pleased with the results of the operation.

There is some controversy as to which level is best. Most agree that for palmar hyperhidrosis, dividing the sympathetic chain between T2 and T3 (third rib) or between T3 and T4 (fourth rib) is acceptable. Most studies confirm the higher the level the drier the hands and the higher the risk of compensatory sweating. To protect the patient and the surgeon, it is wise to always use an adjunct such as fluoroscopy to confirm the vertebral level with certainty. Too high a level of dissection risks injury to the stellate ganglion (T1) and a subsequent Horner syndrome (enophthalmos/ptosis, pupillary constriction, anhidrosis—often with lack of flushing on half of the face or Harlequin syndrome). The energy source used probably makes little difference as long as the collateral injury is avoided and complete transection is achieved. As with most operations, the combination of high surgical volume and access to a multidisciplinary team of dedicated professionals produces the best outcomes.

Further Reading

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