CME/CE Information

CME/CE Released: 02/28/2002; Valid for credit through 02/28/2003

This activity has expired.

The accredited provider can no longer issue certificates for this activity. Medscape cannot attest to the timeliness of expired CME activities.

Target Audience

This activity is intended for dermatologists, neurologists, psychiatrists, primary care physicians, nurses, and psychologists.

Goal

The goal of this activity is to provide practitioners with an understanding of the physiologic and psychological impact of hyperhidrosis and to offer an up-to-date overview of treatment options so that clinicians can evaluate and recommend treatment to patients with this often disabling condition.

Learning Objectives

Upon completion of this self-study activity, participants will be able to:

1. Define hyperhidrosis in the context of the neurobiology of sweating.
2. Describe the psychological and physiologic impact of hyperhidrosis.
3. Discuss current treatments available for hyperhidrosis in the context of a risk/benefit analysis.

Credits Available

Physicians - maximum of 1 *AMA PRA Category 1 Credit(s)*™

Nurses - 1.2 *ANCC* (0 contact hours are in the area of pharmacology)

All other healthcare professionals completing continuing education credit for this activity will be issued a certificate of participation.

Physicians should only claim credit commensurate with the extent of their participation in the activity.

Accreditation Statements

For Physicians

Medical Education Collaborative, a nonprofit education organization, is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Medical Education Collaborative designates this educational activity for a maximum of 1 hour in Category 1 credit towards the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

Contact This Provider

For Nurses

This educational activity for 1.2 contact hours is provided by Medical Education Collaborative.

Provider approved by the California Board of Registered Nursing, Provider Number CEP-12990 for 1.2 contact hours.

Florida BN Provider Number: FBN-2773

Contact This Provider

For questions regarding the content of this activity, contact the accredited provider for this CME/CE activity noted above. For technical assistance, contact CME@medscape.net

Instructions for Participation and Credit

There are no fees for participating in or receiving credit for this online educational activity. For information on applicability and acceptance of continuing education credit for this activity, please consult your professional licensing board.

This activity is designed to be completed within the time designated on the title page; physicians should claim only those credits that reflect the time actually spent in the activity. To successfully earn credit, participants must complete the activity online during the valid credit period that is noted on the title page.

Follow these steps to earn CME/CE credit:

1. Read the target audience, learning objectives, and author disclosures.
2. Study the educational content online or printed out.
3. Online, choose the best answer to each test question. To receive a certificate, you must receive a passing score as designated at the top of the test. Medscape encourages you to complete the Activity Evaluation to provide feedback for future programming.

You may now view or print the certificate from your CME/CE Tracker. You may print the certificate but you cannot alter it. Credits will be tallied in your CME/CE Tracker and archived for 5 years; at any point within this time period you can print out the tally as well as the certificates by accessing "Edit Your Profile" at the top of your Medscape homepage.

The credit that you receive is based on your user profile.

Hardware/Software Requirements

Medscape requires version 4.x browsers or higher from Microsoft or Netscape. Certain educational activities may require additional software to view multimedia, presentation or printable versions of their content. These activities will be marked as such and will provide links to the required software. That software may be: Macromedia Flash, Apple Quicktime, Adobe Acrobat, Microsoft Powerpoint, Windows Media Player, and Real Networks Real One Player.

Supported by an unrestricted educational grant from:

ALLERGAN

Faculty and Disclosures

Author(s)

Jonathan R.T. Davidson, MD

Professor, Department of Psychiatry, Duke University, Durham, North Carolina.

Disclosure: Jonathan R.T. Davidson, MD, has disclosed that he has received grants for educational activities and has served as an advisor or consultant for Allergan. He has also disclosed that he has received speaker fees from Solvay, Pfizer, GlaxoSmithKline, Wyeth-Ayerst, and the American Psychiatric Association. He has received consulting fees from Solvay, Pfizer, GlaxoSmithKline, Forest, Eli Lilly, Ancile, Roche, and Novartis. He owns stock in Pfizer, American Home Products, GlaxoSmithKline, Proctor & Gamble, and Triangle Pharmaceuticals. He has also received research support (PI/Invest) from Pfizer, Solvay, Eli Lilly, GlaxoSmithKline, Wyeth-Ayerst, Organon, Forest, and Pure World.

Dee Anna Glaser, MD

Associate Professor, Vice-Chair, Department of Dermatology, St. Louis University, St. Louis, Missouri.

Disclosure: Dee Anna Glaser, MD, has disclosed that she owns stock, stock options, or bonds, received grants for clinical research, and served as an advisor or consultant for Allergan. She has received honoraria from Novartis. She has also disclosed that she has served as a consultant and speaker for Bristol-Myers Squibb.

Markus Naumann, MD

Assistant Professor, Department of Neurology, University of Wuerzburg, Wuerzburg, Germany.

Disclosure: Markus Naumann, MD, has disclosed that he has received grants for clinical research and has served as an advisor or consultant for Allergan.

From Medscape Neurology

Hyperhidrosis: Current Understanding, Current Therapy

Authors: Markus Naumann, MD; Jonathan R.T. Davidson, MD; Dee Anna Glaser, MD

Posted: 02/28/2002

Preface: The Patient's Perspective

Lisa dates her problem with hyperhidrosis to her sophomore year of high school. It probably started a bit earlier, she thinks, but a humiliating experience during her Oral Communications class marks the symbolic beginning of her struggle with hyperhidrosis. After literally sweating through an oral presentation in front of the class, she heard a

fellow student mutter in disgust, "Oh my God, look at her. Look at how bad she's sweating." Lisa still finds the memory painful.

Being a 15-year-old girl is tough, but being a 15-year-old girl with hyperhidrosis is tougher. The fun of being a cheerleader was overshadowed by the turmoil of constantly worrying about how much she was sweating. She worked up the courage to tell her parents, but they didn't really understand. "I didn't even know that prescription antiperspirants existed, and I was too young to take the situation into my own hands," she remembers today at age 26. So she changed clothes 3 times a day, stuffed tissues, napkins, and paper towels in her armpits, and blamed herself. And that's how she coped with hyperhidrosis for the next 8 years.

A newsmagazine show was on the TV, but Lisa wasn't paying much attention. Then she realized that the woman being interviewed was talking about her constant battle with sweating. "My head just spun around," remembers Lisa. "I thought it was just me, and so I blamed myself. Then I saw this woman on TV and I realized, I'm not the only one."

And so at age 23 Lisa worked up the courage to see a doctor. He prescribed an antiperspirant, but it didn't help. Three months later, she went to a different doctor and got a prescription for a different antiperspirant, but it didn't help either. For the next 3 years, Lisa continued to perfect her routine for dealing with hyperhidrosis:

"I can't buy nice clothes, because I have to throw them away after wearing them once or twice, especially white things. I probably spend 2 hours a day dealing with sweating -- wiping, refreshening, showering, bathing, washing clothes -- but I really spend more time than that because I never stop thinking about it. When I go to a club with my friends, the first thing I do is check out the bathroom. Are there plenty of paper towels for me to stuff in my armpits? Is there an air-dryer I can use to dry my armpits? I don't take off my coat when I make presentations, and I never gesture with my hands -- people would see the sweat stains that go halfway down my arms, or, even worse, the paper towels might fall out. I always keep my arms held close to my body. When I visit friends or relatives, I make sure I hug everyone before I take off my coat."

Of course developing personal relationships has been difficult. Lisa has told only her parents -- who now understand the condition and are supportive -- and her boyfriend. But a favor Lisa recently did for her mother may hold the solution to her problem. Lisa's mother had an appointment with a dermatologist, and Lisa gave her a ride and sat in on the consultation. At the end of the appointment, Lisa asked about sweating. The dermatologist turned out to be a recognized expert in hyperhidrosis, and Lisa will begin treatment soon.

Definition, Epidemiology, and Symptoms

Hyperhidrosis is excessive sweating. The simple qualitative definition of hyperhidrosis as excessive sweating is, of course, completely subjective. For research purposes, hyperhidrosis is defined quantitatively as the production of more than 100 mg of sweat in 1 axilla over 5 minutes.[1]

Hyperhidrosis may be focal or generalized. Focal hyperhidrosis usually affects the axillae, palms, soles of the feet, face, and, rarely, other areas. It can be extremely disabling in both private and professional life. Focal hyperhidrosis affects up to 0.5% of the population and usually appears during the second or third decade of life.

Focal hyperhidrosis is most often essential, or idiopathic, and results from a neurogenic overactivity of the sweat glands in the affected area. The palms and/or soles of the feet (palmoplantar hyperhidrosis) are affected in about 60% of patients, and the axillae are affected in 30% to 40%.[2] Facial sweating is less frequent and affects up to 10% of patients with idiopathic hyperhidrosis. Facial hyperhidrosis should be distinguished from gustatory sweating, which is a secondary form of hyperhidrosis that occurs on the cheek in response to salivation or anticipation of food.

While focal hyperhidrosis is psychologically distressing and anxiety can trigger sweating, the condition is only rarely associated with psychiatric disorders. Patients with focal hyperhidrosis have a physiologic condition, not a psychiatric disorder. Hyperhidrosis can, however, be secondary to social anxiety disorder. (See "Psychiatric Aspects

of Hyperhidrosis," below.)

Focal hyperhidrosis also may be secondary to spinal cord injury and some polyneuropathies. Ross syndrome is a rare form of focal hyperhidrosis of unknown etiology characterized by progressive anhidrosis due to degeneration of sudomotor fibers. There may be disabling compensatory hyperhidrosis in areas in which sudomotor fibers remain intact (mostly the trunk, sometimes the extremities, neck, and face).

Generalized hyperhidrosis, in which sweating occurs over the whole body, has many causes, including diabetes, chronic infectious diseases, and malignancy.

The consequences of hyperhidrosis include dehydration and maceration of the skin, which may result in secondary skin infections.

Neurobiology of Sweating

The human body has an estimated 2-4 million eccrine glands[3] which play an important role in cooling the body in response to increased body temperature. The secretion of eccrine sweat involves the secretion of an ultrafiltrate by the secretory coil in response to acetylcholine (which is released from the sympathetic nerve endings) and reabsorption of sodium by the ductal portion so that the surface sweat is hypotonic.[4] When perspiration is heavy, this absorptive function is crucial for the conservation of electrolytes. The eccrine sweat gland does excrete other compounds, such as heavy metals and organic compounds.

The eccrine gland has a secretory coil and a duct. The coil is composed of clear cells (secretory), dark cells (mucoid), and myoepithelial cells.[5] The myoepithelial cells lie on the basement membrane, abutting the clear cells. The ductal portion has an outer ring of basal cells and an inner lining of cuticular cells. The proximal portion (coiled) of the duct is more active functionally than the distal (straight) portion. In the epidermis, the duct spirals tightly upon itself.

The clear cells are most likely responsible for the secretion of water and electrolytes. These cells have an abundance of membrane villi, membrane infoldings, and mitochondria. The function of dark cells is poorly understood. The contractile myoepithelial cells respond only to cholinergic stimulation and not to alpha- or beta-adrenergic agents.

Innervation of the eccrine glands originates from the hypothalamic preoptic sweat center and travels down through the brainstem and medulla. The nerve fibers synapse in the intermediolateral cell columns of the spinal cord without significant crossing. The myelinated preganglionic fibers pass out in the anterior roots to the sympathetic chain and synapse. Unmyelinated postganglionic sympathetic C fibers arising from sympathetic ganglions join the peripheral nerves and end around the sweat gland. The supply to the skin of the upper limbs is usually from T2 to T8. The trunk is supplied by T4 to T12, and the lower limbs by T10 to L2. There is significant overlap of innervation in the sympathetic dermatome; a single preganglionic fiber can synapse with several postganglionic fibers.

Acetylcholine is the major neurotransmitter, making eccrine gland sympathetic innervation unique; noradrenaline is generally the neurotransmitter in sympathetic nerves. Other mediators have been localized in the periglandular nerves, such as adenosine triphosphate, natriuretic peptide, calcitonin gene-related peptide, galanin, catecholamines, and vasoactive intestinal peptide. The significance of these substances is not fully understood.

Sweating can be induced by thermal stimuli and by emotional stress. Although emotional sweating can occur over the entire skin, it is more often limited to the palms, axillae, and soles. Emotional sweating of the palms and soles stops during sleep, whereas thermal sweating occurs even during sleep.[6] Both, however, are cholinergic.

The hypothalamic sweat center controlling the palms and soles is different from the rest of the hypothalamic sweat centers. It receives nerve inputs from the cerebral cortex and not from the thermosensitive preoptic region of the hypothalamus.

Emotional sweating is not augmented in warm environments. But excessive sweating of the palms and soles lowers the skin temperature of the hands and fingers secondary to excessive evaporative cooling, which increases the sympathetic outflow and aggravates the hyperhidrosis.

Pathophysiology of Hyperhidrosis

The cause of essential focal hyperhidrosis is unknown at present. The sweat glands and their innervation do not show any histologic abnormalities. A dysfunction of the central sympathetic nervous system, possibly of hypothalamic nuclei, or prefrontal areas or their connections is suspected.[5,6] Sufferers display no other signs or symptoms of autonomic dysfunction. A positive family history for the condition in 30% to 50% of cases suggests a genetic component.[7] Gustatory sweating may result from misdirection of autonomic nerves fibers after surgery or in diseases of the parotid gland, and may occur in diabetes and some other rare conditions. Generalized hyperhidrosis can be secondary to a variety of conditions including metabolic disease such as diabetes or hyperthyroidism; chronic infections like tuberculosis; alcoholism; and malignancy.

Psychiatric Aspects of Hyperhidrosis

Hyperhidrosis has been neglected in psychiatric practice, although it is recognized as a distressing and often disabling symptom. While hyperhidrosis often provides the impetus for seeking treatment, little is known about how to treat it, or how effective such treatment might be in psychiatric practice. Goldstein[8] points out how stubborn this symptom can be. As a clinical problem, hyperhidrosis is most likely to be encountered in the context of social anxiety disorder (SAD), where it may command clinical attention. The problem is unlikely to be seen as significant in other mood disorders.

Impact of Hyperhidrosis

Hyperhidrosis exerts a negative impact on the lives of many who suffer from it. Moran and Brady[9] have pointed out the "devastating consequences" that hyperhidrosis has on work and social activities. Lerer and colleagues[10] found that patients with hyperhidrosis had poorer coping abilities and more emotional problems compared with both dermatologic controls with nonpsychogenic problems and normal subjects. Moreover, they suggested a possible genetic predisposition to excessive emotional sweating.

Amir and colleagues[11] found that women were more impaired by hyperhidrosis than were men, and speculated that this finding may relate to the strong esthetic connotations associated with the problem. The researchers also found that subjects who developed the condition early in life suffered more than those with hyperhidrosis of later onset. Rather than becoming habituated to the problem, subjects who had dealt with the condition for a longer time had a lower quality of life than those who had been coping with the condition for shorter periods.

Measurement of Hyperhidrosis in the Psychiatric Context

Two scales developed for use in psychiatric practice include 5-point assessments of sweating. The Brief Social Phobia Scale (BSPS)[12] rates sweating on a 0-4 scale, in which 0 = none, 1 = mild (infrequent or not distressing), 2 = moderate (frequent and/or somewhat distressing), 3 = severe (constant or clearly distressing), and 4 = extreme (incapacitating or painfully distressing).

With the BSPS, the subject is asked to consider any situation that involves contact with other people -- even just thinking about such a situation -- and assess the symptoms experienced. Since subjects may have a history of avoiding distressing situations, it is important to assess patients' views of how they *would* react if they were to place themselves in stressful situations.

The self-rated Social Phobia Inventory (SPIN)[13] also adopts a 5-point range to assess sweating. With the SPIN, the patient is asked to self-rate the extent to which "sweating in front of people causes me distress."

Questionnaires that rate quality of life in regard to sweating include the Amir Hyperhidrosis Quality of Life Scale,[11] a 26-item scale related to the following domains: function, social activity, intimacy, self-appraisals, attributions made to others, and exacerbating conditions. The Dermatology Life Quality Index (DLQI)[14] is a 10-item scale that assesses factors associated with skin disease in general, including embarrassment/self-consciousness, social/leisure/work activities, and intimate and close relationships.

Prevalence Rates of Hyperhidrosis in Psychiatric Practice

No data exist, as far as is known, to indicate rates of hyperhidrosis in psychiatric settings. As mentioned, these data would most appropriately be sought among patients suffering from SAD. In a sample of 338 subjects with SAD, almost 25% reported hyperhidrosis prior to initiating treatment.[15] Approximately 50% had mild to moderate levels of sweating, leaving only one quarter with no excessive sweating at all. In attempting to characterize those with hyperhidrosis, there were no demographic differences with respect to age, gender, or age at onset. Subjects were noted to have heightened physiologic arousal in other areas (eg, trembling, blushing, palpitations), and showed greater disability measures than did a comparison group of subjects with no sweating or only mild sweating. While these findings are not necessarily representative of all clinical populations -- and still less representative of the community -- they are considered typical of subjects seeking treatment for SAD in an academic setting.

Psychiatric Treatment of Hyperhidrosis

No clinical trials have been conducted on hyperhidrosis treatment in the SAD population. It is possible that treatments which are otherwise effective for SAD may not be particularly beneficial for hyperhidrosis, but it is also conceivable that effective treatment of the fear and avoidance components of SAD may also be helpful for hyperhidrosis and, perhaps, other physiologic symptoms.

The largest treatment study of hyperhidrosis in SAD (social phobia) was conducted by Telaranta.[16] In this study, SAD patients were treated with endoscopic thoracic sympathectomy (ETS). (See general "Treatment" section below for description of the procedure.) Subjects suffered from chronic social phobia resistant to psychotherapy and drug therapy. Many patients had a history of addictive behavior, mental and physical abuse, and dysfunctional families. Parental alcoholism had untoward effects in 26% of the sample, and a history of familial violence was reported in 14%. Therefore, this may have been a treatment-refractory group that would be unlikely to respond to nonspecific or placebo treatment, or to achieve spontaneous remission.

Patients were assessed by trained psychiatrists, and the BSPS was used to confirm the diagnosis. Treatment achieved improvement in hyperhidrosis as well as substantial changes in core social phobia features. Thus blushing, palpitations, and anxiety improved by over 50% between pretreatment and follow-up at 4 months. Patient satisfaction was judged at a 4-month follow-up, with almost 50% reporting a great deal of satisfaction, and less than 10% reporting no satisfaction.

This study is important for a number of reasons. First, it is the only study to have seriously looked at hyperhidrosis in SAD. Second, it indicates that resistant cases might benefit from surgical treatment. And third, it indicates that the other features of SAD, such as palpitations and trembling, also improve with ETS treatment.

Pharmacotherapy of hyperhidrosis in psychiatry is poorly researched. There is 1 case report of benefit from clonidine,[8] and there is a conversational reference to the benefit of mirtazapine,[17] but with minimal detail.

Our recent analysis [Dr. Davidson][15] suggests some benefits for selective serotonin reuptake inhibitors (SSRIs) and benzodiazepine drugs, but less for psychotherapeutic approaches. With SSRI treatment, we noted a 53% reduction in sweating, and with a GABAergic anticonvulsant drug we noted a 40% reduction. With cognitive behavior therapy (CBT), a reduction of 25% was observed. Thus, there does seem to be some benefit for SSRI treatment of hyperhidrosis, modest benefit for anxiolytic/anticonvulsant treatment, and limited response to CBT. These findings need to be interpreted in the context that all 3 treatments are generally effective in the SAD population. But we

cannot assume that all treatments are broad-spectrum in their effects, and further adjunctive treatment of hyperhidrosis is perhaps desirable.

Further Questions

Most of the knowledge about SAD and its treatment applies only to the generalized subtype (GSAD). Almost nothing is known about the role of sweating in the more limited nongeneralized type of SAD (ie, performance anxiety). Are the same treatments effective? Is hyperhidrosis as disabling in this condition as it appears to be in GSAD? Also, does secondary anxiety associated with hyperhidrosis of nonpsychogenic origin respond as well to the same treatments? Would targeted treatment against excessive sweating in SAD, such as botulinum toxin, be helpful?

Hyperhidrosis Treatment

Treatment for hyperhidrosis ranges from topical treatment with antiperspirants to surgical procedures. Recently, local injections with botulinum toxin type A (BTX-A) have proved to be a novel, minimally invasive treatment option. (Food and Drug Administration labeling for BTX-A does not include an indication for hyperhidrosis.) An overview of current knowledge about the treatment alternatives for hyperhidrosis with a risk-benefit consideration follows.

Antiperspirants and Deodorants

Although many patients use the terms "antiperspirant" and "deodorant" interchangeably, they are not the same. An antiperspirant is an astringent meant to decrease eccrine and apocrine sweat secretion, while deodorants are designed to remove and mask odor from the axillae. The exact mechanism of action of antiperspirants is unknown, but several theories have been proposed. The most widely held posits that the metal salts contained in antiperspirants physically obstruct the ductal opening of the sweat gland.

Several chemicals can be used to reduce excessive sweating. Today, aluminum and zirconium are the metal salts most commonly used. Early formulations with sodium zirconyl lactate caused granuloma formation, and aerosol zirconium-based products were removed from the market almost 25 years ago due to skin irritation. Aluminum chloride, aluminum chlorohydrate, aluminum zirconium chlorohydrate, and buffered aluminum sulfate are the agents most commonly used.[18]

Topical antiadrenergic drugs could decrease sweating, at least theoretically, but no commercially available antiperspirants in the United States use these agents.

The anticholinergic agents are the most effective antiperspirants. Scopolamine and atropine are poorly absorbed by the skin and require injection or iontophoresis to achieve significant effects. Side effects include dry mouth, urinary retention, and mydriasis. There are no commercially available topical products containing anticholinergic drugs.

The aldehydes can be effective and probably work by blocking the sweat duct. Glutaraldehyde can result in skin staining, and formaldehyde is unpopular due to its sensitizing potential.

Deodorants generally function by masking odor or decreasing bacteria such as *Staphylococcus aureus*, *Aerobacter aerogenes*, and *Corynebacteria*. Antibacterial agents used in deodorants include quaternary ammonium compounds, such as benzethonium chloride, and cationic compounds, such as chlorhexidine and triclosan. Vehicles, such as ethyl alcohol, and certain additives may themselves have some weak antibacterial properties.

In my experience [Dr. Glaser], patients with hyperhidrosis do not find commercially available over-the-counter antiperspirants or deodorants to be effective, although many have difficulty giving them up even when relief has been obtained with other measures.

Aluminum chloride in higher concentrations than that found in over-the-counter products is effective for many of my patients with hyperhidrosis. Typically, I instruct patients to apply these products nightly. Although some physicians

advocate occlusion with gloves or some type of plastic wrap, I don't generally find that this practice increases effectiveness, and it sometimes just decreases patient compliance. After improvement is noticed, the patient should gradually decrease the frequency of application to minimize side effects such as dryness, irritation, and fissures.

Drysol is a prescription-only solution of 20% aluminum chloride in anhydrous ethyl alcohol. It is readily available and covered by most insurance plans. At times, a higher concentration of aluminum chloride is necessary to produce adequate results. Laboratories can supply the physician with suitable preparations, although I tend not to use concentrations higher than 35% due to the high incidence of irritation and fissuring. In palmar hyperhidrosis, these reactions can sometimes be managed with topical over-the-counter lotions and hand creams.

Xerac AC is a solution of aluminum chloride 6.25% in anhydrous ethyl alcohol with a *Dab-O-Matic* head for application. It, too, requires a physician's prescription, but is generally not as effective as the 20% solution for most hyperhidrosis patients.

Other preparations that have been used to control hyperhidrosis include tannic acid 2% to 5% in ethanol and a formalin solution (usually 5% to 20%) in water or ethanol, but allergic sensitization can be a problem.

Iontophoresis

Iontophoresis, the topical introduction of ionized medications into the skin using direct current, can be quite effective for most patients with hyperhidrosis. Iontophoresis is generally used for palmar/plantar hyperhidrosis. Levit[19,20] has shown that simple galvanic devices relieved symptoms in 85% of affected patients. A small direct electronic current (~15 mA) is passed through the skin. Tap water is usually employed, but sometimes anticholinergic agents are added. Iontophoresis may work by "plugging" the sweat ducts or by inducing an electrical change in the sweat gland that disrupts secretion.

Side effects are relatively few. The treated area may become too dry, cracked, or fissured. Reducing the frequency of treatments and applying emollients will usually alleviate the symptoms. Rarely, redness and even vesiculation of the skin develop, and these reactions can be treated with topical corticosteroids. If these adverse reactions occur, the voltage should be decreased during subsequent treatment sessions. Patients sometimes experience tingling and mild discomfort, especially when therapy is initiated. All in all, the greatest drawback of iontophoresis for many patients is the time required to perform the treatments.

Many devices are available for the administration of iontophoresis (Figure 1). In my practice [Dr. Glaser] we generally have the patient begin therapy and training in the office. We use the Fischer MD-1a galvanic unit (RA Fischer Co; Glendale, California). This machine has antisurge protection in the patient circuit, which helps prevent sudden changes in current flow that can occur if patient contact with an electrode or water bath is interrupted. Once it is clear that the patient can tolerate therapy, the patient is instructed to purchase a galvanic unit for home use.

Figure 1. Galvanic iontophoresis unit.

The *Drionic* (General Medical Co; Los Angeles, California) is a battery-operated machine that is commercially available with a prescription. Separate units are required for the axillae and for the palms/soles (Figures 2a,b).

Figure 2a-b. Battery-operated iontophoresis unit, *Drionic*; (a) axillae unit and (b) palms/soles unit.

Twenty minutes of iontophoresis treatment per site is recommended, but response is variable. I suggest that patients begin therapy on a daily basis and then decrease the time or frequency as dictated by response. One study[21] found that an 81% reduction in palmar sweating could be maintained with treatments every second week, but in my practice patients require more frequent maintenance therapy. I have found that patients who use their machines at least 3-4 times weekly -- even for shorter sessions -- experience fewer side effects and can maintain satisfactory

results.

Reinauer[22] found that alternating current (AC) with direct current offset (AC/DC) was just as effective as tap-water iontophoresis in the treatment of palmoplantar hyperhidrosis, but resulted in no signs of cutaneous irritation or discomfort for the patients.

Anticholinergic Drugs

Treatment with systemic anticholinergic drugs has variable success. Glycopyrrolate (*Robinul*) is initiated at doses of 1-2 mg, 1 to 3 times daily, but some patients need higher doses to achieve adequate improvement. The drug does not cross the blood-brain barrier and does not cause central nervous system (CNS) side effects as frequently as some of the other anticholinergic agents. Atropine is shorter-acting but tends to have more CNS effects. Propantheline bromide (*Pro Banthine*) and oxybutynin (*Ditropan*) also may be used.

I [Dr. Glaser] discourage patients from using atropine-like agents because of side effects. Excessive dryness of the mouth, urinary retention, constipation, palpitations, and even failure of accommodation can occur. As discussed above, the topical application of anticholinergics is rarely beneficial, and is probably related to poor cutaneous absorption.

Alternative Therapies

A plethora of homeopathic therapies has been tried by my patients [Dr. Glaser]. Chamomile has been tried for its relaxing properties. Sage, valerian, and St. John's wort have been used solo and in various combinations. Equal parts of St. John's wort, hyssop, sage, and black walnut bark can be brewed into a tea. Different Chinese herbs have also been tried over the years.

In addition to herbal remedies, biofeedback, acupuncture, and hypnosis have been tried by my patients. Results have been universally disappointing.

Surgery

Local surgical management of axillary hyperhidrosis aims to eliminate as many eccrine sweat glands as possible within the vault of the axilla while preserving, as much as possible, its normal appearance and the mobility of the arm. The simplest and most effective method is the en bloc excision of the entirety of the sweating area, which, however, inevitably leads to large, unsightly scars. To overcome this disadvantage, a wealth of surgical techniques has been proposed since the early 1960s. These include partial resection of axillary skin and subcutaneous tissue, removal of subcutaneous tissue without removing skin, shaving procedures, curettage, suction curettage, cryosurgery, and combinations of any of these techniques. Depending on the individual method used, bleeding, hematomas, seromas, wound infection, skin necrosis, prolonged wound healing, prominent scars, wound contractures, and restriction of arm movement may occur. Curettage and suction curettage techniques, usually performed under local or tumescent local anesthesia, appear to be superior to other procedures with regard to cosmetic results and complications.[23,24]

While the many competing approaches of local procedures are often described in detail, only limited information is available about long-term outcome and satisfaction of patients. There may be a place for local surgical procedures in the treatment of axillary hyperhidrosis, but evidence-based benefits are difficult to assess.

Surgical procedures to interrupt the transmission of sympathetic nerve impulses from ganglia to nerve endings for the treatment of hyperhidrosis were introduced as early as 1920. However, the traditional open access to the thorax carried considerable potential for severe complications and sizeable scars. Thus, conventional open surgery was superseded by ETS, which turned out to be equally effective but much less invasive and dangerous (Figure 4). With the spread of minimally invasive surgical techniques and video assistance, ETS has gained broad acceptance in the last decade. Usually, thoracic sympathetic ganglia T2 and T3 are destroyed by electrocautery for treatment of palmar hyperhidrosis and, in addition, T4 in axillary hyperhidrosis. ETS (without removal of ganglia) seems to be equally or

almost as effective as the more extensive sympathectomy, but randomized trials are lacking.[25]

Efficacy. In about 98% of patients with palmar hyperhidrosis, immediate and complete anhidrosis is achieved with ETS, with only low rates of recurrence.[26] Axillary hyperhidrosis does not appear to respond as well to the procedure. In a study[25] that evaluated both early results and long-term outcome of 630 thoracoscopic sympathectomies, 95.2% of patients treated for palmar hyperhidrosis had dry hands immediately or within a few days after treatment. Patients evaluated at long-term follow-up (median 16.1 years; range 1-27 years), had the same results. However, results of patients with axillary hyperhidrosis were significantly worse. Postoperatively, 83.3% of patients treated for axillary hyperhidrosis had dry skin, while only 68.3% had dry skin at long-term follow-up.

Complications. Rare complications of ETS include arterial bleeding possibly requiring conversion to open thoracotomy; intercostal vein bleeding; hemo-, pneumo-, and chylothorax; pleural adhesion or effusion; peripheral nerve injury; chronic postoperative pain and discomfort; and complete or incomplete Horner's syndrome.[27] Compensatory sweating, mainly of the back, abdomen, and legs occurs regularly, with gustatory sweating occurring in up to half of patients.[25] Compensatory and gustatory sweating are the most frequent reasons given by patients for being dissatisfied with the procedure, and may be severe enough to cause an equally troublesome handicap as the original hyperhidrosis.[25,26]

Patient satisfaction. Patients treated for axillary hyperhidrosis and patients treated for palmar involvement have significantly different satisfaction rates after ETS (Figure 3). In one study,[25] 71.7% of patients with palmar hyperhidrosis reported being satisfied with ETS at long-term follow-up; 23% reported being partially satisfied, and 5.4% reported being dissatisfied. In contrast, only 36.6% of patients with axillary hyperhidrosis were satisfied; 43.9% were partially satisfied, and 19.5% were dissatisfied. In another review[26] of 39 patients with excessive axillary sweating alone, only 13 patients (33%) were satisfied with ETS, 18 (46%) were partially satisfied, and 8 (20%) were dissatisfied.

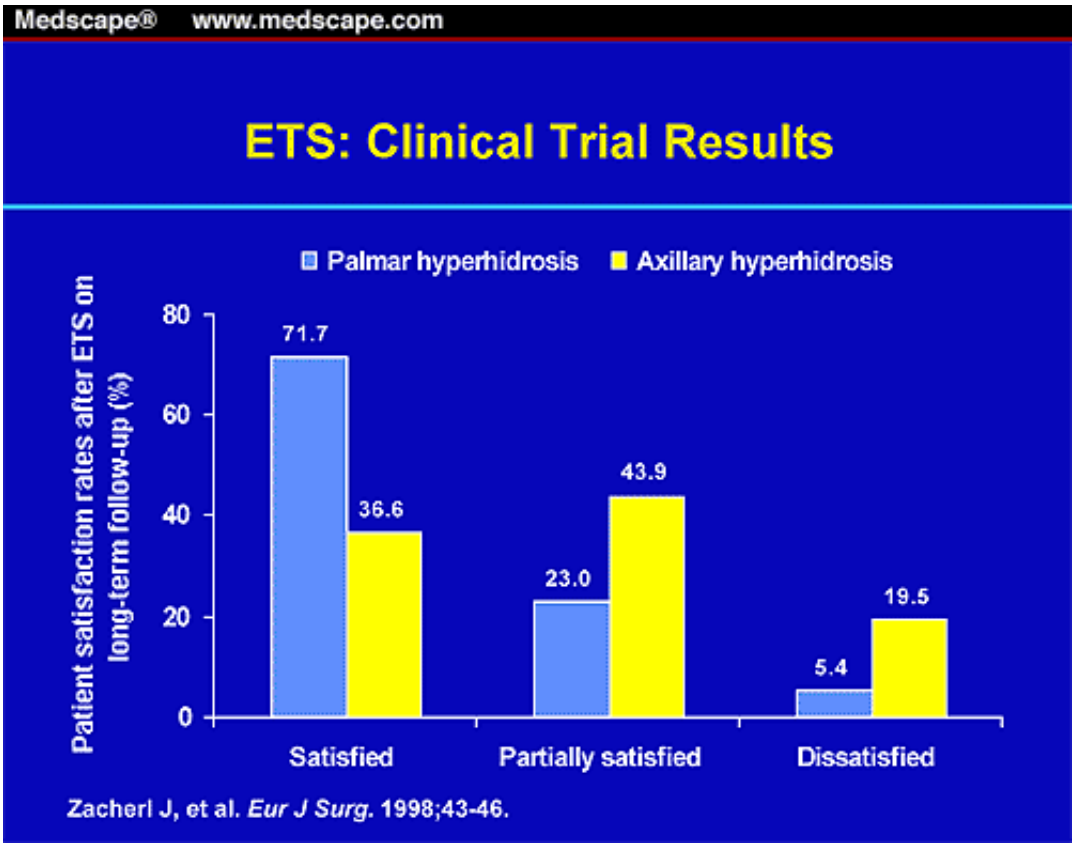

Figure 3. ETS patient satisfaction.

Botulinum Toxin

Botulinum toxin type A (BTX-A) is a novel, minimally invasive treatment option for focal hyperhidrosis of the axillae, the palms, or the forehead. BTX-A acts by temporarily blocking the release of acetylcholine from cholinergic sudomotor fibers. In focal hyperhidrosis, BTX-A is injected intradermally at multiple sites of the affected area. In axillary sweating (Figure 4), usually 10-15 sites equally distributed over the axilla are injected. In palmar sweating (Figure 5), multiple injections at a distance of about 2.5 cm are given over the palm and along the fingers.

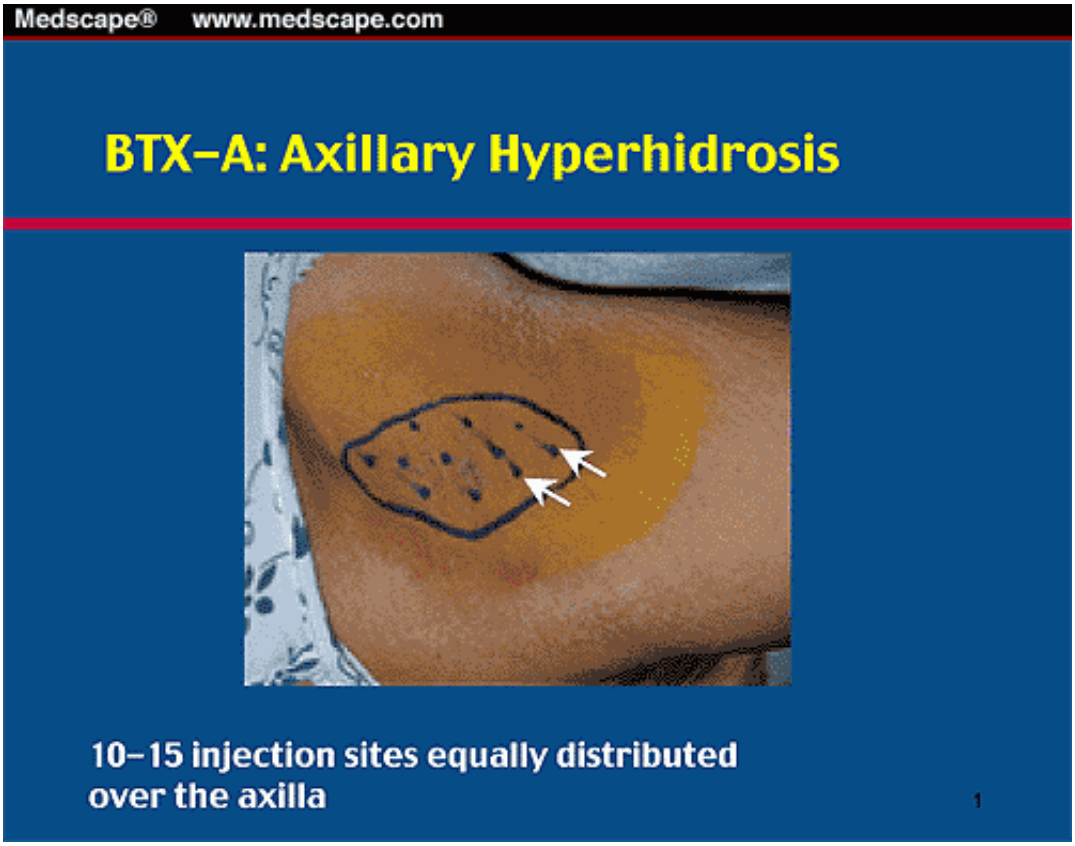

Figure 4. Axillary administration of BTX-A (slide courtesy of Dr. Naumann).

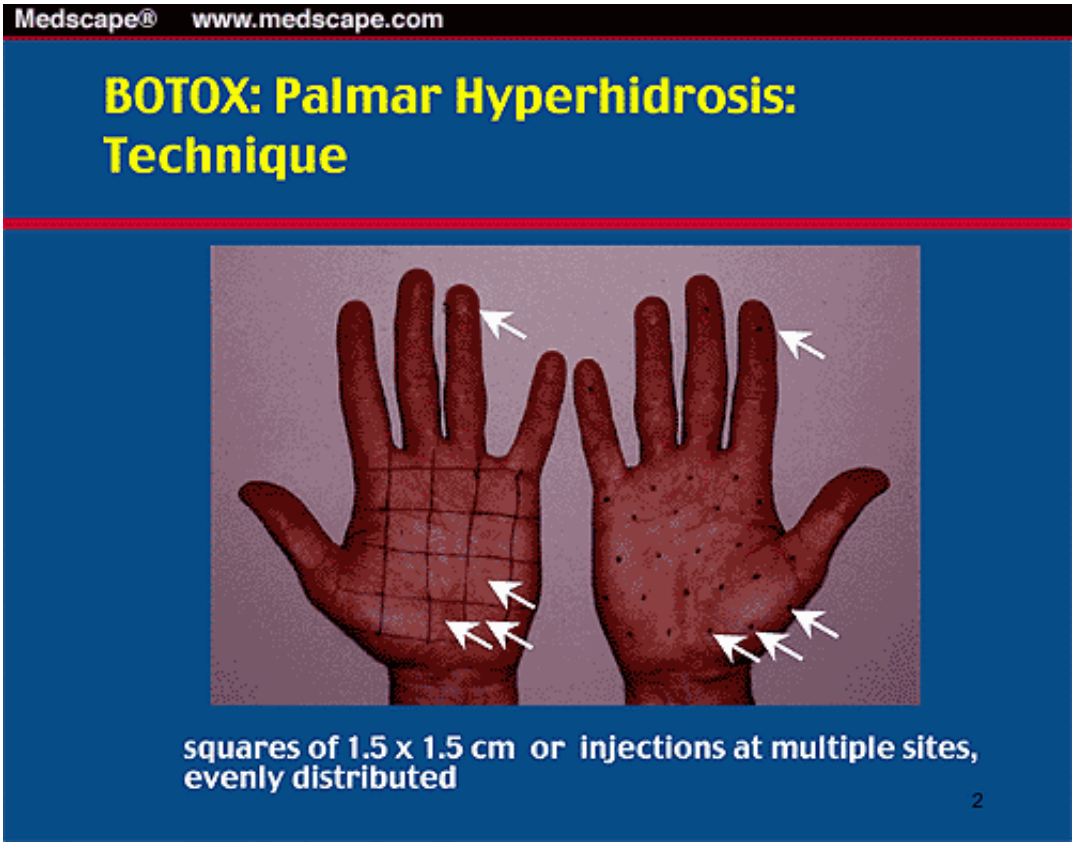

Figure 5. Palmar administration of BTX-A (slide courtesy of Dr. Naumann).

Before injection, the hyperhidrotic field (particularly in axillary hyperhidrosis) may be visualized using the Minor iodine-starch test. In this test, an iodine solution (2 g of iodine in 10 mL of castor oil and alcohol to 100 mL) is painted over the area of the skin to be tested. After it has dried, fine rice or potato starch powder is applied. Sweat causes the mixture to turn dark blue.

Axillary hyperhidrosis. Two large placebo-controlled, double-blind trials[28,29] and several open-label studies[30-32] have documented the beneficial effect of botulinum toxin treatment on reduction of sweat secretion and improvement of quality of life[33] in patients suffering from axillary hyperhidrosis. A large double-blind, placebo-controlled study[28] enrolled 320 patients (307 completed the study) and evaluated the safety and efficacy of intradermal administration of BTX-A (50 U *Botox* per axilla) or placebo for the treatment of bilateral primary axillary hyperhidrosis (Figure 6). Patients were followed for 16 weeks. At week 4, 93.8% of patients treated with BTX-A were classified as responders (> 50% reduction in sweat production from baseline gravimetric measurement), compared with 35.9% of the placebo group ($P < .001$). The mean percentage reduction in sweat production at week 4 was 83.5% in the BTX-A group, compared with only 20.8% in the placebo group ($P < .001$).

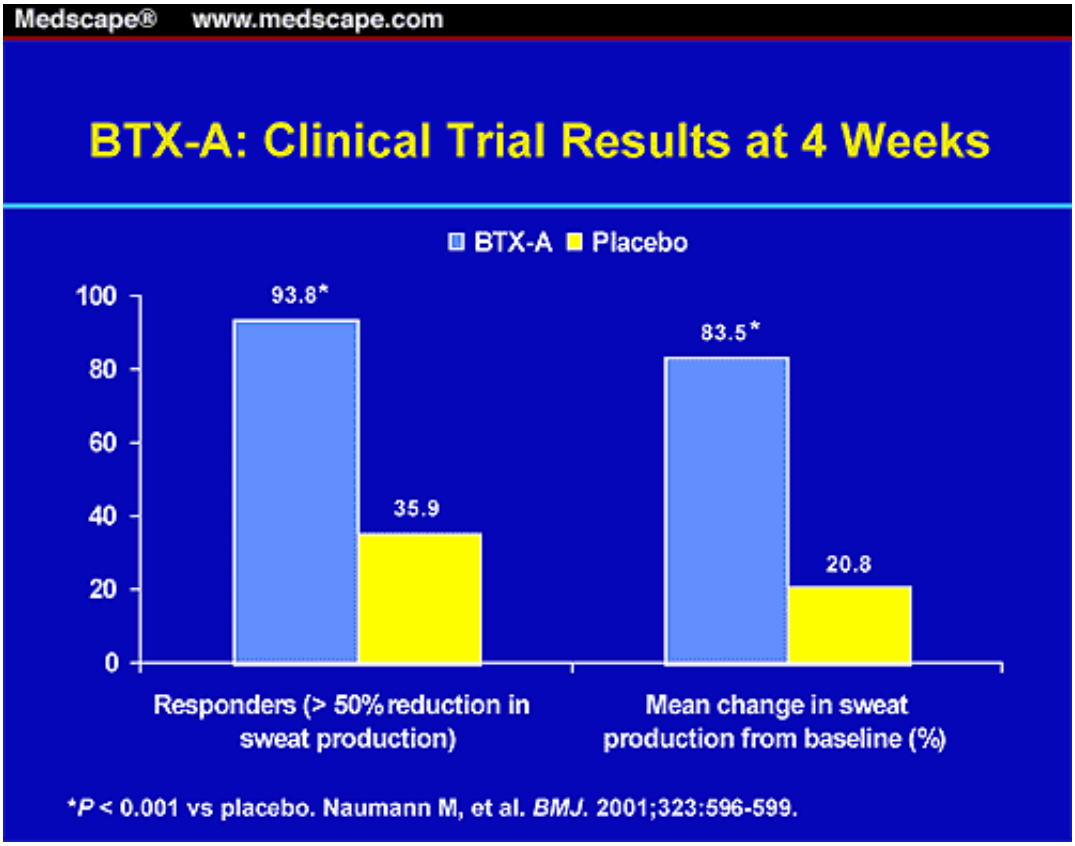

Figure 6. BTX-A clinical trial.

Two hundred seven patients were followed for a further 12 months[30] and received up to 3 further BTX-A injections. Response rates and satisfaction with treatment remained consistently high with no diminution of effect with repeated treatments. Mean duration of benefit was about 7 months after a single treatment session. About 28% of patients did not require more than 1 BTX-A treatment, indicating a long-lasting benefit of more than 16 months in a substantial proportion of patients. No specific side effects occurred in the whole period of 16 months (controlled and follow-up study).

BTX-A treatment markedly improved the quality of life of patients afflicted with hyperhidrosis according to the Hyperhidrosis Impact Questionnaire (*HIQ*) and the *Medical Outcomes Trust SF-12 Health Survey* (SF-12). At baseline, participants reported a marked negative impact of their hyperhidrosis on various measures, including state of mind, emotional status, comfort in social situations, productivity at work, number of clothing changes needed per day, and ability to engage in sex or participate in athletic activities. Posttreatment, significantly greater improvements were observed in all of these parameters in the BTX-A group vs the placebo group ($P < .01$). Patients treated with BTX-A also exhibited significantly greater improvement in the physical-component summary score of the SF-12 at 16 weeks than did placebo-treated patients ($P \leq .019$). Another study in 145 patients with axillary hyperhidrosis (100/200 U *Dysport*/axilla) obtained similar results with regard to efficacy and safety, but no quality-of-life or follow-up data are available.[29] These large controlled studies supported the reports of several previous open-label studies indicating that BTX-A (*Botox* or *Dysport*) is a safe and highly effective treatment for axillary hyperhidrosis. Based on the large controlled trial,[28] BTX-A (*Botox*) is now licensed for the treatment of axillary hyperhidrosis in the United Kingdom, Canada, and other countries.

Palmar sweating. The positive effect of BTX-A on palmar hyperhidrosis has been demonstrated by several open studies[31,34,35] and by 1 small double-blind, placebo-controlled trial.[36] BTX-A was injected using a grid for orientation, or by evenly distributing small amounts of the toxin over the palms. The required total doses were much higher than in the treatment of axillary hyperhidrosis because of the larger area requiring injection to dry up the palms and fingers. The studies used between 120 and 220 U *Botox* per palm or 120 U *Dysport* per palm. Several studies demonstrated a significant decrease in the amount of sweating, well in accordance with the patients' subjective

reports. Sweating was reduced for between 4 and 12 months. Injections were sometimes painful, and side effects included small hematomas and slight transient weakness of small hand muscles due to diffusion of the toxin. A local nerve block of the median and ulnar nerves at the wrist prior to injection avoids the pain of injection. Large placebo-controlled, double-blind studies on BTX-A in palmar hyperhidrosis are lacking so far.

Other indications. Smaller open studies have shown that BTX-A may be effective in patients suffering from craniofacial hyperhidrosis[37] or Ross syndrome.[38] BTX-A has been shown to be effective and relatively safe and to have a long duration of benefit in gustatory sweating.[39]

Review of Treatments

The long-term benefit of local surgical treatments in axillary hyperhidrosis is unclear because no controlled studies with gravimetrical assessment of pre- and postoperative sweat production are available. ETS has proved a highly effective treatment option for axillary hyperhidrosis, but there is a high risk of compensatory sweating, and there are rare perioperative complications. Botulinum toxin type A is a minimally invasive, effective, safe treatment for axillary hyperhidrosis, which due to its temporary effect of about 7 months has to be performed repeatedly.

In view of these pros and cons, I believe [Dr. Naumann] BTX-A should be offered to patients suffering from axillary hyperhidrosis that has failed to respond to conservative topical treatment.[40] Curettage of axillary sweat glands may be an alternative to BTX-A injections because of its longer duration of benefit. However, this procedure is more invasive than BTX-A, and long-term follow-up studies including quality-of-life data are not available. ETS may be considered if BTX-A fails or at patients' request.

In patients with palmar hyperhidrosis, BTX-A may be considered if oral medication and iontophoresis fail. ETS is a highly effective treatment for palmar hyperhidrosis which, however, bears several risks and, in my opinion, would be the treatment of last resort. However, results of future pharmacoeconomic evaluations will have to be taken into account when recommending one of these treatment options.

In my practice [Dr. Glaser], I generally initiate treatment with topical aluminum chloride in both palmoplantar and axillary hyperhidrosis because of ease, time issues, and cost. At that time I also present the patient with a description of the risks and benefits associated with other treatments. If treatment with topical aluminum chloride fails or cannot be tolerated, I let the patient direct therapy based on personality, finances, and time constraints. Iontophoresis can be quite satisfying for patients with palmar hyperhidrosis, but even if they achieve satisfactory results these patients periodically come in to review their options. ETS has achieved excellent results in some patients and very bad results in others who have had complications or severe compensatory sweating. It will be interesting to see if the newer ETS technique that achieves sympathetic blockade by clipping[41] rather than by resection or cautery will indeed be reversible in the event of severe compensatory sweating. My preferred treatment for axillary hyperhidrosis that has not responded to topical aluminum chloride is BTX-A or some form of lipocurette, with most patients choosing BTX-A.

Conclusion

Focal hyperhidrosis can be a disabling condition that affects psychological well-being and renders daily work and social life a struggle. People with this condition should be encouraged to seek evaluation and treatment from a physician, because current treatment options offer significant relief to hyperhidrosis patients.

For a slide presentation summarizing this clinical update, click here to download.

References

1. Hund M, Kinkelin I, Naumann M, Hamm H. Definition of axillary hyperhidrosis by gravimetric assessment.

Arch Dermatol. In press.
2. Naver H, Aquilonius S-M. The treatment of focal hyperhidrosis with botulinum toxin. Eur J Neurol. 1997;4(suppl 2):S75-S79.
3. Goldsmith L. Biology of eccrine and apocrine sweat glands. In: Fitzpatrick's Dermatology in General Medicine [CD-ROM]. 5th ed. New York: McGraw-Hill; 1999.
4. Sato K. The physiology, pharmacology, and biochemistry of the eccrine sweat gland. Rev Physiol Biochem Pharmacol. 1977;79:51-131.
5. Sato K, Kang WH, Saga KT. Biology of sweat glands and their disorders. I. Normal sweat gland function. J Am Acad Dermatol. 1989;20:537-563.
6. Sato K, Kang WH, Saga KT. Biology of sweat glands and their disorders. II. Disorders of sweat gland function. J Am Acad Dermatol. 1989;20:713-726.
7. Mosek A, Korczyn A. Hyperhidrosis in palms and soles. In: Korczyn A, ed. *Handbook of Autonomic Nervous System Dysfunction*. New York: Marcel Dekker; 1995:167-177.
8. Goldstein S. Treatment of social phobia with clonidine. Biol Psychiatry. 1987;22:369-372.
9. Moran KT, Brady MP. Surgical treatment of primary hyperhidrosis. Br J Surgery. 1991;78:279-283.
10. Lerer B, Jacobowitz J, Wahba A. Personality features in essential hyperhidrosis. Int J Psychiatry Med. 1981;10:59-67.
11. Amir M, Arish A, Weinstein Y, Pfeffer M, Levy Y. Impairment in quality of life among patients seeking surgery for hyperhidrosis (excessive sweating): preliminary results. Isr J Psychiatry Relat Sci. 2000;37:25-31.
12. Davidson JR, Miner CM, deVeaugh-Geiss J, Tupler LA, Colket JT, Potts NL. The brief social phobia scale: a psychometric evaluation. Psychol Med. 1997;27:161-166.
13. Connor KM, Davidson JR, Churchill LE, Sherwood A, Foa E, Weisler RH. Psychometric properties of the social phobia inventory (SPIN): A new self-rating scale. Br J Psychiatry. 2000;176:379-386.
14. Finlay AY, Khan GK. Dermatology life quality index (DLQI) -- a simple practical measure for routine clinical use. Clin Exp Derm. 1994;19:210-216.
15. Davidson JR, Foa EB, Connor KM, Churchill EL. Hyperhidrosis in social anxiety. Submitted for publication.
16. Teleranta T. Treatment of social phobia by endoscopic thoracic sympathectomy. Eur J Surgery. 1998;164:27-32.
17. Falkai P. Discussion: Scientific Expert Meeting. J Clin Psychiatry. 1999;60:47.
18. Draelos Z. Personal care products. In: *Cosmetics in Dermatology*. New York: Churchill Livingstone Inc; 1995:215-223.
19. Levit F. Simple device for the treatment of hyperhidrosis by iontophoresis. Arch Dermatol. 1968;98:505-507.
20. Levit F. Treatment of hyperhidrosis by tap water iontophoresis. Cutis. 1980;26:192-194.
21. Dahl JC, Glent-Madsen L. Treatment of hyperhidrosis manuum by tap water iontophoresis. Acta Derm Venereol. 1989;69:346-348.
22. Reinauer S, Neusser A, Schauf G, Holze E. Iontophoresis with alternating current and direct current offset (AC/DC iontophoresis): a new approach for the treatment of hyperhidrosis. Br J Dermatol. 1993;129:166-169.
23. Rompel R, Peros I, Petres J. Subcutaneous curettage for the treatment of axillary hyperhidrosis. Eur J Dermatol. 1997; 7:43-46.
24. Hasche E, Hagedorn M, Sattler G. Die subkutane SchweiÃŸdrÃ¼sensaugkÃ¼rettage in TumeszenzlokalanÃ¤sthesie bei Hyperhidrosis axillaris. Hautarzt. 1997;48:817-819.
25. Zacherl J, Huber ER, Imhof M, Plas EG, Herbst F, FÃ¼gger R. Long-term results of 630 thoracoscopic sympathicotomies for primary hyperhidrosis: the Vienna experience. Eur J Surg. 1998;(suppl 5)80:43-46.
26. Herbst F, Plas EG, FÃ¼gger R, Fritsch A. Endoscopic thoracic sympathectomy for primary hyperhidrosis of the upper limbs. A critical analysis and long-term results of 480 operations. Ann Surg. 1994;220:86-90.
27. Gossot D, Kabiri H, Caliandro R, Debrosse D, Girard P, Grunenwald D. Early complications of thoracic endoscopic sympathectomy: a prospective study of 940 procedures. Ann Thorac Surg. 2001;71:1116-1119.
28. Naumann M, Lowe N, for the hyperhidrosis study group. A randomized, placebo-controlled, double-blind study of botulinum toxin type A in bilateral axillary hyperhidrosis. BMJ. 2001;323:596-599.
29. Heckmann M, Ceballos-Baumann A, Plewig G. Botulinum toxin A for axillary hyperhidrosis (excessive

sweating). N Engl J Med. 2001;344:488-493.
30. Naumann M, Lowe NJ, Hamm H. A multicenter, open-label continuation study evaluating the safety and efficacy of botulinum toxin type A in the treatment of bilateral axillary hyperhidrosis. J Eur Acad Derm Venerol. 2001;15(suppl 2):130.
31. Naumann M, Hofmann U, Bergmann I, Hamm H, Toyka KV, Reiners K. Focal hyperhidrosis: Effective treatment with intracutaneous botulinum toxin. Arch Dermatol. 1998;134:301-304.
32. Naver H, Swartling C, Aquilonius S-M. Palmar and axillary hyperhidrosis treated with botulinum toxin: one-year clinical follow-up. Eur J Neurol. 2000;7:55-62.
33. Hamm H, Naumann M, Lowe N. Effect of botulinum toxin type A on quality of life measures in hyperhidrosis patients. J Eur Acad Derm Venerol. 2001;15 (suppl 2):132.
34. Shelley WB, Talanin NY, Shelley ED. Botulinum toxin therapy for palmar hyperhidrosis. J Am Acad Dermatol. 1998;38: 227-229.
35. Solomon B, Hayman R. Botulinum toxin type A therapy for palmar and digital hyperhidrosis. J Am Acad Dermatol. 2000;42:1026-1029.
36. Schnider P, Binder M, Auff E, Kittler H, Berger T, Wolff K. Double-blind trial of botulinum toxin for the treatment of focal hyperhidrosis of the palms. Br J Neurol. 1997;136: 548-552.
37. Kinkelin I, Hund M, Naumann M, Hamm H. Effective treatment of frontal hyperhidrosis with botulinum toxin A. Br J Dermatol. 2000;143:824-827.
38. Bergmann I, Dauphin M, Naumann M, F et al. Selective degeneration of sudomotor fibers in Ross syndrome and successful treatment of compensatory hyperhidrosis with botulinum toxin. Muscle Nerve.1998;1790-1793.
39. Naumann M, Zellner M, Toyka KV, Reiners K. Treatment of gustatory sweating with botulinum toxin. Ann Neurol. 1997;42:973-975.
40. Naumann M, Hamm H. Does intradermal botulinum toxin type A replace surgery in axillary hyperhidrosis? Br J Surg. In press.
41. Lin TS. Endoscopic clipping in video-assisted thoracoscopic sympathetic blockade for axillary hyperhidrosis. An analysis of 26 cases. Surg Endosc. 2001;15:126-128.

Contents of *Hyperhidrosis: Current Understanding, Current Therapy* [/viewprogram/1540]