REVIEW ARTICLE

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Management of Primary Hyperhidrosis

A Summary of the Different Treatment Modalities

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Abstract

Hyperhidrosis is a common and distressing condition involving increased production of sweat. A variety of treatment modalities are used to try to control or reduce sweating. Sweat is secreted by eccrine glands innervated by cholinergic fibers from the sympathetic nervous system. Primary hyperhidrosis most commonly affects palms, axillae and soles. Secondary hyperhidrosis is caused by an underlying condition, and treatment involves the removal or control of this condition.

The treatment options for primary hyperhidrosis involve a range of topical or systemic medications, psychotherapy and surgical or non-surgical invasive techniques. Topical antiperspirants are quick and easy to apply but they can cause skin irritation and have a short half life. Systemic medications, in particular anticholinergics, reduce sweating but the dose required to control sweating can cause significant adverse effects, thus, limiting the medications' effectiveness. Iontophoresis is a simple and well tolerated method for the treatment of hyperhidrosis without long-term adverse effects; however, long-term maintenance treatments are required to keep patients symptom free. Botulinum toxin A has emerged as a treatment for hyperhidrosis over the past 5–6 years with studies showing good results. Unfortunately, botulinum toxin A is not a permanent solution, and patients require repeat injections every 6–8 months to maintain benefits. Psychotherapy has been beneficial in a small number of cases. Percutaneous computed tomography-guided phenol sympathicolysis achieved good results but has a high long-term failure rate. Surgery has also been shown to successfully reduce hyperhidrosis but, like other therapies, has several complications and patients need to be informed of these prior to undergoing

surgery. The excision of axillary sweat glands can cause unsightly scarring and transthoracic sympathectomy (either open or endoscopic) can be associated with complications of compensatory and gustatory hyperhidrosis, Horner syndrome and neuralgia, some of which patients may find worse than the condition itself.

Hyperhidrosis is the production of excessive quantities of sweat. Primary hyperhidrosis (idiopathic, essential) is most typically limited to the palms, soles or axillae where excess sweating is usually increased by mental stimuli rather than exercise or heat.[1] Sweat is secreted by eccrine glands innervated by cholinergic fibers from the sympathetic nervous system.

The pathophysiology of essential hyperhidrosis is poorly understood but it has been suggested that it could be caused by an unexplained localized overfunctioning of the sympathetic fibers that pass through T_2 and T_3 ganglia.[2] Secondary hyperhidrosis is caused by an underlying condition, and management involves the elimination or control of this condition. In contrast, primary hyperhidrosis requires treatments that will reduce sweating to a level that patients find acceptable by pharmaceutical, psychotherapy or surgical means.

The various modalities used to treat the condition include topical therapies, systemic medications, iontophoresis, behavioral therapy or surgery, and each option has its own advantages, disadvantages, adverse effects (see table I), and complications. Hyperhidrosis can be an extremely disabling condition for patients but as treatments also cause adverse effects, it is important that patients are given precise information regarding the efficacy, adverse effects, and complications of each treatment modality prior to starting any individual therapy. Often the management of hyperhidrosis is tailored to individuals, based on the severity of their symptoms in addition to their personal preferences or circumstances. The aim of this paper is an attempt to summarize the numerous treatment options available for primary hyperhidrosis giving a comprehensive view of their indications, adverse effects and complications.

1. Methods

A Medline search was performed from March 1966 to March 2001 using the search terms hyperhidrosis, treatment, management, botulinum toxin, anticholinergics, iontophoresis, psychotherapy, sympathectomy and sympatholysis.

2. Topical Therapies

2.1 Aluminium Chloride

Aluminium chloride has been reported as one of the most effective topical agents in studies.[3,4,49] It may work by mechanically obstructing the eccrine sweat gland pore[50] or by causing atrophy of the secretory cells.[51]

In an extensive review of the literature on topical antiperspirants Shelley and Hurley[3] concluded that 25% aluminium chloride hexahydrate in absolute ethyl alcohol was the most effective agent for axillary hyperhidrosis. It needed to be applied to a dry axilla (not shaved for 48 hours) and occluded with a vinyl chloride-vinylidine chloride copolymer sheeting (Saran wrap) ideally overnight for 6–8 hours. Adverse effects included tingling, a feeling of warmth and occasionally some branny desquamation was noticed.

Scholes et al.[4] performed a larger study using 20% absolute ethyl alcohol for axillary hyperhidrosis. Of the 65 patients, 64 achieved excellent control of sweating and occlusion of the area was felt to be unnecessary. Axillary skin irritation, which was relieved by applying 1% hydrocortisone cream the morning after, was the most commonly reported adverse effect. Unfortunately, to maintain the control of sweating, the majority of patients had to continue to use the solution every 7–21 days. Goh[5] studied the efficacy of topical aluminium chloride hexahydrate 20% in alcohol solution for the treatment of symptomatic palmar hyperhidrosis in 12 patients. He reported that the absolute ethyl alcohol reduced palmar sweating within 48 hours of application but its effect disappeared within 48 hours of stopping treatment.

The available evidence would suggest that absolute ethyl alcohol is an effective non-surgical, first line treatment for both axillary and palmar hyperhidrosis that has a relatively good safety profile and is easy to apply despite its disadvantages of skin irritation and short duration of action.

2.2 Other Chemical Agents

Other chemical agents used in the past for hyperhidrosis are the aldehydes. Glutaraldehyde 10% in a buffered solution was found to be effective for plantar hyperhidrosis in a study of 25 patients by Juhlin and Hansson.[52] Unfortunately, it stains the skin and can cause allergic sensitization and as a result is only suitable for feet. Formaldehyde also effectively reduced axillary sweating but its use today is not recommended due to its high risk of inducing an allergic contact sensitivity.[53] Although methenamine[54] converts into formaldehyde on the skin, it can be effective and is reported to be less sensitizing. Tannic acid[53] (strong tea) is less effective than glutaraldehyde and it stains the skin.

Table I. Hyperhidrosis treatments and associated adverse effects

Treatments	Adverse effects	References
Medical		
Topical agents	Skin irritation	Shelley & Hurley,[3] Scholes et al.,[4] Goh[5]
Systemic anticholinergic drugs	Dry mouth, blurred vision, constipation and urinary retention	Herxheimer,[6] Canaday & Stanford[7]
Clonidine	Drowsiness, hair thinning and compensatory sweating	Nesathurai & Harvey,[8] Torch[9]
α-Adrenoceptor antagonists	Orthostatic hypotension	Manusov & Nadeau[10]
Iontophoresis	Pins and needles sensation, vesicles, papules, skin irritation and excessive dryness	Hölzle & Alberti,[11] Akins et al.[12]
Botulinum toxin A	Painful injections, temporary muscle weakness, headaches, muscle soreness and hematomas at injection sites	Odderson,[13] Heckmann et al.,[14] Shelley et al.,[15] Solomon et al.,[16] Schnider et al.,[17] Kinkelin et al.,[18] Naver et al.,[19] Naumann et al.,[20] Karamfilov et al.[21]
Psychotherapy		
Biofeedback		Duller & Doyle Gentry[22]
Surgical		
Open sympathectomy supraclavicular/transaxillary/ posterior approach/ anterior transthoraic	Brachial palsy, phrenic nerve damage, chylothorax, recurrent laryngeal nerve damage, pneumothorax, hemothorax, compensatory and gustatory sweating and Horner syndrome	Adar et al.,[1] Greenhalgh et al.,[23] Ellis,[24] Hashmonai et al.,[25] Moran & Brady,[26]
Thoracoscopic sympathectomy	Compensatory and gustatory sweating, neuralgia, Horner syndrome, phantom sweating, hemothorax, pneumothorax, chest pain and wound infection	Zacherl et al.,[27] Shachor et al.,[28] Lin & Fang,[29] Yamamato et al.,[30] Sung et al.,[31] Herbst et al.,[32] Drott et al.,[33] Graham et al.,[34] Rex et al.,[35] Fox et al.,[36] Chiou & Chen,[37] Hsu et al.,[38] Noppen et al.,[39] Hsia et al.,[40] Orteau et al.[41]
Excision of axillary tissue	Scarring, wound infections and abscesses, limitation of arm movement	Ellis,[42] Hurley & Shelley,[43]
Subcutaneous curettage of the axillae	Axillary scarring treatment failure	Jemec,[44] Ellis[42]
Suction-assisted lipolysis	Postoperative pain and temporary limitation of arm movement	Lillis & Coleman[45]
Other invasive techniques		
Chemical sympathectomy	Compensatory hyperhidrosis neuralgia	Kobayashi et al.[46]
Computed Tomography guided thoracic sympatholysis	Pneumothorax, neuralgia, chest pain, Horner syndrome and compensatory sweating	Dordelinger & Kurdziel,[47] Lucas et al.[48]

3. Systemic Therapy

3.1 Anticholinergics

Sweat glands are supplied by sympathetic nerves that are cholinergic in nature[55] and, as a result, systemic anticholinergics may help to relieve symptoms of hyperhidrosis. Unfortunately the doses required to achieve reduced sweating may also result in adverse effects including dry mouth, blurred vision, urinary retention and constipation.[56] These adverse effects keep doses down and put patients off. Consequently the drugs have a limited value. Anticholinergics are also known as antimuscarinics. The earliest reports of systemic therapy for hyperhidrosis described the use of the anticholinergic methantheline bromide in four women following the observation that patients being treated for gastrointestinal disorders with methantheline commented on the dryness of their hands.[57]

Atropine-like drugs[6] have been used to block the effect of acetylcholine on the sweat glands but often their adverse effects can be worse than the condition itself. Frequently, higher doses than recommended by the manufacturers are needed to control symptoms.[6] Today, a commonly used anticholinergic is propantheline bromide, which is initially used at low dose and increased as tolerated.[58] Propantheline bromide has also been reported to reduce the discomfort associated with sweating related to spinal cord injury.[7] Another successfully used anticholinergic drug is glycopyrronium bromide.[59]

In the past, ganglion-blocking agents had been successfully used to suppress hyperhidrosis[6] but because of their serious adverse effects including postural hypotension, they are rarely used today. In cases with a significant emotional factor, anecdotally sedative or tranquilizing drugs are often helpful. Amitriptyline with its anticholinergic action is probably the most useful.[58] Patients with facial hyperhidrosis responded to amitriptyline,[60] while clonazepam, an anxiolytic, successfully treated a patient with unilateral localized facial hyperhidrosis.[61]

3.2 Other Systemic Therapies

There are few studies addressing the use of systemic treatments in primary hyperhidrosis and hence treatments are often based on isolated case reports or anecdotally. Calcium-channel antagonists[62] were tried after Sato[63] elucidated the central role of calcium flux in eccrine secretion. The successful use of diltiazem, a calcium-channel antagonist, in two family members with hereditary emotional hyperhidrosis was described.[62] A case report showed that the αadrenoceptor antagonist phenoxybenzamine, as a possible treatment for hyperhidrosis.[10] Clonidine has been shown to successfully reduce the incidence and frequency of gustatory sweating.[8] Another case report[9] showed the complete remission of facial and scalp hyperhidrosis using a combination of clonidine and a topical solution of 20% aluminium chloride in anhydrous ethyl alcohol. Due to the paucity in the current literature, randomized controlled trials will need to be performed before one can determine if calcium-channel antagonists, αadrenoceptor antagonists and clonidine will become effective treatment modalities for primary hyperhidrosis.

4. Iontophoresis

Iontophoresis is defined[64] as the introduction (by means of an electric current) of ions of soluble salts into the tissues of the body for therapeutic purposes. This method of drug administration has many advantages. Firstly systemic adverse effects of drugs are significantly decreased while a relatively high drug concentration is administered locally where it should achieve the maximum benefit.[65] Commonly used agents include tap water[66] or anticholinergics[67] (e.g. glycopyrronium or hexapyrronium bromide, atropine sulphate, poldine methylsulphate). Secondly, patient acceptance of this technique is usually very good and it avoids the fear that can be associated with injections.[65]

In 1968, Levit[68] was responsible for establishing the use of iontophoresis in practical dermatology and several studies[69-72] have shown its efficacy since. Unfortunately the majority of studies were small with no long-term follow up until Hölzle and Alberti[11] looked at the adverse effects and long-term efficacy of tap water iontophoresis for palmoplantar hyperhidrosis. They compared treatments carried out using a conventional galvanic generator with a more newly developed iontophoresis apparatus, which was suitable for home use. No difference in efficacy or adverse effects between the two devices was found but the authors noted that both groups developed recurrence of sweating within weeks of discontinuing iontophoresis and thus, long-term maintenance therapy is required to sustain the benefit. Patients were treated for up to 4 years without any long-term adverse effects.

Adverse effects associated with iontophoresis include a ‘pins and needles’ sensation, vesicles, erythematous papules and scaling.[12] Decreasing the frequency of treatments and using emollients can reduce the palms from becoming dry, cracked or fissured. Open wounds in the treatment areas need to be covered with petrolatum to avoid unnecessary skin discomfort during iontophoresis. It is recommended that patients with cardiac arrhythmias or with electronic implants e.g. pacemakers should be excluded from iontophoresis.[11] It is contraindicated in pregnancy.[11] Localized adverse effects can be related to individual susceptibility, longer treatment time and dissociation of water into hydrogen or hydroxide ions.[73] Higher amperage and short treatment intervals

also enhance skin irritation.[11] Adverse effects are often more pronounced when anticholinergic[67,74] compounds are used instead of tap water. This is the result of systemic anticholinergic blockade and the symptoms include a dry mouth or throat dryness.

The use of iontophoresis for axillary hyperhidrosis is not as effective as for palms and soles, as only 37.5% of axilla sites responded within 14 days of treatment, using the Drionic portable iontophoretic unit.[12] One of the reasons for this may be the difficulty in maintaining a proper skin contact in the axillary area due to the bulkiness of the Drionic unit. Therefore, using a modified iontophoretic method[75] with an anticholinergic agent and aluminium chloride can obtain better results in the axilla.

Overall, iontophoresis results in a reduction of hyperhidrosis of palms, soles and axillae. It is a simple, effective method without long-term adverse effects and is not associated with any compensatory hyperhidrosis. However, the disadvantages are that it is very time consuming for patients even if self-administered in their own home as patients may need to perform iontophoresis up to several times a week for up to 30 minutes at a time to remain symptom free. It also requires access to equipment that may be too expensive for some patients to afford and treatment may need to be continued long term.

5. Botulinum Toxin A

Botulinum toxin A is a neurotoxin produced by the anaerobic bacterium Clostridium botulinum. There are seven different serotypes (A–G),[76] of which A is the most potent.[77] Types B and F are currently being investigated for use in patients who have developed immunity to toxin type A.[78] Botulinum toxin inhibits the release of acetylcholine from the presynaptic terminal of the neuromuscular junction of striated muscle leading to muscle weakness and paralysis within 1–14 days.[79] Over 3–4 months, new neuromuscular junctions are formed and muscle function slowly returns. The toxin can also produce loss of sweating, in the treated area, by inhibiting the release of acetylcholine from sympathetic nerves that innervate eccrine sweat glands.[80]

Botox®[1] (Allergen) and Dysport® (Ipsen) are the two commercially available forms of botulinum toxin A available for clinical use in the UK and throughout the rest of Europe. Botox® is the only product licensed in US. They both have similar actions, but the two preparations are distinct because of different vehicles, dilution schemes and potency.[81] This is an important fact to consider when comparing studies and treating patients. From experiments in monkeys it has been calculated that the 50% lethal dose (LD_{50}) of Botox® is 2700 units in an average 70kg human;[82] this dose would be much higher than the usual amounts used in the treatment of hyperhidrosis.

The first use of botulinum toxin for therapeutic purposes was in monkeys in 1973,[83] used to demonstrate reversible ocular muscle paralysis. In 1980 it was injected in humans as a therapy for strabismus.[84,85] Since then, botulinum toxin A has had several indications in ophthalmology as a treatment for acute lateral rectus,[86] nystagmus[87] and blepharospasm.[88] In neurology it has been used to treat cervical dystonia[89,90] and hemifacial spasm.[88,91] More recently it has been reported as a cosmetic therapy for glabellar wrinkles.[92]

Bushara and Park[93] first reported the use of botulinum toxin A for the treatment of hyperhidrosis. They studied facial sweating in three patients treated with botulinum toxin A for hemifacial spasm and noticed patients had an area of anhidrosis around the area injected with toxin.

In 1996 a study to determine the dosage, pattern and duration of the anhidrotic effect of botulinum toxin A in healthy volunteers was performed.[94] The conclusion was that subcutaneous injections of botulinum toxin A caused chemodenervation of the sweat glands and although it could be considered, as a possible novel treatment for severe axillary hyperhidrosis, further randomized controlled trials were needed.

Botulinum toxin A has been reported as an effective treatment for gustatory sweating in addition to axillary, palmar, plantar and frontal hyperhidrosis.[13] Several studies (summarized in table II) have shown botulinum toxin as a well tolerated, minimally invasive and effective treatment for primary hyperhidrosis. Unfortunately, most of the studies were performed upon small numbers of patients and it wasn't until more recently a large multicenter randomized controlled trial,[14] on behalf of the hyperhidrosis study group, reconfirmed that intradermal injection of botulinum toxin A was an effective and well tolerated therapy for severe axillary hyperhidrosis.

One of the most common adverse effects associated with botulinum toxin A therapy was temporary weakness of the small muscles of the hand,[15-17,97] which lasted from 3–6 weeks. When botulinum toxin A was used to treat frontal hyperhidrosis, it caused a temporary partial disability in frowning of the forehead, which disappeared after a number of weeks (range of 1–8 weeks).[18] Pain experienced during palmar injections can be reduced by applying cold packs to the area for 15 minutes[19,20] or, alternatively, spraying liquid nitrogen to the area for 5 seconds before injections. Inducing regional anesthesia of the palms by a median or ulnar nerve block, prior to injections, can also reduce pain.[19] Other adverse effects including headaches,[14] muscle

1 Use of tradenames is for product identification only and does not imply endorsement.

Table II. Review of botulinum toxin A as a treatment for primary hyperhidrosis

Studies	No. of pts	Sites treated	Toxin studied		Treatment success	Adverse effects (pts)	Duration of benefit (months)
			type	dose and site			
Bushara et al.[94]	7	Axilla (n = 5)	BOTOX®	15–50U[a]	57% clear	None	6–8 (n = 2 with no sweating; 1 with reduced sweating)
		Dorsum hand (n = 2)	Dysport®	20U	14% improved		11 (n = 2 with no sweating)
Schnider et al.[17]	11	Palms	Dysport®	120U each palm (20U injected into 6 sites)	31% had reduced sweating after 13 weeks	Muscle weakness (n = 3); hematoma (n = 1); Painful (n = 3)	after 3.25 (n = 8/11)
Odderson[95]	2	Axillae	Not specified	50U each axilla (2 sites)	71–76% sweat reduction	Pain with injections; hematomas	2 (n = 2)
Shelley et al.[15]	4	Palms	BOTOX®	100U each palm (50 injection sites with 2U to each, into both palms)	100% of patients had reduced sweating	Mild thumb weakness (n = 1) for a duration of 3 weeks	4 (n = 1/4); 7 (n = 2/4); 12 (n = 1/4)
Naumann et al.[20]	11	Axillae; palms; soles	BOTOX®	3U each site; injected over a 4cm^2 area	100% of patients had reduced sweating	Pain with injection; hematomas	>5 (n = 11/11)
Glogau[80]	12	Axillae	BOTOX®	50U divided into smaller portions into each axilla	100% of patients had reduced sweating	Minor pinpoint hemorrhage at site of entry of needle	5.2 (mean duration)
Schnider et al.[96]	13	Axillae	Dysport®	200U total; each axilla (6 sites)	10 patients 'markedly' improved and 3 patients 'moderately' improved	Minor pruritus (n = 2); constipation (n = 2); increased palmar sweating (n = 2)	At 3.25 (n = 13)
Naver et al.[19]	170	Axillae; palms; face; feet; other sites	BOTOX®	0.5 U/cm^2 or 0.8 U/cm^2 to various areas; mean total dose 170U to palm, 60U to axilla	90% with 0.8 U/cm^2 given, but less for 0.5 U/cm^2	Very dry palms in 25%; reduced finger power in 66% for a mean of 2 weeks	10 (median duration); 3–14
Solomon & Haymann[16]	20	Palms	BOTOX®	2.5U or 5.0U to various areas; total dose of 165U to several areas over 4 weeks	79% in 1st week	Pain during injections, mild muscle weakness in 21%	1 patient lost to follow-up
		Digits	BOTOX®	165U into each hand over a 4-week period	100% in 2 weeks		4 (n = 1); 5 (n = 1); 6 (n = 3); 7 (n = 8); 8 (n = 3); 9 (n = 3)
Karamfilov et al.[21]	24	Axillae	BOTOX®	200U to each axilla; 5–10U injected to several areas	100% after 6 days	Pain and burning during injections	7 (n = 2); 8 (n = 1); 9 (n = 3); >10 (n = 18)
Heckmann et al.[14]	145	Axillae	Dysport®	200U then 2 weeks later 100U; injected into 1 axilla, then into other axillae	81.4% reduction in sweating with 200U, 76.5% with 100U	Headache (n = 4); muscle soreness (n = 2); facial sweating (n = 1)	6 (n = 136 had rates of sweating below baseline)

a 1U is the estimated dose of intraperitoneally injected toxin lethal for 50% of the population (LD_{50}) of female Swiss Webster mice weighing 18–20g.

n = number of patients; **pts** = patients.

soreness of the shoulder girdle,[14] increased facial sweating,[14] axillary itching[14] and minor hematomas at the injection site were also reported.[17,20]

High-dose botulinum toxin A[21] can lower relapse rates by 50% thus inducing a longer-lasting relief of symptoms but reasons for this were unclear. Neutralizing antibodies have been described in patients treated with deep injections of botulinum toxin A for cervical dystonia[98] but, as far as we are aware, there are no published data on the development of antibodies to botulinum toxin A in patients treated for hyperhidrosis.

Most studies conclude that botulinum toxin A is an effective and well tolerated treatment for axillary,[21,80,96] palmar[15-17] and frontal[18] hyperhidrosis. However, further studies are necessary to standardize injection spacing (see figure 1) and dilution techniques.[16]

6. Psychotherapy

Duller and Doyle Gentry[22] used biofeedback to significantly improve the degree of sweating experienced by patients. It is a behavioral technique often used in treating somatic disorders,[99] but it had received little attention in treating skin conditions.[22] The study involved the use of biofeedback training in the treatment of patients whose primary symptom was chronic hyperhidrosis. The rationale behind using biofeedback is that chronic hyperhidrosis can result from anxiety and emotional stimuli and that patients can learn to reduce sweating by learning behavioral-conditioning techniques.

The results of the study showed that 8 of 14 patients significantly improved and two patients appeared to sweat less during the interview but reported little improvement outside the clinic setting. Relaxation was suggested as the active element on this therapy. Although these preliminary results have shown a decreased incidence of sweating in some patients, there have been no long-term follow-up results published and hence this has not become a popular treatment.[56]

7. Surgical Therapy

A number of surgical approaches have been proposed over the past 100 years in the management of axillary and palmar hyperhidrosis. These include surgical sympathectomy, axillary gland excision, subcutaneous curettage of the axillae and suction-assisted lipolysis. Surgical sympathectomy involved either an open approach or, today, the more commonly used endoscopic approach. Open surgical sympathectomy was traditionally performed, as the upper thoracic sympathetic chain was difficult to access.[100] However this procedure has become obsolete as it had several disadvantages over thoracoscopic sympathectomy such as a higher rate of complications, esthetic discomfort and problems with lung function postoperatively.[101,102] Four different approaches had been described for open sympathectomy including supraclavicular[23,103] or cervical, axillary,[24,104] posterior[105,106] and anterior[107,108] sympathectomy but all these have been superseded by endoscopic transthoracic sympathectomy.

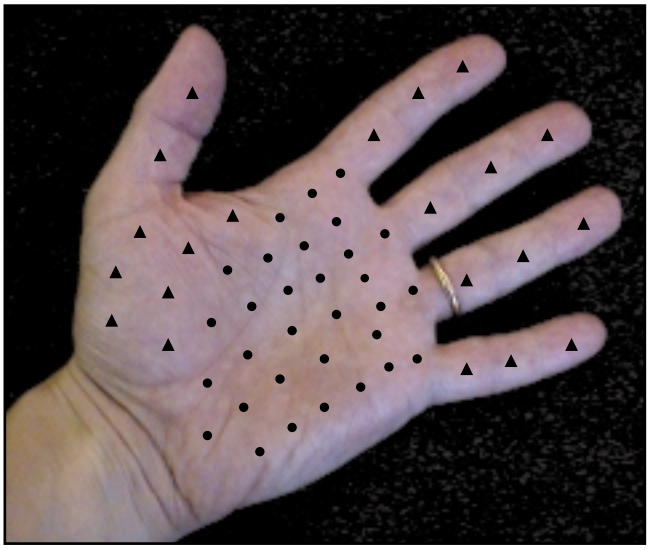

Fig. 1. Sites of injection of botulinum toxin A with increased dose and density of injection in the palmar region (•) in contrast to the fingers (▲).

7.1 Thoracoscopic Sympathectomy

Thoracoscopy was first performed in 1910,[109] but it wasn't until 1942 that Hughes[110] described it as a method for sympathectomy and performed the first operation. Goetz and Marr[107] followed these two years later. In 1954, Kux[111] reported his technique and experience of using endoscopic thoracic sympathectomy in more than 1400 patients. The initial procedures were under direct vision thoracoscopic sympathectomy but this technique has been superseded by the modern technique of video-assisted thoracoscopic sympathectomy (VATS).[27] The advantages of performing thoracoscopic sympathectomy under video guidance are that a better view can be obtained, surgical safety is increased and the procedure is easier to perform without reduced efficacy.[27]

A number of approaches have been described for performing endoscopic thoracoscopic sympathectomy, which includes electrocautery of the sympathetic trunk[112-114] or electroresection of the appropriate ganglia.[25,115] Shachor et al.[28] preferred to cauterize and cut the sympathetic nerve and ganglia where they laid on the ribs, as the area is free of blood vessels and thus reduced the risk of bleeding. Lin and Fang[29] described a half-sitting position under single-lumen intubational anesthesia without artificial pneumothorax for patients undergoing endoscopic transthoracic sym-

pathectomy (ETS). They felt that a good operative view could be achieved after total collapse of the lungs via transient disconnection of the endotracheal tube by the anesthetist without the need to induce an artificial pneumothorax.

Kao et al.[116-119] developed a technique for the treatment of palmar hyperhidrosis involving video endoscopic sympathectomy using a fiber-optic CO_2 laser. This method enabled the sympathetic trunk to be visualized clearly on a television monitor and the correct segment could be confirmed with the aid of sympathetic monitoring by measuring the palmar skin perfusion and palmar skin temperature intraoperatively. The correct segment was then extirpated with a fiber optic laser. The authors believe that segmental ablation is safer, more easily performed than entire trunk ablation and the risk of injuring intercostal veins or nerves is reduced.[117]

More recently the development of a smaller 2mm ultra-thin needle endoscopic instrument, which has been used in urologic and gynecologic procedures for over 10 years, has been designed for thoracoscopic sympathectomy. It is reported to be minimally invasive, very effective and gives a good cosmetic result.[30,31,120] However, some authors report that limitations of the miniaturized instruments are narrow field of vision, lower resolution and difficulty in maintaining control.[121]

Several studies have shown that endoscopic sympathectomy has been used successfully to treat primary hyperhidrosis. These studies are briefly summarized in table III and show the majority of patients as being satisfied. However, more long-term outcome studies showed patient satisfaction declined with time as only 66.7% were completely satisfied and 26.7% partially satisfied after a mean follow-up of 16.4 years.[32] Some of the reasons for patient dissatisfaction were compensatory or gustatory sweating, severe hand dryness and Horner syndrome.[32] Although ETS is a minimally invasive and successful treatment for hyperhidrosis of palms and axillae the adverse effects should be discussed with the patient prior to performing surgery in order to reduce patient's dissatisfaction long-term.

Sympathectomy is an effective treatment for primary hyperhidrosis but unfortunately it is not without complications (table IV). Hashmonai et al.[56] nicely summarizes the five major problems associated with surgical sympathectomy. These include phantom sweating, gustatory sweating, Horner syndrome, neuralgia and compensatory sweating.

Compensatory sweating is a well-recognized complication of upper dorsal sympathectomy. Adar et al.[1] reported 80% of patients who had open sympathectomies experienced compensatory hyperhidrosis, but the incidence in ETS varies from 50–97%. It can become more apparent after bilateral sympathectomy[36] but limiting the extent of sympathectomy to T2 for palmar and T2 and T3 for axillary denervation may reduce the incidence of compensatory hyperhidrosis.[34]

Phantom sweating[132] and gustatory sweating[133] are also complications of upper dorsal sympathectomy. Gustatory sweating is a facial sweating triggered by food, especially spicy and some other specific foods,[56] whereas phantom sweating is the sensation of impending hyperhidrosis in the absence of sweating; the mechanism is poorly understood.[41] In one series, phantom sweating was reported in 26% of patients, normally occurring within 18 months of surgery,[134] but the authors postulated that the reason it is not reported in other series is because patients are not specifically asked about the symptom.[134] The incidence of gustatory sweating may occur in 0–56% of patients.[135] Overall these complications are not usually incapacitating and most patients cope very well with them.[56]

Neuralgia is an important sequela of sympathectomy.[56] It consists of pain in the sympathectomized limb, appearing sometime after the operation and its incidence varies between 0%[134] and 32%.[136] The etiology and mechanism of this complication is unknown but damage to the intercostal nerves during endoscopic electrocautery can result in postoperative regional pain.[56]

Horner syndrome can be produced by damage to the stellate ganglion in particular to the upper C7 portion. The incidence of Horner syndrome varies between studies, and often is related to the operative method used and the experience of the surgeon.[26,114,134] The transthoracic endoscopic approach has a much lower incidence of Horner syndrome than the obsolete open sympathectomy, as it is a minimally invasive procedure with better visualization of the sympathetic trunk. The stellate ganglion lying beneath a fat pad is protected, resulting in a lower incidence of Horner syndrome from 0%[29,36] to 2.5%.[32] It can occur temporarily and resolve spontaneously.[28,114]

Hemothorax and pneumothorax are two further complications encountered in upper transthoracic sympathectomy. Of 290 sympathectomies,[28] three patients developed a hemothorax with one requiring a thoracotomy to stop the bleeding. Hemorrhaging may occur following trauma to an intercostal artery, vein or branch of the azygos vein and thus early recognition and treatment may prevent the development of a hemothorax.[28] Pneumothorax and hemothorax following endoscopic[33,35,137] sympathectomy only require a chest drain to be inserted if they fail to resolve spontaneously.[34] The incidence of pneumothorax varies from 0–10%.[28,29,32,34,35,37,114]

Other minor complications encountered included surgical emphysema,[28,34] chest infection,[34] wound infection,[29,34,114] chest pain[28,32,37] respiratory pain[32] and back pain.[28,114]

Thoracoscopic sympathicolysis causes minimal and subclinical changes in pulmonary function due to a temporary small decrease

Table III. Review of endoscopic transthoracic sympathectomy in the management of primary hyperhidrosis

Studies	No. of patients (no. of patients analyzed)	No. of symp (no. of symp analyzed)	Palmar (no. of patients)	Axillary (no. of patients)	Both palm and axillary or other (no. of patients)	Success rate (patients)	Failure rate (patients)	Patient satisfaction rate	Recurrence (patients)
Byrne et al.[114]	112 (85)	170	20	17	48	98.8%	1.2%	91.8%	
Kao[116]	14	28	14			100%			
Gothberg et al.[113]	450	900					1.8%		0.9%
Chao et al.[122]	150	299	150			99.3%			1.33% immediately
Shachor et al.[28]	150	290	150			98%	2%		2%
Kao et al.[119]	40		40			100%	0%		0%
Herbst et al.[32]	323 (270)	480	175	39	56	98.1%	1.9%	Initial satisfaction: 95.5% total, 2.6% partial; long-term outcome (after 14.6 years): 66.7% total, 26.7% partial	1.5%
Hsu et al.[38]	80	159	80			88.1% rated as excellent; 9.4% rated as good	0%		0%
Chen et al.[123]	180	357	180			98%	2%	95%	2.78%
Drott et al.[33]	850	1700				98%	2%	98%	2%
Graham et al.[34]	47 (45)	92	31	16		96%	4%	91%	4.4%
Noppen et al.[39]	100	199	34		66	98% palm; 62% axilla		100%	
Kao et al.[124]	9988								<3% after 3 years
Kopelman et al.[125]	53	106	53			100%	0%	67.3% total; 21.2% partial	0%
Gossot et al.[126]	124	240	64 (51.6%)	7 (5.6%)	53 (42.7%)				5%
Lai et al.[127]	72	144	72			93.1%	6.9%	77.7%	
Grabham et al.[128]	13 (11)	20 (17)	11			100%	0%		18%
Rex et al.[35]	1152		785	93	274	99.4% palm; 94.5% axilla		87% palm; 68% axilla	
Cohen et al.[129]	223	402				98.7%		98.2%	
Fox et al.[36]	54	91	80 (no. of symp)	11 (no. of symp)		100% palm; 91% axilla	1.85%	52 (96.3%)	5.4%
Chiou & Chen[37]	91	181	91			99%	1%	79 (87%)	16%
Lin & Fang[29]	1360	2715	1360			99.2%	0.80%	95%	1.1% after 3 years

Continued next page

Table III. Contd

Studies	No. of patients (no. of patients analyzed)	No. of symp (no. of symp analyzed)	Palmar (no. of patients)	Axillary (no. of patients)	Both palm and axillary or other (no. of patients)	Success rate (patients)	Failure rate (patients)	Patient satisfaction rate	Recurrence (patients)
Zacherl et al.[27]	369	558 [CTS]; 98 [VATS]	251	47	71	93% [CTS]; 98% [VATS]		67% total [CTS]; 27% partial [CTS]; 80% total [VATS]; 17% partial [VATS]	
Erak et al.[130]	53	92	53			45.6% dry; 45.6% partial sweating	7%	93%	
Imhof et al.[131]	26 (19)					100%	0%	58% total; 36.8% partial	
Hsia et al.[40]	47	94	47			100%			0
Yim et al.[121]	38	76	38			100%		100%	0
Yamamoto et al.[30]	180		180			100%			1.67% relapsed
Lee et al.[120]	117 (94)					99%		95.8%	
Sung et al.[31]	417		375	14	28	100%		99.3%	1.3%

CTS = direct view thoracoscopic sympathectomy; **symp** = sympathectomies; **VATS** = video-assisted thoracoscopic sympathectomy.

in lung volume, which is probably secondary to the thoracoscopic procedure itself and usually has disappeared by 6 months after the procedure.[138]

The immediate failure rate post-sympathectomy varies from 0%–2% (table III) for endoscopic procedures and recurrence rates can be up to 2%. The failure rate could be explained by failure of electrocautery to destroy the second thoracic ganglion or the nerve of Kuntz,[139] which occurs in 10% of persons as an extraneural pathway lateral and parallel to the main sympathetic trunk.

Overall there is a better satisfaction rate for palmar hyperhidrosis[28,29,119,128] than for isolated axillary hyperhidrosis,[35,36] and as a result, some authors[35] would be reluctant to accept patients with axillary hyperhidrosis alone for ETS. They believe other treatment options such as topical aluminium chloride or local excision of sweat glands would be more appropriate. It has been acknowledged that careful selection of patients and meticulous surgical technique would minimize morbidity but there will always be a risk of unpleasant sequelae irrespective of the technique used.[26]

7.2 Excision of Axillary Tissue

Ellis[24] reports that most cases of excessive axillary sweating can be managed with topical proprietary antiperspirants and if these fail, excision of the affected area of skin was extremely effective.[42] The axillary sweat glands were located by the starch-iodine test, which involved painting iodine onto the axilla followed by sprinkling it with starch. Eccrine sweat in combination with the starch and iodine turns purple, demarcating the area of the eccrine sweat glands.

The complications of axillary tissue excision could include hematoma formation, suture abscesses, delayed wound healing,[140] wound infection,[140] skin necrosis, scarring, keloid formation and limitation of shoulder abduction.

Skoog and Thyresson[141] first described the excision of axillary sweat glands in 1962. They created four skin flaps and then excised the glands from the underlying surface of the flaps. The following year, Hurley and Shelley[142] reported good results after excision of the involved ellipse of axillary skin with primary wound closure. This technique was in order to minimize the risk of movement restriction after the operation. However, often a wide and ugly scar resulted. A study by Ellis[42] of 50 patients treated with axillary skin excision showed that 47 were pleased with the result, but three patients had not improved after 1 year. Seven patients were unhappy about the appearance of the scars and three had some limitation of arm movement. In 1966, Hurley and Shelley[43] modified the technique used in patients with severe hyperhidrosis, which involved performing additional peripheral

excisions beyond the central excision with undermining of the area followed by resection of the sweat glands.

In order to reduce scarring, Breach[143] performed three transverse incisions in the axilla and removed all the subcutaneous tissue from the bipedicle flaps, which they created. The authors reported that 23 of 25 patients had a satisfactory result after 1 year. Stenquist[144] reported excellent results in 12 of 14 patients by using bat-shaped axillary excisions.

Although the studies for excision of axillary tissue as a treatment for axillary hyperhidrosis showed fairly good results, it is important to remember that the studies were small and not randomized and thus further randomized controlled trials are needed.

7.3 Subcutaneous Curettage of the Axillae

Jemec[44] described subcutaneous curettage of the axillae as a treatment for axillary hyperhidrosis. The procedure involved using the starch-iodine test to demarcate the affected area, which is then undermined through one or two short incisions, with scissors. A sharp curette is then used to remove all subcutaneous fat in the demarcated area and the incisions are sutured. Jemec reported that 12 out of 20 patients were completely satisfied, four partly satisfied; three dissatisfied and one was lost to follow-up over a 6–9 month follow-up period. None of the patients complained of troublesome scars. This was compared with a similar number of patients who had excision of axillary sweat glands. The results were roughly similar but four of these patients complained of axillary scarring. As a result of these findings, Ellis[42] undertook a trial of the procedure but found his results were disappointing, with high relapse rate and poor patient satisfaction. In view of the high treatment failures, he subsequently abandoned subcutaneous curettage and returned to the well-tried axillary excision operation.

7.4 Liposuction for Treatment of Axillary Hyperhidrosis

Suction-assisted lipolysis has been accepted as a standard surgical procedure for many years,[145] but it has only emerged as a treatment for axillary hyperhidrosis over the past 10–15 years.[146,147] The advantages of liposuction are that it can remove sweat glands without compromising the overlying skin and, as it tends to cause minimal scarring, it is preferable to excision of axillary tissue. It is superior to curettage due to its lower incidence of bleeding as a result of using a blunt cannula. The eccrine sweat glands are located in the deep dermis and upper subcutaneous tissues ensuring that deeper structures such as the brachial plexus are not damaged during the procedure. A review article by Lillis and Coleman[45] eloquently described the procedure, which involves inserting a blunt cannula through an inferior and superior incision and suctioning in a sweeping pattern. After most of the fat is removed the aperture of the cannula is turned up towards the skin surface and is used to scrape the overlying dermis, ensuring the superficial eccrine glands are also removed. The disadvantages of the procedure are that only one side is done at a time. Postoperative patients are advised to apply ice packs and to keep the arm down for the rest of the day. The arm should not be lifted for the week following surgery. Another theoretical risk is the possible development of a small area of full-thickness skin loss after the procedure, although the authors had not seen this. Occasionally secondary procedures need to be performed if there is not a satisfactory decrease in sweating. Overall, Lillis and Coleman[45] believe that a topical trial of antiperspirants followed by iontophoresis should be tried first, and only if these treatments are unsuccessful, liposuction of the axillae should be offered. They feel that liposuction would be the surgery of choice for axillary hyperhidrosis.

8. Chemical Sympathectomy

Sympathetic ganglion blockade with a neurolytic solution is a closed percutaneous needle technique.[148,149] Kobayashi et al.[46] believe that chemical sympathectomy is an effective, albeit often temporary, treatment for severe hyperhidrosis and they have reported successful use of the technique in three patients.

The authors also summarized the results of 10 other patients who had similarly undergone sympathetic ganglion blockade with 100% ethanol for hyperhidrosis in the previous 2 years.[46] Of these, two had bilateral L2 and L3 ganglion blockade (LGB) for plantar hyperhidrosis and the remainder had bilateral T2 and T3 ganglion blockade (TGB) for hyperhidrosis of face, hands and axillae. The results showed the two and three patients who had LGB and TGB respectively, had excellent results; sweating ceased completely. Another two with TGB had satisfactory results but two others experienced poor results with no reduction in sweating. Finally, one patient described an excellent result on his right palm but a poor result on his left palm.

The complications associated with LGB and TGB were neuralgia and compensatory hyperhidrosis. Other known complications include pneumothorax, somatic nerve block resulting in neuralgia, intravascular injection and intradural injection.[46]

Kobayashi et al.[46] concluded that chemical sympathectomy was an effective and useful method for treating severe hyperhidrosis that is refractory to conservative medical treatment. Unfortunately this study had small numbers and does not give long-term follow-up results; therefore, one needs to be slightly cautious when interpreting the results.

Table IV. Complications of endoscopic transthoracic sympathectomy

Studies	Pneumothorax (no. of patients; %)	Hemothorax (no. of patients; %)	Compensatory sweating (no. of patients; %)	Gustatory sweating (no. of patients; %)	Horner syndrome (no. of patients; %)	Pain (no. of patients; %)	Other complications
Byrne et al.[114]	1		54 (64%)		3 transient	12 (14.1%)	Surgical emphysema (n = 3); neuralgia (n = 5); Raynaud syndome (n = 4)
Kao[116]	2	0			0	0	
Gothberg et al.[113]	3	1			1		
Chao et al.[122]		1	28 (21.5%)		0		
Shachor et al.[28]	7 (2.4%)	3 (1.0%)	(50%) of 60 patients followed-up		2 (0.7%) transient		Surgical emphysema (n = 8); rebound sweating (8.3% of patients)
Kao et al.[119]	4		(66%)		0		
Hsu et al.[38]	0	1 (0.6%)					Wound infection (n = 2); air leakage (n = 1); facial anhidrosis (n = 15)
Herbst et al.[32]	11 (2.3%)		(67.4%)	(50.7%)	12 (2.5%)	(26.7%)	Pleural effusion (n = 1); ptosis (n = 7); others (n = 6)
Chen et al.[123]			(70%)		0		Surgical emphysema (n = 3); neuralgia (n = 3)
Drott et al.[33]	4	5	(55%)	(36%)	1 transient; 2 permanent	(39%)	Decreased heart rate (15% of patients)
Noppen et al.[39]	0	0	(45%)	(1%)	1 transient	(80%) post-op lasted 7 days	Neuralgia (n = 6); pleural effusion (n = 2); facial flushes (n = 1)
Graham et al.[34]	9 (10%)		25 (56%)		0		Surgical emphysema (n = 1); chest infection (n = 1); wound infection (n = 1)
Kao et al.[124]		0.30%	>50%		0.10%		
Kopelman et al.[125]	2 (1.9%)	1 (0.9%)	35 (67.3%)		7 transient; 2 permanent	7 (13.5%)	Pneumonia (n = 2); atelectasis (n = 1)
Gossot et al.[126]	3		72.2% TS; 70.9% SS		0		Chylothorax (n = 1); pleural effusion (n = 1)
Lai et al.[127]	6 (8.3%)		71 (98.6%)	12 (16.7%)	5 (6.9%)		Nasal obstruction (n = 5); intercostal neuralgia (n = 5)

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Table IV. Contd

Studies	Pneumothorax (no. of patients; %)	Hemothorax (no. of patients; %)	Compensatory sweating (no. of patients; %)	Gustatory sweating (no. of patients; %)	Horner syndrome (no. of patients; %)	Pain (no. of patients; %)	Other complications
Grabham et al.[128]			11 operations	1		9 (81.1%)	Bleeding trocar site (n = 1)
Rex et al.[35]	12 (1%)	4 (0.3%)	59.80%	28%	5 (0.4%)		Pulmonary embolus (n = 1); thoracic nerve contusion (n = 1)
Cohen et al.[129]	3		99 (44.4%)				
Fox et al.[36]	2		24 (44%)	6 (11.1%)	0	3 (5.6%)	Neuralgia (n = 2); vessel damage (n = 1); arm stiffness (n = 1)
Chiou & Chen[37]		1 (1.1%)	97%	1 (1.1%)	0	2 (2.2%)	
Lin & Fang[29]	6 (0.44%)		84%		0		Segmental lung collapse (n = 4); wound infection (n = 2)
Zacherl et al.[27]	3.8% [CTS]; 1.9% [VATS]		66.8% [CTS]; 69% [VATS]	50.4%[CTS]; 27.6% [VATS]	2.2% [CTS]; 0 [VATS]		Ptosis alone (n = 6); miosis & ptosis (n = 4); intercostal bleeding (n = 1)
Erak et al.[130]	17.5%		34 (64%)	5 (9.4%)	3 transient; 2 permanent		Wound infection (n = 1); neuralgia (n = 1); decreased exercise tolerance (n = 1)
Imhof et al.[131]			63.20%	63.20%	0		Surgical emphysema (n = 1); miosis & ptosis (n = 1)
Hsia et al.[40]			35 (74.5%)		0		
Yim et al.[121]	3		2				
Yamamoto et al.[30]	0		115 (63.9%) moderate; 1 severe	7 (3.9%)	0		
Lee et al.[120]	5		67 (71.2%)		1 partial		
Sung et al.[31]	15 (3.6%)				2 transient		Pleural effusion (n = 14); atrial fibrillation (n = 1); nerve injury (n = 3); parenchymal injury (n = 2)

CTS = direct view thoracoscopic sympathectomy; **n** = number of patients; **SS** = selective sympathectomy; **TS** = truncal sympathectomy; **VATS** = video-assisted thoracoscopic sympathectomy.

9. Computed Tomography Guided Thoracic Sympatholysis

Computed tomography (CT) guided thoracic sympatholysis for palmar hyperhidrosis has developed over the past 15 years.[150] Dordelinger and Kurdziel[47] were the first to report phenol block of the upper sympathetic chain using this method. Although Adler et al.[151] reported good immediate results, the long-term follow-up results showed a failure rate of more than 40%.[152] However, a more recent study by Lucas et al.[48] showed an 80% immediate success rate and a good result in 75% of patients at 20 months follow-up. Sympatholysis was performed under local anesthesia with CT guidance using 6% phenol in 16 patients. Complications included a pneumothorax, intercostal neuralgia, postoperative pain, temporary Horner syndrome and compensatory hyperhidrosis. Despite the results, the authors recommend CT guided thoracic sympatholysis for palmar hyperhidrosis, as they believe the results will get better with experience.

10. Conclusion

Hyperhidrosis can be an annoying and disabling condition. In patients with secondary hyperhidrosis the treatment is that of removing or controlling the underlying cause. The management of primary hyperhidrosis is rather more complex as the cause is not fully known or understood. Therefore treatment is one of reducing sweating to a level that is acceptable to the patient without making the cure worse than the disease itself. There are adverse effects with each of the different treatment modalities but often the management is dictated by the site and severity of symptoms, in addition to patient compliance and expectations. The therapeutic options offered to a patient need to be tailored to the particular individual.

The most symptomatic patients may ascend through the range of treatments and may require surgery when the pattern of sweating is amenable. Such people will have gained an understanding of the risk-benefit profile of their treatments over the course of months or years and be reconciled to the potential risks of surgery. Less symptomatic patients may gain relief from non-invasive medical or psychotherapeutic treatments when the adverse effects are seldom grave and are not permanent. Such treatments need to be maintained to provide continued benefit, although primary hyperhidrosis peaks for a limited period in life and seldom requires medical treatment for more than 10 years.

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