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Hyperhidrosis of the Palms and Soles

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Palmoplantar Hyperhidrosis: General Considerations

Primary focal hyperhidrosis commonly affects the palms of the hands, the soles of the feet or the armpits. Primary hyperhidrosis may be inherited and, although it usually commences in adolescence, may begin in childhood and even in infancy.

Emotional or mental activity increases sweating on the palms and soles. Thermal stimuli increase this effect in many cases. Simultaneous plantar and palmar sweating is not a rare occurrence in the patients affected. The sweating of the palms and soles may be either continuous or phasic. The former is worse in summer and not so clearly precipitated by mental factors. Excessive palmoplantar sweating induces hypothermia of the hands and fingers by evaporative cooling, which may then increase the sympathetic outflow and thus aggravate hyperhidrosis. Palmoplantar hyperhidrosis has been reported to occur in some patients with nail-patella syndrome, keratosis palmaris and plantaris, Raynaud's disease, erythromelalgia, atrioventricular fistula, cold injury and rheumatoid arthritis [1].

Hyperhidrosis is frequently socially embarrassing and occupationally disabling. Patients have a slippery grip and a cold, wet handshake. Excess sweat from the palms may soil paper- and artwork and make it virtually impossible to play many musical instruments. Careers in fields that require contact with paper, metal and electrical components become unattainable. Plantar hyperhidrosis may result in stains and damage to clothing and shoes. Patients who are severely afflicted complain of sweat pouring from the surface of the skin.

Assessment of Hyperhidrosis

The diagnosis can be made following a typical history. Clinical and para-clinical examinations are recommended to exclude secondary hyperhidrosis.

Table 1. Assessment of sweating in patients with palmar and plantar hyperhidrosis

Test	Description	Studies
Iodine-starch test (Minor 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 skin to be tested; after it has dried, fine rice or potato starch powder is applied; sweat causes the mixture to turn dark blue	Naver and Aquilonius [16], 1997 Shelley et al. [4], 1998 Naumann et al. [17], 1998 Naver et al. [19], 1999
Ninhydrin test	Moist palms pressed against paper leave a print which can be dyed with a ninhydrin solution; the paper is sprayed with a 1% dilution in acetone, dried and warmed for a few minutes at about 120 °C in an incubator	Schnider et al. [13], 1996 Schnider et al. [14], 1997
Evaporimetry	Water evaporation is measured with an evaporimeter; the measurement sample is held against the skin for 60 s or more until steady-state values are obtained for at least 15 s; two sites on the palms are measured: at the base of the index finger and in the middle of the hypothenar; the mean is the evaporation value	Naver et al. [19], 1999
Gravimetry	The hyperhidrotic area is blotted dry and then brought into contact with photocopying paper (Xerox) for 1 min; the amount of sweat secreted during the collection period is then determined as the increase in weight	Naumann et al. [17], 1998

It is important to establish the extent and severity of social embarrassment in order to plan appropriate treatment for the patient, mostly those with more than one localization. This can be done by direct questioning, questionnaires, self-rating by the patient and objective tests (visualization of sweat, printing tests, gravimetry, evaporimetry).

The test is not always necessary on the hands because hyperhidrosis is confined to the whole area of the glabrous skin of the palms, plus, in some cases, the periungual skin, where clinical observation is sufficient. Visualization of sweat by an iodine-starch reaction is especially useful on the soles because the hyperhidrosis is not confined to the flat surface only [2].

Printing Tests

The sweat response can be assessed by printing tests such as the ninhydrin method [3] or the iodine-paper test [4] (table 1).



Fig. 1. Ninhydrin test in a patient with palmar hyperhidrosis (before treatment).

Ninhydrin stains amino acids and lower peptides with great sensitivity. For the ninhydrin sweat test, several ordinary kinds of white writing paper have proved useful. The great advantage of the ninhydrin test lies in the fact that the print can be fixed and preserved (fig. 1). This makes it possible to compare prints taken at different times in their original form. The ninhydrin printing test shows the functioning glands as printed dots. The moist skin leaves intense blurred impressions.

The iodine-starch test was modified and improved by having both the starch and iodine put into the paper used for obtaining sweat imprints [1, 4]. In this method, the water in the sweat causes blue spots on the paper when the skin is pressed against it. The iodine-starch test uses an iodine solution that is painted over the area of skin to be tested. After it has dried, potato starch powder is applied. Sweat causes the mixture to turn dark blue (table 1).

The printing tests only provide qualitative evaluation of the sweat response of the palms and soles, plus a fairly reliable method for testing improvement after treatment (fig. 2). It must be emphasized that precise, clean work is always necessary to get reliable prints.



Fig. 2. Ninhydrin test in a patient with palmar hyperhidrosis. Small areas of residual sweating after BTX-A treatment.

Gravimetry

This technique involves the collection of sweat at rest, after exposure to heat or after injection or iontophoresis of cholinergic agonists (pilocarpine, methacholine; table 1).

Other Tests

Evaporation of water is measured with an evaporimeter (table 1). Testing the eccrine sweat glands has provided a useful means of assessing and localizing sympathetic nervous system function in patients with autonomic failure. Skin bio-electric recordings measuring skin conductance and resistance or the sympathetic skin potential provide an alternative measure of sudomotor function. Variability and habituation limit the value of this type of testing, however [5].

Conventional Therapy

Topical antiperspirants can provide useful palliation in some patients with moderate hyperhidrosis, but in many cases they are ineffective. The topical

application of aluminium chloride hexahydrate often causes skin soreness and irritation [6].

Tap water iontophoresis is a safe and inexpensive therapeutic modality but is not always effective. As the effect is only temporary, maintenance therapy, twice to three times a week for several weeks, is required [7].

Sympathectomy or upper thoracic (T₂-T₃) ganglionectomy is frequently offered to patients with severe palmar hyperhidrosis. Lumbar sympathectomy is not usually employed for plantar hyperhidrosis because of the risk of sexual dysfunction. Transthoracic endoscopic sympathectomy is an effective way of treating palmar hyperhidrosis but may be followed by major complications such as compensatory and gustatory sweating (47-67% of cases) or by rare ones such as Horner's syndrome (2.2-3.8%), pneumothorax (~1.3%) or subcutaneous emphysema (~2.1%) [8-10]. A significant decrease in the incidence of Horner's syndrome and gustatory sweating was observed when the procedure was guided by video imaging [10]. Systemic anticholinergic agents may be useful adjuncts to other therapies but are limited by systemic side-effects.

Therapeutic Challenge

In 1994, Bushara and Park [11] performed a brief study and showed that sudomotor efferents are affected by botulinum toxin. They demonstrated localized facial anhidrosis in patients treated for hemifacial spasm, as a side-effect of the botulinum toxin injections. Drobik and Laskawi [12] demonstrated the effectiveness of botulinum toxin A (BTX-A) injections for the management of Frey's syndrome.

A self-experiment showed a long-lasting, marked reduction of spontaneous sweat production on the palms after BTX-A injections [13]. In 1997, the first double-blind, placebo-controlled trial of BTX-A for the treatment of focal hyperhidrosis of the palms was published, showing a significant reduction in sweating in the BTX-A-treated palms [14].

Since then, several studies have demonstrated the safety and efficacy of BTX-A injections in the treatment of hyperhidrosis, and the application technique has been improved [13-18]. In recent years, many patients with focal palmoplantar hyperhidrosis refractory to conventional therapy have requested BTX-A injections.

The therapeutic options and a management algorithm for palmar hyperhidrosis are outlined in figure 3.

If local treatment with an aluminium salt as well as iontophoresis is unsuccessful, BTX-A is a highly effective alternative [13-18]. Before using

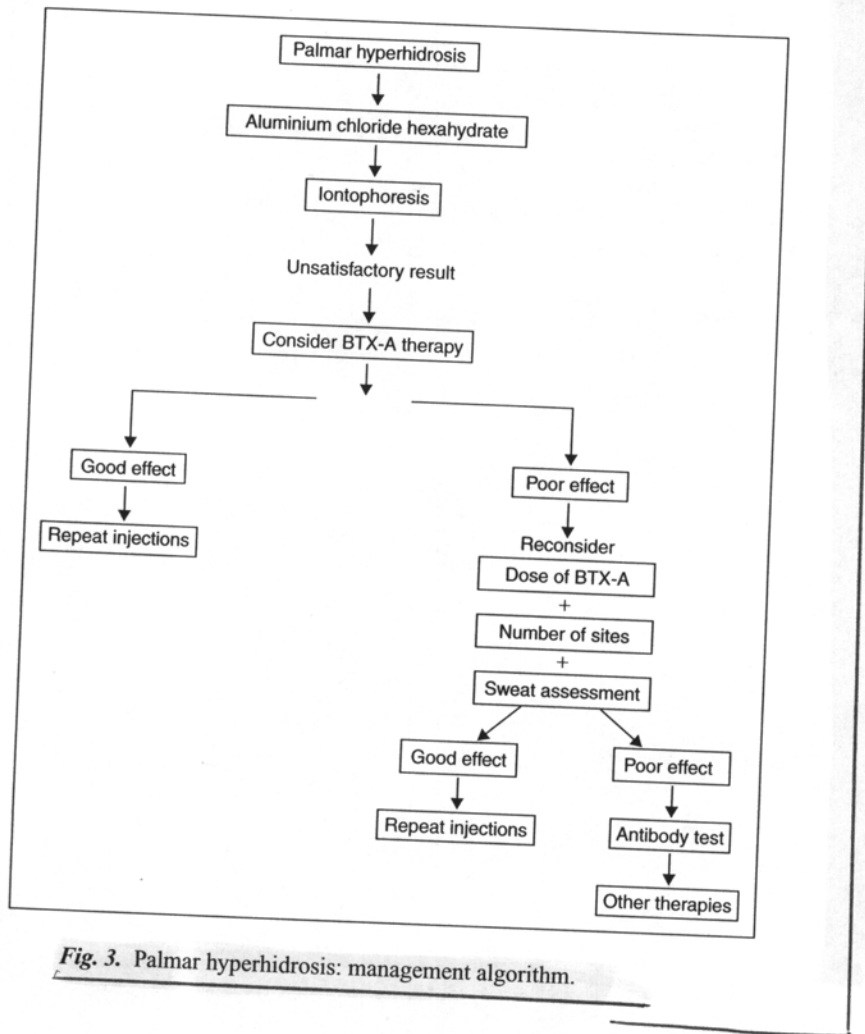


Fig. 3. Palmar hyperhidrosis: management algorithm.

BTX-A, we have to explain the injection technique, the necessity of repeated injections to maintain the effect and the possibility of the development of immunoresistance. The patients treated with BTX-A are supposed to keep a diary to record sweat production (table 2).

The BTX-A treatment technique favoured by most physicians employs intracutaneous injections with small but precise volumes at multiple sites [4, 16–18]. The injections into palms and soles are usually painful. Pain may be alleviated by using a local anaesthetic cream or iontophoresis in tap water containing an anaesthetic or by performing local nerve block prior to treatment. It is usual for some patients to prefer only a local anaesthetic cream and others the nerve block.

Table 2. Assessment summary for hyperhidrosis: injection details

Hyperhidrosis

Date:
Sweat testing:
Self-rating of sweat:
(visual analogue scale: 0 = no sweating, 100 = maximum sweating)
Injection number:
Product, dose, dilution:
Cumulative doses:
Anaesthesia:
Side-effects:

A few patients report only moderate improvement of sweating for a short time (<13 weeks) after BTX-A injections. A higher dose may occasionally improve the efficacy of the treatment.

For patients with palmar hyperhidrosis who desire a permanent effect or who do not experience significant improvement with BTX-A injections and accept the risk of a surgical procedure, the treatment of choice is thoracoscopic sympathectomy [6].

Botulinum Toxin Type A: Doses and Injection Technique

Palms

There are two BTX-A preparations available – Botox® (Allergan, Irvine, Calif., USA) and Dysport® (Ipsen, Biotech, Paris, France). Even though the doses for each are quoted in mouse units (MU), the two preparations have different dose schedules: 1 MU of Botox is not the same as 1 MU of Dysport.

In our patients, we use 5 MU (0.025 ml) or 10 MU (0.05 ml) per site from the 500-MU Dysport vial diluted with 2.5 ml sterile saline [Schnider et al., unpubl. data]. We usually treat the fingers with 5 MU per site and the palms with 10 MU. We treat the fingers with a total of 70 MU (14 sites) and the palms with 160 MU (16 sites) for each hand. The patients who report that sweat is dripping from their fingers or who have large droplets of sweat on inspection may need injections with a shorter distance between injection sites. In severe cases, we use a 500-MU Dysport vial diluted with 1 ml sterile saline and inject 5 MU (0.01 ml) per site at 45 sites for each palm (total dose: 225 MU). We have

observed a better effect when injecting small volumes. The treatment is carried out with Micro-Fine insulin syringes 0.5 ml, 0.33 × 12.7 mm/29 G × 1/2 inch (Becton-Dickinson).

After dilution of the 100-MU Botox vial with 5 ml sterile saline, 2 MU (0.02 ml) or 3 MU (0.03 ml) are injected per site [17, 18]. The total dose injected ranges between 46 and 100 MU for each hand, divided in most cases between 40 and 50 sites. A Botox vial diluted with 1 ml produces a good therapeutic effect with a dose ranging between 70 and 220 MU at multiple injection sites [19].

The potency of a given dose appears to be affected by the dilution applied to the product vial [20]. We observe that use of the appropriate dilution for each product permits us to limit the dose necessary for an anhidrotic effect to a maximum of 500 MU Dysport and 100 MU Botox per treatment, respectively, both for palms and soles. We dilute the 500-MU Dysport vial with 1 ml or 2.5 ml sterile saline in accordance with the Dysport/Ipsen Practice Information. Although there are several possibilities for the Botox vial (from 1 to 8 ml, Botox/Allergan Practice Information), the dilution of 100 MU with 5 ml sterile saline appears to induce the most efficient dose-effect relation (table 2).

The dose applied in the treatment of palmar hyperhidrosis ranges from 60–200 MU Botox to 250–500 MU Dysport (table 3).

Several studies have indicated that the effect will not be immediate and that there is usually a delay of 24–72 h before symptoms improve.

Soles

The technique of application is the same. The dose we apply is 200–250 MU Dysport and 45–50 MU Botox with the same dilutions as mentioned above for the palms. Pedal hyperhidrosis is more tedious and uncomfortable to treat because of the large surface area and sensitivity of the feet [6]. The printing test has to be performed before and at follow-up examinations. The iodine-starch test is recommended for a precise assessment of hyperhidrosis of the soles. The injections are repeated at the necessary intervals, with a minimum of 3 months in between. The anaesthetic procedure is the nerve block described below or the local application of an anaesthetic substance [17].

Regional Anaesthesia

Physicians have attempted to alleviate the pain during BTX-A injection with an anaesthetic cream (EMLA) [18] or with cooling spray [14], but painless injections have only been achieved by nerve block [16–18].

Table 3. Literature review: studies performed on patients with palmar and plantar hyperhidrosis

Study design	Patients	Product (dose and dilution)	Sweat test	Efficacy
Schnider et al. [14], 1997 Double-blind, placebo-controlled	11 patients age: 23–54 years cold packs for 30 min	Dysport 120 MU/0.5 ml 120 MU/6 sites per palm	ninhydrin with digital image analysis	effective for at least 13 weeks in 11 patients
Naver and Aquilonius [16], 1997 Pilot study	4 patients age: 23–43 years median, ulnar nerve block	Botox 100 MU/1 ml 68–90 MU/palm 2 MU/site 34–45 sites/palm	minor test	3 patients: anhidrosis between 1 and 8 months 1 patient: only hypohidrosis
Shelley et al. [4], 1998 Open study	4 patients age: 14–34 years median, ulnar nerve block	Botox 100 MU/5 ml 100 MU/palm 2 MU/site 50 sites/palm	iodine-paper test	good effect: 1 patient for 4 months, 2 for 7 months, 1 for 12 months
Naumann et al. [17], 1998 Open study	5 patients 8 palms and 2 soles	Botox 100 MU/5 ml 3 MU/site/4 cm ² 28–46 MU/palm 42–48 MU/sole	minor test, gravimetry	no recurrence within 16 weeks
Naumann et al. [18], 1998 Open study	16 patients with needle injection or Dermojet with EMLA cream	Botox 100 MU/5 ml 50 MU/palm 60 min before injecting EMLA cream in 6 patients	minor test gravimetry	significantly reduced sweat production with needle injection after 4 weeks
Naver et al. [19], 1999 Open study	113 patients with palms, 10 patients with soles median, ulnar nerve block	Botox 100 MU/1 ml 120–220 MU/palm 0.8 MU/cm ²	minor test (only for testing residual sweating)	duration of effect from 3 to 14 months
Schnider et al., 2000 Unpublished data	21 patients with palms with ethyl chloride BP cooling spray liq.	Dysport 500 MU/2.5 ml 230 MU/palm repeated injections for 3 years	ninhydrin test	median interval between injections: 25 weeks (25th–27th percentile: 21–38 weeks)

Recent studies have shown that topical dermal analgesia may be induced by the iontophoretic administration of 2% lidocaine with 1 : 100,000 adrenaline [21]. Regional anaesthesia by means of median and ulnar nerve block for palms and sural and posterior tibial nerve block for soles has been used regularly in patients with hyperhidrosis.

Nerve Block

Palms

Considering the anatomical distribution of nerves in the hand, regional anaesthesia of the palms [22] may be induced by ulnar, median and radial (ramus superficialis) nerve block at the wrist. Median and ulnar nerve block should be sufficient for botulinum toxin injection.

The needle is placed near the nerve either by inducing paraesthesia, which necessitates its actually coming into contact with the nerve, or by locating the nerve by means of a nerve stimulator. The landmarks for nerve block at the wrist are the ulnar styloid and the palmar crease.

Median Nerve Block. The median nerve is medial to the flexor carpi radialis tendon and lateral and just below the musculus palmaris longus tendon. The m. palmaris longus tendon is identified at the wrist. A skin wheal is raised lateral to it. The injection site is between the m. palmaris longus and m. flexor carpi radialis tendons; 3–5 ml of local anaesthetic (lidocaine 1% or mepivacaine 1% or etidocaine 1% or bupivacaine 0.5%) is injected at a depth of 0.5 cm.

Ulnar Nerve Block. The ulnar nerve lies under the flexor carpi ulnaris tendon on the medial side of the ulnar artery and deep to it.

A skin wheal is raised on the volar surface of the wrist on the lateral side of the flexor carpi ulnaris tendon, and a needle is passed under the tendon to inject 3–5 ml of local anaesthetic. An alternative technique is to inject medially to the flexor carpi ulnaris, directing the needle laterally to pass under the tendon.

Soles

The soles of the feet are anaesthetized by means of posterior tibial and sural nerve blocks at the ankle [22]. The major landmarks for the ankle block are the medial and lateral malleoli.

Sural Nerve Block. A skin wheal is raised between the lateral malleolus and the Achilles tendon. A needle is passed through the wheal and 5 ml of local anaesthetic solution injected.

Posterior Tibial Nerve Block. A skin wheal is raised midway between the medial malleolus and the Achilles tendon. A needle is passed toward the

pulsations of the posterior tibial artery and 5–6 ml of local anaesthetic solution injected after careful aspiration.

Complications

In general, peripheral nerve blocks are safe anaesthetic techniques with a low complication rate.

Some studies have shown that wrist block is an effective analgesic and after 124 nerve blocks in 60 patients, no complications (infections, nerve irritations or lesions) have been observed [23]. Other studies have shown that nerve block repetition may possibly induce neural damage caused by ischaemic, mechanical or chemical damage [24].

In ankle block, temporary paraesthesia, especially of the posterior tibial nerve, may be the most frequent complication. Studies have shown a complete recovery within a few weeks [25]. Systemic toxicity from local anaesthetics after ankle block is rare and may only occur after accidental intravascular administration [25].

Follow-Up

Subsequent management depends on the response to treatment. Printing tests are important for the evaluation of treatment response and assessment of residual hyperhidrotic areas. It is recommended that the first check-up be performed 2 weeks later, to document any transient muscle weakness. Patients should be informed that the weakness is transient and has a median duration of 2–4 weeks.

Side-Effects

Side-effects include small haematomas and transient weakness of small hand muscles [14, 17, 19]. One study which assessed the safety of botulinum toxin in the treatment of palmar hyperhidrosis using a serial nerve conduction study showed a change in nerve conduction to the abductor pollicis brevis in 1 patient treated with subcutaneous injections [26]. If a reduction in the strength of the finger grip occurs, the recommendation is to reduce the dose given over the thenar eminence and to inject it as superficially as possible.

Contra-Indications

Contra-indications include conditions of generalized muscular weakness, such as neuromuscular disorders, progressive myopathies (myasthenia gravis),

profound atrophy of the target muscle and aminoglycoside antibiotic therapy prior to the use of BTX-A, which may potentiate general weakness. Pregnancy and lactation are also contra-indications.

Repeated Botulinum Toxin A Injections

Most patients will experience a satisfactory effect for at least 13 weeks, according to several published studies (table 2). Repeated injections are thus necessary to maintain the treatment effect. The studies demonstrate the efficacy and safety of repeated injections, with a sweating recurrence at longer intervals than with dystonia treatment [19].

Our experience shows a median time interval of 25 weeks (25th–75th percentile: 21–38 weeks) between the sets of injections for palmar hyperhidrosis and a median duration of maximum effect of 11 weeks (25th–75th percentile: 6–20 weeks) [Schneider et al., unpubl. data]. Patients usually experience a fairly anhidrotic plateau phase, followed by a slow recurrence of hyperhidrosis over a period of several weeks. Repeated injections over a period of 3 years were as effective as the first treatment [19, Schneider et al., unpubl. data]. The severity of recurrent sweating is reduced when compared with the initial sweating and remains amenable to re-injection.

Patients who have not improved or experience only slight improvement after the first treatment may be treated with a higher dose (within the range mentioned above), or else other therapies have to be considered.

Poor response to therapy after several BTX-A injections may reflect the development of antibodies [27, 28]. Currently, there are no data concerning the development of resistance to BTX-A therapy in patients with hyperhidrosis. We agree with other physicians' recommendations to reduce immunoresistance: (1) use the smallest possible effective dose, (2) extend the interval between treatments as much as possible, with at least 3 months between them, and (3) avoid using booster injections [27–29].

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