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Abstract

The prevalence of idiopathic hyperhidrosis is between 1% and 2%.
Focal hyperhidrosis has a severe impact on quality of life. Impairment for the patients includes limitations in work, social interaction, physical activities, and leisure as well as emotional and psychological distress.
The first description of iontophoresis was given in the eighteenth century. Its clinical use was manifold, also in dermatology. In 1952 tap water iontophoresis was first described for the treatment of palmoplantar hyperhidrosis.
The most comfortable means of iontophoretic treatment employs pulsed direct current of high frequency (5–10 kHz).
Side effects are minimal and transient. Only slight skin irritation or sensations of discomfort may occur during treatment. Electric burns and electric shock have to be avoided.
The main course of anhidrosis after tap water iontophoresis is most likely a transient functional disturbance of the secretory mechanism of eccrine glands.
It was shown that tap water iontophoresis with pulsed current can extend symptom-free intervals in dyshidrotic palmar eczema.
Contraindications of tap water iontophoresis are pregnancy and metallic implants, such as cardiac pacemakers or orthopedic joint or bone implants.
Defects in the skin barrier, which cannot be protected by petrolatum or insulating tape, also represent a transient contraindication.

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105 Therapy: Iontophoresis

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Core Messages

- The prevalence of idiopathic hyperhidrosis is between 1% and 2%.
- Focal hyperhidrosis has a severe impact on quality of life. Impairment for the patients includes limitations in work, social interaction, physical activities, and leisure as well as emotional and psychological distress.
- The first description of iontophoresis was given in the eighteenth century. Its clinical use was manifold, also in dermatology. In 1952 tap water iontophoresis was first described for the treatment of palmoplantar hyperhidrosis.
- The most comfortable means of iontophoretic treatment employs pulsed direct current of high frequency (5–10 kHz).
- Side effects are minimal and transient. Only slight skin irritation or sensations of discomfort may occur during treatment. Electric burns and electric shock have to be avoided.
- The main course of anhidrosis after tap water iontophoresis is most likely a transient functional disturbance of the secretory mechanism of eccrine glands.
- It was shown that tap water iontophoresis with pulsed current can extend symptom-free intervals in dyshidrotic palmar eczema.
- Contraindications of tap water iontophoresis are pregnancy and metallic implants, such as cardiac pacemakers or orthopedic joint or bone implants. Defects in the skin barrier, which cannot be protected by petrolatum or insulating tape, also represent a transient contraindication.

1 Introduction

Hyperhidrosis is defined as excessive sweating beyond what would be physiologically required for temperature regulation of the body or would be adequate for the emotional state of the individual. Eccrine sweating serves two purposes. First, sweating on the trunk is essential for thermoregulation and sweating on palms and soles optimizes friction during physical activities. Axillary eccrine sweating seems to be an atavistic relict and aids in dissipating axillary odor into the environment by vaporization of odoriferous substances preformed by the action of skin surface bacteria on axillary apocrine sweat. Any amount of eccrine sweat which exceeds these physiological requirements is termed hyperhidrosis.

The prevalence of hyperhidrosis is estimated between 1% (Adar et al. 1977) and 2.8% (Strutton et al. 2004). The prevalence is largest between the age of 18 and 65 years. Males are more often afflicted than females. Palmoplantar sweating frequently starts already in early childhood, axillary sweating usually begins at puberty. In about 50% palms and/or soles are involved.

Idiopathic or primary hyperhidrosis is distinguished from symptomatic or secondary hyperhidrosis, associated with systemic or local disturbances. Primary hyperhidrosis is localized, characteristically symmetric and mostly effects axillae, palms, and soles, sometimes also face, head, and the midline regions of chest and back. It is assumed that it results from overactivity of the sympathetic nervous system. Secondary hyperhidrosis can be focal or generalized and may result from a number of conditions including vertebral illness, endocrine and metabolic conditions, neurologic disorders, cardiovascular disorders, respiratory disorders, medications, drug-use, spinal cord injuries, diabetes, menopause, neoplastic disease, and infection (Hölzle 2002). Further examples are given in > Table 105.1.

Hyperhidrosis has a severe impact on patients' quality of life. Patients have to cope with social, occupational, and medical consequences. Profuse sweating damages clothing, paperwork, and shoes. Obvious sweat marks on clothing or cold wet handshakes are unappealing. The resulting substantial impairment for the patients includes limitations in work, social interaction, physical activities, and leisure as well as emotional and psychological distress. Excessive sweating, or even untimely moderate sweating, in return exacerbate the associated uncertainty and stress and finally lead to a vicious circle. The negative effect of primary hyperhidrosis on quality of life has been evaluated by validated questionnaires and has been reported to be similar or greater than that found in other dermatologic and non-dermatologic chronic diseases (Naumann et al. 2002).

Measures of treating focal hyperhidrosis include the application of aluminum salts in aqueous or ethanolic

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Table 105.1
Pathogenesis of hyperhidrosis

Causative disorder	Example
Physiologic hyperhidrosis	Acclimatization
	Menopause
	Idiopathic gustatory sweating
Endocrinologic disorders	Hyperpituitarism
	Hyperthyreosis
Elevated catecholamines	Hypoglycemia
	Shock
	Phaeochromocytoma
Neurologic disorders	Cervical rib
	Carpal-canal syndrome
	Auriculotemporal syndrome and other types of symptomatic gustatory sweating
	Tabes dorsalis
	Syringomyelia
	Encephalitis
	Diabetic neuropathia
	Hemiplegia
	Plexus lesions
	Sympathetic chain lesions
Compensatory hyperhidrosis in association with wide spread anhidrosis	Ross syndrome
	Diabetic neuropathia
	Miliaria
	Sympathetic chain lesions
Axon reflex sweating	Inflammatory skin lesions
Nevoid disorder	Naevus sudoriferus
Idiopathic hyperhidrosis	Hyperhidrosis axillaris
	Hyperhidrosis manuum
	Hyperhidrosis pedum
	Generalized hyperhidrosis of the thermoregulatory pattern

solutions, the injection of botulinum toxin, iontophoresis, **either for delivering anticholinergic drugs into the skin or as** tap water iontophoresis and, finally, surgery with excision or curettage of the axillary sweat glands or cervicothoracic sympathectomy for excessive sweating on face, axillae, or palms. A treatment algorithm of hyperhidrosis depending on severity of sweating and body site afflicted is given in › Table 105.2 (Hornberger et al. 2004).

Table 105.2
Treatment algorithm for focal hyperhidrosis

	Axillary hyperhidrosis	Palmoplantar hyperhidrosis
1st line	OTC antiperspirants, 15% (10–25%) $AlCl_3{\cdot}6H_2O$ overnight, using proper technique to avoid irritation	OTC antiperspirants, 30% (15–30%) $AlCl_3{\cdot}6H_2O$ overnight, preferably under occlusion, using proper technique to avoid irritation
2nd line	Tap water iontophoresis using special pads as electrodes	Tap water iontophoresis
3rd line	Intradermal injections of botulinum toxin A	Intradermal injections of botulinum toxin[a]
4th line	Surgery: local sweat gland resection, endoscopic thoracic sympathectomy[b]	Endoscopic thoracic sympathectomy[b]

Iontophoresis (Greek, introduction of ions) has been applied to a great many disease conditions for more than 200 years after the first description of the technique by Veratti in 1747 (quoted after Turnell 1921). In dermatology, the list of applications comprises many indications reaching from itchy leg ulcers, plantar warts, lichen planus, vitiligo, scleroderma, lymphoedema, and sclerosis up to the pilocarpine sweat test for diagnosis of cystic fibrosis (Sloan and Soltani 1986).

Up till now, hyperhidrosis has become the most successful application of iontophoresis for dermatologic conditions. In 1936, Ichihashi noted that sweating could be reduced by ion transfer of certain solutions applied to the skin (Ichihashi 1936). Ten years later, Freis used formaldehyde and cupric sulfate iontophoresis for the treatment of dermatophytosis and hyperhidrosis (Freis 1946). Boumann and Grunewald Lentzer were the first ones who published the use of direct current only for the treatment of hyperhidrosis of palms and soles (Bouman and Grunewald Lentzer 1952). They conducted systematic experimental experiments on the efficacy of tap water iontophoresis and found two separate trays more effective than placing the two electrodes into a single water bath. They also reported that adding salts like aluminum chloride or copper sulfate had no additional effect; on the contrary, it diminished the antiperspirant action. Solutions of various compounds have been investigated and anticholinergic agents such as poldine methosulphate (Grice et al. 1972; Hill 1976), glycopyrronium bromide (Abell and Morgan 1974; Dolianitis et al. 2004), and atropine (Gibinski et al. 1973) were shown to have a longer lasting effect after one application than tap water alone. However, side effects of systemic anticholinergic blockade prevented this form of treatment from gaining wide acceptance. Levit, finally, in 1968, introduced tap water iontophoresis into practical dermatology. Its safety and efficacy, since, has been well documented (Levit 1980; van der Schaar 1974; Morgan 1980; Shrivastava and Singh 1977; Ho¨lzle et al. 1984).

In the past decades, tap water iontophoresis has been established as the treatment of choice for palmoplantar hyperhidrosis. In general, direct current of 8–25 mA with a voltage of 20–40 V has been used. In 1993, it was shown that alternating current with direct current offset had the same efficacy despite a lower current of 8–12 mA and a fixed voltage of 16 V. In this mode, handling of the apparatus is very simple and side effects are minimized (Reinauer et al. 1993). This method with pulsed direct current is also suitable for treating children.

Recently, botulinum toxin, type A was applied by iontophoresis to treat palmoplantar hyperhidrosis (Kavanagh and Shams 2005). The authors showed in preliminary experiments that palmar sweating was reduced up to 81% with the effect lasting for about 3 months.

3 Method of Tap Water Iontophoresis and Factors Influencing Its Efficacy

In systematic experiments the influence of major methodological modifications of tap water iontophoresis was investigated. These included the effect of current direction, the duration of a single treatment session, the addition of electrolytes to tap water, and the treatment interval during maintenance therapy.

3.1 Current Direction

It has been known for a long time that the anode exerted a greater suppression of sweating than the cathode (Shrivastava and Singh 1977; Levit 1980). Therefore, the question arises: How should the switch of polarity be performed in order to optimize the anhidrotic effect of tap-water iontophoresis? In a group comparison study the duration of single treatment sessions was kept constant for 30 min. In one group (n = 8) current direction was switched before each treatment session. In the second group (n = 10) polarity was switched when normal sweating was reached on the hand connected with the anode and, then, treatment was continued in this mode until both palms reached normal sweating. In the third group (n = 6) current direction was switched after 15 min midway through each treatment session (Schauf et al. 1994).

Results showed a partial loss of efficacy, if current direction was changed during each treatment session after 15 min. After the switch, side effects caused by the cathode were more frequent and more intense. Patients noticed burning and painful sensations accompanied by erythema. This forced reduction of voltage that finally let to loss of efficacy.

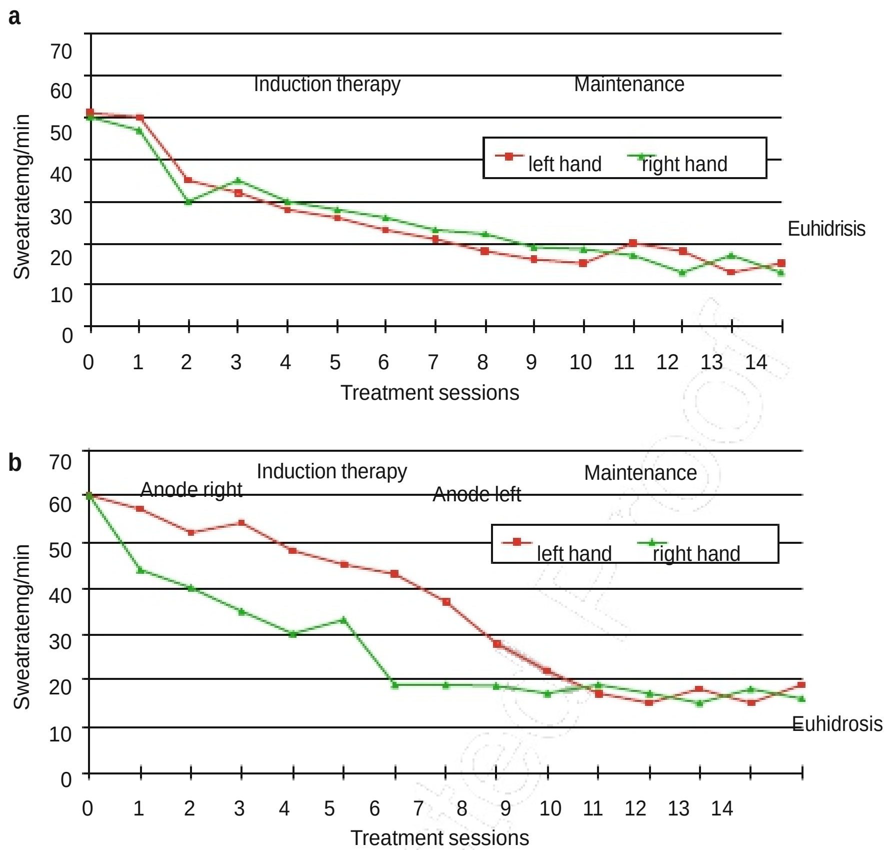
Switching current direction before each treatment session or only once, after reaching normal sweating on the hand treated by the anode, exerted roughly the same overall effect. After about nine treatment sessions, both hands reached euhidrosis, whereby the daily switched mode was slightly more effective; it required eight to nine treatments versus nine to ten treatments in the constant mode. If one hand was constantly treated with the anode, normal sweating already was reached after six treatment sessions. On the contrary, the cathode-treated side showed a reduction of only 45% at that time point. It required, however, only three to four more sessions with switched polarity until, after nine to ten treatments, both hands were euhidrotic, finally (> Fig. 105.1).

These observations led to the following practical procedure. First the dominating hand, mostly the right hand, is treated with the anode and current direction is switched only once after sweating becomes normal on the anodal side. When both hands are satisfactorily dry, patients undergo maintenance therapy, during which polarity is switched before each treatment session.

3.2 Duration of Therapeutic Sessions

In another group comparison study (n = 43), tap water iontophoresis was performed with switching current direction before each treatment session. In the different groups treatment sessions varied from 2 to 5, 15, and 30 min each (Schauf et al. 1994).

Treatments for 10, 15, and 30 min did not substantially differ in their efficacy. In each group patients reached normal sweating after about nine treatments. However, if



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. Fig. 105.1
Reduction of sweating during tap water iontophoresis. (a) Current direction was switched before each treatment. (b) Polarity was kept constant with the right hand connected to the anode for the first six treatments until the right hand had reached euhidrosis. Then polarity was switched and the left hand treated by the cathode until both hands were euhidrotic. Maintenance was, then, performed switching electrodes before each treatment (Adapted from Schauf et al. 1994)

duration of single treatments were shortened further, only 60% of the patients reached normal sweating after 5 min sessions and only 40% after 2 min sessions.

From there it was concluded that treatment between 10 and 15 min would be sufficient.

3.3 Addition of Electrolytes

One might assume that the addition of ions to the tap water would increase current flow and, perhaps, enhance efficacy. Baumann and Grunewald-Lentzer, however, have shown that efficacy was even lowered by adding electrolytes (Bouman and Grunewald Lentzer 1952) Therefore, this issue was further investigated.

In a group comparison study (n = 20) the duration of treatment sessions was 30 min and polarity was switched before each session. Compared were tap water versus physiological saline solution and a solution of ammonium chloride isomolar to physiological saline. In comparison to tap water iontophoresis only two thirds of patients reached euhidrosis when ammonium chloride was added. About 50% of these patients experienced side effects resulting in lowering of the voltage and reduced efficacy. With saline solution, all patients suffered from side effects and voltage had to be drastically reduced resulting in a complete failure of the treatment (Schauf et al. 1994).

3.4 Maintenance Treatment

By means of a questionnaire 28 patients reported on their experience with maintenance treatment for 1 year. About 30% used varying treatment schedules with intervals reaching from few days up to several weeks. Most of the patients (about 60%) were required to use iontophoresis approximately every 6 or 7 days to maintain normal sweating. Side effects were minimal and comprised transient erythema, dry skin with some scaling, or rarely pruritus (Schauf et al. 1994).

3.5 Optimized Method

One treatment session should last between 10 and 15 min. During induction therapy treatments should be performed between three and seven times a week. Treatments twice a day would be less effective (unpublished observation). If treatments are performed less than daily, intervals should be kept fairly constant. Current direction may be switched before each treatment or, even better, kept constant until one side, preferably the dominant hand, has reached euhidrosis. Then polarity is switched until both hands are sufficiently treated. During maintenance current direction is switched before each treatment. Addition of electrolytes is not recommended, if however deionized tap water has to be used, the addition of mineral water is useful. Maintenance treatment is performed once weekly, dependent on the needs of the patients. The goal is to maintain normal sweating. It is one drawback of the method that tap water iontophoresis has to be performed continuously. If treatment is interrupted for 2–3 weeks, hyperhidrosis reoccurs.

3.6 Side Effects

Most patients experience a tingling or slightly burning sensation during tap water iontophoresis. Immediately after treatment sessions, erythema along the waterline may occur and this may be accompanied by some small vesicles. These symptoms are transient and disappear within minutes after treatment. At higher amperages patients experience pain in the extremities connected with the current source.

Small defects in the skin barrier or visible erosions may lead to electric burns. This can also occur, if metallic pieces (jewelry, watches) remain on the skin during the treatment and are submerged to the tap water. Therefore, electrodes must be covered by foam rubber cloths to avoid direct skin contact, metal items worn on hands or wrists should be removed, and skin erosions should be covered with petrolatum or insulating tapes or wrappings.

Iontophoresis with direct current may cause electric shock, if hands or feet to be treated are suddenly submerged into the water or drawn from the water while the electrodes are still under electric tension. These shocks due to rapid changes of the voltage may be prevented by specific electronic devices built into the apparatus to limit speed of voltage change below 5 V/s. Using pulsed direct current of high frequency also prevents this problem (see following paragraphs).

Long-term side effects are absent. Since continuous treatment is necessary to maintain euhidrosis, many patients feel, however, burdened by the time-consuming therapeutic procedure (Brand et al. 2000).

3.7 Iontophoresis with Pulsed Current

In order to minimize side effects and to find the most comfortable mode of performing tap water iontophoresis, a group comparison study using different modes of current was performed. In this investigation, alternating current, direct current and alternating current with a superimposed offset of direct current were used (Reinauer et al. 1993). The alternating current had a sawtooth waveform at a frequency of 5.1 kHz, which produced a current of 8–12 mA. The alternating current with direct current offset consisted of a 0–16 V sawtooth waveform at a frequency of 4.3 kHz, which resulted in a direct current of 8 mA superimposed by a direct current offset between 8 and 12 mA. The conventional direct current apparatus employed an average direct current of 15 mA (range 8–25 mA) and 30 V (range 20–40 V). It was shown that there was no statistical difference in the efficacy of the conventional direct current apparatus in comparison to the alternating current with the direct current offset. Alternating current by itself was ineffective. This has been confirmed more recently in a study using alternating current iontophoresis as a placebo control in the treatment of palmoplantar hyperhidrosis (Karakoc et al. 2004).

With direct current, the usual minimal side effects were observed. Alternating current caused no adverse effects. The use of alternating current with direct current offset almost completely lacked any signs of cutaneous irritation or subjective sensations of discomfort.

In another study (Reinauer et al. 1995) the authors tried to further optimize treatment with pulsed current. In addition to the conventional direct current and the above-described alternating current with direct current offset of 4.3 kHz, pulsed direct current with a rectangular waveform and a frequency of 10 kHz resulting in a voltage from 0 to 16 V was employed. In this study, direct current was most effective (response rate 100% after 10 treatments) followed by high-frequency pulsed direct current (response rate 100% after 12.4 treatments) and pulsed

direct current 4.3 kHz (response rate 80% after 12.3 treatments). Direct current produced the known, but minimal side effects which were somewhat less pronounced using pulsed current of 4.3 kHz. High-frequency pulsed current of 10 kHz was accompanied by only minimal subjective discomfort. Objective adverse findings were absent.
Taken together, the high frequency 10 kHz, rectangular waveform of pulsed current seems to be optimal in terms of practicability. Side effects are virtually absent, electric shock cannot occur, and this treatment is very suitable also for children. If patients with an extreme degree of hyperhidrosis have to be treated, it may be necessary to take advantage of the slightly higher therapeutic effect of direct current. In this case, however, mild side effects and the risk of electric shock, if no further technical preventive measures have been taken, must be accepted.

4 Mechanism of Action of Tap Water Iontophoresis

The exact mechanism of tap water iontophoresis to induce anhidrosis is still elusive. Several hypotheses have been established. The oldest concept is obstruction of the sweat ducts by poral occlusion. This concept is based on the early observations of Shelley et al., who observed in 1948 that iontophoresis could induce experimental miliaria in human skin by sweat retention anhidrosis (Shelley et al. 1948). These authors, however, placed small electrodes directly on back skin of volunteers and generated a rather high current density of 0.125–1.5 mA/cm^2. In tap water iontophoresis current density reaches from 0.04 to 0.125 mA/cm^2 depending on voltage used and skin area being treated, respectively, and size of palms or soles. The high current densities in Shelley's experiments indeed can induce miliaria by poral occlusion (Ho¨lzle 1984). Shelley's findings have been challenged by several authors, but neither by electron microscopic nor by histomorphologic investigations a ductal or poral occlusion could be found in anhidrosis followed by tap water iontophoresis (Bouman and Grunewald Lentzer 1952; Hill et al. 1981; Ho¨lzle 1984; Reinauer et al. 1992).

In one of these studies it was shown that a few days after direct iontophoresis when small pads moistened with saline solution were placed under small metallic electrodes anhidrosis occurs in the treated area reaching a maximum of about 80% sweat retention after 5–7 days. Normal sweating was restored within about 14 days. Histopathologic investigations 1 week after direct iontophoresis showed parakeratotic plugs in the sweat pores containing denatured keratin and cell debris (Hölzle 1984).

The rather high ion flow produced by direct iontophoresis obviously damages the acrosyringium and the resulting repair processes lead to obstruction of sweat pores. In this stage, tape stripping opens the occluded sweat pores again and restores sweat function as was shown by others in early experiments (Gordon and Maibach 1969). These authors used glutaraldehyde and formaldehyde in addition to direct iontophoresis to induce anhidrosis; both agents are known to cause poral closure by denaturation of keratin in the stratum corneum.

In several further experiments it was shown that in the state of tap water iontophoresis-induced anhidrosis intradermal injections of cholinergic agents failed to induce any sweat secretion (Bouman and Grunewald Lentzer 1952; Ho¨lzle 1984; Reinauer et al. 1992). These observations indicate that anhidrosis is caused by loss of secretory function of eccrine acini rather than inhibition of nervous stimulation. The targets of tap water iontophoresis, therefore, are eccrine acini not sympathetic nerve endings.

It is generally understood that the pathways of electric current through the skin follow mainly sweat duct units. Flow through ordinary structured stratum corneum is negligible (Grimnes 1984). In lack of a direct electrophysiological experiment these authors indirectly investigated the patency of sweat ducts by skin resistance measurements. Skin resistance was measured on normal palmar skin, after hyperhydration by soaking the skin with wet dressings, in the state of anhidrosis after tap water iontophoresis, and in the state of anhidrosis after application of 15% aluminum chloride solution for 24 h under occlusion. Skin resistance dropped by about 50% after hydration, increased by a factor of four in anhidrosis induced by tap water iontophoresis, however, it increased by a factor of 150 in anhidrosis induced by aluminum chloride solution. Since it is known that metal salt solutions induce blockage of sweat ducts in the acrosyringium, this blockade also occludes the channels for ion flow and by that increases resistance dramatically. In contrast, tap water iontophoresis induces only a modest degree of skin resistance increase indicating again that complete blockage of the sweat ducts is absent in this anhidrotic state. The modest increase may be explained by empty sweat ducts due to impaired sweat secretion rendering dermal ducts unsuitable as ion channels. The slight drop of resistance after hyperhydration of the skin is the result of enhancing the current flow through the stratum corneum of the inter-follicular or inter-porous epidermis.

In still another approach Wang et al. (1994) investigated the morphology and function of dermal nerves supplying the eccrine sweat glands. By immunofluorescent techniques they compared the presence of several neuropeptides and neuronal markers in hyperhidrotic palmar skin before and after tap water iontophoresis, and in normal palmar skin. They could not find any change in the innervation density or distribution of nerve endings or any alteration of neuropeptides and/or classical transmitter-containing nerves around the secretory coils of the eccrine glands before and after treatment. Nor was there any influence on nerves around the arterioles. The authors concluded that neither sympathetic nerves nor sensory nerves are morphologically altered in palmar hyperhidrosis before or after tap water iontophoresis.

It is well known that the anodal current has a greater inhibitory effect than the cathodal current, that tap water is superior over saline, and that the inhibitory effect is a function of the amperage or, better, the current density in the skin area treated. In search for an explanation for these common observations the pH value of the anodal and cathodal water during tap water iontophoresis was investigated (Sato et al. 1993). It was found that the pH of the anodal water dropped to 3 whereas that of the cathodal water increased to 10 during passage of current through the skin. When sweat glands were isolated from tap water iontophoresis-induced anhidroticpalmar skin they responded to methacholine in vitro, but sweat rate and pharmacological sensitivity were slightly lowered. This, however, is in contrast to in vivo findings, in which injection of cholinergic agents failed to induce sweating. From their results Sato et al. suggested that the strong acidity generated by hydrolysis of water in the anodal bath and the subsequent accumulation of protons in the sweat duct may lead to an as yet unknown change in the function of the eccrine unit.

While using alternating current for the treatment of Palmoplantar hyperhidrosis, Japanese investigators (Ohshima et al. 2008) looked for changes in perspiration volume and Na^+ and K^+ concentrations in the sweat. They found that untreated hyperhidrotic patients had a significantly higher perspiration volume and Na^+ concentration than healthy controls. These findings are expected, since profuse sweating is known to prevent sufficient reabsorption of Na^+ in the distal portion of eccrineacini. After six iontophoresis treatments a significant decrease in sweat rate as well as in Na^+ concentration was observed. After one single treatment perspiration rate was unchanged, however, Na^+ concentration was found significantly decreased already. The authors hypothesized that the effect of alternating current iontophoresis may be due to a complex mechanism involving changes in ductal reabsorption of Na^+. It has to be noticed, however, that with the exception of another Japanese working group (Shimizu et al. 2003) other authors failed to find a satisfying therapeutic effect of alternating current iontophoresis in palmoplantar hyperhidrosis (Reinauer et al. 1993; Karakoc et al. 2004).

Taken together, it seems most likely that a transient functional disturbance of the secretory mechanism is the main cause of anhidrosis after tap water iontophoresis. There are no changes in the sympathetic or sensory nerves nor is there any indication of sweat duct blockade.

Such a mechanism would also fit the clinical observation that decrease of perspiration under tap water iontophoresis does not follow an on-off mechanism, but rather involves a gradual continuous process. First, patients experience that episodes of profuse sweating occur more rarely during the day and tend to last shorter. Then, euhidrosis prevails over longer periods of time interrupted by short bouts of hyperhidrosis, and lastly, palms or soles remain mostly dry whereby sweating remains on tips of fingers or toes. But even in this favorable state hyperhidrosis may break through, if the provoking emotional stimulus is strong enough.

5 Iontophoresis as a Treatment for Dyshidrotic Eczema

Since dyshidrotic eczema is frequently associated with hyperhidrosis of palms and soles, it seemed useful to investigate the effect of iontophoresis on dyshidrotic hand and foot eczema. Several authors were able to show that iontophoresis not only diminished sweating, but also had an efficacious effect on dyshidrotic eczema (Schempp et al. 1996; Odia et al. 1996; Wollina et al. 1998). It is noteworthy that in all studies pulsed direct current was used and that exclusively patients with dyshidrotic eczema were recruited. One important finding is that iontophoresis added only modestly to clearing of eczema, but significantly extended relapse-free intervals, if control of hyperhidrosis by iontophoresis was sufficient (Wollina et al. 1998). These observations triggered widespread use of iontophoresis with pulsed direct current in patients with occupational hand eczema. Controlled trials on larger series of patients, are, however lacking.

As to the mechanism of action it was shown that iontophoresis leads to depletion of substance P (Wollina et al. 1998), which was shown to be elevated in atopic dermatitis (Oesterle et al. 1995) which is most frequently the cause of dyshidrotic eczema of palms and soles. This observation was corroborated by the finding that treatment of hyperhidrosis by botulinum toxin A also improved associated dyshidrotic hand eczema (Wollina and Karamfilov 2002) and since botulinum toxin A also decreased pruritus, it was suggested, that it does not only interact with acetylcholine release but also with substance P. Taken together it seems likely that depletion of substance P by tap water iontophoresis as well as by botulinum toxin A is a major factor improving dyshidrotic eczema.

6 Practial Use of Iontophoresis

The working group on quality control of the German Dermatological Society developed guidelines, which were recently updated (Ho¨lzle et al. 2009). The following instructions are supplemented by recommendations of an international multispeciality working group on the recognition, diagnosis, and treatment of primary focal hyperhidrosis (Hornberger et al. 2004).

6.1 Definition

Tap water iontophoresis is a procedure in which continuous direct or high-frequency pulsed direct current is let through defined skin areas by water bath or wet electrodes. In general, palms or soles, rarely, axillae or other skin sites are treated.

6.2 Iontophoresis Apparatuses

The direct current source must be able to generate a voltage of about 60 V in order to maintain amperage of 10–30 mA even in situations with high skin resistance. The device must be constructed in a way that electric shock would be impossible. Also measures have to be taken that voltage is changed slowly with a maximum of 5 V/s.
Devices with pulsed direct current should generate a frequency between 5 and 10 kHz and should create a rectangular waveform between 0 and 16 V.
The apparatus itself and the entire cable ware must be completely insulated; the electrodes must be kept submerged in tap water and covered by thin sheets of sponge rubber or other insulating materials allowing close contact between skin and water. Water pans should be large enough, to comfortably fit hands or feet with extended fingers or toes. Electrodes should cover the entire bottom of the pan and should be made from stainless steel or aluminum. Patients with sensitizations against nickel, chromium, or cobalt should use aluminum.
A complete disinfection of all accessories inside the pans including the electrodes should be performed before each treatment, if several patients are using the same equipment. In this case sheets of foam rubber must be exchanged for each patient.

6.3 Indications

Tap water iontophoresis is the first line treatment for palmoplantar hyperhidrosis of moderate to severe degree.
In axillary hyperhidrosis iontophoresis by using special electrodes might be useful as well. Topical treatment with aluminum chloride solutions, however, might be superior.
Other types of focal hyperhidrosis may be treated with custom-made electrodes adjusted to the body site, if topical aluminum chloride or injections of botulinum toxin are not feasible. One example is segmental compensatory hyperhidrosis in Ross syndrome (Reinauer et al. 1993).
Further indications for tap water iontophoresis might be dyshidrotic eczema of hands or feet, multiple warts, as well as gram negative infections of toes or keratoma sulcatum.
In the latter cases iontophoresis might be useful for maintenance of disease-free intervals.

6.4 Procedure

Patients should be informed about the procedure, the therapeutic effect to be expected, and possible side effects.

Before each treatment session metallic devices and jewelry must be removed from hands or feet. Defects in the skin barrier, e.g., erosions, should be covered with petrolatum or insulating tape. Tap water is filled in pans so that the patient's hands or feet will be covered up to the dorsal areas of fingers or toes. Pure tap water is preferred. In case of using deionized water, mineral water could be a substitute.

For the treatment of children pulsed direct current should be employed, treatment under the age of 6 is generally not recommended.

Patients undergo three to seven treatments per week for 10–15 min each with constant current direction until the anodal side shows euhidrosis. Then, polarity is turned around until both sides are sufficiently dry. From thereon, current direction is switched before each treatment session.

Complete control of hyperhidrosis is normally achieved after 10–15 treatments. Frequency of maintenance treatment depends on the individual response. Typically it is required once or twice a week. Sometimes, even 2–4 week intervals are sufficient. Since maintenance treatment has to be performed continuously, home treatment is recommended (Ho¨lzle and Alberti 1987; Raulin et al. 1988).

6.5 Side Effects

Using direct current electric shock may occur, if hands or feet are put into or taken out off the water abruptly and technical measures to limit voltage are lacking. This cannot occur with pulsed direct current.

Using direct current dependent on the amperage discomfort and pain may occur in the skin submerged and, at higher amperage the entire limb placed in the electric circuit may hurt.

Immediately after treatment, along the waterline erythema or vesicles may occur. These are asymptomatic and transient.

Metallic items contacting the skin may cause electric burns, if they are submerged. This has to be prevented by removal of all metallic items from the skin to be treated before iontophoresis is started.

Electric burns may also occur, if defects in the skin barrier, such as erosions or vesicles remaining from dyshidrotic eczema or small injuries, are not covered by petroleum or insulated by tape before treatment. One alarming signal would be stinging pain at the site of the barrier defect. Patients should be advised to immediately report such sensations so that appropriate measures can be taken to avoid skin damage.

6.6 Contraindications

Patients with implanted electronic devices like cardiac pacemakers should be excluded from the treatment. Pregnancy is also considered as a contraindication, since therapeutic experience is lacking. Metallic implants within the electric circuit are contraindicated as well. The increased current flow through implanted metallic items might heat up the metal and lead to unwanted damage of the adjacent tissue. The same holds through for metallic intrauterine devices. Larger defects in the skin to be treated, which cannot be covered by petrolatum or an insulating tape, also represent a contraindication, at least transiently as long as they persist.

6.7 Quality Control of the Treatment Outcome

It is recommended to document the therapeutic success by at least qualitative estimates – better by quantitative measurements – of sweat rates before and after the induction treatment. Semiquantitatively the degree of hyperhidrosis might be determined according to the definition given in the table (> Table 105.3).

. Table 105.3

Grading of severity of palmoplantar hyperhidrosis based on clinical features

Grading of hyperhidrosis	
Grade 1	Palms or soles are wet, also dorsal portion of distal phalanges are wet
Grade 2	Palms or soles show sweat beads, visible sweating also involves dorsal portion of distal and mid phalanges
Grade 3	Palms or soles show sweat beads, sweat drips off, sweat beads also occur on dorsal portion of entire phalanges

One easy measurement to indicate intensity of sweating is to determinate the conductivity in mSiev by a simple device measuring skin resistance. Values below 60 mSiev are considered to be normal. In hyperhidrosis measurements may excede150 mSiev.

Exact gravimetric measurements employ determination of weight gain of absorbent pads or sheets of paper kept in contact with the skin area to be evaluated for a fixed time period. For example 20 mg/min per palm would be equivalent to euhidrosis.

The starch iron reaction is most widely used for colorimetric semiquantitative measurements. According to Minor's method an ethanolic solution containing 1.5% iodine and 10.0% castor oil are painted on the skin and subsequently dusted with corn starch. The color reaction reflects intensity of sweating. If a normal typewriter paper is soaked by the solution and, after drying, brought into contact with the perspiring skin surface, imprints can be obtained, which, again, allow a semiquantitative estimate of the severity of hyperhidrosis and can be kept as records.

A simple hygrometric method employs an evaporimeter measuring water vapor dissipating from the skin in $g/m^2/h$. Values 70 $g/m^2/h$ reflect palmoplantar euhidrosis.

7 The Impact of Iontophoresis in Hyperhidrosis and Occupational Skin Diseases

It is out of question that tap water iontophoresis represents a very effective means of treatment in palmoplantar hyperhidrosis and to a certain extent also in axillary hyperhidrosis or in other types of focal hyperhidrosis. It has also been recognized that hyperhidrosis is not only a lifestyle disorder, but it is generally accepted as a skin disease

(Hornberger et al. 2004).There are only few studies addressing the treatment outcome in terms of gain of quality of life. One study (Junker and Kreyden 2008) questioned 251 patients with hyperhidrosis, axillary and palmoplantar, and found that 80% of them felt restricted in their daily activities. After successful treatment a substantial gain in quality of life was achieved.

One of the most frequent occupational diseases in dermatology is hand eczema, especially dyshidrotic eczema associated with atopy and/or cumulative toxic factors. It is shown in some treatment trials that iontophoresis may improve not only hyperhidrosis, which is frequently associated with eczema, but may also improve pruritus and the eczema itself. This mainly holds true for maintenance treatment, after remission of eczema has been induced by conventional topical treatment. Iontophoresis during maintenance treatment has a corticoid sparing effect and prolongs disease-free intervals considerably (Wollina et al. 1998). Although studies on larger patient groups are lacking, iontophoresis may be a valuable aid in controlling chronic hand eczema, especially dyshidrotic eczema. It has to be kept in mind, however, that so far all studies have employed pulsed direct current for treatment of eczema. It is not known whether plain direct current would have the same effect.

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