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*Review Article*

# The Treatment of Primary Palmar Hyperhidrosis: A Review

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**Abstract: Primary palmar hyperhidrosis (HH) is a pathological condition of overperspiration caused by excessive secretion of the eccrine sweat glands, the etiology of which is unknown. This disorder affects a small but significant proportion of the young population all over the world. Neither systemic nor topical drugs have been found to satisfactorily alleviate the symptoms. Although the topical injection of botulinum has recently been reported to reduce the amount of local perspiration, long-term results are required before a definitive evaluation of this method can be made. Hypnosis, psychotherapy, and biofeedback have been beneficial in a limited-number of cases. While radiation achieves atrophy of the sweat glands, its detrimental effects prohibit its use. Iontophoresis has attained some satisfactory results but it has not been assessed long term. Percutaneous computed tomography-guided phenol sympathicolysis achieves excellent immediate results, but its long-term failure rate is prohibitive. Furthermore, percutaneous radiofrequency sympathicolysis may be an effective procedure, but its long-term results are not superior to surgical sympathectomy. On the other hand, surgical upper dorsal (T2–T3) sympathectomy achieves excellent long-term results and the thoracoscopic approach has supplanted the open procedures. Despite some sequelae, mainly in the form of neuralgia and compensatory sweating which cannot be predicted and may be distressing, surgical sympathectomy remains the best treatment for palmar hyperhidrosis.**

**Key Words:** hyperhidrosis, sympathectomy, thoracoscopy

## Introduction

Sweat glands, which are one of the major cutaneous appendages, comprise two types, namely, eccrine glands that exist in all areas of the body, with the highest concentration in the palms and soles, and are responsible for sweating; and apocrine glands that are present only in the axillae, areolas, and anogenital region of adults, and are responsible for body odors produced by bacterial activity and by the excretion of ingested "perfumes" such as garlic.[1] Sweat glands are supplied by sympathetic nerves that are cholinergic in nature.[1] The main function of sweating is thermoregulation, which is achieved by evaporation of the liquid secreted, namely sweat.[1,2] Thermoregulation is required during exposure to a hot environment, during physical exercise,[2] or when the metabolic rate is increased as in thyrotoxicosis.[1] Sweating is also induced by emotions, such as anxiety.[1] Under these circumstances, sweating may be limited to certain regions such as the face or hands. Sweat glands are also excretory organs, sweat being a dilute electrolyte solution that contains mainly sodium chloride, potassium, and bicarbonate, but also lactate, urea, and ammonia.[2]

Hyperhidrosis (HH) is a pathological condition of overperspiration due to excessive secretion of the eccrine sweat glands in amounts greater than required for physiological needs.[3] It may develop secondary to a variety of medical disorders[4,5] or it may be primary, of unknown etiology. An exaggerated response, primarily to emotional stimuli,[6,7] but also to heat and physical effort,[7] has been implied. The major role of the emotional stimuli is emphasized by the observation that during sleep or under sedation, excessive sweating is not prominent,[3] while reports on HH from countries with predominantly cold weather indicate that a warm climate is not an important etiological factor.[8] It has also been claimed that HH is a central phenomenon of excessive stimulation of the sweat glands by an overactive sympathetic system,[9] or that it is an autonomic dysfunction,[10] this statement being based on the equal response to acetylcholine of hyperhidrotic and normal subjects.[9] The possibility of central nervous system dysfunction in patients with HH was suggested by Momose et al.[11] who found electroencephalographic disturbances and evi-

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dence of the hyperperfusion of certain areas of the brain in patients with HH. Primary HH is not a generalized phenomenon of the whole body, but is rather confined to the palms, and in some patients, also to the soles and/or axillae, these being the areas in which the sweat glands are activated predominantly by emotional stimuli.[3] It has also been shown that the total amount of sweat loss during thermal stimulation is not increased in hyperhidrotic patients compared with healthy individuals.[12] Thus primary HH may be, at least in some cases, a condition of shifting in the sweat activity rather than persistent overperspiration.

The natural history of primary palmar HH is poorly documented. The onset is usually either in early childhood, the youngest reported age being 3 months,[13] or adolescence–puberty,[8,14] and it seems to persist throughout life,[15] although it has been claimed that from the fourth decade of life the activity of the sweat glands has a tendency to decrease.[7] The vast majority of patients presenting for treatment are in the second or beginning of the third decade of life.[16–22] This is due to the early onset of symptoms and to the resulting occupational disabilities and social embarrassment which become especially prominent at this age.[5]

The incidence of primary palmar HH is understood even less than its natural history. The only epidemiological study on the subject was performed on the young population of Israel by Adar et al.[8] who reported an incidence of 0.6%–1% of overperspiration in all locations and degrees of severity, and estimated that about 25% of afflicted individuals have frank palmar HH. Males and females are equally afflicted.[5,14,16–22] A familial trait for HH has been described,[23,24] and it has been estimated that 40% of patients have a family history of excessive sweating.[5] Ethnic predispositions have also been implicated;[8,21] however, contrary to the series of Adar et al.[8] in which HH was observed among Jews originating from North Africa, Yemen, and the Balkans, being dark people, the majority of the subjects reported by Borak et al.[7] were of light complexion. Cloward[24] found that in Hawaii, patients of Japanese origin were 20 times more likely to be affected than Caucasians. The largest series is that reported by Shih and Wang,[20] all the subjects of which were Chinese. It is possible that rather than an ethnic predominance, it is the country and personal interest of the authors that determines the ethnic origin of the subjects affected by HH included in the various published series. Primary palmar HH appears to be a worldwide problem.

## Treatments

The different regimes of treating HH are listed in Table 1. For practical purposes they have been divided into two subgroups according to the invasiveness of the procedures.

**Table 1.** Therapeutic modalities for palmar hyperhidrosis

| | |
|---|---|
| 1. Noninvasive treatments | |
| a. With central effect | |
| Hypnosis | Biofeedback |
| Psychotherapy | Tranquilizing drugs |
| b. With sympathicolytic effect | |
| Anticholinergic drugs | |
| c. With peripheral effect | |
| Radiation | Iontophoresis |
| Topical external drugs (astringents, antiperspirants, anticholinergics) | |
| Topical injected drugs (botulinum toxin) | |
| Cryotherapy | |
| 2. Invasive treatments | |
| a. Nonsurgical approaches | |
| Percutaneous phenol sympathicolysis (Computer tomography-guided) | |
| Percutaneous radiofrequency sympathicolysis | |
| b. Surgical approaches | |
| "Open" sympathectomy | |
| supraclavicular approach | dorsal approach |
| transaxillary approach | transthoracic approach |
| Thoracoscopic approach | |
| sympathicolysis | sympathectomy |

### *Non-Invasive Treatments*

Included in this group are various modalities, some of which have become obsolete, while others are still advocated by certain authors. These treatments deal with the problem of HH on three levels: central, sympathicolytic, and peripheral.

A *central effect* is achieved by hypnosis, psychotherapy, biofeedback, and tranquilizing drugs. Hypnosis and psychotherapy have been attempted in the treatment of HH, but found to be beneficial only in few patients.[5] There is no detailed documentation on the effect of such therapies, and their merit in the treatment of HH therefore remains unestablished. Biofeedback has been used by Duller and Gentry,[25] who found significant "improvement" in the degree of sweating in 8 out of 14 patients. Relaxation is the active element of this remedy, but as no long-term follow-up results have been published, this method has not gained popularity. Similarly, the use of tranquilizers has been advocated,[25] but found by others to be of limited value in alleviating oversweating.[5,6] Their benefit, if any, is mainly related to the suppression of anxiety caused by HH.[5]

A *sympathicolytic effect* is achieved by the anticholinergic effect of medications such as atropine, hydegerine, methantheline bromide, bropantheline bromide, glycopyrronium bromide, and phenoxybenzamine.[5,6,26,27] However, the administration of these drugs in the dosages required to attenuate oversweating usually results

in disagreeable and sometimes intolerable side effects, such as blurred vision, dry mouth, urinary retention, and constipation. Thus, this therapeutic modality appears to be ineffective in all but the mildest cases,[28,29] the results being either temporary or unsatisfactory.[30]

A *peripheral effect* has been attempted by various procedures including radiation, topical drugs, and iontophoresis.

Radiation therapy was initially suggested as early as 1901[6] as it induces atrophy of the sweat glands.[4,5,31] Borak et al.[6] reported highly satisfactory results in a series of 122 patients with a follow-up of 2 to 18 years; however, irradiation of the skin is now unacceptable, both because of the unnecessary radiation exposure,[4] and also because of the risk of radiation dermatitis.[5,31]

Topical treatment consists of the local application of drugs which may be applied to or injected into the skin. Drugs applied to the skin are either astringents such as formaldehyde, potassium permanganate, tannic acid, and glutaraldehyde, which act on the epithelium and sweat glands, or antiperspirants, mainly comprised of aluminium chloride salts which block the excretory ducts.[4,32] Although some authors consider them to be highly effective,[27] all of these drugs have a severe drawback in that their effect is not permanent, and they require persistent administration, which is often impossible due to severe skin irritation[4,31,33] observed in about 50% of patients.[27] Moreover, tannic acid and glutaraldehyde produce brown staining of the skin,[27] and a significant number of patients are unresponsive to topical treatment.[26] Topical anticholinergic preparations have also been developed, but have not proved popular because of severe side effects or failure in treatment.[25]

In recent years, intradermal injections with botulinum toxin have been given for the treatment of focal (palmar, axillary or plantar) HH,[34,35] and a 40%[34] to 100%[35] improvement has been observed. To prevent the pain induced by these injections, it has been suggested that the treatment be performed under nerve block anesthesia.[36] A reversible minor weakness in the handgrip has also been reported,[34,35] but compensatory HH has not been observed. Some degree of recurrent sweating of the areas treated by botulinum toxin injections has been successfully treated by reinjection.[35]

Iontophoresis has received wider attention.[27,28,29,37–40] Its inhibiting effect on sweating was noticed almost 60 years ago[41] and its clinical use was established by Levit[42] in the late 1960s. It consists of tap-water electrolysis producing anhidrosis of the immersed limb. After an initial period of about 10–12 treatments, which should be continued until satisfactory results are obtained, maintenance therapy is required once every 1–4 weeks.[28,40] For that purpose, battery-operated units have been devised to allow home therapy.[37] Two mechanisms of action of this treatment have been suggested, namely, a disturbance of the electrical gradient along the sweat ducts which slows sweat flow[29] and "plugging" of the lumen of the eccrine sweat glands;[27,29] however, the exact mechanism is still obscure.[26,28] The majority of series reported in the literature are small, comprised of mixed subjects with palms, armpits, and/or soles affected, the degree of oversweating was not equal in all patients, and no long-term follow-up has been reported.[28,29,37–40] Nevertheless, improvement and a substantial reduction, up to complete alleviation of sweating, was observed in the majority but not all of the patients. Hölzle and Alberti[37] presented a series with a follow-up of more than 1 year, during which time HH was controlled, and only slight discomfort and mild temporary skin irritation were reported. For patients with minor symptoms and those reluctant to undergo surgery, iontophoresis may be a reasonable alternative therapeutic modality.

Cryotherapy has also been attempted but has now been discontinued due to its limited success.[43]

### *Invasive Treatments*

All invasive treatments aim to achieve sympathectomy of the hands. At present, it is almost unanimously accepted that $T_2$–$T_3$ ganglionectomy efficiently achieves sympathetic denervation of the distal part of the upper limb.[14,20,21,44–50] Two basic approaches have been developed: nonsurgical and surgical.

The *nonsurgical approaches* consist of percutaneous phenol block and radiofrequency sympathicolysis.

#### *Percutaneous Phenol Sympathicolysis*

Haxton[51] advocated the use of phenol, instead of the previously used alcohol[30] for the percutaneous sympathetic block, to overcome the problem of prolonged neuritis.[51] Injections were performed by blind percutaneous needle insertion, which resulted in limited success and relapses. Subsequent advances in radiological techniques facilitated positioning of the needle. Walker et al.[52] reported fluoroscopically guided percutaneous sympathetic lysis. Later, computed tomography (CT) was employed,[53] Dondelinger and Kurdziel[54] being the first to report phenol block of the upper sympathetic chain using the latter method. Although the immediate results were very good,[55] the long-term follow-up of patients treated by this method reported by Adler et al.[56] points to a failure rate of more than 40%.

#### *Percutaneous Radiofrequency Sympathicolysis*

In 1984, Wilkinson[57] reported a new method for performing percutaneous sympathicolysis of the upper thoracic ganglia. His technique is based on the fluoroscopically guided introduction of a probe through which radiofrequency is applied to the upper thoracic ganglia,

resulting in high temperatures which destroy the adjacent tissues. Chuang et al.[58] developed a stereotactic method for the application of percutaneous thermocoagulation which resulted in dry hands in 95% of their subjects. Wilkinson[59] reported the results of his method applied to a group of patients with different problems, three of whom had HH. Excellent relief of abnormal sweating was noticed in five of six hands. The long-term effect of this method has been recently examined by Wilkinson[60] who reported that excellent/good results were achieved in 38 patients, partial in 6, and poor in 8.

Nevertheless, the results of these techniques are so far inferior to those of surgical sympathectomy, and a great deal of refinement of the percutaneous techniques is required if they are to supplant surgery.

The *surgical approaches* consist of "open" and thoracoscopic sympathectomy.

*Open Sympathectomy*

Open sympathectomy for palmar HH was first proposed by Kotzareff[61] in 1920. Four major approaches have been described.

*The Supraclavicular Approach.* This approach was developed by Telford[49,62] and was subsequently modified to include resection of the upper thoracic ganglia. Both sides are approached during the same operation. Excellent long-term results achieving dry hands in more than 90% of patients have been reported in several large series of upper dorsal sympathectomies performed by this technique.[15,17,18,63,64]

*The Posterior Approach.* Advocated by Adson,[65] this was further modified by White et al.[66] and Smithwick.[67] This technique enables resection of the intercostal nerves and their posterior roots and root ganglia[67,68] together with the sympathetic ganglia. Both unilateral and bilateral sympathectomy have been performed in one stage. The results, based on several large published series,[19–21] are similar to those of the supraclavicular approach.

*The Axillary Transpleural Approach.* This was devised by Schultze and Goetz, and later described and published by Atkins.[69,70] An extrapleural transaxillary approach with resection of the first rib has also been described.[71] Bilateral sympathectomy by this approach was usually performed as a staged procedure and the results reported in several series[16,72–74] are similar to those of the other surgical methods.

*The Anterior Transthoracic Approach.* Which was first suggested by Goetz and Marr,[46] then later supported by Palumbo,[75] did not gain popularity.

*Thoracoscopic Sympathectomy*

Thoracoscopic sympathectomy was first described by Goetz and Marr[46] in 1944 and employed in a large series of patients reported by Kux[76] in the 1970s. With the advent of endoscopic surgery, numerous reports of thoracoscopic sympathectomy were published.[77] Two basic approaches have been described: one involves electrocautery of the sympathetic chain[78,79] and the other involves electroresection of the appropriate ganglia.[80–85] Ablation of the ganglia with $CO_2$ laser has also been reported,[86] but few large series have been published so far. Using the first technique, immediate "very much to moderate" improvement of 92% of patients was reported by Byrne et al.,[87] while Claes et al.[88] obtained completely dry hands in 81% of patients with an additional 17% achieving some improvement. Success in either curing or improving symptoms of HH was also obtained in the majority of cases reported by Edmondson et al.[45] Chao et al.[89] achieved an immediate cure rate of 99.3% and Shachor et al.[90] achieved dry hands in 98% of their patients, although recurrence developed within a year in 3.3%. Long-term follow-up reported by Byrne et al.[87] showed that "very much to moderate" improvement was reduced to 85%. Thoracoscopic sympathetic resection is less often performed, but in a series reported by us,[83] completely dry hands were achieved in all operated cases. In a more recent study,[84] in which we reported 130 patients who underwent thoracoscopic sympathectomy for palmar hyperhidrosis, there was no conversion into an open procedure, all hands became dry, and in 113 patients available for follow-up over a mean of $25 \pm 13$ months, all hands remained dry with the exception of three in which slight humidity, regarded as normal, developed.

## Discussion

The main functional and social problem associated with HH is excessive palmar perspiration and therefore, treatment should be aimed at alleviating this phenomenon; however, as the mechanism of HH remains unelucidated, no curative remedy exists.

Of all the noninvasive remedies, iontophoresis seems to be the most effective for controlling palmar HH; however, this treatment is messy, and neither devoid of side effects nor definitive. Moreover, it requires permanent maintenance treatment, and knowledge of long-term results is limited, as the longest published follow-up of more than 3 years deals with only four patients.[37] The intradermal injection of botulinum toxin may be the only other noninvasive treatment capable of controlling hyperhidrosis. The absence of compensatory HH in connection with this type of treatment is an important advantage; however, only a few small series

have been published so far,[34–36] and the longest follow-up reported is 5 months.[35] Larger series and longer follow-up results are required to better evaluate this novel technique.

Destruction of the $T_2$–$T_3$ sympathetic ganglia is so far the only means of obtaining permanent relief of HH in the vast majority of patients. Although both percutaneous methods achieve very good immediate results, the long-term results of phenol blocks are relatively poor, even when performed under CT guidance, with a recurrence rate of palmar HH in more than 40% of cases.[56] While the long-term results of percutaneous radiofrequency sympathectomy are much better,[60] they are still inferior to those reported following surgical sympathectomy.

Upper dorsal $T_2$–$T_3$ sympathetic ganglionectomy is currently the most effective proven treatment for palmar HH. When properly performed, it achieves good immediate results in practically all patients, and long-term follow-up has shown that 95% of operated limbs remain dry. For several decades, authors have debated which approach gives the best results while producing minimal complications. With the advent of endoscopic surgery, this debate could become obsolete as evidence is being accumulated that thoracoscopic sympathectomy may achieve results as good as open resection of the two ganglia. Furthermore, similar to all endoscopic procedures, the thoracoscopic approach gives the best cosmetic results and the most rapid recuperation from surgery and earliest return to work. As the open approaches for this procedure are all technically difficult, thoracoscopic sympathectomy does not present a substantial increase in potential complications. Thus, there is no doubt that thoracoscopic sympathectomy is today the gold standard for the surgical treatment of palmar hyperhidrosis.[77] Electroresection of the ganglia seems to give better results than electrocautery; however, definite evaluation of the two techniques, namely, electrocoagulation, adopted by the majority of surgeons, and electroresection, which is technically more demanding, requires compilation and meta-analysis of the data accumulated in the literature.

There have been no reports of mortality in association with surgical sympathectomy. Therefore, its major drawback is the existence of long-term concomitant sequelae, the five major problems being: phantom sweating, gustatory sweating, Horner's syndrome, neuralgia, and compensatory sweating.

Compensatory sweating is another unexplained sequela of upper dorsal sympathectomy that develops in a large proportion of patients. In fact, some authors have observed it in almost all their patients,[91] causing significant discomfort in about one fifth.[91] Its occurrence is unpredictable, it may not necessarily appear at once, and it often abates spontaneously.[20,92] The mechanism of this phenomenon appears to be more complex than simple compensation for thermoregulation as claimed by some authors.[92] The opposite event, namely, decreased sweating in other parts of the body which are not anatomically denervated by upper dorsal sympathectomy, has also been reported.[20,92] The most important observation is concomitant reduction of perspiration of the soles which cannot be explained on an anatomical basis, as sympathetic innervation of the feet originates from the lumbar ganglia. It has been speculated that the hypothalamic sweat center that controls the palms, soles, and in some patients, axillae, is distinct from the rest of the hypothalamic sweat centers and is under exclusive control of the cortex without input from the thermosensitive elements.[3] If such a center exists and is influenced by sympathectomy affecting the palms, it may explain the concomitant palmar and plantar anhidrosis achieved by $T_2$–$T_3$ sympathectomy.

Phantom sweating[93] and gustatory sweating[94] are two complications of upper dorsal sympathectomy, the etiology of which remains obscure. The former is a feeling of sweating in the palms after sympathectomy, without any actual sweating, whereas the latter is mainly facial sweating triggered by spicy and some other specific foods. Phantom sweating has been reported upon specific inquiry in 26%–59% of patients,[18,19,95] whereas gustatory sweating has been described in up to 56% of cases;[18] however, as these complications are usually inconspicuous and not incapacitating, most patients cope very well with them.

Neuralgia is another important sequela of sympathectomy. It consists of pain in the sympathectomized limb, appearing some time after the operation and is presumed to be temporary.[69,96] Its incidence has been reported to range widely between 0%[18–21] and 32%.[97] While the etiology and mechanism of this complication are obscure, damage to the intercostal nerves, especially that caused by the endoscopic electrocautery appliance, may also result in postoperative regional pain.

Horner's syndrome is a distressing but preventable complication resulting from damage to the stellate ganglion, specifically the upper ($C_7$) portion. Its incidence has also been reported to range widely between 0%[20,64] and 40%.[8] This wide variation implicates both the surgical approach and the expertise and experience of the surgeon. Introduction of the endoscopic approach should make this complication extremely rare because the stellate ganglion is anatomically located outside the operative field, although indirect thermic injury is still possible.

Recurrent perspiration of the hands after sympathectomy may be caused either by inadequate resection, or by the return of sympathetic tone to the limb. If the second thoracic ganglion has not been resected, relapse

of the sympathetic tone in the hand can occur and failure would be attributed to inadequacy of the technique. Operative resection of this ganglion should result in effective sympathectomy and the arrest of palmar sweating. The recurrence of palmar sweating despite $T_2$–$T_3$ resection in rare cases may be attributable to the existence of anatomical variations, including accessory or intermediate sympathetic ganglia located outside the sympathetic trunk,[98] or the presence of the inconsistent nerve of Kuntz, which bypasses the second thoracic ganglion.[99] In such cases, resympathectomy should be performed, preferably by the dorsal approach as suggested by Lemmens.[68] As resympathectomy involves a more difficult operation due to local fibrosis and distortion of the tissue planes resulting from the first procedure, it should be reserved for the more severe cases. If undertaken, a different route than the first procedure is advisable.

When appraising the value of upper dorsal sympathectomy for a patient with palmar HH, one should consider the potential benefits of the operation in the functional and social planes versus its possible long-term complications, particularly the prospect of compensatory sweating. For those patients who are severely handicapped by the phenomenon of palmar HH, upper dorsal $T_2$–$T_3$ sympathectomy is the best solution that will grant long-lasting satisfaction. Endoscopic transthoracic ganglionectomy by electrocautery appears to have become the preferred approach for achieving this goal. Improvement in this technique, aiming at reducing the operative time and thermal damage to the adjacent organs, especially the intercostal nerves and vessels, may further ameliorate the results.

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