

# Primary Focal Hyperhidrosis: Scope of the Problem

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*Focal hyperhidrosis (HH) can cause debilitating reductions in the physical and emotional quality of life (QOL) of patients, which can result in numerous restrictions of a patient's personal and professional lifestyle and activities. A variety of treatment options are available for primary focal HH, including topical and oral agents, tap water iontophoresis (TWI), botulinum toxin type A (BTX-A), and surgery. Studies evaluating BTX-A (Botox®) treatment for palmar, plantar, and facial HH reveal that BTX-A provides effective treatment of primary focal HH, with a reasonable duration of effect, and has a good safety profile. Physicians should understand the impact of focal HH and the need to stay abreast of the available treatment options to provide the best care for patients.*

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**H**yperhidrosis (HH) generally is defined as overactivity of the eccrine sweat glands that results in excessive, bilateral, relatively symmetric sweating beyond the amount necessary to maintain a body temperature within normal limits.<sup>1,2</sup> Focal, or localized, HH usually is idiopathic (primary) and most commonly occurs in the axillae, palms, soles, and face.<sup>4</sup> Large epidemiologic surveys were not conducted until recently, so accurate estimates of the scope of this disease state have not been available. A study published in 1977 indicated that approximately 0.6% to 1% of the

population had primary HH<sup>5</sup>; however, a more recent report by Strutton and colleagues<sup>6</sup> suggested that the prevalence of HH may be higher, affecting up to 2.8% of the US population.

Treating primary focal HH is an important aspect of dermatology. Focal HH often results in personal, professional, and social limitations that can cause psychological problems.<sup>7</sup> Primary focal HH considerably reduces patient quality of life (QOL). Patients may experience uncomfortable physical symptoms, including sodden clothing or shoes, and constantly fear odor production. Skin maceration is not a common manifestation; however, if severe, HH can lead to secondary infections such as tinea pedis, viral warts, and dermatitis.<sup>8</sup> Individuals with focal HH also frequently become withdrawn and avoid social interaction; they exhibit self-conscious behavior, embarrassment, a lack of self-confidence, and low self-esteem. In a large study comparing Dermatology Life Quality Index (DLQI) scores among patients with HH or other dermatologic conditions, patients with palmar HH scored higher than patients with eczema or psoriasis that required hospitalization, or contact dermatitis.<sup>7,9</sup>

Satisfactory treatment of primary focal HH is beneficial to a patient's QOL. This article discusses focal HH and reviews available treatment options, including topical agents, oral agents, tap water iontophoresis (TWI), and surgical therapies. We also present available data supporting the use of botulinum toxin (BTX) therapy for focal HH. Because many of the studies evaluating botulinum toxin type A (BTX-A) therapy are small, compare various dilutions and doses, use different numbers and locations of injection sites, and differ in other parameters, we have developed best practice recommendations based on a combination of the published data and our own clinical experiences. Glaser et al<sup>10,11</sup> provide guidance on the treatment process—from diagnosis to insurance reimbursement for BTX-A therapy for palmar, plantar, and facial HH. Glaser<sup>12</sup> reported on treatment recommendations for axillary HH, which will not be discussed in this supplement.

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Table 1.

**Classification and Potential Causes of Hyperhidrosis\*1-3,18-26**

Type of HH	Presentation	Causes
Generalized	Generalized sweating	Physiologic causes (eg, emotions, stress, exercise, temperature); endocrine or metabolic disorders (eg, diabetes mellitus, thyrotoxicosis, hypoglycemia, gout, hyperpituitarism); drugs (eg, antiemetics, antidepressants); neoplasms or tumors (eg, Hodgkin disease, CNS lesions); febrile diseases (eg, acute or chronic infections); spinal cord injury; cutaneous disease
Primary focal	Focal, bilateral, symmetric sweating; childhood or adolescent onset	Idiopathic
Secondary focal	Focal sweating; asymmetrical	Multiple causes (eg, Frey syndrome; neurologic disorders; tumors; cold-induced, compensatory, gustatory, olfactory HH)

\*HH indicates hyperhidrosis; CNS, central nervous system.

Adapted from Hebert.<sup>27</sup>

### Pathophysiology and Etiology

The human body has an estimated 2 to 4 million eccrine sweat glands concentrated in the axillae, palms, and soles.<sup>4,13</sup> Most patients with HH have morphologically and histologically normal sweat glands.<sup>13,14</sup> The pathophysiology of primary focal HH is not completely understood but may result from hyperstimulation of eccrine glands<sup>2</sup> or an abnormal neurologic response to stimuli that raises the basal level of sweat secretion.<sup>1</sup> One hypothesis attributes the cause of focal HH to a dysfunction of the central sympathetic nervous system (ie, hypothalamic nuclei).<sup>13-17</sup>

Table 1 presents the causes of generalized and focal HH.<sup>1-3,18-27</sup> Primary focal HH is idiopathic and not secondary to another cause. Common triggers include heat, stress, emotions, and specific foods or beverages, though patients may experience excessive sweating without an identifiable trigger. Many observations have reported a genetic predisposition for primary focal HH, with the onset of symptoms occurring during childhood or adolescence. The rate of sweating is variable. The main diagnostic criteria for primary focal HH are noted in Table 2.

### Impact on QOL

Focal HH often creates limitations and/or disruptions in a patient's personal and professional lifestyle, which can lead to multiple QOL challenges and psychological consequences. Patients may experience continuous

physical discomfort because of wet, stained, or ruined shoes or clothing. They also may endure functional limitations such as difficulty handling necessary papers or tools, impeding their ability to perform jobs and activities of daily living. For example, an individual may have difficulty handling pens or machinery and also may drop objects more easily; additionally, constantly wet hands may place the patient at risk for shock or cause tools to rust more quickly. These limitations also carry over into the patient's personal life, social interactions, and leisure activities.

The difficulties experienced by patients with HH also may lead to psychosocial effects. Individuals who are embarrassed about their sweating or sweat marks are hesitant to shake hands. Students are embarrassed to raise their hands in the classroom or participate in school activities. These effects often are followed by withdrawal and avoidance behaviors, in addition to emotional distress that manifests as frustration, unhappiness, depression, and decreased confidence.

The DLQI scale has been used in many studies to assess the impact of focal HH on QOL. It is a simple validated tool that is well-suited for routine clinical use.<sup>28,29</sup> This self-assessment survey contains 10 questions in 10 domains: symptoms, embarrassment, daily activities, clothing, social/leisure activities, sports, work/study, partners/friends, sexual activity, and treatment. Most questions have 4 possible responses, ranging from very much to not at all

Table 2.

### Principle Diagnostic Criteria for Primary Focal Hyperhidrosis\*<sup>2</sup>

Focal, visible, excessive sweating for  $\geq 6$  mo without apparent cause and with  $\geq 2$  of the following characteristics:

- Bilateral relatively symmetric sweating
- Sweating that impairs daily activities
- $\geq 1$  HH episode per wk
- Age of onset,  $< 25$  y
- Positive family history of HH
- Cessation of focal sweating during sleep

\*HH indicates hyperhidrosis.

and correlating with scores of 3 to 0, respectively. The degree to which HH affects a patient is based on the total score for all responses—a higher score indicates a greater or more negative impact on QOL.

Another measure of QOL is the Hyperhidrosis Disease Severity Scale. This scale is an HH-specific questionnaire that assesses how patients rate the impact of sweating on their daily activities using a 4-point scale (1=never noticeable, never interferes; 2=tolerable, sometimes interferes; 3=barely tolerable, frequently interferes; 4=intolerable, always interferes).<sup>6</sup> As with the DLQI, a high score on the Hyperhidrosis Disease Severity Scale indicates a severe impact of HH symptoms on QOL.

Several studies have assessed the impact of various forms of primary focal HH on patient QOL.<sup>7,17,28,30</sup> Hamm and colleagues<sup>7</sup> analyzed 165 patients with axillary HH and 116 patients with palmar HH. They found that most patients reported moderate to extreme impairment of their professional (eg, productivity, performance, limitations), emotional (eg, unhappy, depressed, less confident, emotionally "damaged"), social (eg, public places, meeting new people, shaking hands), and personal lives (eg, developing relationships, participating in family events, spending time with friends). These impairments contributed to an overall decrease in health-related QOL. Patients with HH reported a DLQI of 9.2 compared with 0.7 for patients without HH ( $P < .001$ ).<sup>7</sup>

Swartling and colleagues<sup>30</sup> assessed QOL changes using the DLQI in 58 subjects with primary focal HH (30 with axillary HH, 46 with palmar HH, 31 with plantar HH, 18 with palmar and axillary HH, 31 with palmo-plantar HH) who were treated

with BTX-A (Botox<sup>®</sup>). The mean DLQI score significantly decreased from 10.1 to 4.3 in 53 of 58 subjects who answered the questionnaire before and after treatment ( $P < .0001$ ). Excluding 16 subjects who reported relapse (ie, subjectively unacceptable sweating), the mean follow-up DLQI score indicated a statistically significant reduction of 76% in the DLQI score (9.9 to 2.4;  $P < .0001$ ). Among subjects treated for palmar HH, an 80% improvement in DLQI score was observed (9.1 to 1.8;  $P = .00019$ ). Scores significantly decreased for all survey questions ( $P < .05$  for all) except for one question on symptoms (ie, severity of itchy, sore, painful skin), which may be because baseline scores were low.<sup>30</sup>

In a QOL analysis by Tan and Solish,<sup>17</sup> 34 subjects with primary focal HH (22 with axillary HH, 10 with palmar HH, 2 with craniofacial HH) were assessed using a modified version of the DLQI. Mean DLQI scores at follow-up decreased significantly for all subjects treated with BTX-A (Botox), regardless of the location of focal HH (range,  $P < .03$  to  $P < .001$ ); subject satisfaction with treatment ranged from approximately 50% to 95%.<sup>17</sup> Findings from Campanati and colleagues<sup>28</sup> further support the improvements in QOL. Forty-one subjects with primary focal HH (14 with axillary HH; 15 with palmar HH; 5 with plantar HH; 7 with palmar and axillary HH; 1 with palmo-plantar HH; 4 with axillary, palmar, and plantar HH) were evaluated using the DLQI before and after treatment with BTX-A (Botox). Median follow-up DLQI scores demonstrated statistically significant reductions from baseline following BTX-A therapy (13 to 1;  $P < .001$ ).<sup>28</sup>

Satisfactory treatment of focal HH may empower patients and enable them to live their lives more fully because they no longer feel the need to constantly manage their symptoms or avoid potentially uncomfortable situations. When focal HH is managed effectively, patients may have more self-confidence, which provides them with the opportunity to engage in personal, professional, and social interactions and activities.

### Treatment Options

To achieve improved QOL, the physician and patient must work together to identify a treatment option that is both effective and acceptable to the patient. A variety of treatment options are available for primary focal HH,<sup>12</sup> which provides the physician and patient with some flexibility in making the best therapeutic decision. Table 3 lists common treatment options for primary focal HH, which we discuss in greater detail.

**Topical Agents**—Common topical treatments for focal HH include over-the-counter antiperspirants and aluminum chloride ( $\text{AlCl}_3$ ) hexahydrate. Most patients with HH are insufficiently controlled with

over-the-counter antiperspirants and seek alternative treatments.  $\text{AlCl}_3$  generally is considered a first-line therapy and can be effective in milder cases of HH. One study reported good to excellent outcomes in 94%, 60%, and 83% of patients with axillary ( $n=131$ ), palmar ( $n=29$ ), and plantar ( $n=116$ ) HH, respectively, when using a modified  $\text{AlCl}_3$  formulation.<sup>31</sup> Another study of patients with palmar or plantar HH concluded that  $\text{AlCl}_3$  was less effective for these forms of HH than for axillary HH, and that more frequent application was necessary to control sweating and to maintain control.<sup>32</sup> Patients with severe HH usually require more durable treatments than  $\text{AlCl}_3$ , but most insurance companies require a trial of  $\text{AlCl}_3$  before approving other options.

The main concern with the use of  $\text{AlCl}_3$  is concentration-related skin irritation due to a hydrochloric acid by-product.<sup>1,3</sup> Other drawbacks of topical agents include messiness of the product, staining of clothing, inconvenience of application, and cosmetic or aesthetic concerns (especially when applying topical agents to the face). Caution is advised when using these products in patients with eczema or dermatitis, or in patients with open cuts or cracks in their skin. Atrophy of eccrine gland secretory cells with long-term use has been reported but generally is not a clinical concern.<sup>33</sup>

Other topical agents, such as glycopyrrolate, potassium permanganate, glutaraldehyde, and formaldehyde, have demonstrated varying degrees of efficacy in treating HH.<sup>34-36</sup> These agents are not commercially available and may cause skin irritation or staining.

**Tap Water Iontophoresis**—TWI is a US Food and Drug Administration (FDA)-approved treatment for HH.<sup>37</sup> This technique delivers direct current to the areas of skin affected by focal HH using large shallow pans of room temperature tap water and an electrode device. It is preferable to switch the current to the opposite direction halfway through the treatment. Incorporating an anticholinergic agent may lengthen the duration of effect but also may cause side effects. TWI usually requires 6 to 10 treatments to achieve an acceptable degree of sweating; patients then are switched to maintenance treatment every 1 to 4 weeks. TWI is thought to work by plugging the eccrine ducts with ion salts. This treatment method has been shown to be effective for palmar and plantar HH,<sup>20,38-43</sup> but logistical considerations do not render it an option for axillary or craniofacial HH.

Generally, TWI is well-tolerated in patients who do not have skin disorders. The technique can cause discomfort (eg, burning, tingling) and irritation that may produce vesicles or erythema. Improper use may cause burns, cutaneous necrosis, or electric shock. Similar to topical agents, this treatment should be avoided in

Table 3.

## Treatment Options for Primary Focal Hyperhidrosis\*<sup>12</sup>

### Topical Agents

OTC antiperspirants  
 $\text{AlCl}_3$  hexahydrate 10%–35% (OTC and prescription strengths)

### Iontophoresis

Drionic®  
 TWI with or without anticholinergic agents

### Oral Agents

Anticholinergic agents  
 Benzodiazepines  
 Anxiolytics  
 $\beta$ -blockers  
 Clonidine

### Botulinum Toxins

BTX-A  
 BTX-B

### Surgical Treatments

Axillary sweat gland resection  
 Tumescence liposuction  
 Subcutaneous curettage  
 ETS

\*OTC indicates over-the-counter;  $\text{AlCl}_3$ , aluminum chloride; TWI, tap water iontophoresis; BTX-A, botulinum toxin type A; BTX-B, botulinum toxin type B; ETS, endoscopic transthoracic sympathectomy.

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patients with cracked, dry, or cut skin because it will be painful. TWI is contraindicated in females who are pregnant and patients with pacemakers or metal objects such as orthopedic plates or screws in their distal extremities.

TWI is relatively easy to use and can be performed either at a clinic or at home if the patient has purchased a unit. Patients intending to administer treatments at home must be educated about proper use of the machine. In our opinion, the Fischer Galvanic Unit is the preferred unit in the United



States. TWI is a labor-intensive and time-consuming treatment that may not be acceptable for some patients. Teenagers and college students may find it invasive or disruptive to their lifestyles; adults may tire of it after years of use. However, TWI tends to be a good treatment option for young children.

**Oral Agents**—Oral anticholinergic agents have been used to treat HH, with variable results. Use of these drugs has been associated with systemic side effects such as dry mouth, blurred vision, urinary retention, and constipation.<sup>1,2</sup> No oral agents are approved by the FDA for the treatment of HH and none have been tested in controlled clinical trials for this indication. In general, oral treatment should be prescribed with caution. For patients with HH triggered by stress, benzodiazepines, anxiolytics, or  $\beta$ -blockers sometimes are used. Benzodiazepines should be used only for short-term treatment because of their sedating effects and potential for dependency. Treating focal HH with oral agents may not be appropriate because of the potential for systemic side effects, especially if the HH is not generalized and can be controlled locally by other means. However, for a patient with focal HH in multiple locations, an oral agent could be an appropriate treatment. Oral medication is not recommended for patients who frequently need to sweat and are at risk for heat-related problems such as heat stroke. These patients (eg, athletes, manual laborers) may not be able to compensate for diminished generalized sweating.

**Botulinum Toxins**—BTX-A frequently is used for the treatment of other disease states besides HH (eg, cervical dystonia, spasticity) and aesthetics. BTX-A has demonstrated consistent and long-term safety and efficacy with recurrent use in chronic disease states. In 2004, the FDA approved BTX-A (Botox) for primary axillary HH after it was found to be safe and effective for this indication. Positive therapeutic outcomes for focal HH have been achieved with off-label use of BTX-A in other areas such as the palms, soles, and face.

BTX inhibits the release of acetylcholine and blocks sympathetic cholinergic autonomic fibers that innervate sweat glands.<sup>2,44</sup> A grid of intradermal injections in the affected area effectively managed focal HH with minimal safety concerns, aside from slight temporary muscle weakness or decrease in muscle tone. Adequate anesthesia is required when administering BTX injections for HH in sensitive areas such as the palms or soles. Best practice recommendations focusing on the use of BTX-A for palmar, plantar, and facial HH are discussed elsewhere. (See the Glaser et al<sup>10,11</sup> articles in this supplement.)

**Surgical Treatments**—Endoscopic transthoracic sympathectomy (ETS) should be considered only when all other treatment options have failed. The

surgical interruption of sympathetic nerve input to the sweat glands ultimately causes permanent cessation of sweating by those glands. Several analyses showed that after 622 patients had undergone ETS (1110 ETS treatments), up to 33% of patients were partially satisfied or dissatisfied with the results.<sup>2,45,46</sup> Dissatisfaction may result from relapse or compensatory sweating, the latter of which can affect up to 88% (n=1936) of patients receiving ETS.<sup>47</sup> In addition, ETS is associated with the standard risks of surgery, such as pneumothorax, Horner syndrome, brachial plexus injuries, recurrent laryngeal nerve palsy, postsympathetic neuralgia, and phrenic nerve damage. With its potential for adverse events, complications, and compensatory sweating, ETS often is not recommended, especially when safer and more effective treatment alternatives are available.

### Review of BTX-A (Botox) for Focal HH

Additional published studies evaluating BTX-A treatment for palmar, plantar, and facial HH are provided in Table 4; however, only a few studies will be discussed in detail.<sup>8,17,25,30,48-65</sup> Findings from these studies demonstrate that BTX-A provides satisfactory treatment of primary focal HH, with a good safety profile and a reasonable duration of effect.

**Palmar HH**—To date, the published literature has reported more than 250 subjects who received BTX-A for palmar HH. Doses ranged from 25 to 220 U BTX-A per palm, and response rates generally exceeded 90%. Often, the duration of effect outlasted the length of the study; the average BTX-A treatment effect lasts 6 to 7 months. The studies reported the therapy caused mild transient muscle weakness and physicians were challenged with providing adequate anesthesia.

In a study by Naver and colleagues,<sup>53</sup> 19 subjects with palmar HH were treated with 64 to 184 U BTX-A. Sweating cessation was experienced by 5 subjects, and markedly reduced sweating was reported by another 10 subjects. These results were supported by significant improvements in measurements of evaporation and Minor starch-iodine test results ( $P<.001$ ). Evaporation values decreased an average of 57%, and Minor starch-iodine test results revealed both a 5-fold reduction in sweating and a 4-fold reduction in area of sweating. Approximately two thirds of subjects (n=12) experienced slight reduction of power in thumb-index finger grip that lasted 4 to 8 weeks. The subjects classified the weakness as insignificant. Six subjects reported dry skin that required the use of a moisturizer. The median duration of treatment effect was 8 months (range, 5.5–10.8 mo), and re-treatment was successful on relapse.<sup>53</sup>

Lowe and colleagues<sup>49</sup> evaluated 16 subjects who were treated with a total of 100 U BTX-A using a 15-site grid (10 injections in the palm; 1 injection in each digit); 6.67 U were administered per site (0.1 mL). Treatment led to significant reductions in gravimetric measurement of sweat production ( $P=.0037$ ) and improvements as demonstrated by Minor starch-iodine test results, which correlated with significant improvements based on physician and subject assessments ( $P=.008$  and  $P<.0001$ , respectively). All subjects considered the treatment a success; one subject reported minor thumb and finger weakness that resolved within 2 weeks.<sup>49</sup>

In a study by Solomon and Hayman,<sup>59</sup> 19 subjects received 165 U BTX-A in a 3-stage process. In the first stage, 10 sites were injected in the central cup area of the nondominant hand. Two weeks later, 20 sites on the nondominant digits and thenar eminence were injected, and the first-stage treatment was performed on the dominant hand. The third stage was performed 2 weeks later—20 sites on the dominant digits and thenar eminence were injected. All subjects experienced anhidrosis that lasted 4 to 9 months. Most subjects reported a 75% or greater improvement in sweating, even at 12 months. As seen in the other studies, mild muscle weakness that lasted an average of 3 weeks was reported by 4 subjects.<sup>59</sup>

In a prospective, single-blind, randomized study, Saadia and colleagues<sup>55</sup> evaluated the effects of low-dose (50 U) or high-dose (100 U) BTX-A treatments on outcomes for palmar HH. Of 24 subjects beginning treatment, 9 subjects who received the low dose and 11 subjects who received the high dose completed treatment; both groups received the same 20-site injection pattern. Both doses led to dramatically reduced areas of sweating within one month (48%–54% absolute change in area from baseline), which lasted 5 to 6 months in most subjects. A trend toward greater satisfaction with treatment was seen in the high-dose group; 64% ( $n=7$ ) of the low-dose group compared with 92% ( $n=12$ ) of the high-dose group reported excellent improvement of symptoms after one month of treatment. More patients receiving the high dose experienced hand and finger weakness, but in all cases, the weakness was considered mild. Handgrip strength was not affected, but thumb–index finger pinch strength decreased within 2 weeks of treatment by an average of 23% ( $n=11$ ) in the low-dose group and 40% ( $n=13$ ) in the high-dose group, and then steadily improved during a 6-month follow-up period.<sup>55</sup>

**Plantar HH**—As with palmar HH, use of BTX-A for plantar HH has been found to be safe and efficacious; however, there are fewer published studies for plantar HH than for palmar HH (Table 4). Treating plantar HH also shares the same underlying challenge as treating palmar HH—that is, providing sufficient

anesthesia to minimize the pain of injection because the dense innervation in this area is difficult.

In a study by Vadoud-Seyedi,<sup>62</sup> 10 subjects with plantar HH were treated with 50 U BTX-A. Within one week, 8 subjects reported extreme satisfaction with their treatment results; 5 months later, 7 subjects reported their treatment was still effective (5 of 7 subjects described a benefit at up to 6 months).<sup>62</sup>

Sevim and colleagues<sup>56</sup> reported similar findings in their evaluation of 3 subjects with plantar HH who were treated with 100 U BTX-A. Subjects experienced a significant decrease in sweat production (327 to 50 mg/min;  $P<.01$ ). Most subjects reported improvement within one week of treatment and were satisfied with their treatment. The mean duration of effect was 4 to 5 months. One subject manifested mild muscle weakness in the plantar flexors of both feet, which resolved in 10 days.<sup>56</sup>

**Facial HH**—Since 2000, studies have demonstrated the efficacy of BTX-A therapy in gustatory HH (Frey syndrome). In addition, widespread cosmetic use of BTX-A has provided much data on its safety for use on the face. Several studies also have shown the applicability of BTX-A in treating craniofacial HH (not Frey syndrome)(Table 4).

Kinkelin and colleagues<sup>64</sup> described 10 men with severe facial HH who were treated with an average of 86 U BTX-A. Treatment results showed significant reductions in sweat production by gravimetric measurement ( $P<.005$ ) and observable reductions using Minor starch-iodine test results. Five subjects manifested a partial disability to furrow the muscles in the forehead, which resolved within 8 weeks. Nine of 10 subjects were extremely satisfied or satisfied with treatment, and all wanted to repeat treatment when necessary. Subjects indicated that BTX-A treatment reduced their annoyance with frontal sweating by 70%. Nine of 10 subjects continued to express satisfaction with treatment at 5-month follow-up.<sup>64</sup>

A QOL analysis by Tan and Solish<sup>17</sup> provided additional support for the use of BTX-A in facial HH. The study revealed that subjects treated with BTX-A for forehead HH experienced an average maximum efficacy of 100% within 2 weeks; the effect tapered over time, and re-treatment was required about 4.5 months later. One subject reported difficulty wrinkling his forehead after treatment.<sup>17</sup>

### Comment

Treating primary focal HH is an important aspect of the practice of dermatology. Focal HH can cause debilitating reductions in physical and emotional QOL, resulting in numerous restrictions in an individual's personal and professional lifestyle and activities. It is important that physicians understand the impact of focal HH

Table 4.  
**Botulinum Toxin Type A (Botox®) for Palmar, Plantar, and Facial Hyperhidrosis\***

Reference (Year)	No. of Subjects	Dilution	Mean Total Dose, U (Range, U)	Distance Between Injections (Dose Per Site, U)	Anesthesia	Efficacy	Adverse Effects, n	Mean Duration of Treatment Effect (Range)
<b>Palmar HH</b>								
Campanati et al <sup>22</sup> (2003)	27	5 mL	133 (60-200)	1.5 cm (2)	Nerve block, lidocaine 1% (4 mL)	QOL assessment; pooled data showed significant improvement in DLQI score ( $P < .001$ )	Slight muscle weakness, 5; objective EMG measurement of weakness, 1	NA
Holmes and Mann <sup>18</sup> (1998)	8	NA	25	NA (5)	NA	Decreased sweating	Muscle weakness, 2; NA	NA
Lowe et al <sup>19</sup> (2002)	16	1.5 mL	100	10 injections in the palm and 1 injection in each digit, NA (6.67)	EMLA cream under plastic glove occlusion for 1 h, then ice packs for 10 min	Decreased sweating within 1 mo (gravimetric measurement [ $P = .0037$ ]; Minor starch-iodine test); improvement noticeable in 1 wk	Minor thumb and finger weakness, 1; tingling and slight numbness in fingers, 1; pain, 1	NA
Naumann et al <sup>20</sup> (1997)	1	3 mL	100	2.5 cm (3)	NA	Decreased sweating in 1 wk (Minor starch-iodine test)	Slight muscle weakness; pain of injection, 1	$\geq 14$ wk

TABLE CONTINUED ON PAGE 12

Table 4. (continued)

Reference (Year)	No. of Subjects	Dilution	Mean Total Dose, U (Range, U)	Distance Between Injections (Dose Per Site, U)	Anesthesia	Efficacy	Adverse Effects, n	Mean Duration of Treatment Effect (Range)
Naumann et al <sup>1</sup> (1998)	4	5 mL	36±7 (28–46)	2 cm (3)	NA	Decreased sweating in 2 wk (Minor starch-iodine test; gravimetric measurement [ $P<.001$ ])	Small painless hematomas, 2; pain of injection, 3	≥4 mo
Naumann et al <sup>1</sup> (1998)	16 (8 treated using Dermojet <sup>®</sup> )	5 mL	50	2 cm (NA)	EMLA cream 60 min before injection (3 subjects in each group)	Decreased sweating (needle injection [ $P<.0001$ ]; Dermojet [ $P<.05$ ])	Pain of injection, 4/8 in non-Dermojet group; small local hematomas in some subjects	NA
Naver et al <sup>52</sup> (1999)	94	NA	170 (120–220)	1.5 cm (2)	Nerve block, lidocaine 1% (4–5 mL)	Decreased sweating	Slight muscle weakness, 62; skin dryness, 23	10 mo (3–14 mo)
Naver et al <sup>53</sup> (2000)	19	NA	104 (64–184)	2 cm (2)	Nerve block	Markedly decreased sweating or sweat disappearance (15 subjects)	Slight reduction of power in thumb-index finger grip, 12; intense dry skin, 6	8 mo (5.5–10.8 mo)
Rusciani et al <sup>54</sup> (2002)	16	NA	NA	NA (5)	Nerve block	Decreased sweating	Pooled palmar and axillary data reported pain of injection, partial weakness, slight itching, cutaneous xerosis in some patients	Pooled palmar and axillary 10.9 mo (6–13 mo)



Reference (Year)	No. of Subjects	Dilution	Mean Total Dose, U (Range, U)	Distance Between Injections (Dose Per Site, U)	Anesthesia	Efficacy	Adverse Effects, n	Mean Duration of Treatment Effect (Range)
Saadia et al. <sup>55</sup> (2001)	9 (low dose); 11 (high dose)	NA	50 (low-dose group); 100 (high-dose group)	2 cm (2.5) (low-dose group); 2 cm (5) (high-dose group)	Cold packs for 15 min or liquid ethyl chloride	Decreased areas of sweating by 54% or 48% in low-dose and high-dose groups, respectively, within 1 mo	Mild hand and finger weakness, 4 (low-dose group) and 8 (high-dose group); decreased thumb-index finger pinch strength, 11 (low-dose group) and 13 (high-dose group); pain/soreness after injections	5-6 mo
Sevim et al. <sup>56</sup> (2002)	14	4 mL	45-65	1.5 cm (NA)	Nerve block	Decreased sweating at 1 mo ( $P < .01$ ); improvements noticeable within 1 wk	Thenar or general weakness, 5; pain of injection, 2	5.3±1.1 mo (3-7 mo)
Shelley et al. <sup>57</sup> (1998)	4	5 mL	100	1 cm (2)	Nerve block, lidocaine 1%	Decreased sweating after 1 wk	Mild muscle weakness, 1	7 mo (4-12 mo)
Simonetta Moreau et al. <sup>58</sup> (2003)	8	2.5 U per 0.1 mL	69.3±3.1	NA (2.5)	Nerve block	Decreased sweating at 1 mo (Minor starch-iodine test [ $P = .003$ ])	Weakness of thumb-index finger pinch strength, 2	4.5 mo (2-8 mo)
Solomon and Hayman <sup>59</sup> (2000)	19	2 or 4 mL	165	1-1.5 cm (2.5-5)	Cold packs for 15 min or liquid nitrogen; EMLA cream for 8 subjects	Decreased sweating within 2 wk	Mild muscle weakness, 4; pain of injection, 19	7.1 mo (4-9 mo)

TABLE CONTINUED ON PAGE 14

Table 4. (continued)

Reference (Year)	No. of Subjects	Dilution	Mean Total Dose, U (Range, U)	Distance Between Injections (Dose Per Site, U)	Anesthesia	Efficacy	Adverse Effects, n	Mean Duration of Treatment Effect (Range)
Swartling et al <sup>3c</sup> (2001)	44	NA	NA	1 cm (0.8-1)	NA	Decreased sweating; improved DLQI score ( $P < .0001$ )	NA	5.2 mo (3-10 mo)
Tan and Solish <sup>17</sup> (2002)	10	NA	50	NA	NA	Decreased sweating within 2 wk; improved DLQI score ( $P < .02$ )	Mild transient muscle weakness, 3; pain of injection in most patients	7.7 ± 5.0 mo
Trindade de Almeida et al <sup>6c</sup> (2001)	NA	2 mL	NA	1 cm, 40-50 sites (1-2)	Nerve block, lidocaine 2% (3-5 mL)	NA	NA	NA
Vadoud-Seyedi et al <sup>61</sup> (2001)	23	5 mL	50	0.5-1.5 cm (1-2)	Nerve block	Decreased sweating; improvement noticeable within 1 wk	Mild pain of injection, 10; transitory hematoma, 2	7 mo (4-13 mo)
<b>Plantar HH</b>								
Campanati et al <sup>28</sup> (2003)	5	5 mL	150 (50-180)	1.5 cm (2)	Nerve block	QOL assessment; pooled data showed significant improvement in DLQI score ( $P < .001$ )	NA	NA
Naumann et al <sup>9</sup> (1998)	1	5 mL	45 (42-48)	2 cm (3)	NA	Decreased sweating in 2 wk (Minor starch-iodine test; gravimetric measurement [ $P < .001$ ])	Small, painless hematomas, 1	≥ 4 mo

Reference (Year)	No. of Subjects	Dilution	Mean Total Dose, U (Range, U)	Distance Between Injections (Dose Per Site, U)	Anesthesia	Efficacy	Adverse Effects, n	Mean Duration of Treatment Effect (Range)
Sevim et al <sup>56</sup> (2002)	3	4 mL	100 (NA)	1.5 cm	Nerve block	Decreased sweating at 1 mo ( $P < .01$ ); improvements noticeable within 1 wk	Mild muscle weakness of plantar flexors, 1; pain of injection, 1	4–5 mo
Vadoud-Seyedi <sup>62</sup> (2004)	10	5 mL	50	NA <sup>†</sup>	None; Dermojet injections	Decreased sweating within 1 mo (Minor starch-iodine test)	Temporary localized hematoma, 1; pain of injection, 3	5–6 mo
Vadoud-Seyedi et al <sup>63</sup> (2000)	3	5 mL	100	NA	None; Dermojet injections	Decreased sweating (Minor starch-iodine test); improvements noticeable after 1 wk	NA	8 mo (6–10 mo)
<b>Facial HH</b>								
Kinkelil et al <sup>64</sup> (2000)	10	NA	86	1–1.5 cm (3)	NA	Decreased sweating within 4 wk (gravimetric measurement [ $P < .005$ ]; Minor starch-iodine test)	Impaired frowning of forehead, 5; pain of injection	$\geq 5$ mo, excluding 1 subject re-treated after 4 mo
Sanli et al <sup>65</sup> (2004)	1	1 mL	33	1 cm (1)	NA	Marked decrease in sweating within 1 wk	Pain of injection, 1	$\geq 5$ mo
Tan and Solish <sup>17</sup> (2002)	2	NA	<100	NA	NA	Decreased sweating within 2 wk; improved DLQI score ( $P < .03$ )	Difficulty wrinkling forehead, 1; pain of injection	4.5 mo

<sup>†</sup>HH indicates hyperhidrosis; QOL, quality of life; DLQI, Dermatology Life Quality Index; EMG, electromyography; NA, not available; EMLA, eutectic mixture of local anesthetics.

<sup>‡</sup>Median, not mean, for this study.

<sup>§</sup>Fifteen to 20 injection sites.

and the need to stay abreast of the available treatment options to provide the best care for patients.

Patients who are refractory to conventional focal HH treatments (ie, topical agents, TWI) or who find them unsatisfactory should be given the option of BTX-A therapy. However, proper technique in the use of BTX-A is critical to achieving successful clinical outcomes and maintaining safety. Best practice recommendations focusing on the use of BTX-A for palmar, plantar, and facial HH are discussed elsewhere. (See the Glaser et al<sup>10,11</sup> articles in this supplement.)

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