

Assessing, investigating and managing hyperhidrosis

Effective treatment of hyperhidrosis greatly improves the quality of life in patients with the condition. Treatment regimens should be tailored to suit each patient.

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Hyperhidrosis, or excessive sweating, is a common condition and may be overlooked by medical practitioners. It can have a profound impact on patients' lives, limiting work, social interaction and physical activity as well as causing significant emotional and psychological distress.¹ The impact on quality of life is similar to that of many chronic dermatological and systemic diseases, such as psoriasis, rheumatoid arthritis and multiple sclerosis.² Patients with hyperhidrosis may have excessive sweating confined to localised areas such as the palms (focal hyperhidrosis) or over the entire body (generalised hyperhidrosis). In the vast majority of patients, no cause is found and the term primary or idiopathic hyperhidrosis is used.

General practitioners are instrumental in the assessment and treatment of hyperhidrosis. The condition can be difficult to manage and there are

many treatment options available, each with its own advantages and disadvantages. Appropriate treatment often results in a dramatic improvement in quality of life. This article provides an overview of the clinical assessment, investigation and management of this difficult condition.

Epidemiology

Hyperhidrosis is common. A recent epidemiological study involving 150,000 households in the USA revealed that 2.8% of the population experienced excessive sweating in one or more body areas.¹ The reported rate of hyperhidrosis was similar in males and females, although males experienced more axillary hyperhidrosis and females more palmar hyperhidrosis (Figure). Only 38% had discussed their sweating with a health care professional.¹ Females were twice as likely to present for review.

IN SUMMARY

- Hyperhidrosis is a common condition that may result in a significant impairment in social, occupational and recreational activities.
- Symmetrical involvement of the palms, axillae or soles is suggestive of primary or idiopathic hyperhidrosis. Investigations are usually not required unless there are features suggestive of a secondary aetiology, such as fever, weight loss and palpitations.
- Management should be tailored to suit the individual, weighing up the advantages and disadvantages of each treatment. Start with the least invasive treatment, and progress to the more invasive options with higher risks of side effects and complications.
- Topical aluminium chloride is an appropriate first step in treatment but is rarely effective for moderate to severe hyperhidrosis.
- Iontophoresis with glycopyrrolate is very effective for palmo-plantar hyperhidrosis but requires regular visits to specialist clinics.
- Intra-dermal botulinum toxin is an effective treatment, particularly for axillary hyperhidrosis, and usually lasts six months.
- Surgical therapy, although effective and often permanent, should be reserved for patients who have failed less invasive treatments. This is partly because of the risk of postoperative complications and compensatory hyperhidrosis.



PHOTOLIBRARY

Figure. Axillary hyperhidrosis. Intradermal botulinum toxin is usually an effective treatment if topical aluminium chloride does not control the localised sweating.

While all races are affected by hyperhidrosis, Asian populations, and particularly the Japanese, are reportedly affected up to 20 times more frequently than other ethnic groups.

Primary hyperhidrosis can occur at any age but usually manifests in childhood or early adolescence. The age of onset varies dependent on anatomical site, with palmar hyperhidrosis presenting during childhood or adolescence and axillary hyperhidrosis typically presenting later during adolescence.¹

Pathophysiology

Sweating is a normal physiological function, the primary purpose of which is to maintain core body temperature. The human body has two to four million sweat glands distributed on all areas of the skin, with higher concentrations found on the palms, soles, axillae and face. The sweat glands are innervated by cholinergic nerve fibres arising from the sympathetic nervous system. Sweating has both thermoregulatory and emotional variants.

Thermoregulatory sweating, controlled by the hypothalamus, involves the entire body surface and is the human body's most effective mechanism of heat loss. Emotional sweating has input from higher cortical centres and usually involves the palms, axillae, forehead and, to a lesser extent, the soles.

Hyperhidrosis is characterised by the production of amounts of sweat in excess of that required for physiological needs. It is divided into primary or secondary hyperhidrosis. Secondary hyperhidrosis is usually generalised and often has an underlying pathological aetiology (Table 1). Primary hyperhidrosis involves specific sites, usually the palms, soles, axillae or face, and its pathogenesis is poorly understood. It is believed to result from excessive stimulation of sweat glands by the autonomic nervous system; in support of this, the sweat glands of patients with primary hyperhidrosis are histologically normal and not increased in number or size.³ Although anxiety or emotional stimuli play an important role in primary hyperhidrosis, it is not believed to be a neuropsychiatric condition. A family history is present in 30 to 50% of patients, suggesting a genetic component.

Gustatory hyperhidrosis is a form of hyperhidrosis that affects the cheek or mandibular area and occurs in conjunction with salivation. It may be seen following parotid surgery or inflammation of the parotid gland, or in diabetic neuropathy, or it may be idiopathic in nature. Foods that commonly stimulate gustatory sweating include spicy or hot foods, alcohol, coffee and chocolate.

Clinical assessment

The flowchart on page 49 outlines a diagnostic approach for patients with hyperhidrosis. Important aspects of the patient's history include:^{4,5}

- age of onset
- pattern of sweating:
 - areas involved (e.g. palmar, palmoplantar, axillary etc)

Table 1. Aetiology of secondary hyperhidrosis

Endocrine
Thyrotoxicosis
Diabetes mellitus/hypoglycaemia
Menopause
Gout
Phaeochromocytoma
Hyperpituitarism
Carcinoid syndrome
Malignancy
Lymphoma
Leukaemia
Infection
Tuberculosis
Malaria
HIV/AIDS
Neurological
Spinal injury
Cerebrovascular accident
Parkinson's disease
Social anxiety disorder
Drugs (common)
Alcohol (alcoholism)
Aspirin
Insulin (with hypoglycaemia)
Antiemetics
Antidepressants
Amphetamines
Narcotics
Cardiorespiratory
Acute myocardial infarction
Cardiac failure
Respiratory failure

- symmetry of sweating
- triggers (e.g. anxiety, hot weather)
- absence of symptoms during sleep
- family history of hyperhidrosis
- impact on quality of life (e.g. interference with work/school, avoidance of social engagements, choice of clothing etc)
- psychosocial history

- medical comorbidities
- symptoms suggestive of secondary cause (e.g. fever, weight loss, palpitations)
- medication use
- previous treatments to date and their effectiveness (including alternative therapies and over-the-counter medications).

Physical examination should focus on examination for evidence of excessive sweating and its distribution (either focal or generalised). The patient should also be examined for evidence of systemic diseases that may suggest a secondary aetiology. Examination may include the palpation of regional lymph nodes, as well as cardiovascular, gastrointestinal and neurological assessment.

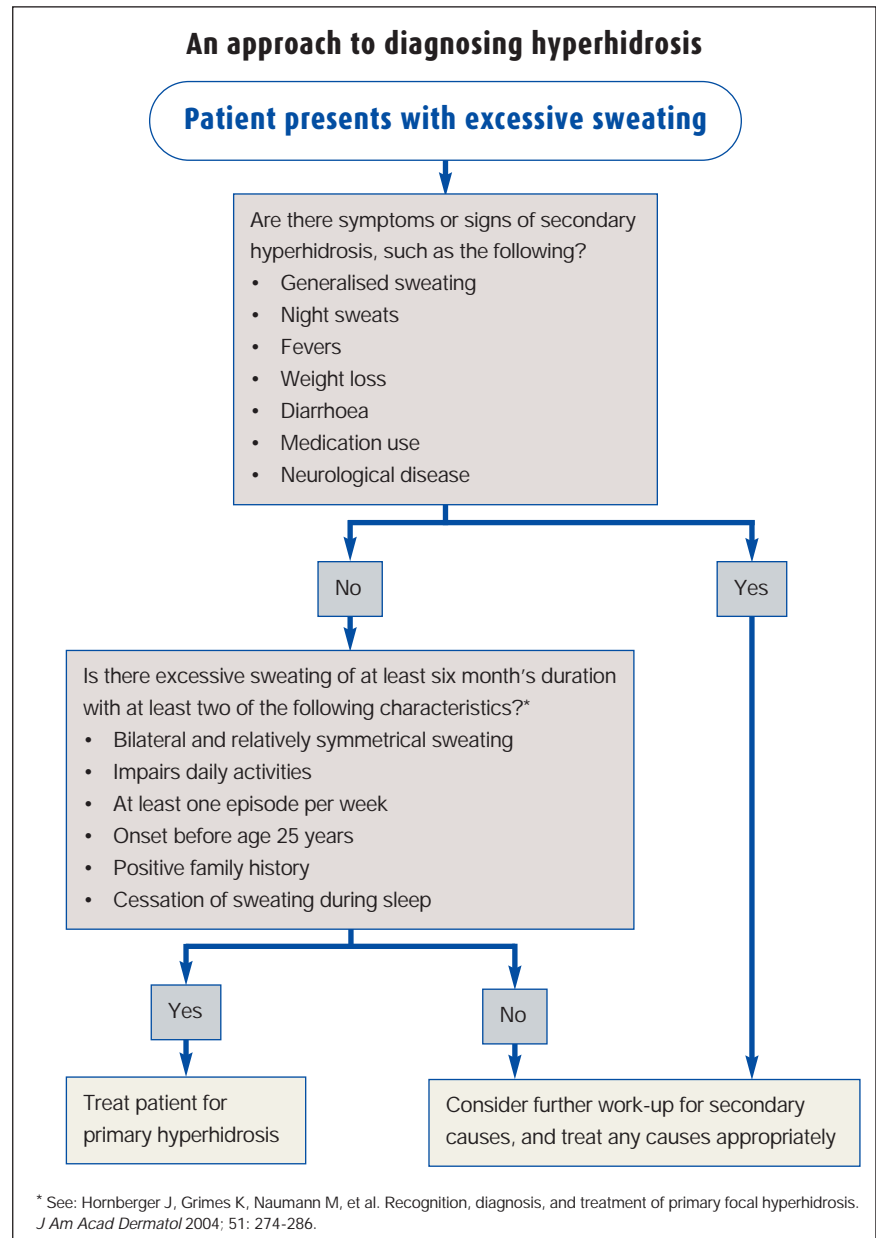
It is important to establish the patient's expectations and goals of treatment as this may dictate which treatment options are appropriate. Patients with mild disease will be less willing to accept potential side effects than patients with severe disease that interferes with activities of daily living.

Investigation

Patients presenting with classical primary focal hyperhidrosis usually do not require laboratory investigation. However, if there are features on history or physical examination suggestive of a secondary cause, investigation or referral of the patient is warranted. Further investigation should be guided by the clinical findings but may include:

- thyroid function testing for hyperthyroidism or thyrotoxicosis
- blood glucose testing for diabetes or hypoglycaemia
- urinary catecholamines when a pheochromocytoma is suspected
- imaging studies (such as chest x-ray or CT scanning) may be used to exclude a neoplastic cause (e.g. lymphoma) or for chronic infections such as tuberculosis.

Quantitative assessment of sweat pro-



duction is generally not required. Gravitric testing of sweat collected on absorbent paper may be used to assess treatment response, but is generally reserved for clinical trials. The starch-iodine test, which leaves dark purple sediment in the presence of sweat, may be useful for mapping areas of excessive sweating prior to treatment with botulinum toxin or local surgery.

Management

The treatment approach will vary depending on the body area involved; treatment algorithms for palmar, axillary and plantar hyperhidrosis are provided on pages 52, 54 and 55. A variety of treatment options are available and these should be tailored to individual patients, based on the severity of disease, tolerance of side effects and personal preference. Some

Table 2. Treatment modalities for hyperhidrosis

Modality	Advantages	Disadvantages
Aluminium chloride	Cheap Can be used at home Few side effects	Less effective for moderate to severe hyperhidrosis Local reactions/irritation
Tap water iontophoresis	Can be used at home	Cost of buying galvanic unit Less effective for moderate to severe hyperhidrosis Local reactions/irritation
Glycopyrrolate iontophoresis	Very effective for moderate to severe hyperhidrosis Reduced sweating elsewhere	Regular attendance at clinic required (every two to four weeks) Systemic side effects (usually mild and transient) Local reactions/irritation (mild)
Botulinum toxin type A injection	Effective (especially for axillary hyperhidrosis) Lasts six to 12 months	Injection trauma Need for nerve block or other anaesthesia Expensive Mild weakness of intrinsic hand muscles (palmar)
Endoscopic thoracic sympathectomy (not performed for plantar hyperhidrosis)	Effective Usually permanent results When used for palmar hyperhidrosis, may improve plantar hyperhidrosis as well	Compensatory hyperhidrosis (60 to 90% of patients) Risk of serious complications (e.g. pneumothorax, Horner's syndrome) Recurrence of symptoms (up to 16% of patients)

advantages and disadvantages of common treatments are summarised in Table 2.

Topical treatments

The main advantage of topical treatments is that they are relatively inexpensive and can be used at home. The most effective topical treatment, especially for axillary hyperhidrosis, is aluminium chloride in concentrations of 20 to 25% (Driclor). Aluminium chloride is believed to act by blocking sweat ducts and causing sweat gland atrophy. Good compliance and correct technique is required for it to be effective. The solution should be applied to dry skin at night and washed off in the morning. Nightly application is required until euhydrosis is achieved, followed by maintenance therapy about once weekly. Skin irritation may occur, and may be managed by reducing the frequency of application and applying a weak topical corticosteroid (such as 1% hydrocortisone cream). It is important to explain to patients that clinical

improvement may not be seen for up to four weeks and that they should not cease treatment until after this time.

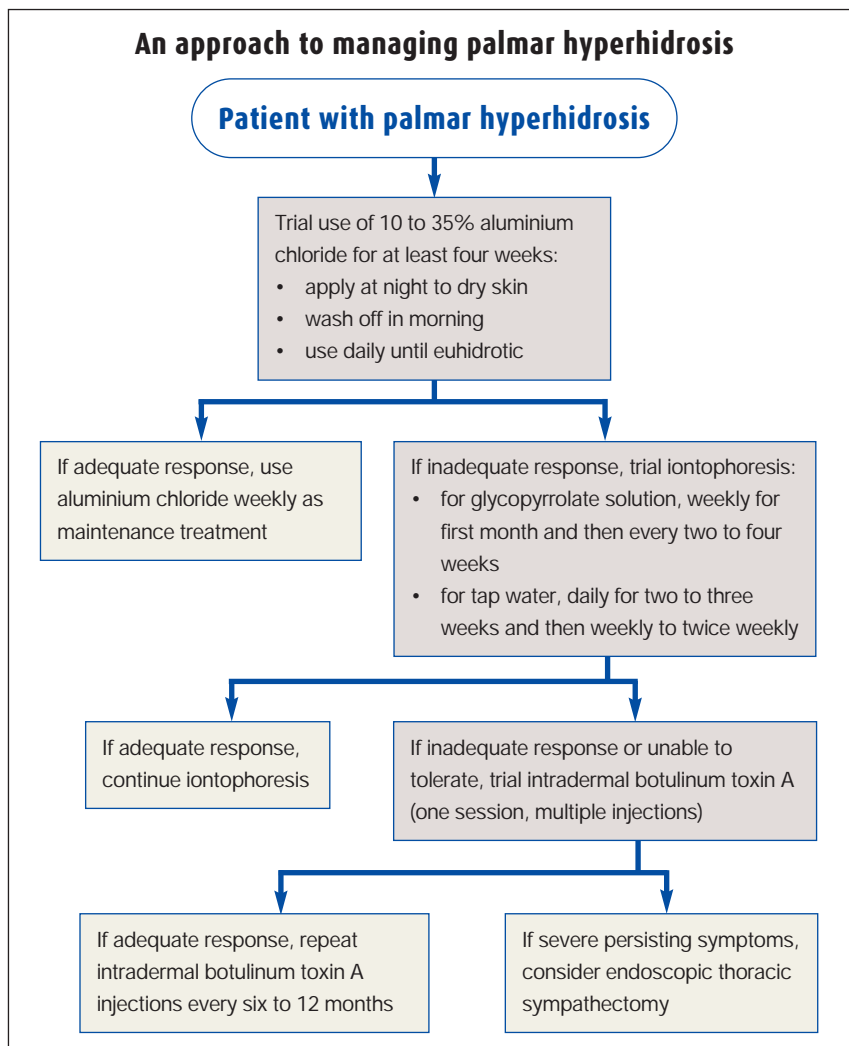
Iontophoresis

Iontophoresis is an effective treatment for palmoplantar hyperhidrosis.⁶ It involves the application of a low intensity electric current (10 to 20 mA) to the palms and soles while they are immersed in either tap water or anticholinergic solution.

Tap water iontophoresis has the advantage that treatment can be performed at home using commercially available and easily portable galvanic units (e.g. available from Wayne Electronics, phone 02-4340 1288; Neurotronics, phone 02-9398 5599 or 1800 636 766, www.neurotronics.com.au). Patients initially use the units on a daily basis for two to three weeks and then repeat treatments as needed, often on a weekly to twice weekly basis. Mild discomfort of the affected area during treatment is the main side effect.

Iontophoresis using an anticholinergic solution has been shown to be superior to tap water without the addition of significant side effects.⁶ Side effects are related to the systemic absorption of small quantities of anticholinergic solution and commonly include dry mouth and less commonly dry eyes or blurred vision. These symptoms are mild and transient, usually lasting 12 to 24 hours. Although it is more effective than tap water, glycopyrrolate iontophoresis has the disadvantage of requiring treatment in specialist centres. Treatment intervals are usually weekly for the first month and then reduced to every two to four weeks, depending on individual response. One advantage of glycopyrrolate iontophoresis is that patients often report reduced sweating from other areas, possibly related to systemic absorption of the anticholinergic solution.

Contraindications to iontophoresis include pregnancy or a history of metallic implants, such as cardiac pacemakers, orthopaedic prostheses and intrauterine



contraceptive devices. In addition, patients with a history of cardiac arrhythmias or narrow angle glaucoma should not use glycopyrrolate solution.

Iontophoresis is less effective for axillary hyperhidrosis because of the technical difficulty of applying the electrodes or sponges to the axilla and an increase in the frequency of local skin reactions.

Botulinum toxin

The use of botulinum toxin type A (Botox, Dysport) is a relatively new but extensively studied treatment modality for hyperhidrosis. Botulinum toxin inhibits the release of acetylcholine from presynaptic

nerve endings. In hyperhidrosis, intradermal injections of botulinum toxin inhibit the sympathetic nerves supplying sweat glands. Multiple intradermal injections are required, about 1 cm apart.

Botulinum toxin is an extremely effective treatment for hyperhidrosis. In one large study, there was an average 83% reduction of sweat production in 94% of patients.⁷ This effect lasts, on average, for six to seven months, although some patients may benefit for up to 16 months following one treatment session, particularly for axillary disease.⁸

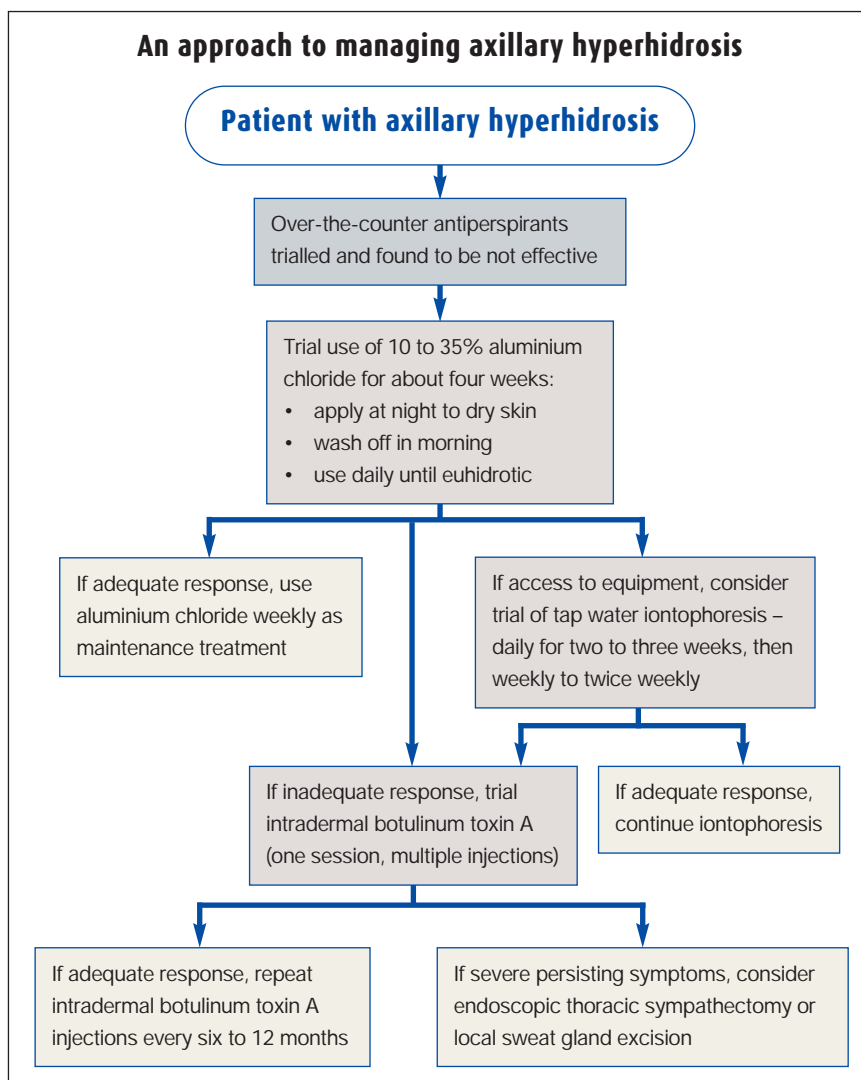
Side effects from botulinum toxin therapy are usually minimal. The only notable

side effect relates to transient weakness of the intrinsic hand muscles with palmar botulinum toxin. This complication is generally well tolerated although patients requiring manual dexterity (such as musicians and surgeons) may be discouraged by this risk.

One limitation of botulinum toxin therapy is the pain of multiple intradermal injections. Axillary botulinum toxin is generally well tolerated without analgesia but palmoplantar injections are considerably more painful and require some form of anaesthetic. Topical anaesthetic creams are generally ineffective and regional nerve block or intravenous sedation is often required. The added cost and risks associated with regional nerve anaesthesia is currently a limiting factor in the application of botulinum toxin for palmoplantar hyperhidrosis. However, newer anaesthetic techniques – including cryoanalgesia, vibration, lignocaine iontophoresis and even botulinum toxin iontophoresis – are currently being explored. Unfortunately, botulinum toxin is expensive and is not currently subsidised by the PBS for use in hyperhidrosis.

Surgical treatments

Endoscopic thoracic sympathectomy
Thoracic sympathectomy for hyperhidrosis has been performed since the 1920s. The procedure has evolved over time from open surgery to minimally invasive endoscopic surgery. The procedure involves ligation, clamping or cauterisation of the thoracic sympathetic ganglia (T2 and/or T3), resulting in denervation of the sweat ducts. The efficacy of endoscopic thoracic sympathectomy (ETS) varies between studies. In a large series of 850 patients treated with ETS, 98% of patients reported 'satisfactory' results after a median follow up of 31 months.⁹ The main advantage of ETS is that it potentially offers permanent resolution of symptoms, although overall relapse rates vary from 0 to 16%. Recurrence rates are significantly higher for axillary symptoms compared to palmar



symptoms (65% v. 6.6%).¹⁰

The main complication following ETS is compensatory hyperhidrosis, the phenomenon of excess sweating in previously euhidrotic areas. Compensatory hyperhidrosis is observed in 60 to 90% of patients following ETS, although the majority find it less disabling than their original symptoms. Gustatory hyperhidrosis is also frequently observed. Serious complications, including haemothorax, pneumothorax, Horner's syndrome and persisting intercostal pain syndromes, are observed in 1 to 2%.

Sympathectomy is not performed for

plantar hyperhidrosis because of the unacceptable risk of sexual dysfunction. However, up to 50% of patients who undergo ETS for palmar hyperhidrosis will experience a reduction in their plantar sweating.

Tumescent liposuction

The permanent removal of sweat glands via tumescent liposuction is an effective treatment for axillary hyperhidrosis. Liposuction has the advantage of being minimally invasive, effective and can be performed in an outpatient setting.¹¹ Complications are uncommon but may

include a recurrence of symptoms and local bruising. It should be considered as an alternative to ETS for axillary hyperhidrosis.

Other procedures

Other surgical methods aimed at the removal of axillary sweat glands include en-bloc excision and curettage. These procedures, however, may result in unacceptable axillary scarring and contractures. In practice, these invasive measures are rarely required since excellent results are achieved with botulinum toxin in isolated axillary hyperhidrosis.

Systemic treatments

Systemic anticholinergic agents such as atropine and glycopyrrolate are occasionally used in treatment-resistant cases, particularly for idiopathic generalised hyperhidrosis. The main disadvantage of these medications is that the dose required to achieve euhidrosis is often associated with significant side effects (for example, drowsiness, dry mouth, constipation and urinary retention).

Anxiolytic or antidepressant agents may be useful when the hyperhidrosis is a manifestation of an underlying psychiatric disorder such as social anxiety disorder. In these situations, liaison with a psychiatrist should be considered.

Alternative therapies

It is difficult to assess the effectiveness of alternative therapies in hyperhidrosis because of the lack of well-designed clinical trials and limited long term follow up. Hypnosis, massage, acupuncture, bio-feedback and relaxation techniques have been used in the treatment of this condition. In some cases, these therapies may be used as an adjunct to other clinically proven treatments.

Conclusion

Effective treatment provides a dramatic improvement in the quality of life of patients with hyperhidrosis. A variety of

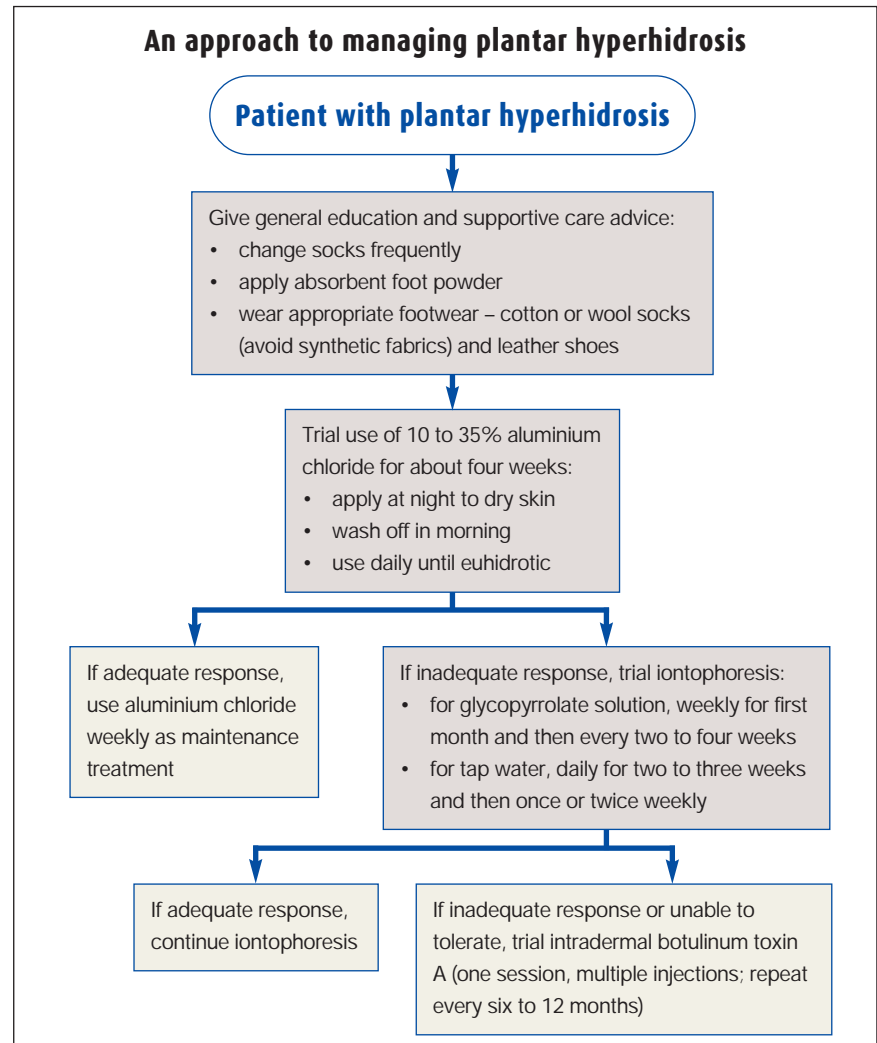
Useful resources

- **Article:** Hornberger J, Grimes K, Naumann M, et al. Recognition, diagnosis and treatment of primary focal hyperhidrosis. *J Am Acad Dermatol* 2004; 51: 274-286.
An excellent clinical review of hyperhidrosis with a consensus opinion from a multispecialty working group using evidence based medicine.
- **Website:** International Hyperhidrosis Society: www.sweathelp.org
A useful website for both doctors and patients offering evidence-based advice.

management options are available but there is no 'gold standard' treatment. Instead, treatment regimens should be tailored to suit each patient, taking into consideration potential side effects, complications and individual patient preference. Useful resources on the condition are provided in the box on this page. **MT**

References

1. Strutton DR, Kowalski JW, Glaser DA, Stang PE. US prevalence of hyperhidrosis and impact on individuals with axillary hyperhidrosis. Results from a national survey. *J Am Acad Dermatol* 2004; 51: 241-248.
2. Swartling C, Naver H, Lindberg M. Botulinum A toxin improves quality of life in severe primary focal hyperhidrosis. *Eur J Neurol* 2001; 8: 247-252.
3. Sato K, Kang WH, Saga K, Sato KT. Biology of sweat glands and their disorders. II. Disorders of sweat gland function. *J Am Acad Dermatol* 1989; 20: 713-726.
4. Hornberger J, Grimes K, Naumann M, et al. Recognition, diagnosis, and treatment of primary focal hyperhidrosis. *J Am Acad Dermatol* 2004; 51: 274-286.
5. Leung AK, Chan PY, Choi MC. Hyperhidrosis. *Int J Dermatol* 1999; 38: 561-567.
6. Dolianitis C, Scarff CE, Kelly J, Sinclair R. Iontophoresis with glycopyrrolate for the treatment



- of palmoplantar hyperhidrosis. *Australas J Dermatol* 2004; 45: 208-212.
7. Naumann M, Lowe NJ. Botulinum toxin type A in treatment of bilateral primary axillary hyperhidrosis: randomised, parallel group, double blind, placebo controlled trial. *BMJ* 2001; 323: 596-599.
8. Naumann M, Lowe NJ, Kumar CR, Hamm H, Hyperhidrosis Clinical Investigators Group. Botulinum toxin type A is a safe and effective treatment for axillary hyperhidrosis over 16 months: a prospective study. *Arch Dermatol* 2003; 139: 731-736.
9. Drott C, Gothberg G, Claes G. Endoscopic thoracic sympathectomy: an efficient and safe method for the treatment of hyperhidrosis. *J Am*

- Acad Dermatol* 1995; 33: 78-81.
10. Gossot D, Galetta D, Pascal A, et al. Long-term results of endoscopic thoracic sympathectomy for upper limb hyperhidrosis. *Ann Thorac Surg* 2003; 75: 1075-1079.
11. Lee MR, Ryman WJ. Liposuction for axillary hyperhidrosis. *Australas J Dermatol* 2005; 46: 76-79.

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