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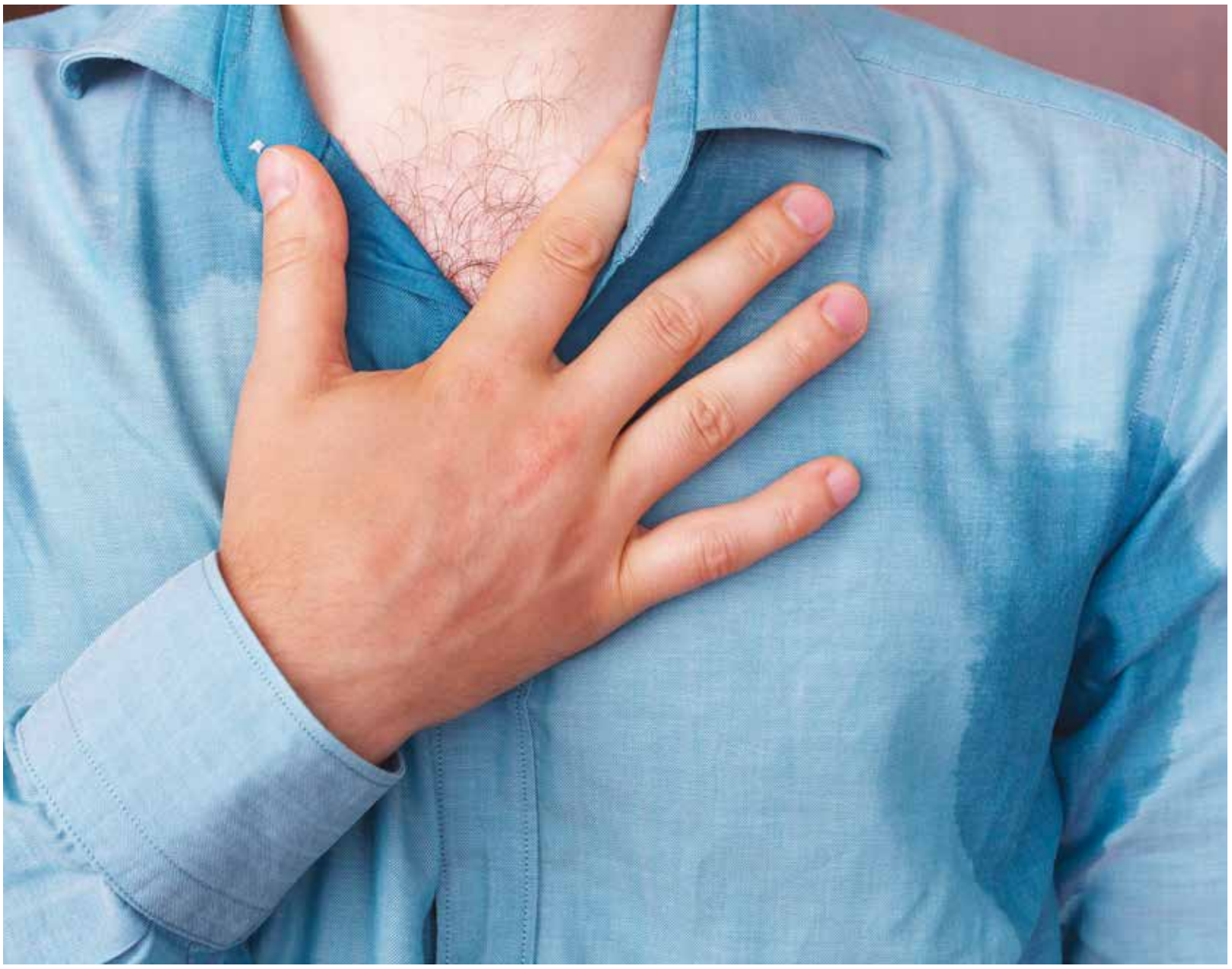

HYPERHIDROSIS AND OTHER SWEAT GLAND DISORDERS

INSIDE

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Background

HYPERHIDROSIS and other sweat gland disorders, including bromhidrosis and hidradenitis suppurativa (HS), have the potential to be deeply distressing conditions.[1] When severe, they impair an individual's daily activities, reduce performance and productivity in the workplace, and lead to higher rates of depression and poor personal image.

Despite the high physical and emotional impact of HS, some patients with hyperhidrosis and bromhidrosis do not seek treatment from their GP. Conversely, other patients present repeatedly until the diagnosis is made and treatment is initiated.

Hyperhidrosis is defined as the production of sweat in amounts greater than physiologically required. It is rarely a sign of significant underlying pathology. More often it is a chronic, primary, idiopathic problem. Idiopathic, primary focal hyperhidrosis is localised to certain areas of the body. The most commonly affected areas are the axillae, palms and soles.

Bromhidrosis refers to offensive body odour. It can cause significant embarrassment and social isolation and impair an individual's quality of life.[2]

Sudiferous (sweat) glands are divided into apocrine (underarm, breast, groin) and eccrine (entire body) glands.[3] Bromhidrosis is thought to occur through biotransformation of odourless secretions into volatile odorous molecules.

In the axilla, *Corynebacterium* is the most common bacterium, which is implicated in the production of unpleasant smelling fatty acids.[4]

Hidradenitis suppurativa is also known descriptively as acne inversa. It is a chronic, relapsing inflammatory condition affecting the pilosebaceous unit.[5,6] It most commonly affects the axillary, groin, perianal, perineal and genital skin. The inframammary skin may also be affected in some women.

Patients repeatedly present to emergency departments or their GP with a solitary painful 'boil'. Delay in diagnosis and failure to initiate prophylactic treatment may result in the formation of sinus tracts, abscesses and scarring.

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Clinical features and diagnosis

Hyperhidrosis

SWEATING is important for thermoregulation, skin hydration, and fluid and electrolyte balance.

Three types of sweat glands have been described: eccrine, apocrine and apoeccrine glands. Eccrine gland overactivity is implicated in the palmer and plantar hyperhidrosis, while overactive apoeccrine glands cause axillary hyperhidrosis.[7]

Eccrine sweat glands are innervated by the sympathetic nervous system, with different regions of the brain controlling thermal and emotional sweating. Acetylecholine is the primary neurotransmitter responsible for innervating eccrine sweat glands. Sweating on the face, chest and back is caused by thermal stimuli, whereas sweating of the palms and soles is triggered by emotional stimuli.

Gustatory sweating, where both salivation and perspiration occur simultaneously in response to hunger or eating, is confined to the peri-oral region of the face.

In primary hyperhidrosis, sweat glands appear histologically normal, and it is believed that the cause of emotional hyperhidrosis is an inappropriate or exaggerated central response to emotional stress. Emotional sweating is rarely experienced during sleep.

Excessive sweating is a common complaint, with a prevalence of between one and three per cent in the population.

It is important for doctors to determine whether the hyperhidrosis is generalised or focal. The medical history should focus on:

- Location of sweating: generalised versus focal, unilateral or symmetrical
- Age of onset
- Duration of symptoms
- Triggers such as heat, emotion, eating
- Concurrent medical and medication history
- Psychological, physical and social impact
- Modifications to personal and professional behaviour[8]

Generalised hyperhidrosis affects the entire body, and a detailed history and examination can distinguish idiopathic from secondary causes, including systemic diseases and medications. The most common cause of generalised hyperhidrosis is excessive heat. Table 1 lists a number of causes to consider when assessing generalised hyperhidrosis.[8]

Focal hyperhidrosis most commonly affects the axilla, palms and soles.[1] Patients may also describe sweating of the scalp, face, inframammary and groin areas.[9]

The most common causes of focal hyperhidrosis are listed in table 2.[8] Primary focal hyperhidrosis is commonly reported in healthy adults younger than 25, with two-thirds of patients reporting a positive family history.

A diagnosis of primary focal hyperhidrosis can be made with a history of focal, visible, and excessive sweating of at least six months duration without apparent cause, accompanied by two of:

- Bilateral, symmetrical sweating
- Impairment of daily activity
- At least one episode per week
- Onset before age 25
- Family history of idiopathic hyperhidrosis
- Focal sweating that ceases during sleep[10]

Rosacea, a common cause of facial flushing, is not generally associated with facial sweating.

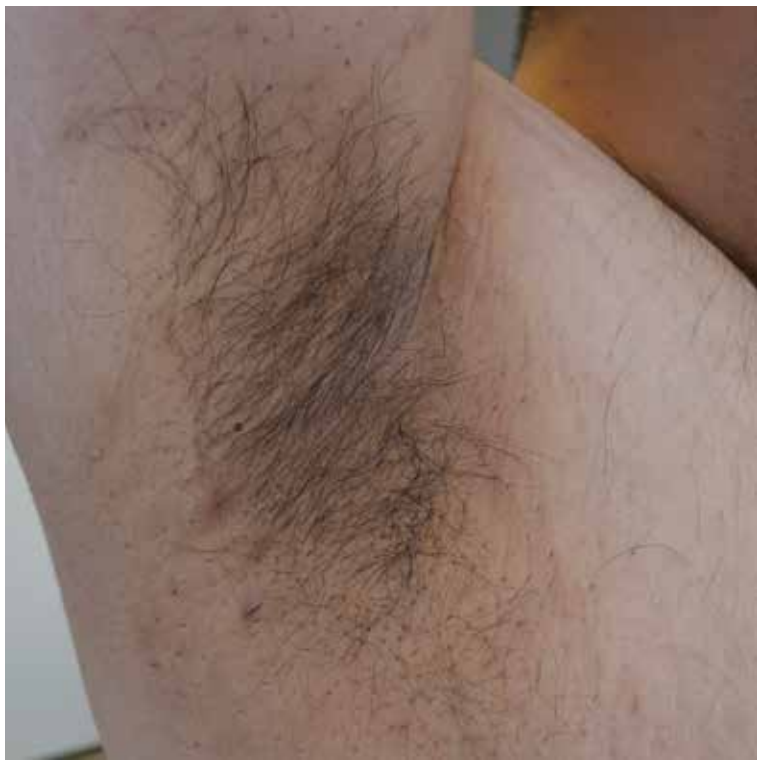

Figure 1. The finding of comedones in the axilla or groin is pathognomonic for HS.

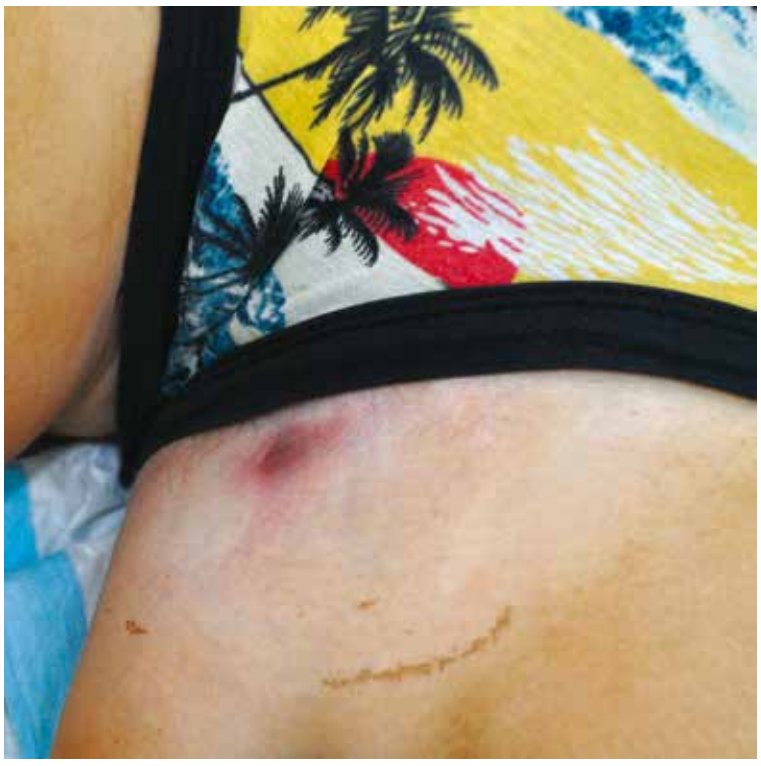

Figure 2. Abscess formation (single/multiple) without sinus tract development or scarring.

Table 1. Causes of generalised hyperhidrosis to consider in general practice

Medications	Propranolol Selective serotonin reuptake inhibitors Tricyclic antidepressants Cholinesterase inhibitors Opioids
Endocrine	Menopause Hyperthyroidism Diabetes mellitus Hypoglycaemia Phaeochromocytoma Hypopituitarism Carcinoid syndrome
Infectious	Tuberculosis HIV Endocarditis Malaria
Congestive heart failure	
Neurological	Spinal cord injury with autonomic dysreflexia Parkinson disease Peripheral neuropathy Intracranial lesions
Malignancy	

Table 2. Causes of focal hyperhidrosis

Type	Features
Primary focal hyperhidrosis (most common)	
Gustatory sweating	Sweating around the mouth, nose and forehead associated with the consumption or sight of food that produces strong salivation. Particularly associated with spicy or hot food
Neurological (secondary)	Spinal cord injuries and peripheral neuropathy

Excessive sweating is a common complaint, with a prevalence of between one and three per cent in the population.

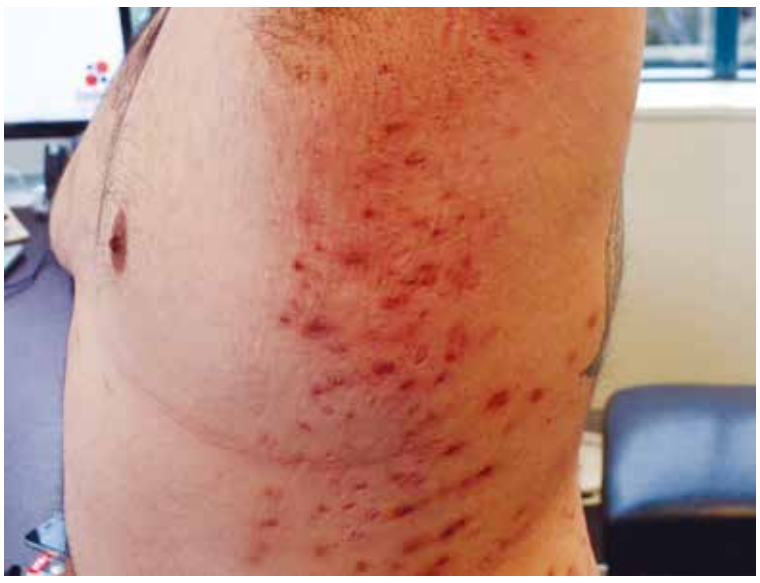

Figure 3. Multiple widespread lesions.

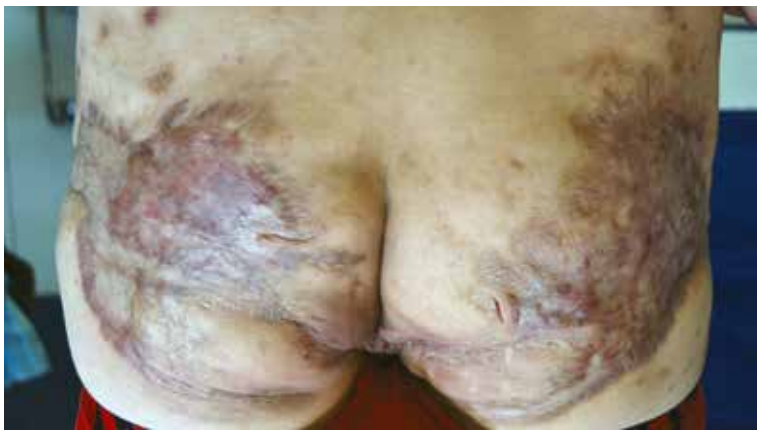

Figure 4. Diffuse involvement, with multiple connected sinus tracts and abscesses across the entire affected area.

Bromhidrosis

While eccrine glands are responsible for thermoregulation, apocrine glands and apoeccrine glands are responsible for pheromonal odours. Apocrine and apoeccrine glands are present in the axillae, groin and inframammary regions. They secrete a small amount of non-odorous oil. Biotransformation of this oily fluid by resident microflora, notably *Corynebacterium*, creates volatile odorous molecules.

Bromhidrosis can be divided into apocrine and eccrine bromhidrosis.[4] Apocrine bromhidrosis is the most prevalent form, occurring exclusively after puberty and producing the distinctive axillary odour reported by many patients. Apocrine bromhidrosis is more commonly reported in males, possibly due to larger and more numerous apocrine glands.

Eccrine bromhidrosis occurs when eccrine sweat degrades keratin, with subsequent bacterial degradation. Eccrine bromhidrosis is most common on the soles, and the odour can linger in footwear and gym clothing. Ingestion of certain foods or medications may worsen eccrine bromhidrosis.

Metabolic disorders including trimethylaminuria, with its distinctive fishy odour, is another rare cause of bromhidrosis.[11] Genetic testing is available in Australia, with the condition managed with dietary modification.

The diagnosis of bromhidrosis is made clinically. A thorough history is important. Bromhidrosiphobia is the abnormal fear of producing body odour and is associated with schizophrenia. Olfactory hallucinations can also be associated with intracranial lesions and a neurological examination is prudent if no odour is clinically apparent.

Although isolation of *Corynebacterium*, *Staphylococcus*, *Micrococcus* and *Propionibacterium* is common in patients with bromhidrosis, bacterial swabs are rarely beneficial for guiding treatment.

Hidradenitis suppurativa

The prevalence of hidradenitis suppurativa (HS) is estimated to be around one per cent of the population, and up to four per cent among young adults attending sexual health clinics.[6,12] HS can occur any time after the onset of puberty. It most commonly presents in the second and third decades of life, and is more common in women.

A positive family history in a first-degree relative is common. Other risk factors include high body mass index, smoking, diet and hormonal factors. Mechanical stress on the skin, or skin friction, is a factor in localising HS to certain body sites.

Classically, apocrine glands have been implicated in the development of HS. However, recent research has demonstrated that follicular occlusion with secondary follicular rupture and localised inflammation are the primary events.[13]

Hormonally induced keratinocyte proliferation leads to follicular hyperkeratosis and follicular occlusion. Rupture of the sebofollicular junction and local inflammation results in destruction of the follicle. Sinus tracts form and are colonised with commensal bacteria. Infection is a late and secondary event.

HS begins in intertriginous regions, most commonly the axillae. Table 3 lists other intertriginous and non-intertriginous areas that may become affected progressively. The hallmark of early HS is acute painful, tender nodules in the axilla or groin.[14]. The nodules may rupture and drain malodourous material. The presence of chronic or relapsing inflammatory nodules, sinus tracts and scarring in intertriginous areas confirm the diagnosis of HS. The finding of comedones in the axilla or groin is pathognomonic for HS (see figure 1).

Table 3. Body sites affected by hidradenitis suppurativa

Type	Affected body site
Intertriginous	Axillae; inguinal area; inner thighs; perianal and perineal area; mammary and inframammary; buttocks; pubic area; scrotum; vulva; chest; scalp and retroauricular area (rare)
Non-intertriginous	Sites of skin compression or friction; waistbands, beltlines, and brassiere straps

Any patient with a single 'boil' in the axilla or groin should be suspected of having HS.

Any patient with a single 'boil' in the axilla or groin should be suspected of having HS. Any patient who has had more than one episode should be referred to a dermatologist for diagnosis and treatment. The nodules of HS are not true boils or furuncles. HS lesions are more deep-seated, rounded and lack a central punctum. Table 4 outlines clinical features that distinguish HS from other differential diagnoses.

The Hurley clinical staging system is used to categorise patients into three disease severity groups.[15] Table 5 outlines the features of each. The severity of disease is directly related to impact on quality of life and mental health. Patients with severe HS are significantly more likely to experience major depression.[16] Complaints of pain, odour and appearance negatively affect performance in social and professional settings.

Hidradenitis suppurativa is a clinical diagnosis. There are no useful diagnostic tests. Disease staging involves a directed history to ascertain the impact the disease is having on social and professional functioning, and examination of all potentially affected areas.

A skin biopsy is rarely required, unless to exclude an overlying squamous cell carcinoma (firm, slow-growing, ulcerated, non-fluctuant mass that is non-draining).

HS is not an infectious diagnosis, making routine bacterial cultures unnecessary. However, bacterial cultures may be useful in cases of secondarily infected lesions or recurrent HS that is refractory to treatment.

Table 4. Characteristics of hidradenitis suppurativa and its differential diagnoses

Condition	Features
Follicular pyodermas (folliculitis, furuncles, carbuncles)	• Superficial inflammatory papules (with or without pustules) that surround hair follicles • Not as deep-seated as HS lesions • Transient lesions that generally respond well to appropriate antibiotic therapy • Do not progress to form sinuses or keloid scarring
Acne vulgaris	• Like HS, hyperkeratinisation leads to formation of comedones, inflammatory nodules and scarring • Generally distributed on the face, upper chest and back • Less likely to form sinus tracts and extensive scar formation
Intergluteal pilonidal disease	• Infection of the skin and tissue of the natal cleft secondary to follicular occlusion • Formation of a sinus, cavity or pit in the natal cleft • May drain purulent, bloody and malodourous material • May coexist with HS
Crohn's disease	• Perianal and vulvar skin manifestations include abscesses, fistulae, sinus tracts, scarring and "knife-cut" ulcers • Most often associated with a history of gastrointestinal illness • Cases of concomitant HS and Crohn's disease rarely reported
Granuloma inguinale	• Sexually transmitted infection caused by *Klebsiella granulomatis* • Characterised by enlarging red ulcers with bleeding granulation tissue • Ulcers confined to the vulva, penis, scrotum, glans, and inguinal and perianal skin

Table 5. Clinical features of the Hurley clinical staging system

Stage	Features
Stage I (Figure 2)	Abscess formation (single/multiple) without sinus tract development or scarring
Stage II (Figure 3)	Chronic/relapsing abscess formation with sinus tract formation and scarring; Single or multiple widespread lesions
Stage III (Figure 4)	Diffuse involvement, with multiple connected sinus tracts and abscesses across the entire affected area

Management

Hyperhidrosis

CONSERVATIVE management of generalised and focal hyperhidrosis involves identifying and treating any associated underlying cause, frequent use of commercially available antiperspirants and deodorants, and lifestyle modifications, such as more frequent showering, wearing lightweight clothing made from natural fibres, changing socks and other affected clothing regularly, and avoiding relevant triggers such as spicy food and hot environments. [8]

Topical therapy

Antiperspirants

Most antiperspirants contain a low-dose metal salt (generally aluminium), which physically obstructs the opening of the sweat gland on the skin. This obstruction damages the epithelial cells within the sweat duct leading to the formation of occlusive plugs.[17] Antiperspirants containing aluminium chloride hexyhydrate are more effective than agents containing aluminium chloride or aluminium chlorohydrate.[8,18]

A concentration of 10-20% aluminium chloride hexahydrate is appropriate for axillary hyperhidrosis, 25% for palmar and plantar hyperhidrosis and 35% for refractory cases.[2,19]

Treatment with stronger antiperspirants is often limited by skin irritation and burning sensation, particularly in the axilla. To minimise this reaction, antiperspirant should be applied to dry skin at night, when hyperhidrosis is reduced, and washed off in the morning.[20] Skin irritation can be controlled with 1% hydrocortisones.[20]

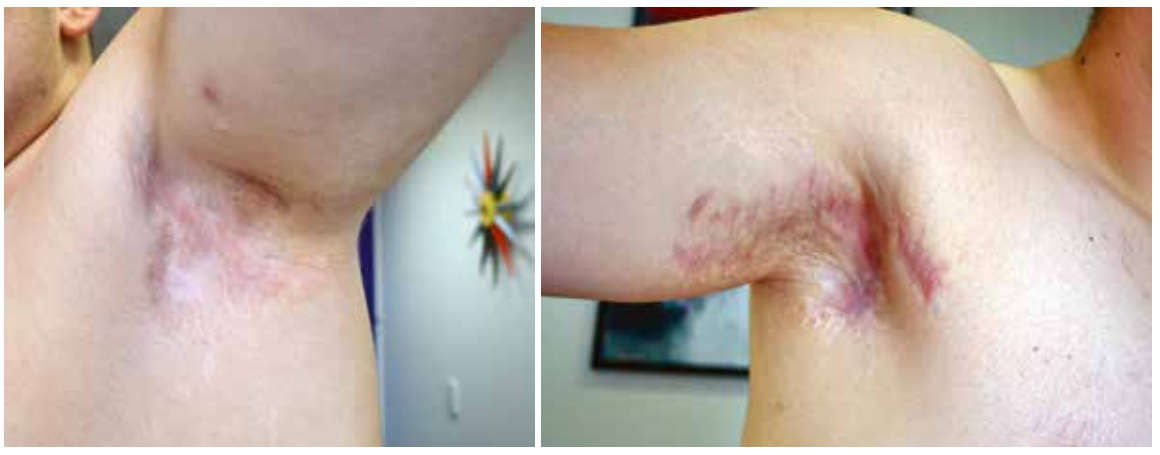

Figure 5. A 19-year-old man with hidradenitis suppuritiva showing left and right axilla nine months post-surgery to excise the axillary sweat glands.

Periodic injection of botulinum toxin A is a safe and effective treatment for focal hyperhidrosis.

Botulinum toxin A

Periodic injection of botulinum toxin A is a safe and effective treatment for focal hyperhidrosis. By blocking the presynaptic release of neuronal acetylcholine from the presynaptic junction of the neuromuscular and autonomic nerves, a single injection of botulinum toxin reduces sweat production for up to 12 months. Several clinical trials support the efficacy of botulinum toxin A in the treatment of axillary hyperhidrosis.[21-24]

Medicare subsidises the use of botulinum toxin A (Botox or Dysport) for severe primary focal axillary hyperhidrosis when administered by a dermatologist.[8] Patients must be aged 12 or over, and failed or are intolerant to topical aluminium chloride hexahydrate for 1-2 months.

Botulinum treatment of the palms and soles are also highly effective but are not subsidised by Medicare. The typical dose of botulinum toxin is 50 IU for each axilla.

Sweating is reduced within 2-4 days, and usually persists for 6-9 months. Limiting factors for botulinum toxin A include pain during injections and non-subsidised cost.

Iontophoresis

Iontophoresis utilises a direct electrical current to deliver polar molecules through intact skin to the sweat glands. Patients place affected hands and/or feet on moistened pads in the iontophoresis unit for 15-20 minutes per session. Tap water is generally utilised in iontophoresis devices available for home use.[26]

Glycopyrronium bromide solution is the most effective liquid medium, however it is only available in specialist centres. Iontophoresis is a safe, efficacious treatment for palmar and plantar hyperhidrosis, alleviating symptoms in 40-85% of cases, depending on the solution used.[25] Iontophoresis is not available in every Australian state.

Reported side effects include dry, cracked hands and feet, erythema and skin irritation, and transient vesiculation.[25] Iontophoresis cannot be used for patients with a pacemaker or implantable device. Patients often trial iontophoresis in specialist skin clinics prior to purchasing a home device.

Microwave thermolysis

Microwave thermolysis utilises microwave energy to destroy eccrine glands and is an emerging therapy for axillary hyperhidrosis.[27-29] Treat-

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ment is generally administered through two 30-minute sessions separated by three months.

A device is available in some Australian specialised skin clinics, however, cost and limited availability preclude many patients from this therapy.

Systemic therapy

The efficacy of anticholinergic medications in focal hyperhidrosis is well established.[30,31] The most commonly prescribed anticholinergic medications in Australia are propantheline bromide and oxybutynin. These are cheap medications that can be used regularly to control hyperhidrosis.

Glycopyrrolate is an effective alternative if not tolerated, although this medication is significantly more expensive.

Anticholinergic side-effects are invariably reported, most commonly dry mouth, blurred vision, headache and urinary retention. Starting oral oxybutynin at a low dose (2.5mg/day) and increasing the dose slowly up to a maximum of 10mg/day reduces the likelihood of experiencing significant anticholinergic side effects. Drowsiness may occur. These agents may aggravate glaucoma. They are contraindicated in myasthenia gravis. There are numerous drug interaction and these agents all need to be used with caution. Specialist referral may be indicated.

Surgical therapy

Surgery is reserved for patients who have failed topical and systemic therapy, and are experiencing serious social, emotional and professional consequences due to hyperhidrosis. Significant cost is a barrier for many patients.

Liposuction or local excision of axillary eccrine and apocrine glands may improve symptoms of axillary hyperhidrosis. Surgical excision is often associated with poor cosmetic outcomes, scarring, restriction of arm movements, and compensatory hyperhidrosis where sweating is paradoxically increased elsewhere on the body.[32] Other complications include bruising, infection, haematoma and dysaesthesia.[33,34] A randomised trial found that botulinum toxin A injection is superior to suction curettage in reducing resting and exercise-induced hyperhidrosis.[33]

Endoscopic thoracic sympathectomy involves cauterising, clipping or cutting the sympathetic chain supplying the upper extremities or cervicofascial region. This surgery is reserved as a last resort for patients with morbidly debilitating disease. While effective for upper limb (including axillary) hyperhidrosis, there is a substantial risk of Horner syndrome, pneumothorax, paraesthesia and bradycardia.[35] Up to 67% of patients will experience compensatory hyperhidrosis following endoscopic thoracic sympathectomy.[36]

Bromhidrosis

It is important to assess the patient's expectations and treatment goals. Conservative management — including routine washing, removal of axillary hair and removal of sweaty clothing — is sufficient for mild cases. However, improvement may be temporary and incomplete.

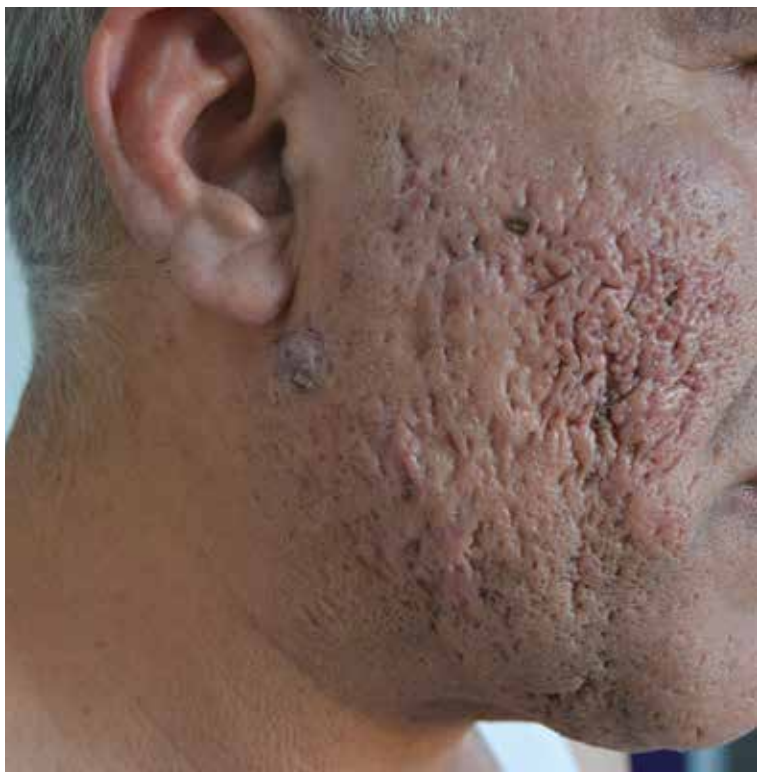

Figure 6. Patient with follicular occlusion tetrad demonstrating acne conglobata with severe acne scarring. Acne conglobata has a similar appearance to severe acne vulgaris, with the additional features of double comedones and dissecting interconnecting subcutaneous abscesses that heal to leave scar bridges.

Microwave thermolysis utilises microwave energy to destroy eccrine glands.

Patients have generally utilised commercially available deodorants and fragrances by the time they present to their GP. These measures remain first-line therapy and their routine use should be encouraged. Deodorants containing antimicrobial metal ions, including calcium phosphate and zeolite antimicrobial ceramics, inhibit axillary bacterial production.[2] Antiseptic soaps and topical antibiotics can be used to reduce the amount of contributory bacteria. In very severe cases, topical or oral metronidazole can be helpful.

For cases where bromhidrosis is associated with excessive sweating, referral to a specialist for treatment of focal hyperhidrosis may be required. Topical aluminium-containing antiperspirants, botulinum toxin A injection and iontophoresis are possible treatment options for bromhidrosis associated with hyperhidrosis.

Hidradenitis suppurativa

The treatment goals of HS are pain relief, specific treatment of individual nodules, prevention of scarring and sinus tract formation, and interventions to reduce the risk of developing further new lesions. Evidence-based European guidelines are currently being developed.[37]

General measures

Lifestyle modifications and general measures to reduce the risk of developing new lesions include:[5,37]

- Education and support: given an increased risk of major depression, all patients should be asked about psychological impact and offered resources for support.[16]
- Hygiene: daily washing of affected areas will improve odour and minimise the risk of secondary infection. Using non-abrasive soap and no abrasive material is essential. Bleach baths may be helpful.
- Non-irritating antiperspirants are recommended: For patients unable to tolerate antiperspirants, botulinum toxin injections are helpful.
- Weight management: excess weight has been associated with HS. Although a causative association has not been established, excess weight is associated with skin occlusion, skin trauma, and hormonal variations.[38]
- Smoking cessation: an association between smoking and HS has been identified in numerous patient populations.[5,38,39] Continuing smoking appears to be a significant factors in patients who fail to achieve remission.
- Diet: dairy and high-glycaemic diets have been implicated in exacerbations of HS.[40,41] Although the effect of dietary modifications has not been evaluated in clinical trials, some dermatologists recommend a low glycaemic diet for patients with HS.
- Avoidance of skin trauma: skin maceration and trauma may perpetuate inflammation, follicular occlusion and rupture. Patients are likely to benefit from wearing loose, light clothing and avoiding excessive heat.[5] Patients must not squeeze or disturb lesions.[5] Shaving and depilatory creams may aggravate hidradenitis suppurativa. Laser hair removal is a generally well-tolerated alternative.

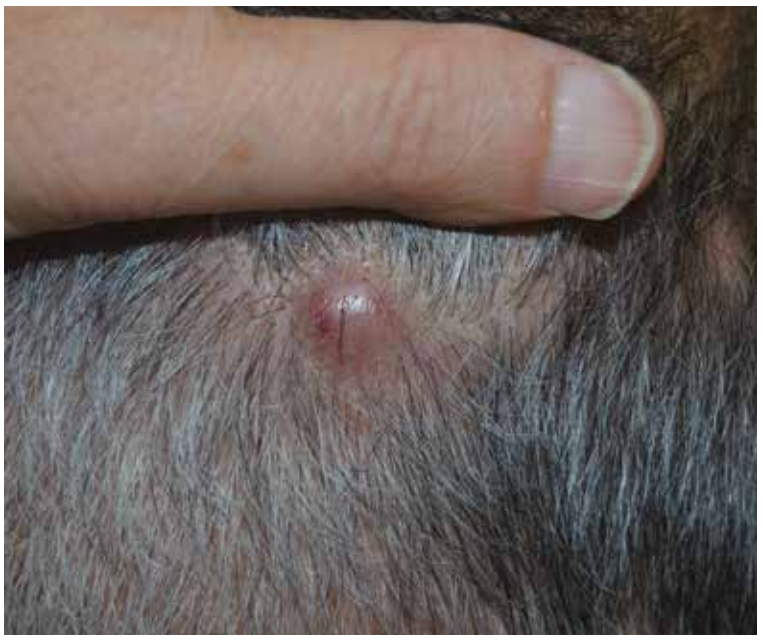

Figure 7. Patient with follicular occlusion tetrad demonstrating dissecting cellulitis of the scalp. Dissecting cellulitis produces dome-shaped nodules of alopecia. These nodules are filled with pus. If untreated these nodules heal with a permanent cicatricial alopecia. Intralesional triamcinolone can lead to partial or total hair regrowth.

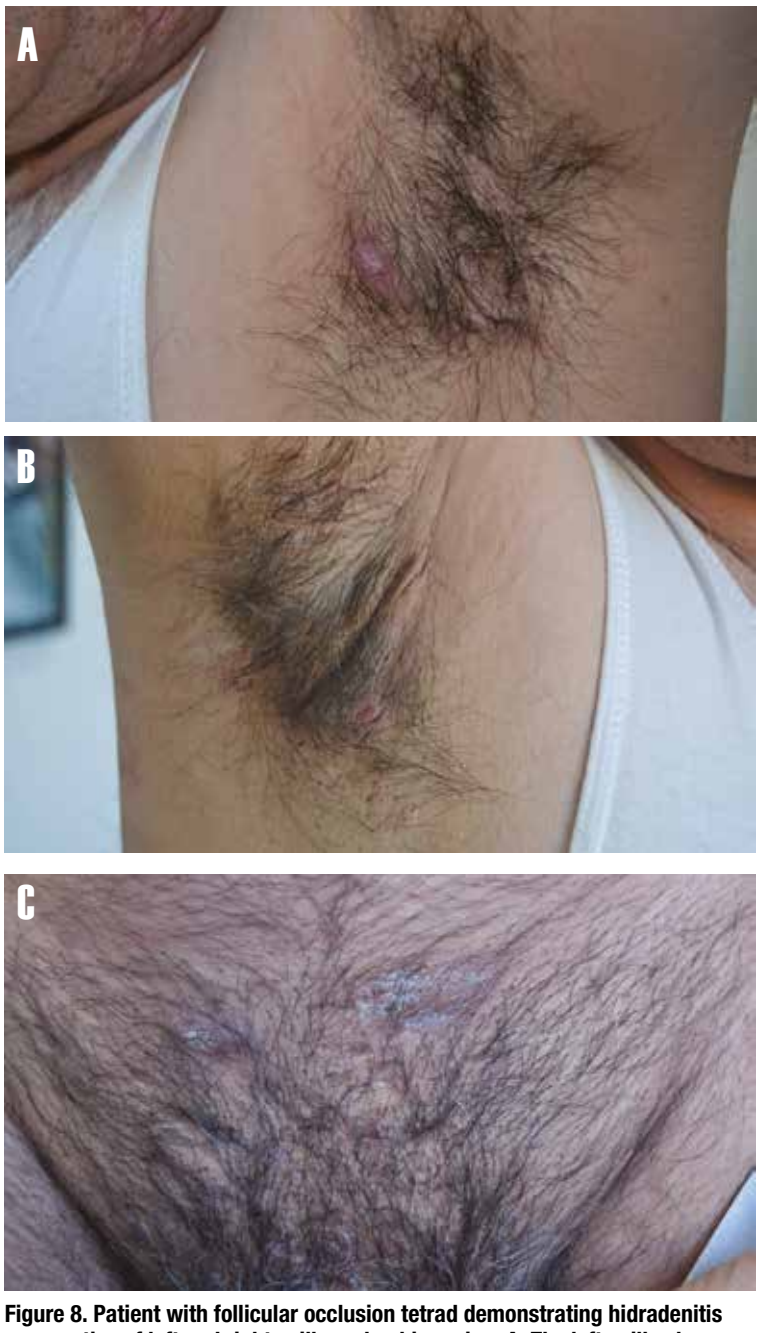

Figure 8. Patient with follicular occlusion tetrad demonstrating hidradenitis suppurativa of left and right axilla and pubic region. A. The left axilla shows thickened scar tissue and sinus tract formation. B. The right axilla show an inflamed nodule and pathognomonic open comedones. C. The pubic region shows multiple inflamed nodules.

Medical and surgical therapy

Treatment is dependent on disease severity, and includes topical therapy, systemic therapy, and surgery. Antibiotics used to treat HS are thought to act both as anti-inflammatory agents, as well as antibacterial agents.

Treatment of mild disease (Hurley stage I) includes topical clindamycin, topical resorcinol, and minor surgery. Patients should be encouraged to bathe using a topical antiseptic or antibacterial soap that is not abrasive to damaged skin.

Clindamycin 1% lotion, applied twice daily to affected areas, is first-line therapy for mild HS. Clindamycin appears to decrease the number of inflammatory nodules and prevent secondary infec-

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tion.[42] Although not confirmed in clinical trials, the short-term use of oral antibiotics, typically doxycycline or minocycline, can alleviate acute flares of mild HS.

Topical resorcinol 15% cream (compounded extemporaneously) is a chemical exfoliant with keratolytic, anti-inflammatory and antiseptic actions.[43] Application of resorcinol cream to new nodules (not the entire region) appears to reduce pain and promote healing of new lesions.[43] Localised desquamation is an expected side effect. However, the availability of resorcinol is limited in Australia.

Given that sinus tract formation is likely due to rupture of the follicular unit, removal of the entire nodule and unit through punch debridement reduces the risk of recurrence and disease progression.[44] Other specialist treatment for mild HS includes intralesional corticosteroid therapy, which may help settle acute flares.

Treatment for moderate disease (Hurley stage II) includes systemic antibiotics, hormonal therapy and surgery. The suggested antibiotic regimen for moderate HS is doxycycline or minocycline 50-100mg twice daily for 3-6 months. Patients with moderate disease should be referred early for further treatment if not responding to systemic antibiotics.

Clindamycin and rifampicin are suggested for patients who fail to respond to tetracyclines.[45,46] These antibiotics are rarely used as initial therapy given the risk of *Clostridium difficile* infection.

Given that androgens contribute to the development of hidradenitis suppurativa, antiandrogen medications can be effective for lesion resolution and prevention of new lesions in a sub-population of affected women.[47,48] A combined oral contraceptive pill containing cyproterone acetate, drospirenone, desogestrel or gestodene is generally used.

Spironolactone 25-50mg daily, increasing up to 100mg daily, is an alternative for women unable to tolerate oral contraceptive medications. All of these agents are contraindicated in pregnancy, which should be excluded prior to initiating therapy. Male patients may respond to either dutasteride or finasteride.

Surgery for moderate hidradenitis suppurativa includes punch debridement of new lesions and debridement of extensive sinuses. Surgery does not arrest the underlying disease process and should accompany medical maintenance treatment.

Treatment for severe and refractory disease (Hurley stage III) requires specialist multidisciplinary care involving dermatologists, plastic surgeons and often psychologists. Medical management includes the addition of TNF-alpha inhibitors, oral retinoids, immunosuppressants and surgery. These agents can be used in addition to the topical and systemic treatments outlined above. Intravenous TNF-alpha inhibitors, notably infliximab, are effective biological agents for severe HS.[49-51]

Early trials have found infliximab superior to adalimumab and etanercept. Availability, cost and significant adverse effects are limitations to biological agents for some patients.

Oral retinoids, including isotretinoin and acitretin benefit only a minority of patients. Retinoids can also aggravate HS in some patients.[52-54] This aggravation may be due to the mechanism of action of isotretinoin, which increases intrafollicular pressure and ruptures the follicular wall. This may trigger an unwanted inflammatory process and worsen the disease.

Immunosuppressants, including prednisolone and cyclosporine, are used to settle acute inflammation. A 3-4-day course of prednisolone 40-60mg daily is usually sufficient to settle acute flares. Cyclosporine can also be used in early disease to prevent new lesions forming. Cyclosporine is less useful in established disease with scarring and sinus tract formation.

Surgery is used in severe HS to remove acute nodules and sinus tracts, and to remove scarred tissue. Surgical procedures considered in severe hidradenitis suppurativa include incision and drainage of lesions, punch debridement of whole follicular units, unroofing of nodules and sinus tracts, and excision of entire affected regions. Surgery is usually combined with general measures and maintenance medical therapy.

Online resources

International Hyperhidrosis Society
www.sweathelp.org

European S1 guideline for the treatment of hidradenitis suppurativa/acne inversa
See: bit.ly/29sfn2L

British Association of Dermatology hyperhidrosis leaflet
See: bit.ly/251vkiu

British Association of Dermatology Hidradenitis Suppurativa leaflet
See: bit.ly/1WlN4le

Prognosis

Hyperhidrosis and bromhidrosis

UNTREATED, focal hyperhidrosis generally develops after puberty and rarely improves. With early diagnosis and initiation of therapy, patients should generally experience significant symptomatic relief.

It is important to assess each patient's goals of treatment. Patients experiencing significant social and professional consequences should be referred to a specialist early to initiate first- and second-line treatments. While carefully considering the adverse effects of each treatment, and the severity and location of the disease, many patients are likely to experience clinical improvement.

Bromhidrosis is generally well managed with an approach including lifestyle modifications, managing excess sweating and the application of fragrances.

Hidradenitis suppurativa

The impact of severe HS on a patient's quality of life can be profound. The average duration of untreated HS is 20 years. The prognosis is improved by early diagnosis, accompanied by lifestyle modifications and intermittent medical treatment. Moderate disease requires specialist intervention and maintenance treatment. Severe HS is very difficult to treat and requires intensive medical and surgical treatment.

Emerging treatments

Hyperhidrosis

THERE have been reports that clonidine, an alpha-2 adrenergic agonist that diminishes the sympathetic outflow, is effective in reducing hyperhidrosis.[55,56] Some studies have suggested that patients experiencing emotional hyperhidrosis may benefit from beta blocker or benzodiazepine therapy.[57,58] However, these should not be considered as part of routine management of hyperhidrosis.

Other treatments with limited data include topical botulinum, laser therapy and ultrasound therapy.[59-61]

Bromhidrosis

A number of studies have suggested that non-invasive treatment of bromhidrosis with laser therapy is effective in reducing axillary bromhidrosis.[62-64] The data available for these therapies is limited and require further investigation.

Hidradenitis suppurativa

Based on current case reports, numerous emerging therapies may benefit patients with severe HS. A number of patients have experienced improvement following subcutaneous injections of the interleukin inhibitors ustekinumab or anakinra.[65-67]

Other emerging adjuvants therapies for severe or refractory HS include metformin, zinc supplementation, hair removal laser therapy, botulinum toxin, vitamin D3 and external beam radiation. The evidence for these therapies is limited and should not be included in routine management regimens.

Case studies

Case study one

ANDREW, 26, presents to his GP complaining of excessive sweating during the day. He reports that he has a supply of shirts at work for when he invariably saturates the underarms of his clothing.

He is unable to wear light-coloured shirts and describes feeling increasingly self-conscious. His work colleagues make light-hearted comments, which compound his poor personal image. He also reports problems dating, given that he is constantly preoccupied by the thought that he will saturate his shirt.

He describes a symmetrical pattern of hyperhidrosis affecting both axillae. The excessive sweating began during his teenage years and occurs multiple times per week. Andrew is surprised he never needs

to change his bedclothes because of excessive sweating.

Andrew has already trialled 'Driclor', an antiperspirant containing 20% aluminium chloride. He reports difficulty using the antiperspirant because of stinging and was dissatisfied with the effect. He is using the aluminium antiperspirant in the mornings as a normal deodorant. Andrew is happy to trial 'Driclor' again, applying the antiperspirant to dry skin at night and washing the area in the morning. These measures, along with a 1% hydrocortisone ointment, minimise skin irritation. However, after two months of treatment, he is unhappy with the degree of improvement.

Andrew is referred to a dermatologist, where further treatment options are discussed. He is concerned about the possible side effects of anticholinergic medications. Given the substantial time and effort required to undergo iontophoresis, he elects to trial botulinum toxin A injections. Following a 50 IU dose into each axilla, there is a significant reduction in the rate of sweat production.

He returns to the dermatologist six months later for repeat injections. Apart from mild pain at the injection sites during the procedures, Andrew tolerates treatment well and reports a significant improvement in his quality of life.

Case study two

Lisa, 34, presents to her GP with recurrent boils in her left axilla and inner thighs. The nodules are exquisitely painful, malodourous and ooze into her clothing. She is highly embarrassed of the condition, becoming socially isolated. She has been unable to become intimate with a recent partner, who became frustrated and ended the relationship. Lisa has presented repeatedly to another GP,

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who has treated her for folliculitis and boils.

The flares started with a single, painful lesion in her inner thigh that affected her ability to walk long distances. She was given a course of oral cephalexin, which did not settle the lesion. She noticed a number of other lesions developing in the inner thigh and in her right axilla. The lesions tended to regress spontaneously within approximately two weeks.

She describes her worst flare consisting of eight painful lesions. An abscess on her inner thigh was incised and drained by her GP, with a significant improvement in her pain. Lisa also has polycystic ovarian syndrome, has smoked one pack of cigarettes each day since adolescence and has a BMI of 31.

On examination during her worst flare, the GP counts 13 painful, deep-seated lesions in the left axilla and inner thighs. The lesions are widely separated and are accompanied by intercommunicating sinuses releasing malodourous bloody discharge. There is extensive scarring in the inner thigh. A diagnosis of hidradenitis suppurativa Hurley Stage II is made.

Lisa is encouraged to bathe regularly using a non-soap cleanser, cease smoking, modify her diet and avoid skin trauma. It is imperative that she does not squeeze or manipulate the lesions in any way. Topical 1% clindamycin cream is applied twice daily for three months.

A course of oral doxycycline 100mg daily is prescribed and, as she has no contraindications and is not currently planning to become pregnant, a combined oral contraceptive pill containing cyproterone acetate is commenced.

Given there have been worsening acute attacks, Lisa is referred to a specialist dermatologist. Punch debridement is performed to remove recurring lesions and the offending follicular units. With aggressive medical management and minor surgical management, she experiences significant clinical improvement within three months.

Lisa follows up routinely with the GP and dermatologist to monitor recurrence, and encourage ongoing lifestyle modifications.

Summary

HYPERHIDROSIS, bromhidrosis and hidradenitis suppurativa are conditions that cause major distress and have significant deleterious effects on quality of life. Accurate diagnosis and early referral of patients with debilitating disease may minimise the effects these conditions have on personal and professional functioning.

Key points

- Accurate clinical evaluation of hyperhidrosis will help differentiate primary focal hyperhidrosis from generalised hyperhidrosis, which is likely secondary to medications or a systemic illness. The history should include questions about the consequences of hyperhidrosis on a patient's life.
- Patients with significant hyperhidrosis unresponsive to aluminium-based antiperspirants should be referred early to a specialist for further treatment, including topical, systemic and surgical therapies. The selection of each treatment follows careful consideration of their specific adverse effects.
- Bromhidrosis can have substantial, negative consequences in social and professional settings. A clinical diagnosis is generally sufficient. Treatment consists of reducing the volume of sweating, optimisation of hygiene and application of fragrances to mask body odour.
- Hidradenitis suppurativa is a chronic follicular occlusive disorder that is characterised by recurrent nodules, sinus tracts and keloid scarring. It is not a primary disorder of apocrine glands as previously thought. It classically affects the intertriginous axillary, groin, perianal, perineal and mammary skin. The severe pain, odour, discharge and permanent scarring greatly impacts quality of life and psychological wellbeing.
- All patients with HS should be encouraged to undertake general measures and lifestyle modifications to prevent developing new lesions, particularly smoking cessation and dietary modification. Treatment thereafter depends on the clinical stage, with topical, systemic and surgical therapies available. Early referral to a dermatologist will help prevent disease progression.
- Patients with moderate to severe HS are at high risk of developing major depression. Resources for psychological support are beneficial for patients whose quality of life is negatively affected.
- Treatments for HS to consider prior to dermatology referral include topical antibiotics, oral antibiotics and hormonal therapy. Severe disease may require immunological therapy or extensive surgical treatment.

How to Treat Quiz

Hyperhidrosis and other sweat gland disorders — 12 August 2016

INSTRUCTIONS

Complete this quiz online and fill in the GP evaluation form to earn 2 CPD or PDP points.
We no longer accept quizzes by post or fax.

The mark required to obtain points is 80%. Please note that some questions have more than one correct answer.

GO ONLINE TO COMPLETE THE QUIZ

www.australiandoctor.com.au/education/how-to-treat

1. Which TWO statements regarding disorders of sweating are correct?
a) Sweat gland disorders have the potential to be deeply distressing conditions.
b) Sweat disorders, even when severe, are not associated with any impaired functionality of quality of life.
c) Bromhidrosis refers to offensive body odour.
d) Sudiferous (sweat) glands are divided into eccrine (underarm, breast, groin) and apocrine (entire body) glands.

2. Which THREE statements regarding hyperhidrosis are correct?
a) Hyperhidrosis is defined as the production of sweat in amounts greater than physiologically required.
b) Hyperhidrosis can rarely be a sign of significant underlying pathology, particularly when generalised.
c) More often it is a chronic, primary, idiopathic problem.
d) Idiopathic, primary focal hyperhidrosis occurs most commonly in the groin and buttock cleft.

3. Which TWO statements are correct regarding the clinical features of hyperhidrosis?
a) Three types of sweat glands have been described, eccrine, apocrine and apoeccrine glands
b) Eccrine sweat glands are innervated by the sympathetic nervous system.
c) Apoeccrine gland overactivity is implicated in the palmar and plantar hyperhidrosis, while overactive eccrine glands cause axillary hyperhidrosis
d) Gustatory sweating may be stimulated by either thermal or emotional stimuli.

4. Which THREE statements are correct regarding the clinical features of hyperhidrosis?
a) Emotional sweating is commonly experienced during sleep.
b) In primary hyperhidrosis, sweat glands appear histologically normal, and it is believed that the cause of emotional hyperhidrosis is an inappropriate or exaggerated central response to emotional stress.
c) Generalised hyperhidrosis affects the entire body, and the most common cause is excessive heat.
d) Primary focal hyperhidrosis is commonly reported in healthy adults younger than 25, with two-thirds of patients reporting a positive family history.

5. Which TWO statements regarding bromhidrosis are correct?
a) Eccrine glands are responsible for pheromonal odours.
b) Apocrine bromhidrosis is the most prevalent form, occurring exclusively after puberty and producing the distinctive axillary odour reported by many patients.
c) Eccrine bromhidrosis is most common on the soles and the odour can linger in footwear and gym clothing.
d) The diagnosis of bromhidrosis is made by identifying the offending organism on culture, which then guides treatment.

6. Which THREE statements regarding hidradenitis suppurativa are correct?
a) Risk factors include high BMI, smoking, diet and hormonal factors.
b) Mechanical stress on the skin, or skin friction is a factor in localising HS to certain body sites.
c) HS is more common in men.
d) Follicular occlusion with secondary follicular rupture and localised inflammation are the primary events.

7. Which TWO statements regarding hidradenitis suppurativa are correct?
a) The hallmark of early HS is acute painful, tender nodules in the axilla or groin.
b) HS begins in intertriginous regions, most commonly the groin.
c) The finding of nodules in the axilla or groin is pathognomonic for HS.
d) The presence of chronic or relapsing inflammatory nodules, sinus tracts and scarring in intertriginous areas confirm the diagnosis of HS.

8. Which THREE are differential diagnoses of hidradenitis suppurativa?
a) Follicular pyodermas
b) Granuloma inguinale
c) Nummular eczema
d) Crohn's disease

9. Which TWO statements regarding the management of hyperhidrosis are correct?
a) Botulinum toxin A is still in the experimental stages and not recommended for the treatment of hyperhidrosis.
b) Conservative management of generalised and focal hyperhidrosis involves identifying and avoiding relevant triggers such as spicy food and hot environments.
c) Anticholinergic medications are cheap, effective and safe, and are regarded as first line treatment for hyperhidrosis.
d) Surgery is reserved for patients who have failed topical and systemic therapy and are experiencing serious social, emotional and professional consequences due to hyperhidrosis.

10. Which THREE statements regarding the management of hidradenitis suppurativa are correct?
a) The goals of treatment of HS are pain relief, specific treatment of individual nodules, prevention of scarring and sinus tract formation and interventions to reduce the risk of developing further new lesions.
b) Mild disease (Hurley stage I) requires only lifestyle measures, such as weight loss and smoking cessation, as treatment.
c) Treatment for moderate disease (Hurley stage II) includes systemic antibiotics, hormonal therapy and surgery.
d) Treatment for severe and refractory disease (Hurley stage III) requires specialist multidisciplinary care involving dermatologists, plastic surgeons and often psychologists and psychiatrists.

CPD QUIZ UPDATE

The RACGP requires that a brief GP evaluation form be completed with every quiz to obtain category 2 CPD or PDP points for the 2014-16 triennium. You can complete this online along with the quiz at **www.australiandoctor.com.au.** Because this is a requirement, we are no longer able to accept the quiz by post or fax. However, we have included the quiz questions here for those who like to prepare the answers before completing the quiz online.

Australian Doctor Education

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NEXT WEEK

Next week's How to Treat discusses coeliac disease, one of the most common chronic autoimmune diseases. This condition is commonly overlooked, leading to significant morbidity and mortality, reduced quality of life and increased healthcare use. The author is **Dr Jason Tye-Din**, consultant gastroenterologist, Royal Melbourne Hospital, and laboratory head, at the Walter and Eliza Hall Institute, Melbourne, Victoria.