Sweating and hyperhidrosis

Pharmacists should be prepared both to give general advice on sweating and on treatment options for hyperhidrosis. In this article, Christine Clark looks at these sometimes embarrassing problems

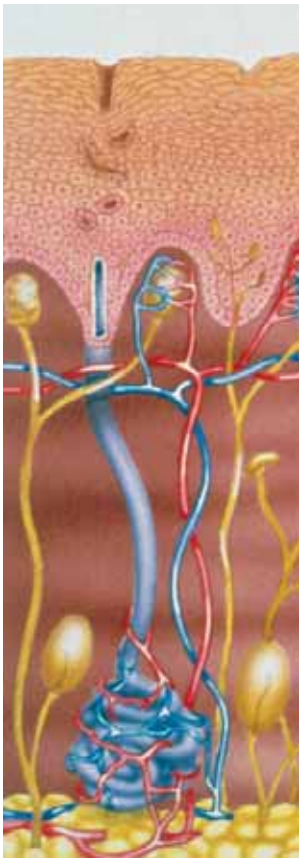
Sweating is essential for temperature regulation. In humans, body temperature is maintained at about 37C by the thermoregulatory centre in the hypothalamus. This receives input from two sets of thermoreceptors; receptors in the hypothalamus itself monitor the core temperature as blood passes through the brain and skin receptors monitor external temperature. Both measures are needed so that the body can make appropriate adjustments. The thermoregulatory centre sends impulses to several effectors to adjust body temperature, for example, by increasing peripheral vasodilation and sweating to lose heat. Sweating can also occur as a response to other triggers, including:

- Anxiety
- Intense concentration
- Spicy foods (capsaicin in chillies is thought to activate the same sensory receptors as heat)

Sweat glands are coiled, tube-like structures in the dermis. There are two main types: eccrine and apocrine. About 2.5 million eccrine sweat ducts open on to the skin surface. These are more numerous on the palms, soles, axillae and forehead than elsewhere on the body. In these areas, the glands are under both psychological and thermal control whereas elsewhere on the body they are under thermal control only.

Eccrine sweat glands are innervated by sympathetic cholinergic fibres. This makes eccrine gland sympathetic innervation unique, because noradrenaline is generally the neurotransmitter in sympathetic nerves. When first formed, eccrine sweat is an isotonic mixture of water, sodium, potassium, urea, amino acids, enzymes, organic compounds and heavy metals. As it passes through the eccrine duct, sodium, chloride and bicarbonate are actively (but incompletely) reabsorbed so that the solution that reaches the skin surface is hypotonic. This mechanism is believed to be important for conservation of electrolytes when sweating is heavy.

Apocrine sweat glands are larger than eccrine sweat glands and they open into hair follicles, rather than on to the skin surface. Apocrine sweat glands are predominantly found in the axillae and the anogenital region. Apocrine glands appear to be vestigial scent glands. Apocrine sweat is much more viscous than that from eccrine glands and is produced in smaller volumes. The sweat is odourless when secreted but develops an odour after coming into contact with skin bacteria. Apocrine glands are inactive until puberty and they are under sympathetic (adrenergic) control.



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Eccrine sweat ducts are most numerous on the palms, soles, axillae and forehead

There are about 2.5 million eccrine sweat ducts opening on the skin surface

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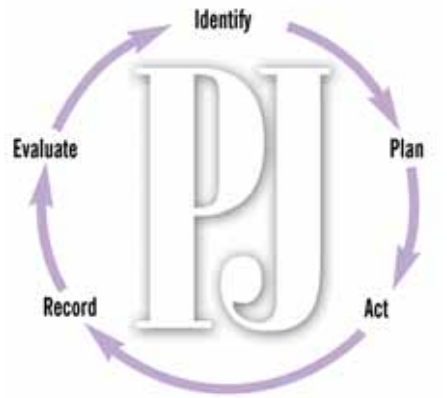


Identify knowledge gaps

1. What are the treatment options for hyperhidrosis?
2. How should aluminium salts for hyperhidrosis be applied?
3. Is there a link between antiperspirants, deodorants and breast cancer?

Before reading on, think about how this article may help you to do your job better. The Royal Pharmaceutical Society's areas of competence for pharmacists are listed in "Plan and record", (available at: www.rpsgb.org/education). This article relates to "common disease states".

At puberty, a third type of gland,the apoeccrine gland, appears. These are hybrid sweat glands found in the armpits and may play a role in axillary hyperhidrosis (see below). Similar to eccrine glands, they respond mainly to cholinergic stimuli, and their ducts are long and open directly on to the skin surface. Apoeccrine glands secrete nearly 10 times as much sweat as eccrine glands.

Composition of sweat

Sweat delivered to the skin surface contains about 0.2–1.0 per cent solutes (low concentrations of sodium and chloride and relatively high concentrations of potassium, lactate, urea, ammonia and amino acids and has a pH of 4.0–6.8. The daily water loss in sweat is variable — from 100 to 8,000ml/day. This is almost entirely eccrine sweat.

The maximum rate of sweating is up to 50 ml/minute in an acclimatised adult. This rate cannot be sustained but losses of up to 25 per cent of total body water are possible under severe stress and this can be fatal.

Antiperspirants

Antiperspirants suppress sweating. Aluminum salt solutions are the most common antiperspirants in use. Aluminum chloride hexahydrate is among the most effective antiper-

spirants currently available. It is an astringent but its mechanism of action as an antiperspirant is believed to be either mechanical obstruction of the eccrine gland sweat pore or induction of atrophy of the secretory cells. Skin irritation, due to the active ingredient or to other components (eg, perfumes and preservatives), is a common problem. The skin in the armpit is thin and relatively sensitive. Moreover, products applied to this area are trapped there by virtue of the anatomy.

Deodorants Deodorants do not prevent sweating but either mask body odour or reduce the commensal bacterial population. Aluminium or zinc-containing deodorants have antibacterial actions — alum has been used for many years for water purification. For example, "natural, crystal" deodorants are usually potassium alum (aluminium potassium sulphate) or ammonium alum (ammonium aluminium sulphate) crystals. Crystal deodorants are moistened and rubbed over the skin. Other products that have been recommended as deodorants include vinegar, bicarbonate of soda and isopropyl (rubbing) alcohol. Natural deodorants contain strongly perfumed natural oils such as sage and lemongrass.

Body odour (bromhidrosis) is a chronic condition in which excessive odour, usually an unpleasant one, arises from the skin. This is caused mainly by bacterial decomposition of apocrine gland secretions to give ammonia and short-chain fatty acids, which have characteristic strong odours. Feet can also produce odour. Often this is associated with footwear that makes feet sweat excessively and provides a breeding ground for bacteria and fungi. The smell of body odour can be influenced by diet. Some foods, such as onions, fish and garlic, can cause the sweat to smell more strongly.

Body odour can be managed by regular washing using antibacterials, wearing clean clothing, washing clothing at high temperatures and avoiding, as far as possible, occlusive footwear and clothes made of synthetic fibres. As in so many fields, prevention is better than cure. Deodorants, however, can be used.

Panel 1 discusses the possible association between antiperspirants and deodorants with breast cancer given recent coverage in newspapers and on the internet.

Hyperhidrosis can be an embarrassing condition

Hyperhidrosis

About 1 per cent of the population suffers from hyperhidrosis (excessive sweating). This condition appears to serve no physiological purpose and can be socially and psychologically disabling. Hyperhidrosis can be generalised or focal. Generalised hyperhidrosis, in which sweating occurs over the whole body, has many causes, including diabetes, chronic infectious diseases and malignancy. People who complain of generalised hyperhidrosis should have organic causes rules out. Panel 2 lists some causes of abnormal sweating.

Focal hyperhidrosis (excessive sweating of one body part) is more likely to be idiopathic, although it can occur as a result of spinal cord injury and some polyneuropathies. The palms or soles of the feet (palmoplantar hyperhidrosis) are affected in about 60 per cent of patients and the axillae are affected in 30 to 40 per cent of patients. Facial sweating is less frequent and affects up to 10 per cent of patients with idiopathic hyperhidrosis.

Hyperhidrosis is more than just being a bit hot and sweaty in response to normal stimuli; people with focal hyperhidrosis describe profuse sweating to the point where cold sweat drips off their hands or face, soaking clothing, smudging documents and (when hands are affected) making it difficult to grip implements, such as cutlery and pens. It is not usually associated with excessive body odour, but the wetness is embarrassing. In addition, the affected skin can become macerated and prone to infection as a result of being constantly wet. There is also an increased risk of developing eczema on the affected skin.

Treatment General measures to reduce the problems of excessive sweating should always be considered before embarking on active treatment (see Panel 3, p760, for advice that pharmacists can give). Treatment for hyperhidrosis should start with topical antiperspirants. If this fails, people with hyperhidrosis should be referred to a dermatologist in order to find the most suitable treatment. Iontophoresis or botulinum toxin may be suitable, depending on the area(s) affected (see below). Only as a last resort should surgery be considered.

Signposting patients to appropriate support groups and other sources of information is also helpful. Many people with hyperhidrosis feel isolated and a listening ear, coupled

Panel 1: Breast cancer?

Although there is no conclusive research linking the use of underarm antiperspirants or deodorants and breast cancer, scare stories continue to appear on the internet and in newspapers. One popular hypothesis is that sweating enables the body to rid itself of unnamed toxins and that antiperspirants prevent this. The toxins accumulate in the armpits and their proximity to the breasts led to the suggestion that antiperspirants could cause breast cancer. Another hypothesis is that antiperspirants contain toxic materials that could reach the breast tissue through the skin, especially if the axillary skin is damaged by shaving. Both hypotheses make numerous assumptions.

In 2002, a case control study involving 1,600 women (about 800 with breast cancer and about 800 controls) examined the use of razors and underarm antiperspirants or deodorants in the two groups.[1] The results did not show any increased risk for breast cancer in women who reported using underarm antiperspirants or deodorants. The results also showed no increased breast cancer risk for women who reported shaving their armpits and applying an underarm antiperspirant or deodorant, or for women who used an underarm antiperspirant or deodorant within one hour of shaving.

In 2003, a different study showed that the age of breast cancer diagnosis was significantly lower in women who used underarm antiperspirants or deodorants and shaved their underarms more frequently.[2] Although these results suggest that underarm shaving with the use of antiperspirants or deodorants might be related to breast cancer, they do not demonstrate a causal link.

In 2004, a study showed that 18 out of 20 samples of tissue from breast tumours contained parabens.[3] Parabens (hydroxybenzoates) have been shown to mimic oestrogen activity and they are widely used in pharmaceuticals and cosmetics (as preservatives), including in some antiperspirants and deodorants. This led to the hypothesis that parabens derived from antiperspirants or deodorants might accumulate in breast tissue and contribute to the development of cancer. Although the 2004 study supports this hypothesis, it is important to note that the study did not examine healthy breast tissue or other tissues, nor did it establish that the source of the parabens was antiperspirants or deodorants.

with helpful contacts, can make a difference.

Formaldehyde, glutaraldehyde and tannic acid denature proteins in the skin lining the sweat pore, causing temporary plugging of the pore, but are no longer used to treat hyperhidrosis. Formaldehyde induces contact sensitivity and glutaraldehyde and tannic acid cause skin discolouration.

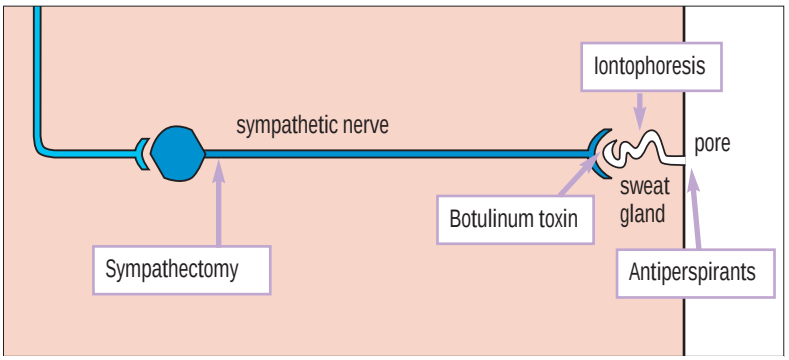
Antiperspirants Aluminium chloride hexahydrate 20 per cent (a higher concentration than for cosmetic antiperspirants) is available as a roll-on application. It should be applied to the hyperhidrotic area at night, when the sweat glands are inactive. The theory is that the sweat ducts are plugged and the effects will last for the next few days. It is important that the skin is dry otherwise there is a high risk of irritation (hydrochloric acid may form) and any residue should be washed off in the morning, to reduce the possibility of irritation. Initially, aluminium products need to be used every 24–48 hours but it should be possible to reduce the frequency of application to every one to three weeks as the condition improves. If used in the armpits, patients must be reminded not to shave the area for 24 hours before or after applying the antiperspirant. Common side effects include dryness, irritation and fissuring of the skin.

Contact with the eyes and mucous membranes must be avoided and for this reason aluminium products are not recommended for use on the hands — it is difficult to avoid touching the face during sleep. Aluminium antiperspirants are not recommended for hyperhidrosis affecting the face.

A dusting powder of aluminium dihydroxyallantoinate (Aldioxa) is also available.

Anticholinergics Systemic antimuscarinic agents can be used to block the cholinergic drive to the sweat glands. They are not licensed for this indication but they may be the only option available for hyperhidrosis affecting the face or groin. The main problem is that they are non-selective and typical anticholinergic side effects, including blurred vision, urinary retention and constipation, are common. Oxybutinin, glycopyrronium bromide and propantheline bromide have all been used for this purpose. Glycopyrronium bromide is often recommended because it does not cross the blood-brain barrier. A starting dose for propantheline bromide of 15mg three times a day has been suggested.

Topical anticholinergics are said to be poorly absorbed, unless used for iontophoresis (see below) and are not generally used. A topical anticholinergic powder (diphemanil methylsulfate 20mg/g) is available in Australia and New Zealand.



Target sites of treatments for hyperhidrosis

Treatment for hyperhidrosis should start with topical antiperspirants

Iontophoresis Iontophoresis involves the topical introduction of ionised medicines into the skin using direct current. In hyperhidrosis, iontophoresis is generally used for palmar-plantar problems and can relieve symptoms in 85 per cent of affected patients. The hands or feet are placed in shallow baths which are filled with water and a small, direct electronic current (~15mA) is passed through the skin. The procedure usually causes no more than a pins-and-needles sensation. The usual treatment time is 20 minutes. Tap water alone is

Panel 2: Causes of abnormal or excessive sweating

Anxiety	Generalised anxiety disorder often causes excessive sweating.
Cardiovascular disease	Sweating is a common symptom of heart failure, probably due to increased sympathetic activity. Sweating often occurs with myocardial ischaemia.
Drugs	Drugs reported to cause sweating include aspirin, paracetamol, anti-emetics, insulin, morphine, fluoxetine and amphetamines. Alcohol or narcotic withdrawal can also cause sweating.
Endocrine disorders (eg, hyperthyroidism, diabetes mellitus*, menopause, acromegaly and phaeochromocytoma)	In hyperthyroidism, excessive sweating is due to an increase in body metabolism and an increase in sensitivity to circulating adrenaline. In diabetes mellitus, sweating can occur during an episode of hypoglycaemia. Autonomic neuropathy can cause sweating (postprandial sweating, especially affecting the face and neck area is typical). Hot flushes and drenching sweating are usually attributed to oestrogen deficiency during the menopause. Excessive sweating is a common presenting feature of acromegaly, and is probably due to an increase in body metabolism. In phaeochromocytoma, the sudden release of catecholamines result in paroxysmal sweating, palpitations and headaches.
Infection (eg, malaria)	Brucellosis and tuberculosis can cause nocturnal sweating.
Injury*	Spinal cord or hypothalamic lesions can cause hyperhidrosis
Malignancies (eg, Hodgkin's disease intrathoracic malignancy or carcinoid tumour)	Hodgkin's disease often presents with nocturnal sweating. Mesothelioma can cause ipsilateral hyperhidrosis, due to an increase in sympathetic activity from pressure on the thoracic sympathetic trunk or postganglionic fibres.
Respiratory failure	Sweating is a common feature, probably due to increased sympathetic activity.

Adapted Prodigy guidelines

*Injury to the sympathetic trunk or diabetic neuropathy can lead to an area of the body in which sweating is absent and heat can trigger a compensatory hyperhidrosis in another part of the body.

Panel 3: General advice pharmacists can give

- Avoid sweating triggers, such as heat or spicy food.

For armpit sweating:

- Try to use antiperspirants regularly.
- Avoid clothes that more easily show up sweat marks. For example, as a rule, white and black clothes are less noticeable when wet than other colours — although dark clothes show white ("tide") marks from dried sweat.
- Wear loose clothing under the armpits, and preferably not made with man-made fibres such as nylon and polyester.
- Consider using dress shields (armpit shields) to absorb excess sweat and protect delicate or expensive clothing. Dress shields can be obtained via the internet or the Hyperhidrosis Support Group (UK)
- If you find that armpit skin is easily irritated, avoid further irritation caused by soap. Instead, use a soap substitute or emollient wash product.

For excessive feet sweating, it can help to:

- Change socks at least twice daily.
- Use an absorbent foot powder twice daily.
- Wear a different pair of shoes on alternate days, to allow them to dry fully.
- Avoid sport shoes or boots, because these are likely to have an occlusive effect.

Adapted from list on Prodigy PIL

usually used, but sometimes anticholinergic agents are added. Iontophoresis may work by plugging the sweat ducts or by inducing an electrical change in the sweat gland that disrupts secretion.

There are few side effects; the treated area may become too dry or cracked. Reducing the frequency of treatments and applying emollients usually alleviates this. Rarely, redness and small blisters develop, and this can be treated with topical corticosteroids. If these adverse reactions occur, the voltage should be decreased for subsequent sessions. Patients sometimes experience tingling and mild discomfort, especially when therapy is initiated. The greatest drawback of iontophoresis is the time required to perform the treatments. Most people need six or seven treatments over three to four weeks initially. After this, treatment may be needed less frequently. Treatments can be given in hospital but it is also possible to purchase equipment for home use, at a cost of about £280.

Iontophoresis should not be given to anyone who is pregnant, or has a metal implant or a pacemaker.

Botulinum A toxin Botulinum A toxin (BTX-A) acts by temporarily blocking the release of acetylcholine from cholinergic sudomotor (sweat driving) fibres. BTX-A is authorised for use in axillary hyperhidrosis. A single treatment involves 10 to 15 intradermal injections of BTX-A into each axilla. In one large double-blind randomised control trial, 82 per cent of the treatment group achieved a reduction in axillary sweating of 50 per cent or more compared with 21 per cent of the placebo group, at 16 weeks.[4] The effects can last from four to eight months and the treatment can be repeated.

BTX-A treatment is too painful to be used on the hands or feet and, if necessary, it is done under nerve block or general anaesthetic. BTX-A treatment is offered by some hospitals but there is often a long waiting list. Private treatment is also available and the usual cost per treatment is about £400.

Surgery Surgical options are usually only considered if other treatment options have failed. Surgery needs to be considered carefully and patients need to be aware of the potential risks. There are two main types of surgery: local axillary surgery or endoscopic (trans) thoracic sympathectomy (ETS). Local axillary surgery aims to remove or destroy as many eccrine sweat glands in the axillae as possible. Procedures include complete excision of the sweating area and removal of the subcutaneous tissue without removing the skin. The main problems include unsightly scarring, wound contractures, poor wound healing and restriction of arm movement.

ETS involves cutting the sympathetic chain to abolish sweating. It is usually carried out endoscopically via the transthoracic route. This is a major surgical procedure that requires the partial collapse of one lung. The main problem is compensatory hyperhidrosis in a different area of the body such as the chest, back, thighs or groin. Many patients say that this is worse than the original hyperhidrosis and so it is worth remembering that ETS is not reversible. A support group for patients in this predicament has been established (see below). Other problems include risks associated with the procedure itself, such as pneumothorax (1–5 per cent), brachial plexus injuries, post-operative neuralgia, and recurrent laryngeal nerve palsy. ETS can be used for hyperhidrosis affecting the hands but is generally not used for hyperhidrosis of the feet because interruption the lumbar sympathetic chain can cause sexual dysfunction.

Action: practice points

Reading is only one way to undertake CPD and the Society will expect to see various approaches in a pharmacist's CPD portfolio.

1. Discuss with a colleague how you would respond to a customer asking for an "antiperspirant that doesn't cause cancer".
2. Be aware of which deodorants and antiperspirants are parabens free.
3. Look up the contraindications and side effects for botulinum A toxin in the British National Formulary.

Evaluate

For your work to be presented as CPD, you need to evaluate your reading and any other activities. Answer the following questions:
What have you learnt?
How has it added value to your practice? (Have you applied this learning or had any feedback?) What will you do now and how will this be achieved?

References

1. Mirick DK, Davis S, Thomas DB. Antiperspirant use and the risk of breast cancer. Journal of the National Cancer Institute 2002;94:1578–80.
2. McGrath KG. An earlier age of breast cancer diagnosis related to more frequent use of antiperspirants/deodorants and underarm shaving. European Journal of Cancer Prevention 2003;12:479–85.
3. Darbre PD, Aljarrah A, Miller WR, Coldham NG, Sauer MJ, Pope GS. Concentrations of parabens in human breast tumours. Journal of Applied Toxicology 2004;24:5–13.
4. Naumann M, Lowe NJ. Botulinum toxin type A in treatment of bilateral primary axillary hyperhidrosis: randomised, parallel groups, double blind, placebo controlled trial. BMJ 2001; 323:596.

Resources

- Hyperhidrosis Support Group (UK), www.hyperhidrosisuk.org/faqs.htm e-mail: info@hyphidrosisuk.org
- The Radisson Group, founded by British and Irish sympathectomy patients who are suffering the side effects of endoscopic transthoracic sympathectomy. www.noetsuk.com
- ESFB channel — a website based in Canada dealing with excessive sweating and facial blushing. Has stimulated establishment of local groups worldwide. www.esfbchannel.com.
- Prodigy guidelines — hyperhidrosis. www.prodigy.nhs.uk
- Embarrassing Problems. www.embarrassingproblems.co.uk