Non-prescription Medicines

Second edition

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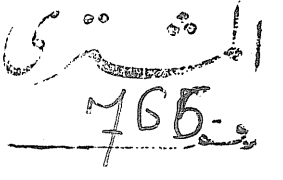

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To my wife and family

Alan Nathan

Since qualifying in 1964 Alan Nathan has spent most of his career as a community pharmacist, and was an independent proprietor for 14 years. In 1989 he was appointed Boots Teacher/Practitioner in the Department of Pharmacy, King's College London, and became a full-time lecturer in community pharmacy in 1994. Alan Nathan has been a member of the Council of the Royal Pharmaceutical Society since 1986.

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Introduction

THE IMPORTANCE OF NON-PRESCRIPTION MEDICINES

In the preface to the first edition of this book in 1998 it was indicated that non-prescription medicines were becoming increasingly important within the overall scheme of healthcare in the United Kingdom. Since then there have been several developments, mainly as a result of the implementation of government health policies, which have increased their importance and are likely to carry on doing so for the foreseeable future. These include the following:

- For some years now general practitioners (GPs) have been increasingly recommending to patients who are not exempt from paying National Health Service (NHS) charges for prescriptions that they buy for themselves non-prescription treatments for minor illnesses. This usually saves money for both the patient, as over-the-counter (OTC) medicines generally cost less than the NHS charge, and the NHS, as the cost is borne by the patient and not charged against the GP's prescribing budget. This trend is set to continue, as more prescription-only medicines are to be reclassified for OTC sale.
- The NHS plan for pharmacy, launched in September 2000, declared that makers of medicines would be encouraged to apply for OTC status for their products (Prescription-only Medicine (POM) to Pharmacy (P) medicine reclassification), so that pharmacies would have a growing range of medicines to offer.
- NHS Direct, the government's telephone health helpline, now officially includes pharmacies as a referral resource for help and advice, alongside GP surgeries and hospital accident and emergency departments. There may, therefore, be an increase in people coming to pharmacies for advice about minor ailments and the medicines to treat them.

- The NHS is opening up walk-in centres where people can go for medical attention without appointment. These are able to supply medicines, including non-prescription medicines.
- The range of medicines that can be prescribed by nurse prescribers has been extended to include all Pharmacy (P*) and General Sale List (GSL) medicines that are allowable on NHS prescriptions.
- Medicines, including non-prescription medicines, can be supplied to patients in GP practices and elsewhere by practice nurses and other staff acting under patient group directions.
- Prescribing rights are to be granted to groups of health professionals who have not previously had them, including pharmacists, chiropodists, optometrists, physiotherapists, etc. The lists of prescribable medicines for these groups will doubtless include non-prescription medicines. (Paradoxically, pharmacists are unlikely to be allowed to prescribe non-prescription medicines on the NHS, as they can already supply P and GSL medicines without prescription. Allowing them to prescribe them, usually to patients exempt from NHS prescription charges, is likely to be seen as a cost increase to the NHS, mainly due to administration costs.)

These developments mean that, as well as pharmacists, who will remain the main purveyors, several other groups of health professionals will now have a direct interest in, and will need to have a good knowledge of, non-prescription medicines. While this book was written mainly with pharmacists in mind, when revising it for this edition I have also taken account of the interests and needs of other health professionals, particularly GPs, practice and district nurses and health visitors.

*Under the Medicines Act 1968, Pharmacy (P) medicines are all medicines that are not specified in a prescription-only order or included on a General Sale List (GSL). There is no actual list of P medicines. P medicines may only be sold from registered pharmacies and all sales must be made under the supervision of a pharmacist. GSL medicines can be sold from any retail premises, and do not require the involvement of a pharmacist in their sale.

AIM OF THE BOOK

The aim of this book is to help pharmacists and other primary health-care professionals to make well-informed recommendations, and to give patients sound advice on non-prescription medicines. To this end, all the main categories of OTC medicines are reviewed in this book, under alphabetically arranged sections on the diseases and conditions they are designed to treat. Information is provided on the following aspects of products and their constituents:

- Compounds or constituents
- Mode of action
- Indications
- Side-effects
- Cautions and contraindications
- Interactions
- Dosage ranges
- Presentations and formulations
- Products available and manufacturers (either all products in a category or, in categories where there are a large number of products, a representative selection)

Each section concludes with a summary of key points and suggestions for the most appropriate products to recommend.

This edition has been completely revised and brought up to date. New products have been included and assessed, and discontinued products deleted. New opinions on, and approaches to, treatment (e.g. head lice) have been included where appropriate. One entirely new section – on emergency hormonal contraception – has been added.

EVIDENCE-BASED MEDICINE AND OTCS

It is now a well-established principle that clinical decision making should be based on the evidence of effectiveness, i.e. on clinical trials and postmarketing surveillance, rather than relying on custom and

practice and anecdote and, where possible, information given in the book will be similarly based. However, this evidence is relatively rare for OTC medicines and there is much less research-based, peer-reviewed, published material available in comparison with that for prescription drugs. Manufacturers often say that they have relevant data on file but, in general, they are reluctant to make such information available. In some cases results of trials conducted on similar products or their constituents as POMs are available, but they may not be applicable, as both the products themselves and the circumstances of their supply are different from their OTC counterparts. Many non-prescription medicine constituents are established and thoroughly tested as prescription drugs, but they may be marketed at a lower strength than the prescription equivalent and for different indications.

Another problem about trying to apply the principles of evidence-based therapy to non-prescription medicines is that clinical trials of prescription drugs tend to concentrate on efficacy, which may be described as an objective measure of effectiveness, based on observed, measurable and verifiable results. With non-prescription medicines, on the other hand, it is often the patient's perception of the medicine's effectiveness that is paramount, and this may be described as the patient's experience of efficacy. Pharmacists will be able to testify that there are many examples of OTC medicines which, judged against purely pharmacological criteria, would not be expected to work, or for which efficacy has not been proven, but which patients find work for them.

There are several factors which may influence patients' perceptions of the effectiveness of non-prescription medicines and which make it difficult to apply evidence-based principles to them.

- Expectations may be enhanced because the patient has much greater involvement in, and control over, the selection of an OTC than a prescribed medicine. In the latter situation, patients usually have little or no input into the choice of medicine, they may be given very little information about it, and they have a passive and dependent role, all of which may undermine their confidence in the medicine. When buying a medicine, on the

other hand, patients are essentially in control. The decision to purchase is theirs, and their expectation of effectiveness may have been raised by advertising or recommendation by an acquaintance. Even when patients ask the pharmacist to recommend a medicine, they are much more likely to be offered options and to play a part in selection than is the case with a prescribed medicine. This greater sense of involvement may well increase expectations, and consequently increase placebo effect and perceived effectiveness.

- Many conditions for which OTC medicines are used are self-limiting, and would improve anyway without treatment within a short time. Patients are therefore likely to ascribe their recovery to the medicine they have taken rather than to the natural course of events, increasing their confidence in the medicine and possibly in OTC medication generally.
- Recommendation often has an important role in creating the expectation of effectiveness. Media advertising is powerful, as is recommendation from family members or trusted friends.

These factors may explain why products which seem to have little rational pharmacological basis for their claimed actions are often successful sellers. To users, what counts is their experience that a medicine works for them, not that in theory it should not. Any criticism of a medicine in a product selection discussion in this book should not, therefore, be interpreted as a condemnation, but simply as a statement that there may be little theoretical or clinical evidence to support its claimed effectiveness.

In the absence of other evidence, a medicine's track record in terms of sales and user satisfaction may be as good a reason for recommendation as any other. What this book sets out to do is present and objectively assess the available scientific and clinical information, in order to help pharmacists and other health professionals to make reasoned judgements on the best choice of non-prescription medication for their patients.

Acne

Acne is largely a condition of young people, and resolves in the large majority of patients by the age of 25. It is believed to be nearly universal in adolescents, and about 60 per cent of teenagers consider their condition sufficiently serious either to self-treat with non-prescription products or to seek medical advice. In most cases it is a minor problem from a medical point of view. However, its psychological impact on sufferers can be enormous as it affects young people at a stage in their lives when they are especially sensitive about their appearance, and they are anxious to find a cure for what they consider a highly embarrassing problem. A large number of products for acne are available over the counter, and pharmacists therefore have an important role in helping young people to choose effective, good-value treatments, and in advising them on how to get the maximum benefit from them. Several effective products for mild to moderate acne are available without prescription, but correct use and persistence are necessary to increase the chance of success.

CAUSES

Acne is the result of a combination of several factors. The main processes involved are as follows:

- The pilosebaceous units in the dermis of the skin consist of a hair follicle and associated sebaceous glands; these glands secrete sebum, a mixture of fats and waxes, the function of which is to protect the skin and hair by retarding water loss and forming a barrier against external agents. The hair follicle is lined with epithelial cells which become keratinised as they mature.
- During puberty the production of androgenic hormones increases in both sexes and levels of testosterone rise. Testosterone is taken up into the sebaceous glands where it is converted into dihydrotestosterone, stimulating the glands to secrete increased amounts of sebum.
- At the same time, the keratin in the follicular epithelial walls becomes unusually cohesive and sebum accumulates within it to

form keratin plugs. These block the openings of the follicles in the epidermis and cause them to dilate beneath the surface of the skin.

- If the orifice of the follicular canal opens sufficiently the keratinous material is extruded through it and an open comedone results. This is also known as a blackhead because the keratinous material is dark in colour. Because this material can escape, the comedone does not become inflamed. If the follicular orifice does not open sufficiently, a closed comedone (whitehead) results, in which inflammation can occur. Most acne sufferers have a combination of both types.
- The actions of micro-organisms, principally *Propionibacterium acnes*, cause the follicular wall of closed comedones to disrupt and collapse, spilling their contents into the surrounding tissue and provoking an inflammatory response. In addition, bacterial enzymes bring about the decomposition of triglycerides in the sebum to produce free fatty acids, which also cause inflammation. This process leads to the formation of papules around the follicular openings in the more common, milder form of acne and to cyst formation in the deeper layers of the skin in the more severe form.

TREATMENT

Only topical products are available for treatment of mild to moderate acne without prescription. Antibiotics – both systemic and topical – are available on prescription for more severe conditions. The overall aim of topical therapy is to remove follicular plugs to allow sebum to flow freely, and to minimise bacterial colonisation of the skin. Four main types of preparation are available without prescription:

- Keratolytics
- Antimicrobials
- Abrasives
- Anti-inflammatory agents

Keratolytics

Compounds available

Compounds available are:

- Benzoyl peroxide
- Salicylic acid
- Sulphur
- Resorcinol

Mode of action

Keratolytic agents (also known as comedolytics in relation to acne) promote shedding of the keratinised epithelial cells on the surface of the skin, although the various compounds used may cause this effect via different mechanisms. Through their action, keratolytics prevent both closure of the pilosebaceous orifice and the formation of follicular plugs, and facilitate the flow of sebum. They also possess varying levels of antimicrobial activity, which contributes to their effectiveness.

Benzoyl peroxide has been in use for the treatment of acne for more than 60 years, and is generally accepted as the most effective topical treatment for mild conditions. There is some difference of opinion over its principal mechanism of action. It was generally thought that its activity was mainly due to a comedolytic effect through an irritant action, leading to an increased turnover of the epithelial cells lining the follicular duct and increasing sloughing. However, it has recently been suggested that its principal mode of action is as a bactericide against *P. acnes*. Benzoyl peroxide is lipophilic and therefore penetrates the follicle well; once absorbed it releases oxygen, which suppresses the bacteria, thereby reducing the production of irritant free fatty acids. Some studies have shown 5 per cent benzoyl peroxide to be more effective in reducing *P. acnes* counts than topical erythromycin or oral tetracycline.

Salicylic acid is used in concentrations of up to 3 per cent for acne. Exerting its keratolytic effect by increasing the hydration of

epithelial cells, it may also have some bacteriostatic activity and a direct anti-inflammatory effect on lesions. It is also believed to enhance penetration into the skin of other medicaments, and is combined with sulphur in some formulary preparations. Sulphur is claimed to possess keratolytic and antiseptic properties, although this is debatable; but it does appear to hasten the resolution of inflammatory pustular lesions. Some authorities consider preparations based on salicylic acid or sulphur to be obsolete for the treatment of acne.

Resorcinol is a keratolytic agent which now only appears in combination with sulphur in a single proprietary preparation. It is not regarded as efficacious, has several drawbacks, and is not recommended.

Adverse effects, cautions and use

Benzoyl peroxide is mildly irritant and may cause redness, stinging and peeling, especially at the start of treatment, but tolerance usually develops with continued use. To minimise these effects, the lowest available strength (usually 5 per cent) should be used and applied at night for the first week so that any erythema caused subsides by the next morning. If there is no adverse reaction, frequency of application may then be increased to twice daily. Several weeks of regular application are usually required to produce real benefit; if the lower strength is ineffective, the higher strength (10 per cent) can be tried.

Treatment should not be prolonged beyond three months with the 5 per cent preparations or beyond two months for 10 per cent preparations.

True allergy occurs in a very small proportion of patients, but allergic contact dermatitis is more common; if troublesome skin irritation occurs, the product should be stopped for a day or two, and if the same reaction occurs when the product is used again it should be discontinued. Care should be taken to keep all keratolytics away from the eyes, mouth and other mucous membranes. Benzoyl peroxide is an oxidising agent and may bleach clothing and bedclothes.

Concerns were expressed a few years ago in the United States that benzoyl peroxide, although not a carcinogen, may promote the growth of tumours, and research on this is continuing. No such fears have been expressed by medicine safety or regulatory bodies in the United Kingdom, and it is considered safe for human use.

Salicylic acid is a mild irritant and similar precautions should be adopted as for benzoyl peroxide. Preparations are applied two or three times a day. Salicylic acid is absorbed readily through the skin and excreted slowly, and salicylate poisoning can occur if preparations are applied frequently, in large amounts and over large areas.

Patients who are sensitive to aspirin should avoid preparations containing salicylic acid.

Sulphur – there is some evidence that sulphur, as well as resolving comedones, actually promotes their formation.

Resorcinol should not be applied over large areas of skin or for long periods, as it is absorbed and can interfere with thyroid function or cause methaemoglobinaemia. Resorcinol may cause dark-brown scaling on the skin in darker-skinned individuals. Both sulphur and resorcinol can cause skin irritation and sensitisation.

Formulations

Benzoyl peroxide is available in the form of creams, lotions, gels and washes, and in concentrations of 2.5, 5 and 10 per cent. There is little difference in clinical response to the three concentrations in terms of reducing the number of inflammatory lesions, but formulation appears to make a difference. The drying effect of an alcoholic gel base enhances the effectiveness of the active constituent, and it is more effective than a lotion of the same concentration. However, gels have a greater potential for causing drying of the skin and irritation than preparations in aqueous bland bases. Washes containing benzoyl peroxide have been found to have little or no comedolytic effect, although in a small-scale trial a skin wash containing 2 per cent salicylic acid has been found to be more effective than a 10 per cent benzoyl peroxide wash. Brevoxyl (Stiefel) contains benzoyl peroxide 4 per cent formulated in a hydrophase base. The manufacturers claim

that the formulation holds the benzoyl peroxide in solution, increasing its bioavailability in comparison with traditional formulations and preventing the crystallisation of benzoyl peroxide on the skin, which leads to particulate irritation. Their studies show that this formulation is as effective as benzoyl peroxide 10 per cent, but with no more irritant effect than a 2.5 per cent preparation.

The bases of some products may themselves reduce the number of comedones. For example, in trials on Quinoderm cream (Quinoderm Ltd) (see below), the base alone produced marked improvements in about half the subjects treated with it, compared with similar improvements in about two-thirds of the group treated with the product containing the active constituents.

Some bases, particularly those of the older formulary products, may reduce the effectiveness of acne products by making the skin more greasy.

Quinoderm contains potassium hydroxyquinoline sulphate, which has both antibacterial and keratolytic properties, in addition to benzoyl peroxide.

Products

- Benzoyl peroxide (5 per cent and 10 per cent unless otherwise stated)

  Creams

  — Boots Mediclear
  Boots

  — Brevoxyl (4 per cent in hydrophase base)
  Stiefel

  — Oxy On-the-Spot (2.5 per cent)
  GlaxoSmithKline Consumer

  — PanOxyl 5
  Stiefel

  — Quinoderm (with 0.5 per cent potassium hydroxyquinoline sulphate)
  Quinoderm Ltd

Lotions

— Boots Mediclear
Boots

— Oxy 5, Oxy 10
GlaxoSmithKline Consumer

Gels

— Acnecide
Galderma

— PanOxyl
Stiefel

— PanOxyl Aquagel (2.5 per cent)
Stiefel

— Quinoderm Lotio-gel (5 per cent with 0.5 per cent potassium hydroxyquinoline sulphate)
Quinoderm Ltd

Wash

— PanOxyl (10 per cent)
Stiefel

- Salicylic acid

— Acnisal face wash (2 per cent)
DermaPharm

— Salicylic Acid and Sulphur Cream BP 1980
(2 per cent salicylic acid and 2 per cent sulphur)

— Salicylic Acid and Sulphur Ointment BPC 1973
(3 per cent salicylic acid and 3 per cent sulphur)

- Resorcinol

— Eskamel Cream (2 per cent with 8 per cent sulphur)
Goldshield

Antimicrobials

Compounds available

Compounds available are:

- Cetrimide
- Chlorhexidine
- Povidone-iodine
- Triclocarban
- Triclosan

Mode of action

As two of the contributory factors to acne are increased sebum production and *P. acnes*, one approach to treatment is to remove excess sebum from the skin and reduce the bacterial count. To this end, several products are available formulated as astringent lotions and detergent-based washes containing antibacterial or antiseptic ingredients, and there are also some antimicrobial creams. There is little in the way of evidence to support their effectiveness, but part of any value these products may have may lie in the placebo effect on patients generated through participating in an active routine to deal with their problem.

Products

Products available are:

- Cetrimide
  - — Torbetol (0.7 per cent with 0.75 per cent chlorhexidine)
    Torbet

- Chlorhexidine
  - — Cepton lotion (0.1 per cent), Cepton medicated skin wash (1 per cent), Cepton medicated clear gel (2.5 per cent)
    Eastern Pharmaceuticals

- Povidone-iodine
  - — Betadine skin cleanser (7.5 per cent)
    SSL International
- Triclocarban
  - — Valderma soap (1 per cent)
    Roche Consumer Health
- Triclosan
  - — Clearasil treatment cream regular (0.1 per cent with 8 per cent sulphur)
    Crookes Health Care

Abrasives

Constituents and products

The constituents and products containing them are:

- Polyethylene granules and silica in a detergent, foaming, gel base
  - — Ionax Scrub
    Galderma
- Fused synthetic aluminium oxide particles, in two grades, in a soap-detergent base
  - — Brasivol, No. 1 and No. 2
    Stiefel

Mode of action, use and cautions

Abrasive products are formulations containing small, gritty particles in a skin wash, intended to remove follicular plugs mechanically.

Their effectiveness is uncertain. Use is recommended from once to four times daily, and the duration of each application is from 15 seconds to two minutes, depending on the product. Abrasive products are contraindicated in the presence of superficial venules or capillaries (telangiectasia), and over-enthusiastic use can cause irritation.

Anti-inflammatory agents

Compounds and product

There is only one product:

- Nicotinamide
  - — Papulex gel (4 per cent)
    Pharmagenix

Mode of action and use

Nicotinamide is the physiologically active amide of nicotinic acid, and its deficiency in the diet can lead to a range of symptoms, including skin problems. In the topical treatment of acne it is claimed to have anti-inflammatory activity, although its mechanism of action is unknown. It is postulated that it might act directly on inflammatory mediators, perhaps through inhibition of neutrophil chemotaxis. In a double-blind clinical trial it was found to be as effective as 1 per cent clindamycin gel in the treatment of mild to moderate acne. It does not appear to have been tested against benzoyl peroxide. It is applied twice daily, and as it may produce side-effects of dryness, peeling and irritation similar to those produced by benzoyl peroxide, the same precautions in use should be taken. The main drawback of nicotinamide gel appears to be its price (its recommended price before abolition of resale price maintenance was more than £14 per tube), which could deter many purchasers.

PRODUCT SELECTION POINTS

- Benzoyl peroxide is the first-line treatment for mild to moderate acne. It has a proven record of efficacy and few drawbacks. A higher strength (10 per cent) formulation of benzoyl peroxide should only be used if three to four weeks' treatment with a 5 per cent product has produced no improvement. Nicotinamide gel also appears to be effective, but is expensive.
- Alcoholic or astringent gel formulations of benzoyl peroxide are more effective than lotions or creams. However, water-based formulations are less likely to cause skin drying and irritation, and may improve compliance. Washes containing benzoyl peroxide have been found to have little comedolytic effect.
- Antibacterial creams, washes and lotions may have little more than a placebo effect.
- All acne treatments must be used regularly for up to three months to produce real benefits.

PRODUCT RECOMMENDATIONS

First choice of treatment for mild to moderate acne – an alcoholic or astringent based gel containing 5 per cent benzoyl peroxide. An aqueous cream or lotion formulation may be preferred by patients with more sensitive skins.

Athlete's foot

Athlete's foot (tinea pedis) is a fungal infection, most commonly causing itching and weeping between the toes, although other areas of the foot may also be involved.

CAUSES

The causative organisms are a group of fungi known as dermatophytes which colonise the horny, outermost layer of the skin. They produce keratinase, which destroys the keratin layer of the epidermis, and also exotoxins which may cause erythema.

TREATMENT

Preparations for athlete's foot are available in a range of formulations, including ointments, creams, paints, sprays and powders. Powders are usually recommended for dusting into shoes, socks and stockings, either as adjuncts to creams and ointments or to prevent the recurrence of infection once cleared, particularly in individuals who tend to be chronic sufferers. The powder formulation itself helps inhibit the propagation of fungi by adsorbing moisture and preventing skin maceration.

Good foot hygiene is also important for effective treatment, and patients should be advised to wash and dry their feet thoroughly before each application of medicament. They should not share towels with others (this helps to prevent the spread of infection), should change their socks, tights or stockings daily, and should be advised to avoid occlusive footwear. Pharmacists should also emphasise the need to apply the medication well beyond the area that can be seen to be infected, and to use it regularly for the full recommended treatment period.

There are three groups of drugs available for the treatment of athlete's foot:

- Antifungals
- Keratolytic agents
- Other antimicrobial compounds, contained in some products

Antifungals

Compounds available

Compounds available are:

- Imidazoles
- Terbinafine
- Tolnaftate
- Undecenoates
- Benzoic acid

Mode of action and usage

Terbinafine, an allylamine derivative, and imidazoles are widely accepted as being the most effective treatments for athlete's foot. They act by inhibiting the biosynthesis of ergosterol, a constituent of the fungal cell membrane, resulting in disruption of the cell. Overall little difference has been found between the efficacy of topical terbinafine and imidazoles in the treatment of fungal infections of the foot, although the former clears infections up to four times more quickly.

Imidazoles licensed for treatment of the condition without prescription are bifonazole, clotrimazole, econazole, ketoconazole and miconazole. They are considered to be more or less equally effective. These compounds also possess activity against Gram-positive bacteria, which is useful, as secondary bacterial infection may complicate the fungal infection.

Twice or three-times daily application is recommended for most imidazoles, except for the bifonazole preparation. This compound, being highly lipophilic, penetrates the skin more effectively and binds rapidly at high concentration, and requires application only once daily. Treatment is generally advised for at least a month to ensure that this tenacious infection is eradicated. Terbinafine is used once or twice daily for one week. Local irritation and sensitivity are possible with all compounds.

Tolnaftate is believed to act by distorting fungal hyphae and stunting mycelial growth. It is active against all species responsible for tinea pedis but has no antibacterial activity. It is used twice daily and treatment should be continued for up to six weeks. It is well tolerated when applied to intact or broken skin, although it usually stings slightly when applied. Skin reactions are rare and include irritation and contact dermatitis.

Undecenoates – undecenoic acid is an antifungal agent which is effective in mild chronic cases of tinea pedis. Both the acid and its salts are used in proprietary athlete's foot preparations. Undecenoic acid is co-formulated with its zinc salt in one proprietary brand (this is also an official formulary preparation in the United States – Compound Undecylenic Acid Ointment USP). Zinc undecenoate has astringent properties, which help to reduce the irritation and inflammation caused by the infection. Undecenoic acid, the active antifungal entity, is also liberated from the zinc salt on contact with moisture on the skin. Undecenoic acid and its derivatives are thought to be suitable for mild forms of athlete's foot characterised by dry scaling of tissue, but to be less effective where the skin is macerated and moist. Up to four weeks' treatment may be needed to produce therapeutic results. Irritation may rarely occur following application of undecenoic acid or its salts.

Benzoic acid has antifungal activity, acting by lowering the intracellular pH of infecting organisms. It is combined with salicylic acid (a keratolytic agent, see below), in an emulsifying ointment base in Benzoic Acid Ointment, Compound, BP (Whitfield's ointment). This preparation has stood the test of time, having been in use for around 90 years, but more cosmetically acceptable products are now available. The same ingredients in the same proportions are included in Toepedo cream (Dendron). Benzoic acid may cause irritation of the skin, and should not come into contact with the eyes or mucous membranes.

Products

- Terbinafine
  - — Lamisil AT
    Novartis Consumer Health
- Imidazoles

  Bifonazole
  - — Canesten AF Once Daily Cream
    Bayer Consumer Care

  Clotrimazole
  - — Candiden Cream
    Akita Pharmaceuticals
  - — Canesten AF Cream, Powder and Spray; Canesten Hydrocortisone Cream
    Bayer Consumer Care
  - — Medisport Athlete's Foot Cream
    Medisport International

  Econazole
  - — Ecostatin Cream
    Bristol-Myers Squibb
  - — Pevaryl Cream, Lotion and Powder
    Janssen-Cilag

  Ketoconazole
  - — Daktarin Gold Cream
    Johnson & Johnson MSD

  Miconazole
  - — Daktarin Dual Action Cream, Spray Powder and Powder
    Johnson & Johnson MSD

  - Daktacort HC cream
    Johnson & Johnson MSD

- Tolnaftate
  - Mycil Ointment, Powder and Spray
    Crookes Healthcare
  - Tinaderm Cream, Tinaderm Plus Powder and Aerosol
    Schering-Plough
  - Scholl Athlete's Foot Cream, Powder, Solution and Spray
    SSL International

- Undecenoic acid
  - Healthy Feet Cream
    Pickles
  - Mycota Cream, Powder and Spray (undecenoic acid/zinc undecenoate)
    SSL International
  - Monphytol Paint (contains methyl and propyl undecenoates together with salicylic acid and methyl and propyl salicylates)
    LAB

- Benzoic acid
  - Toepedo Cream
    Dendron

Keratolytic agents

Compounds available

Compounds available are:

- Salicylic acid
- Benzoyl peroxide

Mode of action and usage

Salicylic acid – at concentrations above 2 per cent salicylic acid – has a keratolytic effect, causing the keratin layer of the skin to shed. (Below this concentration it aids normal keratinisation.) Keratolysis is achieved by increasing the hydration of the stratum corneum (the outermost layer of dead cells), softening the cells and facilitating the dissolution of the intracellular cement bonding them together so that they separate and detach (desquamate). Moisture is essential to this process and is provided either by water in the formulation or by the occlusive effect produced by its application to the skin.

Salicylic acid alone has little or no antifungal activity but it facilitates the penetration of other drugs into the epidermis; preparations for athlete's foot containing salicylic acid therefore also contain antifungal constituents. Salicylic acid is present at a concentration of 3 per cent in Whitfield's ointment, Toepedo cream and Monphytol paint. Although salicylic acid is readily absorbed through the skin, salicylate poisoning is highly unlikely to result from its application to a small area for the limited period of treatment for athlete's foot.

Benzoyl peroxide has a mild keratolytic effect and also antimicrobial activity. It is widely used in the treatment of acne, but is also included in one product for athlete's foot, Quinoped Cream (Quinoderm Ltd), in which it is formulated with potassium hydroxyquinoline sulphate, an antimicrobial with antifungal and antibacterial properties. Benzoyl peroxide can produce redness of the skin and stinging, especially when first used. It can also bleach clothing.

Other antimicrobial compounds

Halquinol and potassium hydroxyquinoline sulphate are quinoline derivatives which possess antibacterial and antifungal activity. The former is included at very low concentration as the active constituent of Valpeda Cream (Roche Consumer Health), and the latter is combined with benzoyl peroxide in Quinoped Cream (Quinoderm Ltd).

PRODUCT SELECTION POINTS

- Terbinafine or imidazole antifungals are generally regarded as the first-line treatment. Tolnaftate has also been shown to be clinically effective, but the former have additional activity against bacterial supra-infection. Undecenoates appear to be less effective than imidazoles for deeper-seated infections. Other athlete's foot treatments offer no advantage over the above.
- Antifungal powders and sprays may be helpful in preventing recurrence of infection in chronic sufferers.

PRODUCT RECOMMENDATIONS

First choice of treatment – terbinafine or an imidazole antifungal cream. Tolnaftate cream for patients sensitive to these.

Powders containing the above or undecenoates can be dusted on to the feet and into hosiery and footwear as prophylaxis for chronic sufferers.

Colds

Colds normally present as a complex or sequence of symptoms. Products marketed for their treatment are usually compound formulations of several ingredients, each intended to alleviate a different symptom. As is frequently the case with self-treatment, the psychologically beneficial effect on the sufferer of doing something to relieve the discomfort caused by the cold, plus the expectations raised by advertising or recommendation, may be as important as the intrinsic therapeutic properties of a product's ingredients. Although it is probably better to recommend individual medicines in response to specific symptoms, the public seems to prefer 'all-in-one' remedies and they often work out cheaper than two or three separate products.

CAUSES

Colds and influenza are commonly confused by patients, who appear to believe that influenza is a more severe form of a cold. Both conditions are viral in origin, and as long as there are no complications treatment is symptomatic and essentially the same.

A common cold usually begins with a sensation of smarting or tingling in the nose, throat and possibly eyes, and progresses to sneezing and rhinorrhoea (runny nose). Inflammation and swelling of the mucosae of the nasal passages may then occur, leading to congestion (blocked nose, stuffiness). The throat often also becomes inflamed, causing soreness and possibly reflex coughing, which may also be provoked by mucus dripping down from the nasopharynx into the bronchus (postnasal drip). In children, a raised temperature may accompany a common cold.

Cold remedies contain constituents intended to relieve these symptoms. They also often include analgesics/antipyretics, although raised temperature and muscular pains are not usual features of the common cold in adults, but are characteristic of influenza – a different and more serious infection. (Patients who have genuine influenza are usually too ill to get out of bed, and would not present in the pharmacy for advice and treatment but would have to send a representative.)

TREATMENT

Most systemic products for colds contain combinations of two or more of the following:

- Sedating antihistamines
- Sympathomimetic decongestants
- Vitamin C
- Cough suppressants
- Analgesics/antipyretics

The last two groups of ingredients are described in some detail in the sections on cough and pain and only additional information relating specifically to their inclusion in cold remedies is given here.

In addition, a number of volatile substances are included in products to be inhaled for the relief of cold symptoms.

Antihistamines

One of the antimuscarinic side-effects of sedating antihistamines – the drying up of nasal secretions – is exploited in cold remedies to counteract rhinorrhoea. The suppression of rhinorrhoea in its turn provokes congestion, and antihistamines are usually co-formulated with sympathomimetics to offset this effect. Sympathomimetics may also help to counteract the sedation caused by antihistamines, but not other antihistamine side-effects such as dry mouth, urinary retention and blurred vision.

Product examples

Antihistamines are formulated with sympathomimetic decongestants in two products:

- Actifed tablets and syrup (triprolidine/pseudoephedrine)
  Pfizer Consumer Healthcare

- Eskornade capsules (diphenylpyraline/phenylpropanolamine) *Goldshield Pharmaceuticals*

There is no evidence that any compound is preferable to another in the treatment of rhinorrhoea. The antihistamine constituent appears to be present at therapeutic dose levels in both products.

Systemic decongestants

In cold remedies decongestants are used to constrict the swollen mucosae and dilated blood vessels of the nasal passages to improve air circulation and mucus drainage. The same compounds are used as in cough preparations, plus phenylephrine, although this drug is not considered to be very effective and it is also subject to first-pass metabolism in the liver. Phenylephrine is the only systemic decongestant licensed for use in GSL products.

Local decongestants

For local use compounds are employed which exert a rapid and potent vasoconstricting effect when applied directly to the affected tissue.

Compounds available

The following compounds are available:

- Ephedrine
- Oxymetazoline
- Phenylephrine
- Xylometazoline

Mode of action and cautions

When used topically inside the nose, the vasoconstricting action of sympathomimetic decongestants prevents their absorption, confining

activity to the area of application. They can therefore generally be used by patients for whom systemic decongestants are contraindicated. Although the likelihood of interactions is also reduced, patients taking monoamine oxidase inhibitors (MAOIs) should not use topical decongestants.

Topical sympathomimetic decongestants have a rapid and potent action. Their disadvantage is that, if used for prolonged periods, they cause a rebound effect (rebound congestion, also known as secondary hyperaemia or rhinitis medicamentosa), with the congestion returning, often worse than before. This is thought to be due to compensatory vasodilatation as the tissues become conditioned to the drug and its effects wear off.

The longer-acting compounds, xylometazoline and oxymetazoline, take longer to produce rebound congestion than the shorter-acting ephedrine and phenylephrine. Dosing is also more convenient with longer-acting compounds, as they are effective for up to 12 hours and need only be used twice or three times daily compared with every three to four hours for the shorter-acting compounds.

To prevent rebound congestion, the shorter-acting topical decongestants should not be used for more than five days or the longer-acting compounds for more than seven days. Rebound congestion does not occur when sympathomimetic decongestants are taken orally.

Product presentation

Topical decongestants are available as sprays or drops. Sprays are preferable for adults and older children, as a fine mist provides better distribution of medicament around the area of application; drops are more likely to be swallowed and absorbed systemically. Greater ease of application makes drops more suitable for children under six years.

Product examples

Products available include:

- Ephedrine
  - — Ephedrine Nasal Drops BP (0.5 per cent)
- Oxymetazoline spray (0.05 per cent)
  - — Afrazine
    Schering-Plough
  - — Dristan
    Whitehall
  - — Vicks Sinex
    Procter & Gamble (H&BC)
- Phenylephrine
  - — Fenox drops and spray (0.5 per cent)
    SSL International
- Xylometazoline
  - — Otrivine Adult Formula drops and spray (0.1 per cent) and Otrivine Children's Formula drops (0.05 per cent)
    Novartis
  - — Sudafed Decongestant spray (0.1 per cent)
    Pfizer Consumer Healthcare

Inhalants

A wide variety of volatile substances is included in products intended to be inhaled, either directly or via steam inhalations, for the relief of cold symptoms. They all have a pungent, aromatic odour. There is no objective evidence that they improve cold symptoms, but products containing these substances have been popular for generations and

they undeniably produce a temporary sensation of clearing the nasal passages.

In theory, at least, use of volatile products in steam inhalations should be helpful as the steam itself could be expected to liquefy mucus secretions and make removal easier, although one research study found no benefit from steam inhalation. Excessive use of inhalants without steam, on the other hand, may make matters worse by reducing clearance of mucus by impairing the action of cilia in the upper respiratory tract.

Constituents and presentation

Inhalant preparations contain between two and six volatile ingredients, the combinations being different for each product. There is little information available about their action on respiratory tract tissue, and their use appears to be empirical and based on tradition. The most frequently included constituent is menthol, and other popular ingredients are eucalyptus oil, benzoin, camphor, methyl salicylate, thymol, pine oil and peppermint oil. Creosote, clove oil, aniseed oil, juniper berry oil, turpentine oil, cajuput oil, terpineol, chlorbutol and chlorocresol are also included in some products. Concentrations of constituents vary widely between products.

Nearly all ingredients of inhalant products have a counterirritant effect when applied locally. Thymol, chlorbutol and chlorocresol are phenolic antiseptics with antibacterial and antifungal activity, although their inclusion in inhalant preparations would seem to be for their strong, 'medicinal' aroma.

Inhalants are presented as steam inhalations (e.g. Menthol and Eucalyptus Inhalation BP 1980), oils which can be inhaled directly or via steam inhalations (e.g. Karvol capsules, Crookes Healthcare; Olbas Oil, G R Lane), and salves which are applied around the throat and upper chest or used in steam inhalations (e.g. Snufflebabe, Pickles; Vicks VapoRub, Procter & Gamble (H&BC); Mentholatum Vapour Rub, Mentholatum). Volatile substances are also presented as pastilles which are sucked (e.g. Potter's Catarrh Pastilles, Ernest Jackson). The fairly complicated procedure involved in steam

inhalations may well improve the efficacy of any product used, through an attention-placebo effect.

Vitamin C

Several compound cold treatments contain vitamin C, in the range of 50–100 mg per dose. The use of this vitamin in the treatment of the common cold has been the subject of debate for more than 30 years, since Linus Pauling advocated 'mega-doses' as both prophylaxis and cure. Current opinion is that relatively high doses of vitamin C produce a modest benefit in reducing the duration of cold symptoms, but long-term daily supplementation in large doses does not appear to prevent colds. Various theories have been advanced to account for the effects of vitamin C on common cold symptoms, including a direct antimicrobial action, inhibition of prostaglandin synthesis, an antihistaminic action, stimulation of repair of damaged respiratory tissue and stimulation of immune function. The last of these has the best supporting experimental evidence.

There are some adverse consequences of taking large doses of vitamin C, particularly for groups of patients who are already at risk. Vitamin C is a reducing agent and may interfere with diabetic urine glucose tests; it has been reported to counteract the action of anticoagulants, and it may increase the production of urinary oxalate, leading to renal stones.

The adverse effect likely to be of greatest relevance to community pharmacists results from the formulation of high doses of vitamin C as effervescent tablets. Large quantities of sodium bicarbonate are required in this formulation, which could disturb the electrolyte balance of patients with cardiovascular conditions, especially those whose sodium intake is restricted.

PRODUCT SELECTION POINTS

- Although from a clinical point of view it is preferable to recommend individual products in response to specific cold symptoms,

patients tend to find combination products more convenient, and they often work out cheaper than two or three individual medicines.

- Local sympathomimetic decongestants (drops or sprays) can generally be used by patients in whom systemic decongestants are contraindicated.
- The longer-acting local sympathomimetic decongestants, oxymetazoline and xylometazoline, are preferable to shorter-acting compounds, as they need less frequent application and can be used for slightly longer periods without risk of rebound congestion.
- For adults, spray presentations of local decongestants are preferable to drops, but sprays should not be used in children under six years.
- Although there is no objective proof that volatile inhalants improve cold symptoms they enjoy a long-standing popularity with patients, and are safe to use in patients of all ages (the proprietary products have different minimum ages) and in all risk groups.

PRODUCT RECOMMENDATIONS

For some products for colds and 'flu' there is little evidence of effectiveness, and others might be regarded as examples of inappropriate polypharmacy. Nevertheless, two factors create a strong demand for these: the desire of sufferers to alleviate their symptoms and their willingness to try anything that might bring relief, and the expectations created by advertising. Thus, while 'all-in-one' night-time cold treatments or antihistamine/decongestant combinations might not accord with the principles of rational product selection, there is a heavy demand for them.

Some formulations can, however, be recommended with confidence that they are rational and normally effective choices, while others will provide some symptomatic relief and are harmless. These include:

- For colds and 'flu' with nasal congestion (in normal healthy adults) – analgesics/antipyretics combined with sympathomimetic decongestants, e.g. paracetamol/phenylpropanolamine (Sinutab Tablets, Pfizer Consumer Healthcare), and ibuprofen/ pseudoephedrine (Nurofen Cold and Flu tablets, Crookes Healthcare), Lemsip Pharmacy Powercaps (Reckitt Benckiser). Some decongestant/analgesic combinations are available as powders to prepare hot drinks; the making of a hot drink may add to any placebo effect.
- For nasal congestion – decongestant nasal sprays (drops for children), e.g. xylometazoline.
- As inhalations – Menthol and Eucalyptus Inhalation; but inhalant oils (e.g. Karvol capsules, Crookes Healthcare; Olbas Oil, G R Lane) and salves (e.g. Vicks VapoRub, Procter & Gamble) may be preferred for convenience.

Cold sores

Cold sores (herpes simplex labialis) are a recurrent infection of the area around the lips and mouth.

CAUSE

Cold sores are caused by the herpes simplex type 1 virus (HSV-1). They are very common; about 80 per cent of the population are asymptomatic carriers of the virus, and 20 to 25 per cent of these (about 8 million people) suffer, on average, two symptomatic outbreaks per year. Once contracted, the virus is never eliminated from the body, but following the attacks it regresses to the ganglia of the trigeminal and lumbosacral nerves, where it lies dormant until one of several trigger factors or lowered immunity allows it to break out again. Cold sores frequently occur in association with the common cold, hence the name. The condition also often follows exposure to the sun, giving rise to its other common name, sun blisters. Outbreaks follow a characteristic pattern, with a prodromal phase of up to 24 hours before any visible signs appear, during which the area on or around the lips begins to tingle, burn or itch. Erythema then develops, followed by the formation of painful and irritating fluid-filled blisters which break down into shallow, weeping ulcers. The ulcers then dry and form crusts which are shed, and the area heals within about seven days. The total length of an episode is about 10 to 20 days.

TREATMENT

Cold sores are difficult to treat – even systemic antiviral therapy has not proven very effective. A number of topical non-prescription products are available:

- Aciclovir – an antiviral agent
- Povidone-iodine – an antimicrobial agent with some antiviral activity

- Antiseptics, astringents and local anaesthetics – intended to alleviate symptoms

Aciclovir

Mode of action

Aciclovir is a synthetic analogue of guanine. Its spectrum of activity is specific to human pathogenic viruses which produce thymidine kinase, of which HSV-1 is one. The activity of aciclovir depends on its conversion by thymidine kinase within infected cells to aciclovir monophosphate, which is then converted by cellular enzymes to aciclovir triphosphate. Aciclovir triphosphate is incorporated by virus-specific DNA polymerase into viral DNA instead of the deoxyguanosine triphosphate required for DNA synthesis and replication. The DNA chain is thereby terminated and replication cannot occur. Aciclovir also inhibits the virus-specific DNA polymerase by acting as a 'decoy' substrate.

Use and efficacy

The manufacturers recommend that aciclovir cream should be used as soon as prodromal symptoms occur, to prevent progress of the cold sore, either stopping it altogether or limiting the severity of the attack. The cream should be applied five times daily, at four-hourly intervals, but omitting an application in the middle of the night, and treatment should be continued for five days. If healing is not complete after this time, treatment can be continued for a further five days. Patients should be referred to a doctor if lesions are not healed within three weeks.

There is limited evidence of the effectiveness of aciclovir as a treatment for cold sores and the *Drug and Therapeutics Bulletin* has stated that it probably has little effect. Most clinical trials have shown little or no benefit of aciclovir over placebo in reduction of pain or itching, and little or no effect on shortening of the infection if the product is used after lesions have appeared. Some trials have demonstrated a

reduction of a day or two in the median time to healing if the cream is used from the first onset of prodromal symptoms, although the severity of symptoms was not reduced. In one trial, lesions did not progress beyond the erythema stage in a small proportion of subjects treated with aciclovir, compared with none in the placebo group. Another trial found aciclovir cream to have no clinical advantage over placebo, although both were better than no treatment. It has been suggested that use of aciclovir cream may reduce the length of subsequent cold sore attacks by reducing the reservoir of virus in the nerve ganglia, although there is no evidence from clinical trials for this.

Aciclovir cream has been found not to have any prophylactic action against the recurrence of cold sores caused by ultraviolet radiation, one of the most common triggers of the condition. High-factor sunscreens, on the other hand, have been found to provide effective protection.

Adverse effects and cautions

Transient burning and stinging may occur following application, and a small proportion of patients experience erythema, itching, or mild drying or flaking of the skin. Care should be taken not to get cream inside the mouth or in the eyes, as it is irritant to mucous membranes. (Particular care should be taken by all patients with cold sores not to touch their eyes, as transfer of the virus can cause herpes keratitis, a serious and potentially sight-threatening infection.) Aciclovir cream is licensed for use in children and pregnant women, and is only contraindicated in patients hypersensitive to the antiviral itself, or to propylene glycol, which is contained in the base.

Products

- Zovirax Cold Sore Cream
  GlaxoSmithKline Consumer
- Herpetad
  Eastern Pharmaceuticals

- Soothelip
  Bayer Consumer Care
- Virasorb
  SSL International

All these products contain aciclovir 5 per cent.

Povidone-iodine

Mode of action and use

Povidone-iodine is an iodophore in which povidone, a polymer, acts as a carrier and slow-release delivery system for iodine. Iodine has a broad spectrum of antimicrobial action, including some anti-viral activity. There is no good evidence that povidone-iodine is effective against cold sores. It is applied as a solution twice daily to the cold sores and allowed to dry. It can be used for both adults and children.

Caution

Caution is recommended with the use of iodine-containing products in pregnancy and breast-feeding, due to the possible effect on fetal and infant thyroid function.

Product

There is only one product:

- Brush-Off Cold Sore Treatment
  SSL International

Other treatments

Compound preparations containing antimicrobial, local anaesthetic, counterirritant and astringent constituents in various combinations are available.

Mode of action

As cold sores are uncomfortable and often painful, but self-limiting, the principal aim of treatment is to reduce discomfort while the infection takes its course. Constituents with local anaesthetic and analgesic effects, such as lidocaine (lignocaine), choline salicylate and phenol are included for this purpose. Counterirritants such as ammonia solution and menthol respectively produce sensations of warmth and coolness and may mask discomfort. The bland cream bases of some products may also have a soothing effect.

Astringents such as zinc sulphate and tannic acid precipitate proteins in the lesions, and are presumably included to promote faster healing, although there is no evidence that they do this. Lotions and gels with alcoholic bases may also be employed to accelerate healing as they have a drying effect on the sores. Antimicrobials are presumably included to prevent secondary bacterial infections from complicating and prolonging attacks, although this rarely occurs.

Combination preparations for cold sores are relatively innocuous, although repeated use of local anaesthetics can cause sensitisation. The cream formulations can be applied as frequently as necessary; the use of lotion and gel formulations is, however, limited to three or four applications per day.

Products

- Blistex Relief Cream (strong ammonia solution, aromatic ammonia solution and phenol)
  Dendron

- Bonjela Antiseptic Pain Relieving Gel (choline salicylate and cetalkonium chloride. This product can also be used in the treatment of mouth ulcers – see section on mouth ulcers)
  Reckitt Benckiser
- Colsor Cream and Lotion (tannic acid, phenol and menthol)
  Pickles
- Cymex Cream (urea, cetrimide, chlorocresol and dimethicone)
  E.C. De Witt
- Lypsyl Cold Sore Gel (lidocaine (lignocaine), zinc sulphate and cetrimide)
  Novartis Consumer Health

PRODUCT SELECTION POINTS

- Aciclovir cream appears to have little effect on cold sore symptoms, but may reduce the length of an attack if used as soon as prodromal symptoms begin. It has been suggested that use of aciclovir cream may reduce the severity of future attacks in chronic sufferers.
- Combination preparations are unlikely to shorten attacks, but they contain constituents that may provide symptomatic relief.
- Aciclovir cream is considerably more expensive than the combination products, and it is therefore probably more cost-effective for people who suffer cold sores only occasionally to use the latter. Chronic sufferers may find it useful to keep aciclovir cream ready to use at the first sign of an attack.
- For sufferers whose attacks are triggered by sunlight, an ultraviolet-blocking lip salve is an effective prophylactic.

PRODUCT RECOMMENDATIONS

For occasional sufferers – a combination product containing analgesic ingredients.

For chronic sufferers to have ready to use at the onset of prodromal symptoms – aciclovir cream.

As prophylaxis against sun blisters – a sun-blocking lip salve.

Constipation

(continued . . .)

Constipation that is not secondary to underlying disease or caused by factors such as side-effects of drugs or laxative abuse is known as simple or functional constipation and may be self-treated with advice from a pharmacist.

CAUSES

Simple constipation has various causes but it is often due to insufficient fluid and fibre in the diet. This results in low stool volume, and the consequent lack of stimulus of the colon to peristalsis inhibits bowel evacuation. Correcting these dietary deficiencies often resolves the problem, although patients sometimes fail to appreciate that time needs to be allowed for them to take effect. Some patients are unable to take dietary measures or find them unsuccessful and laxatives may in these cases be a useful short-term measure.

TREATMENT

Laxatives can be broadly classified into five groups depending on their mode of action:

- Bulk-forming laxatives
- Stimulant laxatives
- Osmotic laxatives
- Faecal softeners
- Faecal lubricants

There are also several products available for use as bowel evacuants prior to abdominal investigation procedures. Although these can be sold without prescription they should be used only under medical direction and will not be discussed here.

Bulk-forming laxatives

Constituents

Bulk-forming laxatives contain one of the following:

- Wheat bran
- Ispaghula husk
- Sterculia
- Methylcellulose

Mode of action

Bulk-forming laxatives provide the closest approximation to the natural process of increasing faecal volume, and are normally the first-line recommendation for functional constipation. They contain natural or semi-synthetic polysaccharides or cellulose derivatives which pass through the gastrointestinal tract undigested. All bulk-forming laxatives are more or less equally effective but some patients find some preparations more palatable than others.

These products increase faecal volume through three mechanisms, the relative contribution of each depending on the composition and properties of the substance. The first action is to add directly to the volume of the intestinal contents; bran consists almost entirely of water-insoluble fibre and acts in this way. Other bulk-forming laxatives contain mucilloid constituents which bind water and swell in the colonic lumen forming a gel, thereby softening the faeces and increasing their bulk. Ispaghula husk (which consists of the seed coats of various species of *Plantago*, a plantain) and sterculia (also known as Indian tragacanth or karaya gum, a gum from the tropical shrub *Sterculia urens*), both act in this way. Methylcellulose is a semi-synthetic hydrophilic colloid with a similar action. Bulk laxatives also add to faecal mass by acting as substrates for the growth of colonic bacteria.

Dosage and administration

- Bran: adults, one sachet (Trifyba) twice or three times daily, mixed with food; children, half or one sachet twice daily. At least one glass of water or other liquid should be drunk with the meal. Unprocessed wheat or oat bran, sprinkled on food or mixed with fruit juice, is also effective.
- Ispaghula: adults, one sachet (Fybogel, Konsyl, Regulan) or two teaspoonfuls (Isogel) twice daily; children 6 to 12 years, half adult dose. The preparation should be stirred into about 150 ml of cold water and taken immediately, preferably after meals.
- Sterculia (Normacol, Normacol Plus): adults, one or two heaped 5-ml spoonfuls or one or two sachets once or twice daily after meals; children 6 to 12 years (Normacol only; Normacol Plus not recommended), half adult dose. The granules should be placed on the tongue and washed down, without chewing, with plenty of water.
- Methylcellulose: adults, three to six 500 mg tablets (Celevac) twice daily, swallowed with at least 300 ml of water.

None of the above preparations should be taken immediately before going to bed, because there may be a risk, which is more likely with water-insoluble fibre products, of oesophageal blockage if patients lie down directly after taking them. As bulk laxatives have a natural action, patients should be warned not to expect an immediate effect. They usually act within 24 hours, but two to three days of medication may be required to achieve a full effect.

Cautions and contraindications

As bulk-forming laxatives are not absorbed they have no systemic effects; also, they do not interact with other medicines and do not appear to interfere significantly with drug absorption. However, there is a risk of oesophageal and intestinal obstruction if preparations are not taken with plenty of water. It is therefore important to stress to patients that instructions for administration are carefully followed.

Abdominal distension and flatulence are possible side-effects, and for this reason bulk-forming laxatives may cause discomfort if taken in the later stages of pregnancy. They are not contraindicated in pregnancy, although the general precautions that apply to use of any medicine should be observed.

Some bulk-forming laxative preparations contain glucose, which would need to be taken into account when making recommendations for patients with diabetes. Bran contains gluten and should not be taken by patients with coeliac disease or gluten enteropathies. Bulk laxatives may not be suitable for patients who need to restrict their fluid intake severely.

Products

- Wheat bran
  - — Trifyba sachets
    Sanofi-Synthelabo
- Ispaghula husk (also known as plantago or psyllium)
  - — Fybogel sachets
    Reckitt Benckiser
  - — Isogel granules
    Pfizer Consumer Healthcare
  - — Konsyl Orange, Konsyl Sugar Free sachets (contain twice as much ispaghula husk as Konsyl Orange)
    Eastern Pharmaceutical
  - — Manevac granules and sachets (also contains senna)
    Galen
  - — Regulan sachets
    Procter & Gamble Pharmaceuticals
- Sterculia
  - — Normacol granules and sachets; Normacol Plus granules and sachets (also contain frangula)
    Norgine

- Methylcellulose
  - Celevac tablets
    Shire Pharmaceuticals

Stimulant laxatives

Mode of action and use

It is thought that the effect of stimulant laxatives is mainly produced by stimulation of the intestinal mucosa to secrete water and electrolytes. This is achieved through one or both of two possible mechanisms. The first is inhibition of the 'sodium pump' (the enzyme sodium/potassium adenosine triphosphatase (Na^+K^+ATPase)). Inhibition of the sodium pump prevents sodium transport across the intestinal wall and leads to the accumulation of water and electrolytes in the gut lumen. The second mechanism is increased production of fluid in the intestine through the action of the laxative on cyclic adenosine monophosphate (cAMP) and prostaglandins, which promote active secretory processes in the intestinal mucosa. It is also thought that stimulant laxatives may cause direct damage to mucosal cells thereby increasing the permeability of these cells and allowing fluid to leak out.

The length of time for individual stimulant laxatives to take effect varies according to their site of action, which may be in the small intestine, the large intestine or both, but they normally work within 4 to 12 hours of administration. For this reason, doses are usually taken at bedtime to produce an effect the next morning. Suppository presentations (e.g. bisacodyl) produce much faster results, usually within an hour.

Cautions and contraindications

The main adverse effects of stimulant laxatives are griping and intestinal cramps. Prolonged use can result in fluid and electrolyte imbalance, and loss of colonic smooth muscle tone. This can lead to a vicious circle in which larger and larger doses of laxative are needed

to produce evacuation, until eventually the bowel ceases to respond at all and constipation becomes permanent.

Stimulant laxatives should be used for only short periods of a few days, at most, to re-establish bowel habit. They are not contra-indicated in pregnancy, but should be avoided in the first trimester. Stimulant laxatives are generally not recommended, and most are not licensed, for use in children under five years of age. Several stimulant laxative agents are contained in products marketed for OTC sale. They fall into two main groups: diphenylmethane derivatives and anthraquinones.

Certain cautions should be observed in the use of anthraquinones in view of their side-effects. They are secreted in breast milk and large doses may cause increased gastric motility and diarrhoea in infants; this class of laxative should therefore be avoided by nursing mothers. Anthraquinone glycosides are excreted via the kidney and may colour the urine a yellowish-brown to red colour depending on its pH.

Diphenylmethane derivatives

Compounds available are:

- Bisacodyl
- Sodium picosulfate

Bisacodyl acts mainly via stimulation of the mucosal nerve plexus of the large intestine, so takes rather longer to act (six to ten hours after oral administration) than laxatives that act within the small intestine. It is minimally absorbed and appears to exert no systemic effects. Bisacodyl causes gastric irritation; there are therefore no oral liquid presentations and tablets are enteric-coated. Tablets should be swallowed whole and should not be taken within one hour of an antacid as this will lead to dissolution of the coating and release of the drug in the stomach.

Sodium picosulfate becomes active following metabolism by colonic bacteria; it therefore has a relatively slow onset of action,

usually acting within 10 to 14 hours. It is useful because it can be used in young children.

Dosages of these preparations are:

Bisacodyl (children under 10 years, under medical supervision only): by mouth – adults and children over ten years, 5 to 10 mg at night; by rectum – adults and children over ten, 10 mg (one suppository), children under ten, 5 mg (one paediatric suppository). Suppositories should be administered in the morning as they act within 15 minutes to one hour. Bisacodyl suppositories may cause a burning sensation in the rectum.

Sodium picosulfate: adults and children over ten years – 5 to 15 mg at night; children from two to ten years – 2.5 to 5 mg, according to age.

The availability of these products is:

- Bisacodyl
  - — Bisacodyl tablets (5 mg; non-proprietary)
  - — Biolax tablets
    Chatfield Laboratories
  - — Dulco-lax tablets and Dulco-lax adults' and children's suppositories
    Boehringer Ingelheim Self Medication Division

- Sodium picosulfate
  - — Dulco-lax Perles
  - — Laxoberal elixir
    Boehringer Ingelheim Self Medication Division

Anthraquinones

Anthraquinones are naturally occurring glycosides used in the form of standardised plant extracts. They are hydrolysed by colonic bacteria to release derivatives of 1,8-dihydroxyanthraquinone, which are absorbed to a moderate degree but with little systemic consequence.

They are believed to act through a combination of direct stimulation of the intramural nerve plexus and interference with absorption of water across the intestinal wall. The effects of individual preparations vary according to the speed of hydrolysis of the glycosides they contain and their anthraquinone constituents. Anthroquinone glycoside-containing preparations derived from several plant sources were for many years popular ingredients of laxative products, but in recent years they have been dropping out of use. With the exception of senna they are now only found in herbal laxative medicines, which generally contain mixtures of plant-derived materials rather than a single constituent.

Senna

Senna is obtained from the dried leaves or pods of *Cassia senna* (= *C. acutifolia*) (known as Alexandrian senna) or *C. angustifolia* (Tinnevelly senna). Preparations are usually standardised to the content of sennoside B (7.5 mg per tablet or 5 ml syrup). Infusions made from senna pods were popular, but they are becoming increasingly difficult to obtain. Their action may be unpredictable as they are unstandardised and they tend to cause cramping and griping, possibly due to extraction into the infusion of oxidised glycosides which have this effect.

Dosages of senna: adults – 15 mg at night; children between six and 12 years – 7.5 mg. (Califig, which contains senna in fig syrup, is licensed for use in children from one year at a dose from 1.25 mg.)

The availability of this product is:

- Senna
  - — Senna Tablets 7.5 mg BP
  - — Califig syrup
    Merck Consumer Health
  - — Ex-Lax Senna chocolate
    Novartis Consumer Health
  - — Nylax with Senna tablets
    Crookes Healthcare

— Senna tablets
Potter's

— Senokot tablets, syrup and granules
Reckitt Benckiser

— Sure-Lax Senna tablets
Peter Black Healthcare

— Senna is also an ingredient of Manevac
Galen

Other stimulant laxatives

Other anthraquinone plant derivatives used in OTC laxative products include powdered rhubarb, frangula and cascara. Powdered rhubarb is an ingredient of Fam-Lax Senna tablets (Torbet) and other herbal laxative products; it contains tannins and exerts an astringent action. Frangula, from the bark of *Rhamnus frangula*, is contained in Normacol Plus (Norgine) and in some herbal laxative products. Cascara, from the bark of *Rhamnus purshiana*, has a strong purgative action and griping effect. One of the most popular laxatives a generation ago, it is now only found in herbal preparations.

Castor oil has been traditionally used as a laxative; it contains ricinoleate, which is hydrolysed in the small intestine to produce glycerol and ricinoleic acid, the latter producing a drastic purgative effect which may give rise to dehydration and electrolyte imbalance and can also cause colic. The stimulant effects are sufficient to cause uterine contraction in pregnant women and may provoke abortion. Castor oil is mentioned here because it is sometimes requested by the public as a laxative, but it should not be sold for constipation under any circumstances.

Aloin is an extract of aloes. It has a similar but more drastic action to senna and is very irritant. Aloin is the sole constituent in Calsalettes tablets (Torbet), and aloin or powdered aloes is included in several herbal products.

Osmotic laxatives

Constituents

Osmotic laxatives contain one of the following:

- Magnesium sulphate
- Magnesium hydroxide
- Sodium sulphate
- Lactulose
- Glycerol

Mode of action

Osmotic laxatives are either inorganic salts or organic compounds which are very poorly absorbed from the intestine. In the intestine their presence creates a hypertonic state. In order to equalise osmotic pressure, water is drawn from the intestinal wall into the lumen, raising the intraluminal pressure by increasing the volume of the contents, thereby stimulating peristalsis and promoting evacuation. The effects of the inorganic salts are very rapid: large doses produce a semi-fluid or watery evacuation within three hours and smaller doses act in six to eight hours. Magnesium salts are also believed to act through stimulating the secretion of the hormone cholecystokinin, which promotes fluid secretion and motility in the intestine.

Lactulose, a synthetic disaccharide, takes much longer to act than the inorganic osmotic laxatives because it has first to be broken down by colonic bacteria, mainly to lactic acid. This produces a local osmotic effect. It may take 72 hours of regular dosing to produce an effect, and this is seen as a disadvantage by patients seeking rapid results. It has a sweet taste which makes it more palatable for children, to whom it can be safely given, but many adults find the large dose volumes required (up to 30 ml) sickly and a deterrent to compliance.

Glycerol is a highly hygroscopic trihydric alcohol which appears to exert its principal laxative action by attracting water of hydration into the intestine. It is also believed to have a direct mild irritant effect and may also have some lubricating and softening actions. Glycerol

is administered in the form of suppositories, which usually act within 15 to 30 minutes. It is a useful treatment for babies and young children. Glycerol is inactive by mouth as it is readily absorbed and extensively metabolised in the liver.

Sorbitol is a polyhydric alcohol with a similar action to glycerol. It is not used as a laxative but is commonly employed as a sweetener in sugar-free confectionery and medicines. Unlike glycerol, it is poorly absorbed from the gastrointestinal tract, and regular consumption of products containing it can cause diarrhoea.

Cautions and side-effects

Some absorption of inorganic laxative salt ions does occur, but in normal, healthy individuals the amounts are too small to cause toxic effects, and the ions are rapidly excreted via the kidney. However, accumulation of magnesium ions can occur in the presence of renal impairment, causing toxic effects in the central nervous system (CNS) and altered neuromuscular function through hypermagnesaemia. As renal function tends to decline with age it may be advisable to discourage regular use of magnesium-containing laxatives by elderly patients.

Absorption of sodium salts can result in water retention and a rise in blood pressure, and chronic use should be avoided in patients with renal insufficiency, oedema, high blood pressure or congestive heart failure.

The main side-effects of inorganic osmotic laxatives are nausea and vomiting. In addition large doses can produce significant dehydration, so sufficient water should always be administered with a dose to ensure that no net loss of body water occurs.

Serious adverse effects with lactulose are rare. Relatively minor side-effects, although they may be sufficient to discourage compliance, occur in about 20 per cent of patients taking full doses and include flatulence, cramp and abdominal discomfort, particularly at the start of treatment. Lactulose is a disaccharide of galactose and fructose and also includes some lactose. It cannot therefore be used by patients with galactose or lactose intolerance and must be used with caution in patients with diabetes.

Products

- Magnesium sulphate
  - — Epsom Salts
  - — Andrews Original Salts
    GlaxoSmithKline Consumer
  - — Kest tablets
    Torbet

- Magnesium hydroxide
  - — Magnesium Hydroxide Mixture BP (Cream of Magnesia)
  - — Milk of Magnesia liquid
    GlaxoSmithKline Consumer
  - — Milpar (also contains liquid paraffin)
    Merck Consumer Health

- Sodium sulphate
  - — Glauber's Salt
  - — Fynnon salts
    SSL International

- Lactulose
  - — Duphalac solution and dry sachets
    Solvay Healthcare
  - — Lactugal solution
    Intrapharm Laboratories
  - — Lemlax solution
    Co-Pharma
  - — Regulose solution
    Novartis Consumer Healthcare

- Glycerol
  - — Glycerol Suppositories BP (70 per cent in a gelatin base – mould sizes: 4 g for adults, 2 g for children, 1 g for infants)

Faecal softener – docusate sodium

This is the only compound available.

Mode of action and cautions

Docusate sodium (dioctyl sodium sulphosuccinate) is an anionic surfactant which acts by lowering the surface tension of the intestinal contents. This allows fluid and fat to penetrate, emulsify and soften faecal material for easier elimination. The faeces are kept soft and evacuation is achieved without straining. Docusate is also thought to exert a stimulant laxative effect similar to the anthraquinones. A laxative effect usually occurs within one to three days of administration. Used alone, docusate is a weak laxative, but it is considered useful for patients in whom straining at stool must be avoided, for example, following an operation or myocardial infarction. Docusate is non-absorbable and non-toxic but it is believed to facilitate the transport of other drugs across the intestine, and could thereby increase their action and adverse effects.

Dose

Adults – up to 500 mg daily in divided doses; children – 12.5 to 25 mg three times a day; infants, over six months – 12.5 mg three times a day.

Products

- Dioctyl capsules (100 mg)
  Schwarz Pharma

- Docusol Adult (50 mg/5 ml) and Paediatric (12.5 mg/5 ml) Solutions
  Typharm

Faecal lubricant – liquid paraffin

This is the only compound available.

Mode of action and side-effects

Liquid paraffin is indigestible and absorbed only to a small extent. It penetrates and softens the faeces and coats the surface with an oily film which facilitates its passage through the intestine. It is considered to have a limited usefulness as an occasional laxative in situations where straining at stool must be avoided, but it has several drawbacks which make it unsuitable for regular use.

Liquid paraffin can seep from the anus and cause irritation; it may interfere with the absorption of fat-soluble vitamins; it is slightly absorbed into the intestinal wall where it may set up foreign-body granulomatous reactions; and it may enter the lung through aspiration and cause lipoid pneumonia. As a result of problems caused by chronic use, liquid paraffin was reclassified from GSL to P status and its maximum pack size restricted. It should not be used in the presence of abdominal pain, nausea or vomiting and should never be used for children.

Products

The only product available is Liquid Paraffin Oral Emulsion BP (non-proprietary), but liquid paraffin is an ingredient of Milpar (Merck Consumer Health).

PRODUCT SELECTION POINTS

- Ideally, simple or functional constipation should be corrected by dietary means through increasing fibre and fluid intake. These measures are not always successful, but should be tried first.
- Bulk-forming laxatives are the first choice for the treatment of constipation. They are not absorbed, are pharmacologically inert and exert their effect by mimicking the natural action of food on the gut. They can be used long-term if necessary.
- The short-term use of stimulant laxatives is justified to re-establish a bowel habit if dietary measures and bulk-forming laxatives have failed. Bisacodyl or a standardised senna preparation are the best choice. Stimulant laxatives are reliable, act relatively quickly and generally produce few side-effects. There is little to commend the use of other laxatives in this class.
- Regular use of inorganic osmotic laxatives should be avoided in the elderly and by patients with cardiovascular problems or renal impairment.
- Several factors may deter patients from using lactulose: it must be taken for up to three days before producing an effect; it is intensely sweet; it may cause cramping and flatulence; and it is relatively expensive.
- There is no justification for the use of liquid paraffin as a non-prescription laxative.
- Constipation is common in the later stages of pregnancy. Bulk-forming laxatives and bisacodyl or senna are suitable and safe to use, although the former may add to abdominal discomfort. Breast-feeding mothers should avoid senna.
- Medical opinion is that the use of laxatives in children is undesirable and, if necessary, should only be used under medical supervision. However, if dietary means fail, a single glycerol suppository of the appropriate size may be sufficient to correct the problem. Several other products are licensed for use in children, and have recommended doses.
- Constipation is often the result of side-effects of prescribed medication. Before recommending a laxative, the pharmacist

should consult with the patient's GP to see if an alternative drug could be prescribed.

- Pharmacists should be alert to laxative misuse, both intentional and unwitting.

PRODUCT RECOMMENDATIONS

First-line – dietary, i.e. increased fibre and fluid intake. Second-line – bulk-forming laxatives. Third-line – a short course of a stimulant laxative, either bisacodyl or standardised senna. Refer the patient if constipation is not resolved within a week.

Corns and calluses

Corns and calluses are localised formations of thick, horny skin (hyperkeratinisation) on the feet.

CAUSES

Corns and calluses are caused by pressure or friction on the feet. Pressure on the nerve endings in these areas gives rise to pain. Hard corns occur over bony prominences, generally on or around the toes; soft corns occur between the toes and have a soft and whitened appearance caused by maceration of the skin by perspiration. Calluses form on the flatter, weight-bearing and fleshier areas of the foot.

TREATMENT

Treatment is either by epidermabrasion or by the use of hydrocolloid plasters or keratolytic agents.

Epidermabrasion

Epidermabrasion does not involve the use of pharmacological agents but is a physical process involving removal of the horny skin by the use of a mechanical aid.

Several gently abrasive materials and appliances are available, ranging from emery boards and pumice stones to specially designed files such as the Scholl corn and callus file, and synthetic pumice-like blocks such as Newton's Foot Therapy chiropody sponge.

Careful technique is important for the successful and safe removal of hard skin by epidermabrasion, and the following are the main points of advice that should be given to patients:

- Soak the foot (to soften the skin) in mild soapy water for a few minutes, or apply a moisturising or softening cream.
- Rub some soap on to the appliance, and gently rub the corn or callus for five minutes.

- Repeat the process nightly for one week, then review. There is no need to remove the hard skin completely, just enough to relieve pain or irritation.
- Do not wear ill-fitting shoes (often the cause of the hyperkeratinisation) to help prevent recurrence of the problem.

Hydrocolloid plasters

Hydrocolloids are complex polymer formulations used in wound management. They swell in the presence of moisture absorbed from the skin, and in corn and callus plasters the hydrocolloid forms a soft, protective gel-like cushion which rehydrates and softens the hardened tissue. The plaster is left *in situ* for about a week, and on removal the corn or callused skin should be removed with it.

Product examples

- Compeed Hydrocure system for calluses and corns
  Coloplast
- Scholl Polymer gel corn removers
  SSL International
- Scholl Gelactiv callus remover
  SSL International

Keratolytic agent – salicylic acid

Mode of action and use

In the removal of corns and calluses the function of salicylic acid is to remove a thick layer of cornified skin cells, mainly through loosening the attachment of the area of hardened skin to the normal skin (see also the section on athlete's foot). Salicylic acid concentrations in products used for this purpose range from about 11 to 50 per cent, depending on the type of formulation.

Corn and callus caps and plasters contain high concentrations of salicylic acid (usually 40 per cent) in a semi-solid base spread on to a suitable backing material, contained within a ring which is either self-adhesive or attached to an adhesive plaster. Such systems provide direct and prolonged contact with the affected area. They should be applied and changed every one or two days for about a week, after which time the callosity should lift away easily. If it cannot be removed after 10 to 14 days of treatment professional help should be sought. An ointment containing 50 per cent salicylic acid is also available; it should be applied nightly for four nights.

Paints and liquids are available which contain salicylic acid in a concentration of 11 to 17 per cent, often in a collodion-based vehicle. Collodions contain pyroxylin, a nitrocellulose derivative, dissolved in a volatile solvent such as ether, acetone or alcohol. On application, the solvent evaporates, leaving on the skin an adherent, flexible, water-repellent film containing the medicament. This has the advantage of maintaining the salicylic acid at the site of application and also assists maceration of the skin by preventing moisture evaporation. Liquid preparations are usually applied daily for several days until the corn or callus can be easily removed.

Cautions

As salicylic acid is caustic to normal skin, care should be taken to prevent preparations from spreading beyond affected areas. True sensitivity to salicylic acid is very rare, but a few patients react to colophony present in collodions and plaster bases. Preparations containing high concentrations of salicylic acid should be avoided by patients who are sensitive to aspirin. (For remarks regarding risk groups, see section on foot problems.)

Product examples

- Carnation Corn Caps
  Cuxson Gerrard

- Carnation Callus Caps
  Cuxson Gerrard
- Scholl Corn Removal Plasters (original, fabric and washproof)
  SSL International
- Scholl Callus Removal Pads
  SSL International
- Pickles Foot Ointment
  Pickles
- Salicylic Acid Collodion BP
- Dispello Corn & Wart Paint
  Ayrton Saunders
- Bazuka (contains lactic acid 4 per cent in combination with salicylic acid 12 per cent; licensed for the treatment of corns and calluses: see also sections on verrucas and warts)
  Dendron
- Salatac (contains lactic acid 4 per cent in combination with salicylic acid 12 per cent; licensed for the treatment of corns and calluses: see also under verrucas and warts)
  Dermal

PRODUCT SELECTION POINTS

- Epidermabrasion or hydrocolloid plasters are the safest and most suitable methods for treating corns and calluses.
- A wide range of preparations containing salicylic acid is available, all of which should be effective if properly used.

PRODUCT RECOMMENDATIONS

First-line treatment – epidermabrasion or hydrocolloid plasters.
Second-line treatment – plasters or a liquid application containing salicylic acid.

Cough

(continued . . .)

Cough remedies have had no significant additions to their range of active ingredients in recent years, although new products continue to be introduced as a result of reformulations and permutations of constituents. There are now about 40 proprietary brands and well over 100 products marketed specifically for cough.

NATURE OF COUGHS

There are three types of cough:

- Dry (irritating and non-productive)
- Chesty with production of mucus
- Chesty but non-productive (no mucus is produced but there is a feeling of 'tightness' or wheezing due to congestion of the bronchial airways).

The effectiveness of cough treatments has been questioned by some medical and pharmaceutical authorities, and the *British National Formulary* is sceptical about the value of some of them. However, cough remedies can be effective if products are selected rationally to treat specific symptoms. Also, as in most areas of self-medication, placebo effect plays a significant part, with consumers' high expectations of cough remedies often being reinforced by manufacturers' advertising. If a placebo effect enhances pharmacological effectiveness, so much the better.

Product choice depends on the type of cough. The active ingredients of cough remedies fall into four main categories:

- Suppressants, to treat dry, irritating coughs
- Expectorants for chesty, productive coughs
- Decongestants for chesty, non-productive coughs
- Demulcents, to soothe any kind of cough

Products which contain combinations of ingredients should be carefully selected to ensure that they are suitable for the symptoms.

TREATMENT OF DRY IRRITATING COUGHS – SUPPRESSANTS (ANTITUSSIVES)

Two classes of compounds, opioids and antihistamines, are used as antitussives in cough preparations.

Opioids

Compounds available

Compounds available are:

- Codeine
- Pholcodine
- Dextromethorphan

Mode of action

Infection of the upper respiratory tract produces inflammation and irritation of the throat and trachea, stimulating the cough reflex in an attempt to remove what the brain perceives as a foreign object, resulting in a dry, non-productive cough. Such coughing serves no beneficial purpose, is inconvenient and can eventually become debilitating. It can justifiably be suppressed with antitussives.

Opium alkaloids act on the medullary cough centre in the brain to depress the cough reflex. Both dextro- and laevo-isomers of opioid compounds possess antitussive activity, but dependence liability resides only in laevo-isomers.

Dextromethorphan, a dextro-isomer which has been developed as an orally active antitussive with little or no dependence liability, is now the most widely used opioid constituent of OTC cough remedies.

Evidence as to which of codeine, pholcodine and dextromethorphan is the most effective antitussive is conflicting. Codeine and pholcodine are generally rated as more potent than dextromethorphan.

Dosage

- Codeine
  - Adults: 15 to 30 mg three or four times daily
  - Children, 5 to 12 years: half adult dose
  - Children, one to five years: 3 mg three or four times daily (not suitable for infants under one year)

- Pholcodine
  - Adults: 5 to 10 mg three or four times daily
  - Children, 1 to 12 years: 2.5 to 5 mg three or four times daily
  - Infants, three months to one year: 1 mg three or four times daily
  - Pharmacokinetic studies have shown pholcodine to have a long half-life, and twice or only once-daily dosing may be sufficient

- Dextromethorphan
  - Adults: 10 to 20 mg every four hours
  - Children, 6 to 12 years: 5 to 15 mg up to four-hourly to a maximum of 60 mg in 24 hours
  - Children, one to six years: 2.5 to 5 mg to a maximum of 30 mg in 24 hours

Cautions and side-effects

Codeine is partially demethylated in the body to morphine. This may contribute to its antitussive activity but also accounts for its liability to cause sedation, respiratory depression (although this is not normally a problem at OTC doses), constipation and addiction.

Codeine is now little used in proprietary formulations. Pholcodine has a generally lower side-effect profile than codeine, and dextromethorphan is claimed to be virtually free from side-effects.

Interactions

At antitussive doses, opioids have no significant interactions with other drugs.

Product examples

- Codeine
  - — Codeine Linctus BP (no proprietary product marketed primarily for OTC sale contains codeine as sole constituent)
- Pholcodine
  - — Pholcodine Linctus BP
  - — Expulin Dry Cough Linctus
    Shire Pharmaceuticals
  - — Tixylix Daytime
    Novartis Consumer Health
- Dextromethorphan
  - — Robitussin for Dry Coughs
    Whitehall
  - — Strepsils Cough lozenges
    Crookes Healthcare

Many products contain opioids in combination with other ingredients. The use of combination cough remedies is discussed below.

Antihistamines

Compounds available

Compounds available are:

- Brompheniramine
- Chlorphenamine (chlorpheniramine)

- Diphenhydramine
- Promethazine
- Triprolidine

Mode of action

The above compounds are all sedating-type antihistamines and exert a central and peripheral inhibitory action on neuronal pathways involved in the cough reflex. The sedative properties of these compounds may be an important factor in their use, in so far as they will help cough sufferers to sleep if taken near bedtime. They also exert anticholinergic side-effects, including the drying-up of bronchial and nasal secretions, which may be helpful in some situations.

Uses

As for opioids.

Dosage

The maximum dose recommended by the manufacturers of cough remedies containing brompheniramine, diphenhydramine and triprolidine is at the lower end of the therapeutic range for these compounds. The two products containing promethazine contain quantities which appear to be below the therapeutic level.

Side-effects and cautions

Side-effects include sedation, and anticholinergic effects, such as dry mouth, urinary retention, constipation and blurring of vision. The elderly are more susceptible to these. Because of these side-effects, cough preparations containing antihistamines should not be recommended to patients with glaucoma or prostate problems. Paradoxical CNS stimulation can also occur, particularly in children, and there have been occasional reports of hallucinatory episodes.

Interactions

The sedative effects of antidepressants, anxiolytics and hypnotics are likely to be enhanced by antihistamines, as are the antimuscarinic actions or side-effects of drugs such as trihexyphenidyl (benzhexol), orphenadrine, tricyclic antidepressants and phenothiazines.

Product examples

- Brompheniramine: Dimotane range
  Whitehall
- Chlorpenamine (chlorpheniramine): some products in the Expulin range
  Shire Pharmaceuticals
- Diphenhydramine
  - some products in the Benylin range
    Pfizer Consumer Healthcare
  - some products in the Bronalin range
    SSL International
- Promethazine: Tixylix Night-Time SF
  Novartis Consumer Health
- Triprolidine: Actifed Compound Linctus and Actifed Expectorant
  Warner Lambert Consumer

TREATMENT OF CHESTY, PRODUCTIVE COUGHS – EXPECTORANTS

Compounds available

Compounds available are:

- Guaifenesin
- Ammonium chloride

- Ammonium carbonate
- Ipecacuanha
- Squill
- Senega
- Guaiacol
- Creosote
- Sodium citrate

Mode of action and efficacy

In a productive cough, mucus produced in the bronchial passages as a result of infection is moved upwards towards the pharynx by ciliary action and is then expelled by coughing. As the cough is clearing mucus and helping to keep the airways open it should not be suppressed.

Expectorants are used to assist mucus removal. They are substances that when given in large doses are emetic. As emetics they act through vagal stimulation of the gastric mucosa, producing a reflex response from the vomiting centre in the brain. The same mechanism stimulates the bronchial glands and cilia and it is postulated that in sub-emetic doses this stimulation will still occur.

Although expectorants have long been used in the treatment of cough there is little objective evidence of their effectiveness. Guaifenesin is the most frequently used in proprietary preparations, and is recognised by the United States Food and Drug Administration as being effective, at doses of around 200 mg three times a day. However, the drug has a short half-life and more frequent dosing may be necessary to ensure effectiveness.

As is often the case with OTC products, many expectorant preparations contain what appear to be sub-therapeutic levels of constituents. Manufacturers may do this to reduce to an absolute minimum the possibility of any adverse effects from substances for which, even at full doses, there is little proof of efficacy. Even at the highest strengths included in OTC formulations there is little risk of adverse effects, and expectorants do not interact with other drugs.

Product examples (guaifenesin as sole constituent)

- Expulin Chesty Cough Linctus
  Novartis
- Famel Expectorant
  Shire Pharmaceuticals
- Jackson's All Fours
  Anglian Pharma
- Tixylix Chesty Cough
  Novartis Consumer Health

TREATMENT OF CHESTY, NON-PRODUCTIVE COUGHS – DECONGESTANTS

Compounds from two groups are used as decongestants and bronchodilators in cough remedies: sympathomimetics and methylxanthines (theophylline).

Sympathomimetics

Compounds available

Compounds available are:

- Ephedrine
- Pseudoephedrine

Action, uses and dosage

Sympathomimetics mimic the action of noradrenaline (norepinephrine), the principal transmitter between the nerve endings of the sympathetic nervous system and the adrenergic receptors of the innervated tissues. They stimulate both alpha-receptors, causing constriction of smooth muscle and blood vessels, and beta-receptors,

producing bronchodilatation. They are therefore useful in coughs where the tissues of the upper respiratory tract are congested, as they shrink swollen mucosae and open up the airways. Sympathomimetics also have CNS-stimulant activity and their vasoconstricting property tends to raise blood pressure.

Both sympathomimetics used in cough preparations have more or less equivalent action on the respiratory tract, but ephedrine has greater CNS and pressor activity and is used in few products. The recommended adult dose of pseudoephedrine is 60 mg up to four times daily, and for ephedrine up to 60 mg three times a day.

Side-effects and cautions

Because of their pressor effects, and because they can also increase heart rate, sympathomimetic decongestants should be avoided by patients with any kind of cardiovascular condition or glaucoma. They also interfere with metabolism, including glucose metabolism, and should not be taken by patients with diabetes or those with thyroid problems. As they are CNS-stimulants, doses should not be taken near to bedtime.

Interactions

MAOIs prevent the breakdown of noradrenaline and increase the amount stored in adrenergic nerve terminals. Administration of sympathomimetics in conjunction with MAOIs will increase the level of adrenergic transmitter substances and can result in potentially lethal hypertensive crises. Sympathomimetic decongestants must therefore not be given to patients on MAOI therapy.

Oral decongestants should also be avoided in patients taking beta-blocking drugs. Sympathomimetics stimulate both the alpha-adrenergic receptors of the cardiovascular system to produce vasoconstriction, and the beta-receptors to produce vasodilatation and stimulation of the heart. The overall effect is a slight increase in both blood pressure and heart rate. If the beta-receptors are blocked, unopposed alpha-vasoconstriction can lead to a rise in blood pressure.

Product examples

- Pseudoephedrine
  - — Actifed and Sudafed range
    Pfizer Consumer Healthcare
  - — Dimotane range
    Whitehall

- Ephedrine
  - — Do-Do Chesteze Tablets
    Novartis Consumer Health

Theophylline

Action, uses and dosage

Bronchodilatation is mediated by cyclic adenosine monophosphate (cAMP), which causes smooth muscle relaxation through intracellular modulation of calcium ion levels. cAMP is depleted when bronchoconstriction occurs, being broken down by the enzyme phosphodiesterase. Methylxanthines inhibit the action of phosphodiesterase and it was thought until recently that their bronchodilator action was due to this. It is now believed that another, as yet unknown, mechanism may be responsible.

Theophylline is used mainly in the treatment of asthma, but it is included in one OTC product – Do-Do Chesteze tablets (Novartis) – marketed for the treatment of bronchial cough, breathlessness and wheezing.

The adult dose of theophylline is from 60 to 250 mg up to four times a day.

Interactions and cautions

Theophylline is metabolised in the liver and interacts with several commonly prescribed drugs which inhibit its metabolism, causing serum

levels to rise. This is important because theophylline has a narrow therapeutic index, and concentrations can rise rapidly to toxic levels. Commonly used drugs with which there are significant interactions include cimetidine, ciprofloxacin (and other quinolone antibacterials), erythromycin (and other macrolides), fluvoxamine, St John's wort, calcium-channel blockers and fluconazole. Smoking speeds up the metabolism of theophylline, necessitating larger doses to be effective.

Theophylline should be used with caution in patients with liver or cardiac disease, epilepsy, the elderly and pregnant and breast-feeding women.

In view of the problems associated with theophylline, and the availability of a wide range of alternative treatments, it would seem best not to recommend this single OTC theophylline-containing product.

TREATMENT TO SOOTHE ANY KIND OF COUGH – DEMULCENTS

Compounds available

Compounds available are:

- Glycerol
- Liquid glucose
- Syrup
- Honey
- Treacle

Action and uses

Demulcents coat the mucosa of the pharynx and provide short-lived relief of the irritation that provokes reflex coughing. They are used mainly for their placebo effect. Pastilles (e.g. glycerin, lemon and honey) provide a more prolonged soothing effect as they promote production of saliva, which has a demulcent effect, while they are being sucked. Demulcents have the advantage of being pharmacologically inert and they can be safely taken by anyone. Their only drawback is

the high sugar content of some preparations. These should be used with caution in patients with diabetes, and in children because of their cariogenic potential. Several sugar-free linctuses are available, both of the demulcent type and containing active ingredients.

Product examples

- Glycerin, Lemon and Honey Linctus
- Simple Linctus BP
- Meltus Baby Linctus Blackcurrant
  SSL International

TREATMENT WITH COMBINATION REMEDIES

Proprietary cough remedies containing a single ingredient are the exception rather than the rule. Some products contain just an antitussive (usually dextromethorphan) or an expectorant (usually guaifenesin), but the majority are mixtures containing up to six ingredients, plus vehicle and flavouring. Many products contain pharmacologically rational combinations, such as an antitussive with a decongestant/bronchodilator, which is sensible for a dry cough with wheeziness or congestion, or an expectorant with a decongestant, suitable for a productive cough with congestion.

The number of irrational formulations has been reduced in recent years, but there are still some available combining an expectorant with an antihistamine, which have mutually antagonistic effects on clearance of mucus, or an antitussive to suppress coughing with an expectorant to promote it.

Some products contain, in addition to a more or less therapeutic quantity of an active constituent, a number of 'traditional' ingredients in very small concentrations. It is unlikely that these could have any therapeutic effect, and they are presumably included to present a suitably impressive formula on the label to increase placebo effect. Menthol and volatile oils, which provide a suitably 'medicinal' aroma and flavour, are also often included.

Some products contain sub-therapeutic amounts of several ingredients with the same action, such as expectorants, perhaps in the belief that they will have an additive effect and be effective while minimising any adverse effects. Such combinations are unlikely to have any therapeutic effect beyond that of a placebo.

PRODUCT SELECTION POINTS

- Placebo effect plays a more important part in the perceived effectiveness of cough remedies than in most other groups of OTC products. Nevertheless, many products do contain constituents of recognised effectiveness. Products should be chosen rationally with ingredients matched to symptoms, and the possibility of contraindications and interactions taken into account.
- Cough suppressants are indicated for dry, irritating, non-productive coughs, expectorants for productive, chesty coughs, and decongestants for cough accompanied by congestion. Demulcent preparations can be used for any kind of cough, are harmless and have a useful placebo effect.
- Combinations of a suppressant or an expectorant with a decongestant are appropriate for certain types of cough. Other combinations are irrational, and may contain mutually antagonistic ingredients.
- Products should be selected which contain a therapeutic dose of active ingredient(s); some products contain sub-therapeutic amounts and are likely to have no effect.
- Products containing antihistamines should be used with caution in the elderly, and avoided in patients with glaucoma or prostatic hypertrophy.
- Products containing sympathomimetic decongestants should not be taken by patients with diabetes or patients with glaucoma, cardiovascular or thyroid problems, nor by patients taking beta-blockers or MAOIs.
- Products containing theophylline should not be taken by patients taking cimetidine, quinolone and macrolide antibacterials,

fluvoxamine, St John's wort, calcium-channel blockers or fluconazole because of an interaction which can raise plasma theophylline to toxic levels.

- There is a wide range of sugar-free linctuses for patients with diabetes who wish to avoid sugar-containing medicines, and of sugar-free children's cough medicines.
- The symptoms and history of a cough should be carefully assessed and diagnosed as trivial before recommending any OTC treatment. Coughs persisting for more than two weeks should be referred for further investigation.

PRODUCT RECOMMENDATIONS

- Cough suppressants – pholcodine, dextromethorphan
- Expectorants – guaifenesin, preparations containing 200 mg per adult dose
- Combination products – non-productive cough with congestion (dry, wheezy, 'tight') – dextromethorphan with pseudoephedrine
- Productive cough with congestion – guaifenesin with pseudoephedrine
- Demulcents – products such Simple Linctus BP, and Glycerin, Lemon and Honey Linctus are cheap, harmless and have a useful placebo effect. They may be used for any type of cough.

Cradle cap

Cradle cap appears as scaling and crusting of the scalp in infants. Its appearance may be worrying to parents, but it is not usually serious.

CAUSES

Cradle cap is a form of seborrhoeic dermatitis of the scalp, causing scaling and crusting. It usually appears within the first three months of life and resolves spontaneously within a year.

TREATMENT

Products available

There are four licensed products available without prescription:

- Capasal Therapeutic Shampoo (shampoo licensed for use in several scalp conditions; it contains salicylic acid, coconut oil and coal tar. It is quite expensive)
  Dermal
- Dentinox Cradle Cap Shampoo (contains sodium lauryl ether sulphosuccinate and sodium lauryl ether sulphate – both anionic surfactant detergents commonly used in medicated shampoos)
  Dendron
- Pragmatar (contains a cetyl alcohol-coal tar distillate with sulphur and salicylic acid. It is applied to the scalp after shampooing, and can be diluted with a little water in the palm of the hand before application. It can be used daily if necessary)
  Alliance Pharmaceuticals
- SCR (contains 1.5 per cent salicylic acid in an aqueous cream base. It is applied to the scalp and washed off after between 30 minutes and two hours, depending on the baby's age and the severity of the condition. Care must be taken to avoid contact with the eyes)
  Pickles

Effectiveness

These treatments have not been shown to be any more effective at treating cradle cap than the method recommended in the *British National Formulary*, which involves rubbing olive oil, arachis oil or baby oil into the scalp, leaving it on overnight then removing by shampooing. However, parents may feel reassured by using a product that is specifically marketed for the condition.

Cystitis

Cystitis is an inflammation of the bladder and urethra, characterised by the frequent urge to pass urine with a burning or stinging sensation on urination.

CAUSES

Bacterial infection is responsible for about half of all cases, and *Escherichia coli* is the most common causative organism. *E. coli* infection results in increased acidity of the urine, which causes the inflammation that produces the symptoms of cystitis. Cystitis among males is relatively rare and is often associated with abnormalities of the genito-urinary tract; men reporting symptoms of cystitis should always be referred to a doctor. Children should also always be referred as they are susceptible to permanent kidney and bladder damage as a result of urinary tract infections.

TREATMENT

Most treatments are based on alkalinising agents which restore the pH of the urine to normal levels, but it has been argued that this is only justified where *E. coli* is known to be involved as the urine is not acidic otherwise. It has also been suggested that, even where *E. coli* is involved, increased fluid intake alone may be as effective as the use of alkalinising agents.

Compounds available

Alkalinising agents used are:

- Sodium bicarbonate
- Sodium citrate
- Potassium citrate

Administration and dosage

Sodium bicarbonate alone is an effective alkalinising agent and is very cheap. It is kept in most homes and is useful when nothing else is to hand. The recommended dose for the alkalinisation of urine is 3 g (a level teaspoonful) in water every two hours until the symptoms subside.

Sodium citrate is contained in several proprietary products (often together with sodium bicarbonate) for the relief of symptoms in cystitis. In each of these products the combined alkalinity of the salts is equivalent to about 4 g of sodium citrate per dose.

Potassium citrate is contained in several preparations in a dose of 3 g. One product contains citric acid and potassium bicarbonate.

The recommended dosage for all these proprietary preparations is three times daily for 48 hours. The full course should be completed even if the symptoms have gone, but if symptoms persist beyond the length of a course patients should be referred. All products should be well diluted with water, and an additional large intake of fluid is recommended to reduce the acidity of the urine through dilution and to flush any infecting organisms out of the bladder.

Cautions, contraindications and interactions

The sodium content of preparations for cystitis is high, i.e. about 35 mmol (800 mg) per dose, and can lead to increased fluid retention and raised blood pressure. These products should, therefore, be avoided by patients with hypertension, heart disease, diabetes, impaired renal function and during pregnancy. (Pregnant women presenting with symptoms of cystitis should in any case always be referred to a doctor.)

Sodium-containing preparations should also be avoided by patients on lithium. Sodium is preferentially absorbed by the kidney and the excretion of lithium is increased, resulting in reduced plasma lithium concentrations.

There is a theoretical risk of hyperkalaemia if potassium citrate is taken together with potassium-sparing diuretics or other potassium-sparing drugs such as angiotensin-converting enzyme (ACE)

inhibitors or aldosterone antagonists. The risk is negligible with the short courses recommended for cystitis preparations, but the advice generally given on package inserts is that patients taking any medication for cardiovascular conditions should consult their doctor.

Products

- Sodium bicarbonate
  - — Sodium Bicarbonate BP
- Sodium citrate
  - — Canesten Oasis sachets
    Bayer Consumer Care
  - — Cymalon sachets
    SSL International
  - — Cystemme sachets
    Abbott
  - — Cystocalm sachets
    Galpharm
  - — Cystoleve sachets
    SSL International
- Potassium citrate
  - — Potassium Citrate Mixture BP
  - — Cystopurin sachets
    Roche Consumer Health
  - — Effercitrate effervescent tablets
    Typharm
- Citric acid and potassium bicarbonate
  - — Effercitrate sachets
    Typharm

PRODUCT SELECTION POINTS

- Alkalinising agents may not be strictly necessary, and may only be helpful when cystitis is due to bacterial infection caused by *E. coli*. However, as pharmacists are unable to ascertain the cause of an attack they are justified in offering treatment.
- Plain sodium bicarbonate is as effective an alkalinising agent as any other treatment, but proprietary products offer the convenience of accurately measured doses and useful information for sufferers on treating and coping with the condition.
- Products containing sodium salts should not be sold to patients with hypertension or heart disease, to pregnant women or to patients taking lithium.
- The risk of hyperkalaemia from short courses of potassium-containing products is very low, but package information may deter patients who are taking medication for cardiovascular conditions from using these OTC products.
- Potassium Citrate Mixture BP may be relatively cheap, but is less convenient and less palatable than proprietary preparations.

PRODUCT RECOMMENDATIONS

Any proprietary product, taking into account contraindications.

Dandruff and seborrhoeic dermatitis

(continued . . .)

Dandruff is seen as excessive shedding of the cornified cells of the scalp in the form of scales. Seborrhoeic dermatitis results from accelerated epidermal proliferation and sebaceous gland activity on the scalp, face and trunk.

CAUSES

Dandruff

Dandruff (pityriasis capitis) is a chronic, non-inflammatory scalp condition characterised by excessive shedding of the cornified cells of the scalp in the form of scales, which is sometimes accompanied by itching and redness of the scalp. Dandruff is rare in young children, but incidence increases rapidly and reaches its peak in the second decade of life, declining gradually thereafter. It is a widespread condition and estimates of prevalence vary, but it has been claimed that 75 per cent of the population is affected at some time in their lives. It appears to affect both sexes equally.

Dandruff is due to a naturally increased rate of horny substance production and cell turnover on the scalp, and may be associated with raised androgen levels. It has been said that the condition is a normal physiological state elevated to the status of a disease solely on cosmetic grounds. However, people with dandruff have been found to have high levels of micro-organisms on the scalp, particularly the yeast *Pityrosporum ovale*, compared with those who do not have the condition. It has not been conclusively determined whether this organism is implicated in the cause of dandruff or is merely encouraged by the abundance of nutrients from shed skin cells, but antimicrobial shampoos active against *P. ovale* appear to control the condition.

Seborrhoeic dermatitis

Seborrhoeic dermatitis (seborrhoea) is the result of accelerated epidermal proliferation and sebaceous gland activity on the scalp, face

and trunk. On the scalp, the condition may be difficult to distinguish from more severe forms of dandruff, as characteristic features are the presence of greasy scales and often pruritus. Seborrhoeic dermatitis is common in infants, when it is known as cradle cap (see section on cradle cap), relatively rare in children and occurs again from puberty, reaching its peak incidence between the ages of 18 and 40. The condition may also involve the area in and around the ears, the eyebrows and eyelashes. As in dandruff, growth of *P. ovale* is increased in the scaly epidermis and may be a causative agent – a theory supported by the fact that ketoconazole improves the condition.

TREATMENT

Topical treatments for dandruff and mild forms of seborrhoeic dermatitis are the same and are available without prescription. Regular use (at least twice weekly) of an ordinary mild detergent shampoo will effectively control dandruff by removing scales, and is recommended in the *British National Formulary* as the treatment of choice.

A wide range of medicated treatments is available, containing ingredients such as:

- Pyrithione zinc
- Selenium sulphide
- Ketoconazole
- Coal tar
- Keratolytic agents
- Antimicrobial detergents

Pyrithione zinc and selenium sulphide

Mode of action

Both compounds are cytostatic agents which act by reducing the rate of epidermal cell turnover. The compounds are generally accepted as being effective in controlling dandruff and are of approximately equal

efficacy. Pyrithione zinc's action is thought to be due to a non-specific toxicity for epidermal cells, whereas selenium sulphide is believed to have a direct antimitotic effect. It has also been suggested that selenium sulphide has an inhibitory action against *P. ovale*, exerting its activity by irreversibly changing free sulphydryl groups in the yeast cells into rigid polysulphide bonds, thereby preventing cell division.

Administration

The effectiveness of pyrithione zinc is dependent on the extent of binding to the hair and epidermis, and is a function of time, temperature, concentration and frequency of application. Early formulations required contact times of five to ten minutes, but for current products about two to three minutes is sufficient at a frequency of use of twice or three times weekly.

Selenium sulphide is used twice weekly for two weeks, then weekly as necessary to control the condition. Each of the two applications per treatment should be left on the hair for three minutes.

Contraindications, cautions and side-effects

Pyrithione zinc binds strongly to both the hair and epidermis but does not penetrate into the dermis, and long-term use has not been associated with toxicity. Selenium sulphide also appears safe for long-term external use, although it is highly toxic if ingested orally. Regular use of selenium sulphide shampoo tends to leave a residual odour of hydrogen sulphide and makes the scalp oily; dyeing or perming of the hair should not be carried out for at least two days either side of using the shampoo. Rare contact dermatitis and hypersensitivity are possible with both compounds. Neither compound should be applied to broken or abraded skin and contact with the eyes should be avoided. Neither is contraindicated in pregnancy or breast-feeding, although the manufacturers of selenium sulphide shampoo advise against its use during the first trimester of pregnancy. Selenium sulphide preparations are not recommended for use in children under five years.

Products

- Pyrithione zinc
  - — Polytar AF shampoo (contains pyrithione zinc 1 per cent with coal tar extracts and cade oil. It is the only licensed medicine to contain pyrithione zinc)
    Stiefel
  - — The compound is contained in several 'medicated' shampoos which are not licensed as medicines, including Head and Shoulders
    Procter & Gamble (HB&C)
- Selenium sulphide
  - — Selsun shampoo (2.5 per cent)
    Abbott

Ketoconazole

Mode of action

Ketoconazole is available as a 2 per cent shampoo. It is an azole anti-fungal which inhibits replication of yeast cells by interfering with the synthesis of ergosterol – a vital component of the cell membrane. Several studies have shown ketoconazole to be effective in clearing dandruff and scalp seborrhoea, but not significantly more so than selenium sulphide or pyrithione zinc. Ketoconazole does, however, appear to be better tolerated than selenium sulphide. It is more expensive than selenium sulphide and 'medicated' pyrithione zinc preparations.

Administration

To clear dandruff and seborrhoeic dermatitis, the shampoo is used twice weekly for two to four weeks; on each application it should be left on the hair for three to five minutes. The condition can then be controlled with weekly or fortnightly use.

Contraindications, cautions and side-effects

Ketoconazole shampoo appears to be extremely safe to use. The compound has not been detected in plasma following topical use, so the shampoo is not subject to the adverse effects and interactions associated with systemic use. Skin irritation has been reported only very rarely. It is not contraindicated in pregnancy.

Product

There is only one product:

- Nizoral Dandruff Shampoo
  Johnson & Johnson MSD

Coal tar and other tar products

There is a wide range of products licensed for dandruff, seborrhoeic dermatitis and psoriasis of the scalp and available without prescription. Most of these products contain combinations of ingredients, of which coal tar is the most popular.

Mode of action

The mode of action of coal tar is unclear; it does not appear to reduce cell proliferation but appears to prevent the formation of squames or flakes of dandruff by interfering with the formation of intracellular cement. It also appears to impede the formation of sebum, and to have antipruritic properties.

Products

At least a dozen formulations are available for use on the hair, containing different coal tar solutions and extracts in varying concentrations, often in association with other tar derivatives and other constituents. The rationale for these combinations is unclear as there

is little evidence for synergistic or additive effects of constituents in the treatment of dandruff. Concerns have recently arisen over possible carcinogenicity and mutagenicity of coal tar and special precautions for handling the raw material are now required, but so far no restrictions have been placed on the use of manufactured products.

Some examples of coal tar containing preparations are:

- Alphosyl 2 in 1 Shampoo and Alphosyl Lotion
  Stafford-Miller
- Clinitar Shampoo
  Cambridge Healthcare Supplies
- Pentrax Shampoo
  DermaPharm
- Polytar Liquid
  Stiefel

Keratolytic agents

The keratolytic properties and possible adverse effects of salicylic acid are described in the sections on athlete's foot and acne.

Mode of action

In the treatment of dandruff, salicylic acid, at adequate concentration, would be expected to help break up dandruff squames and loosen them from the scalp.

Administration

Three proprietary shampoos containing salicylic acid (in combination with other constituents), with concentrations varying from 0.5 to 3 per cent, are licensed for the treatment of dandruff, seborrhoeic dermatitis and other scaly conditions of the scalp. A minimum concentration

of 1 per cent is reported to be necessary to show a keratolytic effect on the scalp, but a prolonged contact time is needed and the effect takes up to 10 days to develop. Shampoos containing salicylic acid are greatly diluted on application, contact time is minimal and there is unlikely to be sufficient left on the scalp after rinsing to exert a residual effect, so casting doubt on their effectiveness. Some shampoos contain other keratolytic agents, including sulphur which is believed to cause increased sloughing of cells via an inflammatory process, and allantoin which is claimed to have chemical debriding properties.

There are also two ointment formulations containing salicylic acid and coal tar; these are likely to be more effective than shampoos but are messy to use and the risk of adverse effects is greater.

Products

- Capasal Therapeutic Shampoo
  Dermal
- Ionil T Shampoo
  Galderma (UK)
- Meted Shampoo
  DermaPharm
- Pragmatar Cream
  Alliance Pharmaceuticals
- Cocois Coconut Oil Compound
  Medeva Pharma

Antimicrobial detergents

Ceanel Concentrate (Quinoderm Ltd) contains cetrimide, a quaternary ammonium antiseptic and cationic surfactant, together with an antifungal agent, undecenoic acid, at very low concentration. It may be no more effective for dandruff than an ordinary shampoo used regularly.

PRODUCT SELECTION POINTS

- Pyrithione zinc, selenium sulphide and ketoconazole shampoos are all effective in controlling dandruff, and there is little difference between them in effectiveness. Selenium sulphide is slightly less pleasant to use, and ketoconazole shampoo is more expensive than shampoos containing the other two compounds.
- There is only one product containing pyrithione licensed as a medicine, but there are several brands and own-label versions available as 'medicated' shampoos.
- A wide range of shampoos containing coal tar, keratolytic agents and microbial detergents is available, but they should not be the first choice for the treatment of dandruff.
- According to the *British National Formulary* the treatment of choice for dandruff is the frequent use of a mild detergent shampoo.

PRODUCT RECOMMENDATIONS

Regular (twice weekly) use of an ordinary shampoo should be tried initially. If this is not effective, the treatment of choice on grounds of cost and cosmetic acceptability would be a 'medicated' pyrithione zinc shampoo, although ketoconazole and selenium sulphide shampoos are equally effective.

Diarrhoea

Diarrhoea of an acute self-limiting nature can be treated with non-prescription medicines.

CAUSES

Diarrhoea of the acute self-limiting type is generally caused either by bacterial or viral infection through ingestion of contaminated food or drink. Some bacteria (e.g. toxigenic *Escherichia coli* and *Staphylococcus aureus*) produce toxins which bind to the mucosal cells of the small intestine, causing hypersecretion of fluid. This overwhelms the reabsorbing capacity of the colon and results in watery diarrhoea, often with little or no fever or other symptoms. Other bacteria (e.g. invasive *E. coli*, salmonella and shigella) directly invade mucosal epithelial cells and cause an inflammatory reaction, producing an often less fluid diarrhoea accompanied by nausea, vomiting, cramps and sometimes low-grade fever. Viral infections, which often affect babies and young children, also produce watery diarrhoea. Acute diarrhoea can also have non-infective causes, such as stress, alcohol and hot, spicy food.

Normal faeces contain 60 to 85 per cent water, and between 70 and 200 ml of water per day is lost from the body through defecation. In diarrhoea, water loss of up to four times this volume per loose stool occurs, and sodium and potassium alkaline salts are excreted along with it, leading to a fall in plasma pH (acidosis), which can have serious metabolic consequences. Fluid and electrolyte losses are increased if vomiting also occurs.

In babies and young children the situation is especially hazardous, as a relatively high proportion of total body weight is lost, and dehydration can occur very rapidly. The elderly are also particularly sensitive to the effects of fluid and electrolyte loss, especially if they are taking diuretics. Reduction in blood volume due to excessive loss of fluid through diarrhoea may stimulate the secretion of aldosterone from the adrenal cortex, causing excretion of potassium and leading to hypokalaemia. Excessive fluid loss may also lead to renal failure through reduction of renal artery blood flow.

TREATMENT

Oral rehydration therapy

The first line of treatment for acute diarrhoea is fluid and electrolyte replacement by oral rehydration therapy (ORT). This is particularly important in the very young and the elderly. ORT is not intended to relieve symptoms. As diarrhoea is regarded as the natural way to 'flush out' the causative organisms and toxins from the bowel, the use of antidiarrhoeals, which are either intestinal antimotility agents or adsorbents, is regarded as unnecessary and sometimes undesirable from a therapeutic viewpoint. It is recognised, however, that sufferers will often wish to curtail diarrhoea for reasons of comfort or convenience, but the use of antidiarrhoeals should be regarded as an adjunct to fluid and electrolyte replacement.

Before recommending any treatment, serious underlying causes of diarrhoea must be considered and excluded. In addition, referral should be made for any episode lasting more than 72 hours in adults and older children, 48 hours in children under three years and the elderly, and 24 hours in children under one year. Infants under three months should be referred immediately.

Mode of action

Oral rehydration salts (ORS) are designed to replace water and electrolytes lost through diarrhoea and vomiting. They contain sodium and potassium to replace these essential ions and citrate and/or bicarbonate to correct acidosis. Glucose is also an important ingredient as it acts as a carrier for the transport of sodium ions, and hence water, across the mucosa of the small intestine.

The composition of the ORS preparations available in the United Kingdom varies between products, but all are designed to correct fluid loss and electrolyte imbalance associated with mild to moderate diarrhoea. The sodium content is in the range of 50 to 60 mmol/l and the glucose content up to 200 mmol/l. World Health Organization (WHO) oral rehydration salts contain a higher concentration of sodium

(90 mmol/l), and are intended for use mainly in developing countries where conditions causing severe diarrhoea and fluid loss are relatively common.

ORT is not intended to stop diarrhoea, but acute diarrhoea is self-limiting and normally ceases within 24 to 48 hours. ORT can be recommended for patients of any age, even when referral to a doctor is considered necessary.

An oral rehydration product (Dioralyte Relief, Aventis Pharma) is available containing powdered rice starch in place of glucose. It is claimed to achieve even greater rehydration than glucose over time, and the rice starch is claimed to help produce firmer stools, leading to faster recovery compared with glucose. A Cochrane Review found that the product was effective in reducing stool output and consequent fluid loss in people suffering from cholera, but that it had little effect in infants and children with non-cholera diarrhoea.

Dosage and administration

The contents of one sachet of ORS (or two Dioralyte effervescent tablets, Aventis Pharma) should be dissolved in 200 ml of water (250 ml in the case of Rehidrat, Searle); for infants the water should be freshly boiled and cooled. It is important to make up the solution exactly to the recommended volume; too concentrated a solution will be hyperosmolar, drawing more water into the intestine, exacerbating the diarrhoea and dehydration. To avoid risk of possible exposure to further infection, the solution should be discarded not later than one hour after reconstitution, or it may be kept for up to 24 hours if stored in a refrigerator.

The recommended dose of ORS for an adult is 200 to 400 ml after every loose motion, or two to four litres over four to six hours. (Diabetic patients can use ORS, but they should be reminded to monitor blood glucose levels carefully.) Patients may prefer to sip one or two teaspoonfuls every few minutes rather than drink large quantities less frequently. Children over two years should be offered a cupful (200 ml) of solution after each loose stool, and children under two years should be offered a quarter to half a cupful. Infants should be given one to

one-and-a-half times the normal feed volume. Both breast- and bottle-fed babies should continue to be fed normally during diarrhoea; formula feed should not be diluted.

Contraindications and cautions

There are no contraindications to ORT unless the patient is vomiting frequently and unable to keep the solution down, in which case intravenous fluid and electrolyte replacement may be necessary. Fluid overload from excessive administration of ORS is highly unlikely, but possible if it is continued in babies and young children for more than 48 hours. Fluid overload is recognised by the eyelids becoming puffy, and is rapidly corrected by withholding ORS and other liquids.

Products

- Dioralyte sachets and tablets
  Aventis Pharma
- Dioralyte Relief sachets
  Aventis Pharma
- Electrolade sachets
  Eastern Pharmaceuticals
- Entrocalm Replace sachets
  Galpharm International
- Rehidrat sachets
  Searle
- Replavite
  Sussex Pharmaceuticals

Opioids

Compounds available

The following compounds are available:

- Loperamide
- Morphine
- Codeine

Mode of action

One of the effects of morphine and the opioid drugs is to cause constipation by increasing tone of both the small and large bowel and reducing intestinal motility. They also increase sphincter tone and decrease secretory activity along the gastrointestinal tract. Decreased motility enhances fluid and electrolyte reabsorption and decreases the volume of intestinal contents.

Loperamide has a high affinity for, and exerts a direct action on, opiate receptors in the gut wall. It also has a high first-pass metabolism so very little reaches the systemic circulation, and at the restricted dosage permitted for non-prescription use it is unlikely to cause any of the side-effects associated with opiates. Studies have shown it to be effective in reducing the duration of diarrhoea, although it should be remembered that acute diarrhoea is in any case self-limiting and relatively short-lived. A recent study showed that dosing with 2 mg loperamide produced complete relief from diarrhoea in a median time of 25 hours, compared with 40 hours for placebo.

Morphine acts promptly on the intestine (within one hour of administration), because of its direct action on intestinal smooth muscle and quick absorption from the gastrointestinal tract. Its action peaks within two to three hours and lasts about four hours. Morphine is not well absorbed orally and its availability may be reduced in combination products because of its adsorption on to other constituents.

Codeine is a weaker opioid than morphine.

Dosage

Loperamide – adults and children over 12 years, two capsules initially, followed by one after each loose bowel motion up to a maximum of eight capsules in 24 hours. If symptoms have not subsided within 24 hours the patient should be referred. Loperamide is not licensed

for non-prescription use in children under 12 years, and should not be recommended to pregnant or breast-feeding women.

Morphine – the morphine content per recommended dose of the products listed below ranges between 0.5 and 1 mg. The effectiveness of these small amounts in controlling diarrhoea is debatable; no specific effective dose has been stated by the United Kingdom authorities, but the United States Food and Drug Administration considers dosages in the range 1.5 to 2 mg morphine to be effective.

Side-effects and cautions

The use of opioids as antidiarrhoeals is limited by their actions on the CNS, which include CNS depression and the risk of dependence. However, the risk of dependence at usual dosages for acute diarrhoeal episodes is low. Community pharmacists will none the less be well aware of the abuse potential of OTC products containing morphine and codeine.

Products

- Loperamide (all 2 mg – licensed for use in adults and children from the age of 12 years)
  - — Arret capsules
    Johnson & Johnson MSD
  - — Diah-Limit capsules
    Wallis
  - — Diasorb capsules
    Norton
  - — Diocalm Ultra capsules
    SSL International
  - — Imodium capsules
    Johnson & Johnson MSD
  - — Normaloe tablets
    Tillomed Laboratories

- Loperamide with simethicone (Imodium Plus, Johnson & Johnson MSD)

  Loperamide (2 mg) is formulated with the surfactant compound simethicone (125 mg) in a chewable tablet. The manufacturers claim that the combined formulation relieves the cramping and bloating that can accompany diarrhoea, and that it improves the effectiveness of loperamide. A study involving nearly 500 patients has shown that the combination product considerably reduced the duration of diarrhoea and relieved gas-related discomfort in comparison with loperamide alone. The dose of this product is two tablets initially for adults over 18 years of age (one tablet for young adults between 12 and 18 years) followed by one tablet after each loose stool (for all ages from 12 years). The maximum dose is four tablets daily for two days.

- Morphine (licensed for use in adults and children from the age of six years)

  — Kaolin and Morphine Mixture BP

  — J. Collis Browne's Mixture and Tablets
  SSL International

  — Diocalm Dual Action tablets (also contains attapulgite)
  SSL International

  — Opazimes tablets (also contains aluminium hydroxide, kaolin and belladonna dry extract)
  Co-Pharma

- Codeine

  — Kaodene (contains 10 mg codeine phosphate and 3 g kaolin in 10 ml – licensed for use in adults and children from the age of five years)
  Sovereign Medical

At the time of writing reclassification from POM to P had been proposed for co-phenotrope tablets, containing diphenoxylate hydrochloride

2.5 mg and atropine sulphate 0.025 mg, for the treatment of acute diarrhoea. The preparation is likely to be available without prescription from early 2002. Diphenoxylate is a synthetic opioid derivative with similar activity to loperamide. Atropine is a naturally occurring antimuscarinic alkaloid with an inhibitory effect on gastrointestinal motility. Under the proposed licensing conditions use will be restricted to persons aged 16 and over, the maximum dose will be ten tablets daily, and the maximum pack size will be 20 tablets. Co-phenotrope, marketed as Lomotil (Goldshield), has been available as a POM since 1973.

Adsorbents

Compounds available

The following compounds are available:

- Kaolin
- Pectin
- Attapulgite
- Bismuth subsalicylate

Kaolin is a natural hydrated aluminium silicate which has been used in the treatment of diarrhoea since ancient Greek times. It is not absorbed from the gastrointestinal tract, and about 90 per cent of the drug is metabolised in the gut and excreted in the faeces.

Attapulgite is another naturally occurring clay mineral, consisting of hydrous magnesium aluminium silicate. Its adsorptive capacity can be increased by thermal treatment; the heat-treated form is known as activated attapulgite, and alkaloidal adsorptive studies have shown it to have an *in vitro* adsorptive capacity for certain toxic compounds which is five times greater than kaolin. Both kaolin and attapulgite have been shown to have varying and relatively weak adsorptive properties in respect of diarrhoea-producing bacteria.

Pectin is a purified carbohydrate obtained from the rind of citrus fruit or pomace (crushed apple); its mode of action is uncertain.

Bismuth subsalicylate is claimed to possess adsorbent properties, and some studies have shown it to be effective in treating diarrhoea. Large doses are required and salicylate absorption may occur; it should be avoided by individuals sensitive to aspirin.

Mode of action

The rationale behind the use of adsorbents is that they are capable of adsorbing microbial toxins and micro-organisms on to their surfaces. Because the drugs are not absorbed from the gastrointestinal tract, adsorbed toxins and micro-organisms are ultimately excreted in the stool. In addition, adsorbents, particularly hydrophilic organic polymers (e.g. pectin and bulk-forming agents), bind water within the intestine causing watery stools to become more formed. Bulk-forming agents (e.g. ispaghula, methylcellulose and sterculia), which are plant-derived polysaccharide products that absorb water and add bulk to stools, are used to treat some forms of chronic diarrhoea. They are more usually used as laxatives (see constipation section).

Adsorbents are used as the main constituents in antidiarrhoeal preparations for young children, in whom opiates and antimuscarinics are contraindicated. As they are largely unabsorbed from the intestine, adsorbents are relatively harmless and safe to use, but there is little evidence that they are effective. An argument has also been put forward that if they do reduce evacuation of faeces, they may prolong the presence of offending pathogens and toxins in the bowel. Adsorption is a non-specific process, and as well as adsorbing toxins, bacteria and water, the drugs may interfere with the absorption of other drugs from the intestine. This should be borne in mind if recommending adsorbent antidiarrhoeals to patients taking other medicines.

Products

(See also products listed above under morphine and codeine.)

- Kaolin
  - — Kaolin Mixture BP

- — Entrocalm tablets
  Galpharm International
- — Junior KaoC suspension (also contains calcium carbonate)
  Torbet Laboratories

- Attapulgite
  - — Entrotabs (also contains pectin and aluminium hydroxide)
    Shire Pharmaceuticals

- Bismuth subsalicylate
  - — Pepto-Bismol
    Procter & Gamble

Belladonna

Belladonna dry extract is a constituent of Opazimes (Co-Pharma) tablets. The mode of action of belladonna extract, its contraindications and interactions are described under antispasmodics in the section on indigestion.

Mode of action

The function of belladonna in this product is presumably to reduce the frequency and force of movement of the smooth muscle of the intestine, in order to relieve pain and reduce the intensity of the diarrhoea.

Dosage

Belladonna Dry Extract BP 1988 contains 1 per cent alkaloids calculated as hyoscyamine, and the hyoscyamine content of the recommended dosage of Opazimes tablets is 60 µg. The recommended dose of hyoscyamine as an antispasmodic is 150 to 300 mg, and it would therefore appear that the content of belladonna dry extract in these products is at virtually homeopathic level. In addition, belladonna dry

extract is formulated together with morphine which directly opposes the effect of belladonna on intestinal tone, so the inclusion of both would seem to be irrational from a pharmacological viewpoint.

PRODUCT SELECTION POINTS

- Acute infective diarrhoea is a self-limiting condition which normally resolves without treatment within a couple of days. It is debatable whether any attempt should be made to stop acute diarrhoea, although patients' desire not to want to suffer the discomfort and inconvenience it causes is understandable. If the patient will accept the advice, normally the best course of action is to recommend ORT and provide reassurance.
- Patients with diarrhoea should be referred to a doctor if it persists for more than 24 hours in babies under one year, for two days in children under three and in elderly patients, and three days in older children and adults. Infants under three months with diarrhoea should be referred immediately.
- The most important thing in managing acute diarrhoea is to ensure that the fluid and electrolytes lost are replaced and that dehydration is avoided. This is especially important for elderly and very young patients.
- ORT can be safely recommended to any patient with diarrhoea, even if an antidiarrhoeal is also supplied or the patient has to be referred to a doctor.
- Loperamide is probably the most effective antidiarrhoeal, and is unlikely to cause any adverse effects at the recommended licensed dosage. It cannot be supplied without prescription for children under 12 years. Loperamide with simethicone appears to be more effective than loperamide alone.
- Antidiarrhoeals containing morphine may not be very effective due to the low concentration of the drug in OTC products. Co-formulation with adsorbents may also reduce its availability. Nonetheless, morphine-containing products are liable to abuse.

- There is little evidence that adsorbents are effective as antidiarrhoeals, but they should do no harm. They can be safely taken by younger children if a parent insists on wanting to stop the diarrhoea, although ORT should always be strongly recommended as well.
- Products containing belladonna extract would appear to have little value due to the low concentration of the drug. The combination of belladonna with morphine in antidiarrhoeal products seems pharmacologically irrational.

PRODUCT RECOMMENDATIONS

Based on rational criteria, the choice of products available for diarrhoea is very limited. First-line treatment for all patients and in all circumstances, but especially for babies, young children and the elderly – ORT; for adults who want to curtail diarrhoea – loperamide or loperamide with simethicone.

Dry skin

Dry skin is a common condition from which nearly everybody suffers at some time.

CAUSES

Dry skin results from an inadequate moisture content in the stratum corneum. It is associated with a range of skin conditions, including contact dermatitis, atopic eczema and psoriasis, and with various systemic disorders such as hypothyroidism, arthritis and autoimmune conditions.

Dry skin becomes more common with increasing age because of thinning of the epidermis and its reduced ability to retain moisture. In healthy people, dehydration of the skin may be caused by cold weather or over-exposure to the sun, or by occupational exposure to dehydrating agents. The symptoms of dry skin include roughness and flaking, loss of flexibility, fissures, hyperkeratosis, inflammation and pruritus, in varying degrees of severity depending on the cause and individual response.

TREATMENT

Dry skin is treated with the use of moisturisers and emollients.

The symptoms of dry skin begin to appear when the water content of the stratum corneum falls below 10 per cent, and the principle of treatment is rehydration to its normal level of between 10 and 20 per cent. Moisturising and emollient preparations are formulated to achieve this by replacing water lost from the epidermis (although this is only possible to a limited extent) and by preventing further evaporation. The latter may be achieved simply by applying a film of oil to the skin while it is wet or directly after it has been wetted and dried, for example by adding oil to a bath or applying it directly afterwards. However, for minor dry skin conditions, oil-in-water emulsions provide a more aesthetically acceptable method.

Emulsions first hydrate the skin, with various constituents being used to enhance water penetration or uptake by the epidermis (see

below). Loss of water from the emulsion, due mainly to evaporation and to a lesser extent absorption into the skin, in addition to the mechanical stress caused by its application, then causes the emulsion to crack, releasing the oil phase. The layer of oil forms a hydrophobic seal over the skin which retards further water evaporation. Oil-in-water creams and lotions also have a cosmetic effect through smoothing down the rough, scaly surface of dry skin and reducing mechanical drag, making it feel smooth to the touch. Water evaporation, especially from emollients with a higher water content, produces a cooling effect on the skin which alleviates pruritus accompanying dry skin conditions such as eczema.

The degree of occlusiveness and of prevention of water evaporation can be varied by varying the oil content of emulsions. Water-in-oil preparations with a very greasy texture are also available; these may be suitable for more severe dry skin and eczematous conditions but they are generally less aesthetically acceptable for use in mild dry-skin conditions.

A wide range of proprietary emollient products is available, in a variety of presentations, including creams, ointments, lotions, bath oils, water-dispersible bath additives, an aerosol spray and a shower gel. Although some are expensive and usually supplied on prescription, all can be bought over the counter. There are also some inexpensive formulary emollient preparations, including Emulsifying Ointment BP and Aqueous Cream BP, which consists of emulsifying ointment 30 per cent with water. These may be as effective as more expensive products, although less cosmetically elegant than some. There has been some controversy over the appropriateness of using Aqueous Cream purely on the grounds of cheapness: the Skin Care Campaign, an alliance of groups including United Kingdom national dermatology patient organisations and health professionals, has expressed concern that it causes sensitisation in substantial numbers of people, especially children. Sensitisation has been ascribed to the partitioning of the emulsifying agent, sodium lauryl sulphate, in the formulation.

With such a wide choice of products and little objective evidence of relative effectiveness, choice is often a matter of personal preference.

Emollient preparations are generally very safe to use, the only contraindication being sensitivity to constituents. The principal constituents of emollient products are reviewed below.

Paraffins

Hard, soft and liquid paraffins are mixtures of hydrocarbons obtained from petroleum; liquid paraffin is also known as mineral oil. Soft and liquid paraffins can be used on their own as emollients and are effective occlusive agents. However, they are usually not cosmetically acceptable as they are greasy and difficult to wash off the skin, and their occlusive effects can sometimes lead to maceration of the skin, which may aggravate existing dermatitis. Mixtures of hard, soft and liquid paraffins are used as bases in many emollient and other dermatological creams.

Product examples

- Aqueous Cream BP
- Emulsifying Ointment BP
- Alcoderm Cream and Lotion
  Galderma (UK)
- Alpha Keri Bath Oil
  Bristol-Myers Squibb Pharmaceuticals
- Diprobase cream
  Schering-Plough
- Diprobath bath additive
  Schering-Plough
- E45 Cream
  Crookes Healthcare
- Oilatum Cream and Bath Formula
  Stiefel

- Ultrabase cream
  Schering Health Care
- Unguentum M Cream
  Whitehall

Glycerol, propylene glycol and sodium pidolate

Glycerol is a trihydric alcohol; it is hygroscopic and used in emollient and hydrating products to promote the retention of water in the skin. It also improves the feel and consistency of formulations, making them more pleasant to use. In concentrations above 50 per cent glycerol acts as a dehydrating, rather than a hydrating, agent. This property is exploited in Magnesium Sulphate Paste BP used in the treatment of boils and carbuncles, where it attracts water-containing pus towards the area of application, preventing it spreading into the tissues.

Propylene glycol and sodium pidolate have hygroscopic properties similar to glycerol, and are used in emollients to increase hydration of the skin.

Product examples

- Hydromol Cream
  Quinoderm Ltd
- LactiCare lotion
  Stiefel
- Neutrogena Norwegian Formula Dermatological Cream
  Neutrogena UK
- Probase 3 Cream
  Schering-Plough

Urea

At a concentration of 10 per cent, urea increases hydration of the skin. (At higher concentrations, it is claimed to have keratolytic and antipruritic properties.) Urea can cause burning or stinging, and may irritate inflamed skin, but this is usually minimised by formulating products to a pH of 6.

Product examples

- Aquadrate cream
  Procter & Gamble Pharmaceuticals
- Calmurid cream
  Galderma (UK)

Both of the above contain urea 10 per cent.

Lactic acid

Lactic acid and other alpha-hydroxy acids increase hydration of the skin and control keratinisation.

Product examples

- Calmurid
  Galderma (UK)
- LactiCare lotion
  Stiefel

Natural products

Lanolin (anhydrous wool fat) is derived from the sebum of sheep and is thought to be similar to human sebum. It is an excellent emollient,

being highly water-absorbent (up to about 30 per cent) and therefore a useful water-in-oil emulsifier. It is also occlusive. Lanolin has been less popular as an emollient in recent years due to reports of sensitisation, but purified and hypoallergenic derivatives have been developed and it is still included in several products.

Isopropyl myristate is a fatty acid ester derived from coconut oil. It is included as an ingredient in several emollients as it is stable in formulations, fairly readily absorbed into the skin and has a good 'skin-feel'. Soya, arachis and almond oils are also used in emollient products.

Product examples

- Balneum bath treatment
  Crookes Healthcare
- Dermol 500 Lotion
  Dermal Laboratories
- Diprobath bath additive
  Schering-Plough
- Emulsiderm Emollient emulsion
  Dermal
- Hydromol Cream
  Quinoderm Ltd
- Imuderm Therapeutic Oil
  Goldshield Pharmaceuticals

Administration

Treatment regimens depend on the condition, and can range from daily baths containing oils or emollient additives followed by liberal application of further emollients, to the occasional application of a cream to a patch of dry skin. Patients needing the former are likely to

be under medical supervision, but pharmacists should be able to advise them how to use their products to the best effect.

A bath is good therapy for atopic eczema or severe dry skin as it hydrates the skin and provides a good base for the application of emollients. Between 10 and 30 ml of bath additive (the exact amount depends on the product) should be added to a lukewarm bath at about 37°C. (If the water is too hot it will cause dilation of the blood vessels and can make the itching of eczema worse.) Emulsifying Ointment BP can be used as a bath additive; about 30 g should be whisked up with hot water in a jug and then poured under the running tap. After bathing the skin should be patted, not rubbed, dry.

Hydration is claimed to increase the efficacy of topical medication tenfold, so an emollient should be applied immediately, before the skin dries out. Emollients are safe to use and can be applied as frequently as needed during the day. For patients with atopic eczema the emollient can be applied liberally over the entire body, including the face and scalp if needed.

PRODUCT SELECTION POINTS

- There is a wide range of emollient products in a variety of presentations, although some are intended primarily for use in atopic eczema and chronic dry skin conditions. Oil-in-water creams or lotions are generally the most suitable and cosmetically acceptable preparations for mild dry skin conditions.
- With little or no evidence of comparative effectiveness, choice is generally based on personal preference and cost.
- Some products, particularly emollient bath additives and other preparations used mainly for atopic eczema or chronic dry skin conditions, seem very expensive in relation to the intrinsic value of their constituents and their relatively simple formulations.

PRODUCT RECOMMENDATIONS

For mild dry skin conditions – an oil-in-water emollient cream or lotion.

For atopic eczema and chronic dry skin conditions – emollients, with the choice of product and presentation depending on the situation and individual preference.

Ear problems

Ear problems offer little scope for pharmacists to advise on treatment as patients' descriptions of their symptoms and their own self-diagnoses may be misleading, and medical examination is usually necessary for accurate diagnosis.

CAUSES

Earache

In adults, earache may sometimes be associated with an upper respiratory tract infection, and so long as the pain is not severe it may be treated with oral analgesics for up to 48 hours before referral if the condition does not improve. Earache in children should always be referred, as otitis media is fairly common and repeated attacks can lead to permanent damage if not properly managed; use of an oral analgesic can be advised until a doctor can be seen. Analgesic ear drops are available without prescription, but are not generally recommended.

Ear wax

Cerumen (ear wax) is a complex oily fluid secreted by sebaceous and apocrine glands in the external auditory canal, which combines with exfoliated skin cells to form a protective waxy layer. This is normally moved outwards by movement of the jaw in speaking and chewing, and removed by washing. In some individuals excessively cohesive cerumen is produced. This forms a waxy plug which affects hearing and causes discomfort, and the prophylactic use of a cerumenolytic preparation is sometimes recommended. Generally, however, syringing is necessary to remove ear wax, although cerumenolytics can be used in advance to soften, loosen and partially dissolve it.

Otitis externa

Otitis externa is an inflammation of the external auditory canal. The acute form is usually caused by bacterial infection, but may be fungal or viral. The chronic form is eczematous and may be atopic or a contact dermatitis. A dermatitis may become infected and the two types of otitis externa can exist together.

TREATMENT

Earache

Compound available – choline salicylate

There is only one formulation available without prescription which contains an analgesic constituent: choline salicylate; the product also contains glycerol. It is available as two brands – Audax and Earex Plus – both marketed by SSL International and licensed for the relief of earache and softening of ear wax.

Mode of action

Choline salicylate is used as a local analgesic, and it is also included in gels for the treatment of sore mouths and mouth ulcers. It has a counterirritant effect, and is also hydrolysed by cutaneous esterases to produce salicylic acid, which probably exerts some anti-inflammatory effect due to antiprostaglandin activity. One small double-blind trial found Audax ear drops to be more effective as an analgesic than placebo. However, the *British National Formulary* states that choline salicylate is of doubtful value when applied topically.

Audax and Earex Plus also contain glycerol, and in a comparative trial Audax was found to be a more efficient cerumenolytic than Earex drops, another brand marketed by the same company, containing fixed and volatile oils. Glycerol has been claimed to be as effective as anything else for softening ear wax.

Although marketed as cerumenolytics and not for the relief of ear pain, some other brands of ear drops contain constituents with counterirritant or local analgesic properties, such as camphor oil, chlorbutol, turpentine oil and terpineol, which may have some analgesic effects.

Ear wax

Cerumenolytic ear drops are available for the softening of ear wax, but should generally only be supplied if a doctor or a nurse trained to diagnose ear conditions has advised their use following examination, as patients will often mistakenly ascribe any ear problem, including loss of hearing, discomfort and pain, to this cause. Cerumenolytics may soften ear wax and make it easier to remove by syringing, but they are unlikely to dissolve and remove compacted plugs on their own.

Several approaches are taken to loosening and dissolving wax in the ear, including the use of aqueous and oily solvents, and surfactants and oxygen generation to facilitate penetration of water into the plug. Constituents of cerumenolytic products include fixed and volatile oils, glycerol, docusate, urea hydrogen peroxide and paradichlorobenzene. However, in an *in vitro* study performed to compare the efficacy of a number of wax-dispersing preparations, it was found that water, originally intended to be a control, proved to be the most effective agent.

Constituents of cerumenolytic ear drops

- **Fixed and volatile oils**

  As wax contains a high proportion of oily components, it is logical to assume that it can be at least partially dissolved by oils, and the *British National Formulary* recommends the use of olive oil or almond oil to soften wax before removal.

However, in the *in vitro* study mentioned above, olive oil appeared to be almost totally ineffective as a wax dispersant. Turpentine oil is widely used as a solvent, and terpineol also has solvent properties, and both are included in Waxwane ear drops (Thornton & Ross). Earex ear drops (SSL International) contain arachis, almond and camphor oils in equal proportions.

- **Docusate sodium**

  Docusate sodium is a surface active agent which increases water penetration into the wax plug. In an *in vitro* comparison with four other proprietary cerumenolytic products with different formulations, Waxsol (Norgine), an aqueous preparation containing 0.5 per cent docusate sodium, was found to be the most efficient. However, this test was carried out in the company's own laboratories. Clear Ear (Co-Pharma) and Molcer (Wallace) ear drops both contain 5 per cent docusate sodium; Waxsol originally contained this concentration, but was reformulated in the mid-1980s following reports of local irritation.

- **Urea hydrogen peroxide**

  Exterol (Dermal) and Otex (Dendron) ear drops both contain 5 per cent urea hydrogen peroxide in a glycerol base. In contact with tissues containing the enzyme catalase, hydrogen peroxide releases its oxygen to create effervescence which helps to break up wax by a mechanical action. The glycerol assists in softening the wax, and the urea in increasing penetration of the solution into the plug. Hydrogen Peroxide Solution BP 20 volume (6 per cent), diluted one part with three parts of water, may also be used but may not penetrate so effectively.

- **Sodium Bicarbonate Ear Drops BP**

  This preparation contains 5 per cent sodium bicarbonate and 30 per cent glycerol in water. In an *in vitro* test it performed well in comparison to proprietary preparations.

- **Paradichlorobenzene**

  This is contained in Cerumol ear drops (LAB), in an oily base with chlorbutanol. The compound is claimed to assist the oil to penetrate ear wax plugs, but in a comparative test it fared less well than other proprietary products and water. It is also reported to be irritant. Nevertheless, it has been a popular product for many years.

Administration of cerumenolytic ear drops

The following technique is recommended for the most effective use of ear drops:

- It is best to have another person instil the ear drops.
- Before use the drops should be slightly warmed by holding in the hands for a few minutes.
- Patients should lie their head on a flat surface such as a table, with the affected ear uppermost.
- The auricle (pinna) should be lifted upward and backward in adults, or downward and backward in children, to straighten the ear canal.
- The requisite number of drops should be instilled.
- The tragus (the small projection in front of the external opening) should be pressed gently once or twice, to assist the drops down the ear canal and expel air bubbles.
- The patient should remain with the head down for at least five minutes, and then a cotton-wool plug moistened with the drops should be put into the ear.
- Unless otherwise directed, the drops should be used night and morning for three or four days prior to syringing.

Otitis externa

- **Hydrocortisone cream**

  Mild eczematous otitis externa affecting the pinna can be treated with hydrocortisone cream. (For details, see section on irritant and allergic dermatitis.)

- **Aluminium acetate**

  Aluminium aceate is astringent, hygroscopic and produces an acidic environment hostile to pathogenic bacteria. Aluminium Acetate (13 per cent) Ear Drops BP can be used as an anti-inflammatory for eczematous otitis externa in the external ear canal. However, it is not readily available and may have to be obtained from a specials manufacturer, making it prohibitively expensive for sale over the counter.

- **Acetic acid**

  Acetic acid has antibacterial activity, and is reported to be active against *Haemophilus*, *Pseudomonas*, *Candida* and *Trichomonas* species. A 2 per cent solution of acetic acid is available as a pump-action spray (EarCalm Spray; Stafford-Miller), licensed for the treatment of superficial infections of the external auditory canal in adults and children over the age of 12 years. It is used between three and eight times daily until two days after symptoms have disappeared, for up to a maximum of seven days. Use should be discontinued and medical advice sought if symptoms do not improve within 48 hours of starting treatment.

PRODUCT SELECTION POINTS

- Analgesic ear drops should not be recommended for earache unless the cause is known with certainty, and known not to be serious. Earache from an unknown cause should be treated with oral analgesics until a doctor can be seen.

- Cerumenolytic ear drops should not be recommended unless the presence of ear wax has been identified.
- There is conflicting evidence about the effectiveness of the various cerumenolytic products, but preparations with an aqueous base appear to be more effective than those with an oil base.
- Products formulated with glycerol seem to be quite effective.

PRODUCT RECOMMENDATIONS

For earache – oral analgesics only until a medical diagnosis is made.

For ear wax (confirmed as such) – sodium bicarbonate ear drops, or other aqueous based product.

For mild eczematous otitis externa on the pinna – hydrocortisone cream.

For mild infective otitis externa (confirmed as such) – acetic acid 2 per cent solution.

Emergency hormonal contraception (EHC)

TREATMENT WITH LEVONORGESTREL

An emergency hormonal contraception (EHC) product containing levonorgestrel became available as a Pharmacy (P) medicine in January 2001.

EHC has been available since the launch in 1984 of a high-dose oestrogen–progestogen product (Schering PC4, withdrawn October 2001), and a progestogen-only product (Levonelle-2) was introduced in 1999. Both products have proven to be safe in use and effective, but availability was limited to prescription because it was considered that a physical examination was necessary before they could be supplied. However, the effectiveness of EHC depends upon a course being started very soon after unprotected sexual intercourse, and the need to see a doctor can delay this. In addition, it was thought that many potential users were being deterred by the prospect of having to undergo an examination. Recently it has been shown that examinations, and indeed the involvement of doctors, are not necessary for the supply of EHC.

The progestogen-only form of EHC has been shown to be more effective than the oestrogen–progestogen combination and to have a higher safety and lower side-effect profile, and a version licensed for pharmacy sale became available in 2001.

Active constituent and presentation

The course consists of two tablets of levonorgestrel 750 μg each.

Mode of action and efficacy

Levonorgestrel is thought act in one of several ways, depending on at what point in the menstrual cycle it is used:

- Before ovulation it may prevent ovulation taking place by delaying or inhibiting the release of the ovum from the ovary.
- After ovulation it may prevent fertilisation by affecting the motility of the fallopian tube and preventing sperm meeting the ovum.

- After fertilisation it induces changes in the endometrium that render it unreceptive to the ovum and prevent ovum implantation.

All of the above mechanisms are considered to be contraceptive rather than abortifacient, as from a clinical viewpoint fertilisation is not considered to have taken place and a fetus cannot develop until a fertilised ovum is implanted in the endometrium.

Clinical trial data show that, overall, levonorgestrel EHC prevents 85 per cent of expected pregnancies if used within 72 hours of unprotected intercourse, but effectiveness declines with time. It is 95 per cent effective if the first dose is taken within 24 hours, 85 per cent if used within 24 to 48 hours, and 58 per cent effective if used within 48 to 72 hours. It is not licensed for use after 72 hours. It is also important that the second dose is taken 12 hours (and not more than 16 hours) after the first.

Dosage

Levonorgestrel EHC is licensed for use by women of 16 years and over. The first tablet is taken as soon as possible after unprotected sexual intercourse, with the second 12 hours later. The first tablet must be taken not more than 72 hours after intercourse. Unprotected intercourse may have occurred in cases of suspected barrier method failure, or if part of a course of an oral contraceptive has been missed. In the latter situation contraceptive effectiveness can be considered to be compromised, and EHC offered, if intercourse has taken place within seven days of the following:

- with a combined contraceptive:
  - — two or more pills missed from the first seven pills in a pack, or
  - — four or more pills missed mid-course

(If two or more pills are missed from the last seven in a pack, EHC is not necessary providing that the next pack is started immediately, i.e. without the normal pill-free break.)

- with a progestogen-only contraceptive: if one or more pills has been missed or taken more than three hours after the usual time

In all the above situations additional contraceptive precautions should be taken until consecutive daily pill taking at the correct time has been resumed for at least seven days.

Taking levonorgestrel EHC may delay or bring forward the onset of the next period by a few days, but should not otherwise disrupt the cycle. Repeated courses are not dangerous, but can disrupt the cycle. Levonorgestrel EHC is not suitable as a regular means of contraception, and women who ask repeatedly for supplies should be advised to consider long-term methods.

Contraindications

There are very few situations in which levonorgestrel EHC cannot be safely recommended. The only contraindications are:

- Hypersensitivity to levonorgestrel
- Pregnancy, because it will be ineffective, although there is no evidence that the fetus will be harmed if the preparation is taken by a pregnant woman. (Before making a supply a pharmacist should ask appropriate questions to verify that a prospective purchaser is not already pregnant: if she is pregnant, she should be referred)
- Severe hepatic dysfunction
- Conditions, such as severe diarrhoea or Crohn's disease, in which there is a high risk that the medication will not be absorbed

A relative contraindication is breast cancer, although the risk to a sufferer from the medication is much less than that of pregnancy.

Breast-feeding is not a contraindication as only very small amounts of levonorgestrel appear in breast milk. Any potential problem can be overcome by taking a dose immediately after feeding and not feeding the baby for at least three hours after taking a dose.

Side-effects

Side-effects of levonorgestrel EHC are as for progestogens generally and include abdominal pain, headache, dizziness, fatigue and breast tenderness, but these are not usually serious. The main undesirable effect is nausea, which in clinical trials affected 23 per cent of subjects. Vomiting occurred in about 5 per cent of subjects. If vomiting occurs within three hours of a dose of levonorgestrel absorption will be impaired, and another dose must be taken as soon as possible. Two consecutive 12-hourly doses must be kept down within 84 hours of intercourse to ensure effectiveness. There is no medication licensed for non-prescription sale to prevent nausea and vomiting, but antihistamines for motion sickness and domperidone are available without prescription, although supply would be outside of their licensing conditions.

Interactions

Levonorgestrel is metabolised in the liver and drugs which induce liver enzymes will increase its metabolism, and could reduce its effectiveness. Drugs with this effect include primidone, phenytoin, carbamazepine, St John's wort, griseofulvin, rifampicin, rifabutin and ritonavir. Levonorgestrel itself inhibits the metabolism of ciclosporin, raising plasma levels and increasing the risk of toxicity. Patients taking these drugs would need to be referred to their doctor.

Other issues

Repeated requests for EHC

Although there is no evidence that repeated use is harmful, levonorgestrel EHC is not intended to be a means of regular contraception. Repeated use is also likely to disrupt the menstrual cycle. If a client asks repeatedly for supplies, the pharmacist should explain this and advise on conventional methods of contraception.

Third-party requests for EHC

It is not a requirement of the licensing conditions that the supply of EHC must be made to the client in person. However, a pharmacist is unlikely to be able to obtain all the necessary information from a third party to decide that supply is appropriate. Supply to a third party should therefore be made only in exceptional circumstances.

Requests in advance of need

The licensing conditions for levonorgestrel EHC allow supplies only if unprotected intercourse has occurred within the previous 72 hours, which precludes sales in advance of need. This rationale for this restriction has been questioned by some, who argue that as an emergency form of contraception it should be able to be kept available for use without delay should the emergency arise.

Age of clients

The rate of unplanned teenage pregnancies in the UK is the highest in Europe, and 10 000 per annum occur in girls under the age of 16. To try to reduce this figure several health authorities have introduced schemes allowing pharmacists to supply levonorgestrel EHC to girls under the age of 16 under patient group directions. However, the licensing conditions for pharmacy sale of the product do not permit supply to girls under 16.

Moral objections to supply

Some pharmacists have moral or religious objections to hormonal contraception. Others may be prepared to supply contraceptives but regard EHC as a form of abortion, as they believe that life commences with fertilisation of the ovum and not with implantation of the fertilised ovum into the uterine wall. The Royal Pharmaceutical Society's Code of Ethics respects the rights of such pharmacists not to supply EHC themselves, but they must not obstruct a client's right to obtain it and are expected to treat requests sensitively and advise where a supply can be obtained quickly.

Privacy and confidentiality

It is extremely important that a client is able to discuss a request for EHC with a pharmacist in privacy. Arrangements should be made to facilitate this, and the pharmacist should personally deal with all requests for EHC.

Product

- Levonelle tablets
  Schering

Foot problems

Foot problems generally have OTC treatments available, at least for most common minor foot problems. They are usually very effective when properly used, but patience is often required. Encouraging patients to persevere with treatment to a successful conclusion, as well as providing advice on foot care measures to prevent recurrences, is therefore very important.

CAUSES

See under athlete's foot, corns and calluses and verrucas for causes of these common foot problems.

TREATMENT

Products available

See under athlete's foot, corns and calluses and verrucas for details of products available for these conditions.

Cautions

Particular care is needed with certain groups of at-risk patients. Patients with diabetes, for example, often suffer from poor peripheral circulation. They are therefore more liable to ischaemic foot lesions than healthy people, and will recover less readily from any minor foot damage. In addition, peripheral neuropathy may result in a decreased perception of pain so that any injury to the feet may not be noticed. Vision may also be impaired, particularly in elderly patients with diabetes, making it more difficult to see any damage that may have occurred. Pharmacists should, therefore, never recommend any treatment to patients with diabetes for foot problems, and if asked for advice should always refer patients either to a chiropodist or their GP.

This caution also applies to patients with peripheral vascular disease and to the elderly who, like diabetes patients, tend to suffer

more with foot problems, may have declining peripheral circulatory and sensory nerve function, and often do not have the physical mobility or the dexterity to manage their own treatment properly.

Haemorrhoids

Haemorrhoids ('piles') are common and estimated to affect at least 50 per cent of the adult population at some time. Incidence is equal in both sexes and is highest in individuals between 20 and 50 years old. Embarrassment over the site of the lesion and the need for a rectal examination may deter some patients from seeking medical attention as early as they might for other conditions. It is therefore important for pharmacists to have a sound knowledge of the symptoms and to know when patients should be advised to see a doctor.

CAUSES

Haemorrhoids are the result of swelling and dilatation of the veins that line the anal canal. They are classified into two types: internal haemorrhoids, which are confined to the anal canal and are not visible; and external haemorrhoids, which become enlarged through straining at defecation and prolapse through the anal sphincter to protrude outside the anus. External piles either retract spontaneously after defecation or can be pushed back inside by the patient with a finger; if straining at defecation is not addressed and corrected, the haemorrhoids may remain prolapsed.

Symptoms of haemorrhoids include pain and discomfort, as a result of swelling in the area of the rectum and anus, which often becomes worse on defecation. Itching and a burning sensation also occur. Pruritus ani is intense itching around the anus which is often associated with haemorrhoids. It may result, in part, from irritation caused by seepage of rectal contents due to sphincter dysfunction.

Internal piles may bleed. The blood will be fresh and bright red in colour and may be seen on the faeces and splashed around the toilet bowel after defecation. Although this is not normally serious, all patients with rectal bleeding should be referred.

Haemorrhoids are often self-diagnosed and mild cases can be treated without medical intervention, although recurrent episodes or those that fail to clear up within a week should be referred.

TREATMENT

Most cases of haemorrhoids can be managed by local symptomatic treatment, plus use of laxatives where necessary (see section on constipation), and dietary adjustment is an important contributory factor as constipation is often caused by a low-residue diet. A wide range of products, in a variety of dosage forms, is available without prescription for the symptomatic treatment of haemorrhoids (see Table on p. 152). Most products contain a combination of ingredients. The rationale for the use of most of these seems logical but, as is often the case with non-prescription medicines, there is little objective evidence of their effectiveness. The various types of ingredients are reviewed below.

Local anaesthetics

Compounds available

Compounds available are:

- Benzocaine
- Cinchocaine
- Lidocaine (lignocaine)

Mode of action, uses and adverse effects

Local anaesthetics reversibly block excitation of pain receptors and sensory nerve fibres in and around the area of application. Local anaesthetics used in haemorrhoidal preparations are weak basic amines with the same basic chemical structure of an aromatic lipophilic group joined to a hydrophilic amino group by a linking ester or amide moiety. They reach their site of action by penetrating the lipophilic nerve structure in their lipid-soluble uncharged form, but exert their anaesthetic action in the ionised form. All compounds used in haemorrhoidal preparations, except for benzocaine, are

hydrochloride salts which are converted to the un-ionised base at tissue pH. Benzocaine is used in the free base form.

At the cellular level, activity is due to the ionised form of the anaesthetic, which blocks conduction of nerve impulses across cell membranes by decreasing their permeability to cations, mainly sodium ions. The degree of penetration and effectiveness of individual compounds depends on their lipid solubility, their dissociation constants (p*K*a) and on the pH of the surrounding environment, which is often influenced by the formulation of the products containing them. Compounds with high lipid solubility tend to be more potent and have a faster onset and longer duration of action than those with low lipid solubility. (Local anaesthetics are less effective on inflamed than on normal tissue as the pH of inflamed tissue is lower, resulting in a higher degree of ionisation, leaving less of the uncharged lipophilic drug available to penetrate the tissues.) Generally, amide-type anaesthetics are more potent and produce less sensitisation than ester-type compounds.

In haemorrhoidal preparations local anaesthetics are used to relieve pain, burning and itching. Use should be restricted to the perianal region and lower anal canal; they should not be used in the rectum as there is little sensory tissue there and anaesthetic can be rapidly absorbed through the rectal mucosa to cause potentially toxic systemic effects. Local anaesthetics are also rapidly absorbed through damaged skin. Skin sensitisation and systemic allergic reactions are possible with prolonged use, and use should be restricted to five to seven days.

Benzocaine is an ester-type local anaesthetic. Allergic reactions and sensitisation have been reported relatively frequently. Recommended concentrations are in the range of 5 to 10 per cent with a frequency of application of up to six times daily. Lanacane Cream (Combe International), which is licensed for the treatment of anal irritation, has a content of 3 per cent benzocaine and a recommended application of three times daily, which would appear too low a concentration to be effective. The concentration may be deliberately low in order to reduce the possibility of sensitivity reactions.

Cinchocaine is a potent and long-acting amide-type compound,

used at strengths of 0.5 to 1 per cent in haemorrhoidal preparations. It has less sensitising potential than benzocaine.

Lidocaine (lignocaine) is an amide-type compound with a relatively long duration of action and is the most widely used local anaesthetic in haemorrhoidal preparations. Although it is poorly absorbed through the skin, it may be rapidly and almost completely absorbed through mucous membranes and broken skin, and can cause systemic toxicity. But most non-prescription formulations contain low concentrations and are safe if used in accordance with the manufacturer's directions.

Astringents

Compounds available

Compounds available are:

- Allantoin
- Bismuth oxide
- Bismuth subgallate
- Peru balsam
- Zinc oxide

Mode of action and uses

Astringents coagulate protein in skin and mucous membrane cells to form a superficial protective layer. By reducing the secretion of mucus and intracellular contents from damaged cells, they help relieve local irritation and inflammation. Some astringent substances, such as zinc oxide and bismuth salts, also provide a mechanical protective barrier on the surface of damaged skin; Peru balsam has additional mild antiseptic properties. It has been suggested by United States licensing authorities that in products containing constituents with a mechanical protective effect they should constitute at least 50 per cent of the dosage unit, in order to provide a protective layer of

adequate thickness. This level is not reached in any of the products marketed in the United Kingdom.

Anti-inflammatories

Compound available

There is only one compound – hydrocortisone acetate.

Mode of action and uses

Hydrocortisone has a long history of prescription usage as a topical anti-inflammatory, and there is abundant clinical proof of its efficacy. (For a description of the mechanism of action of hydrocortisone, see the mouth ulcers section.)

Haemorrhoidal preparations containing hydrocortisone have been available on prescription for many years. Hydrocortisone was reclassified from POM to P in 1987 for limited dermatological indications, and in 1995 licensing was extended for use in haemorrhoidal preparations.

Two brands are available:

- Anusol Plus HC ointment and suppositories (containing 0.25 per cent hydrocortisone acetate in the ointment and 10 mg per suppository, together with astringent constituents)
  Pfizer Consumer Healthcare

- Perinal spray (containing 0.2 per cent hydrocortisone with lidocaine (lignocaine))
  Dermal

Use of haemorrhoidal preparations containing hydrocortisone is subject to several licensing restrictions: they should not be used for patients under 18 years, or during pregnancy or lactation, and they should not be used for more than seven days. The possibility of infection should be excluded before starting use because of the possibility of immunosuppression by the corticosteroid. The manufacturer of

Anusol Plus HC advises that the products should not be recommended to new sufferers who have not consulted their doctor, and that its use should be reserved for the relief of pain associated with the inflammation of more severe haemorrhoids.

Other agents

Fibrinolytic agent

Mucopolysaccharide polysulphate has a chemical structure similar to heparin and is claimed to promote fibrinolysis and break up small blood clots, and also to possess anti-inflammatory and antiexudative properties. It is also claimed to strengthen weak connective tissue in the anus and rectum. There is little evidence of its effectiveness.

Sclerosing agent

Lauromacrogol 400 is a non-ionic surfactant which has been used as a sclerosing agent in the treatment of varicose veins. Sclerotherapy involves injecting a sclerosing agent into a varicosed vein to create fibrosis and close off the lumen and the technique is used, although rarely, for the treatment of haemorrhoids. There appears to be no evidence that lauromacrogol 400 is effective when applied externally.

Skin protectant

Shark liver oil has been used as a source of vitamin A, and both it and cod liver oil have been used as skin protectants. However, claims of their value have not been substantiated by controlled observations, and a United States Food and Drug Administration advisory review panel found both substances lacking in demonstrated effectiveness.

Wound-healing agent

Yeast cell extract is a water-soluble extract of brewer's yeast which has been claimed to be effective in promoting wound healing or tissue

repair in haemorrhoids. Extensive tests have been carried out on *in vitro* and *in vivo* wound-healing models, and the substance has been found to stimulate oxygen consumption, increase angiogenesis and promote collagen synthesis, but no acceptable evidence exists that it has any effect on haemorrhoids.

Administration and dosage forms

The recommended treatment regimen for most preparations is twice daily, morning and evening, and after each bowel motion; products containing hydrocortisone should not be used more than three or four times in 24 hours. The bases of all products are likely to contribute an additional emollient and soothing effect, and the lubricating effect of suppositories may ease straining at stool. However, suppositories may slip into the rectum and melt there, bypassing the anal areas where the medication is needed and increasing the possibility of systemic absorption of local anaesthetics and hydrocortisone. This possibility is increased if the patient is lying down. Creams and ointments are generally considered to be preferable to suppositories for self-treatment of haemorrhoids.

PRODUCT SELECTION POINTS

- There is little evidence of the effectiveness of non-prescription haemorrhoidal preparations, but most have been available and used with apparent satisfaction for many years, and many are also frequently prescribed. The bases of products may themselves have a soothing effect.
- Products containing a local anaesthetic and constituents with mechanical protective or astringent properties would appear to be logical choices, as long as the content of these is sufficient to exert an effect.
- Products containing hydrocortisone may be useful for inflammation and irritation associated with haemorrhoids and pruritus

ani, and may also be worth trying if other products have not proved effective.

- Creams or ointments are considered preferable to suppositories.

PRODUCT RECOMMENDATIONS

For mild cases – a compound preparation containing a local anaesthetic and astringent or skin-protective constituents.

For cases with additional inflammation and irritation – a preparation containing hydrocortisone.

For underlying constipation – short-term treatment with a stimulant laxative, followed by an increase in fibre and fluid in the diet or regular use of a bulk laxative.

Haemorrhoidal products and constituents

Constituent type	*Constituent*	*Product*	*Maker*	*Dosage form*
Local anaesthetic	Benzocaine	Lanacane	Combe	C
	Cinchocaine	Nupercainal	Eastern	O
	Lidocaine (lignocaine)	Anodesyn	SSL International	O, S
		Germoloids	Bayer Consumer Care	C, O, S
		Hemocane	Eastern	C
Astringents	Allantoin	Anodesyn	SSL International	O, S
	Bismuth oxide	Anusol	Pfizer Consumer Healthcare	C, O, S
		Anusol Plus HC	Pfizer Consumer Healthcare	O, S
		Hemocane	Eastern	C
	Bismuth subgallate	Anusol	Pfizer Consumer Healthcare	O, S
		Anusol Plus HC	Pfizer Consumer Healthcare	O, S
	Peru balsam	Anusol	Pfizer Consumer Healthcare	C, O, S
		Anusol Plus HC	Pfizer Consumer Healthcare	O, S
	Zinc oxide	Anusol	Pfizer Consumer Healthcare	C, O, S
		Anusol Plus HC	Pfizer Consumer Healthcare	O, S
		Germoloids	Bayer Consumer Care	C, O, S
		Hemocane	Eastern	C
Anti-inflammatory	Hydrocortisone	Anusol Plus HC	Pfizer Consumer Healthcare	O, S
		Perinal	Dermal	Spray
Fibrinolytic	Mucopolysaccharide polysulphate	Anacal	Sankyo Pharma	O, S
Sclerosing agent	Lauromacrogol	Anacal	Sankyo Pharma	O, S
Skin protectant	Shark liver oil	Preparation H	Whitehall	O, S
Wound-healing agent	Yeast cell extract	Preparation H	Whitehall	O, S

O = ointment, C = cream, S = suppository.

Hay fever

(continued . . .)

Hay fever (seasonal allergic rhinitis) affects as many as 12 per cent of the population and the incidence is thought to be increasing. However, it appears that only around 20 per cent of sufferers consult their GPs. For pharmacists, it is in treatments for hay fever, perhaps more than any other condition, where the changes from POM to P status in recent years have had the greatest impact; most treatments for hay fever available to GPs can be bought in pharmacies.

Non-prescription treatments for hay fever are available in both oral and topical formulations. Ingredients in oral products include antihistamines (both sedative and non-sedative) and combinations of sedative antihistamines with decongestants. Topical formulations include products for use in the nose and in the eyes.

CAUSES

Hay fever is the result of a type I allergic reaction, in which initial exposure of a sensitive individual to an antigen (usually tree or grass pollens) results in the production of antigen-specific immunoglobulin E (IgE). IgE attaches to mast cells and basophils, which become sensitive to further antigenic material. On further exposure the antigen binds to IgE, causing degranulation of the mast cells and release of chemical mediators, including histamine, leukotrienes and prostaglandins, which produce the inflammatory response. Prolonged exposure to the allergen may result in sustained response, causing nasal congestion.

TREATMENT – ORAL FORMULATIONS

Histamine is the principal chemical mediator responsible for the inflammatory response of hay fever (and other allergic reactions). All oral formulations for treatment of hay fever are antihistamines and act through competitive antagonism of histamine at the H_1-receptor.

The older, sedative antihistamines (known as first-generation antihistamines) are lipophilic and cross the blood–brain barrier readily.

In the brain, in addition to binding to H_1-receptors, sedative antihistamines bind to and block muscarinic (cholinergic), and in some cases alpha-adrenergic and serotonergic receptors. As a result, they cause several generally undesirable side-effects including sedation, dry mouth, blurred vision, urinary retention, constipation and gastrointestinal disturbances.

The newer, non-sedative antihistamines (second-generation antihistamines) are less lipophilic and do not penetrate the brain to a significant extent; they are therefore much less likely to cause centrally mediated adverse side-effects. However, about 6 per cent of individuals exhibit drowsiness and other CNS side-effects in response to placebo; in addition, impairment of function, if it occurs, is not always accompanied by subjective feelings of drowsiness. Patients should therefore be warned that these antihistamines may affect driving and other skilled tasks, and that excess alcohol should be avoided.

Antihistamines are generally effective in controlling symptoms of hay fever, including sneezing, nasal itching, rhinorrhoea and, to a lesser extent, allergic conjunctivitis, but have little or no effect on nasal congestion. The maximum effect of antihistamines is not achieved until several hours after peak serum levels have been reached; in addition they cannot reverse the consequences of H_1-receptor activation, and are effective only if they are able to block histamine release before it occurs. For maximum effectiveness, therefore, antihistamines should be taken when symptoms are expected, rather than after they have started.

Non-sedative antihistamines

Compounds available

Compounds available are:

- Acrivastine
- Cetirizine
- Loratadine

Uses

These compounds are used mainly for the treatment of hay fever and perennial rhinitis, but they are also licensed for treatment of insect bites and allergic skin reactions. However, because of their lack of central activity they are of no use for motion sickness. In hay fever, they are generally preferable to the older antihistamines because of the much lower incidence of side-effects, but they are slightly more expensive. All drugs in this group are of equal efficacy. Acrivastine has a rapid onset of action and a short half-life, necessitating more frequent dosing than cetirizine or loratadine, but it may be useful to give rapid relief. Peak plasma levels of cetirizine and loratadine are reached in about an hour; they have a long elimination half-life and are long-acting, requiring only once-daily dosage. Loratadine is metabolised in the liver by cytochrome P450 enzymes, and theoretically can interact with drugs that inhibit or are metabolised by this enzyme system. However, no interactions of clinical significance have been reported. Although the incidence of sedation is extremely low for all three drugs (fewer than one patient in 140 complained of drowsiness with any of these drugs in a prescription-event monitoring study of more than 43 000 patients), loratadine has a much lower incidence of sedation than acrivastine or cetirizine, and has been recommended as the antihistamine of choice for people in occupations in which any degree of sedation is undesirable.

Dosage

- Acrivastine: adults and children over 12 years, 8 mg three times daily (not recommended for use in children under 12 or people over 65 years)
- Cetirizine: adults and children over 12 years, 10 mg daily (not licensed for children under 12 years)
- Loratadine: adults and children over six years, 10 mg daily

Products

- Acrivastine – Benadryl Allergy Relief capsules
  Pfizer Consumer Healthcare
- Cetirizine – Zirtek Allergy Tablets
  UCB Pharma
- Loratadine – Clarityn Allergy tablets and syrup
  Schering-Plough

Acrivastine (in Benadryl Plus Capsules) is formulated with a sympathomimetic decongestant (pseudoephedrine) in a combination product used for hay fever.

Sedative antihistamines

Compounds available

Compounds available are:

- Azatadine
- Brompheniramine
- Chlorphenamine (chlorpheniramine)
- Clemastine
- Diphenhydramine
- Promethazine

Uses

There is no evidence of difference in effectiveness between older antihistamines, although individual response to specific drugs varies widely. Choice is often based on personal preference and factors such as degree of sedation caused and duration of action, which do differ between compounds. Price may also be a factor.

Azatadine exhibits significantly less sedating and other CNS effects (6 per cent greater than placebo) than other older antihistamines

and is fairly long-acting, requiring only twice-daily dosing. Promethazine is highly sedative but has a long half-life, and a single dose may provide relief of symptoms for up to 24 hours. The dose is preferably taken at night, on the supposition that the sedative effect will have largely worn off by the following morning. Clemastine has an intermediate sedative effect (about 20 per cent greater than placebo) and a duration of action of up to 12 hours. Chlorphenamine (chlorpheniramine) is about as sedating as clemastine, with a faster onset but shorter duration of action; it is also the cheapest oral antihistamine. Brompheniramine has moderate, and diphenhydramine pronounced, sedative properties.

Dosage

- Azatadine – adults and children over 12 years, 1 mg twice daily; children 6 to 12 years, 0.5 mg
- Brompheniramine – adults and children over 12 years, 12 to 24 mg twice daily; children 6 to 12 years, 6 to 16 mg daily; children 3 to 6 years, 6 to 8 mg daily
- Chlorphenamine (chlorpheniramine) – adults and children over 12 years, 4 mg three to four times daily; children 6 to 12 years, 2 mg
- Clemastine – adults and children over 12 years, 1 mg twice daily; children 6 to 12 years, 0.5 mg
- Diphenhydramine – adults and 12 over 12 years, 75 to 200 mg daily (not recommended for children under 12 years)
- Promethazine – adults and children over 12 years, 25 to 50 mg at night, or 10 to 20 mg two or three times daily; children over five years, 10 to 25 mg daily

Side-effects, cautions and interactions

See above, and the section on cough.

Product examples

- Azatadine
  - — Optimine syrup
    Schering-Plough
- Brompheniramine
  - — Dimotane Elixir
    Wyeth
- Chlorphenamine (chlorpheniramine)
  - — Calimal Tablets
    Sussex
  - — Piriton Allergy Tablets and Syrup
    Stafford-Miller
  - — Pollenase Antihistamine Tablets
    Peach Pharmaceuticals
- Clemastine
  - — Tavegil Elixir and Tablets
    Novartis Consumer Health
- Diphenhydramine
  - — Histergan Syrup and Tablets
    Norma Chemicals
- Promethazine
  - — Phenergan Elixir and Tablets
    Aventis Pharma

Combination products

Some oral products containing combinations of antihistamines with sympathomimetic decongestants are marketed for treating nasal congestion associated with hay fever and the common cold. (See also section on colds, and for a description of systemic sympathomimetic decongestant compounds, see the section on cough.) Antihistamines on their own are effective for treating the typical symptoms of acute hay fever, known as the early phase. Prolongation of the condition by continued exposure to the allergen leads to a late-phase sustained response, producing mucus secretion in the nasal passages and increased permeability of the capillaries, resulting in submucosal swelling and blockage. First-generation antihistamines reduce rhinorrhoea through their anticholinergic action but do little to relieve nasal congestion, but co-administration of a sympathomimetic decongestant may be helpful.

Combination products marketed for hay fever include:

- Dimotane Plus Elixir (brompheniramine/pseudoephedrine) *Wyeth*
- Haymine (chlorphenamine (chlorpheniramine)/ephedrine) *Pharmax*

TREATMENT – NASAL PREPARATIONS

Nasal products contain anti-inflammatory, sympathomimetic decongestant or antihistamine constituents.

Anti-inflammatory agents

Compounds available

Compounds available are:

- Beclometasone
- Sodium cromoglicate

(Budesonide and flunisolide are classified as P, but there are currently no OTC products available.)

Mode of action

Beclometasone is a corticosteroid. Corticosteroids down-regulate the inflammatory response of type I allergic reactions by reducing the number of basophils and mast cells and blocking release of mediator substances. They inhibit both early and late responses to allergen exposure, and are therefore effective in relieving nasal congestion. Intranasal corticosteroids are now regarded as the treatment of choice in patients with moderate to severe hay fever and superior to oral antihistamines.

The mode of action of sodium cromoglicate remains uncertain; it was thought to act by stabilising mast cell membranes and preventing their degranulation, but new evidence indicates that other factors are involved. The drug is effective against both early and late type I responses.

Uses and dosage

Beclometasone and sodium cromoglicate are used intranasally. (Sodium cromoglicate can also be used in the eyes: see below). As they counteract both the early and late response to allergen exposure, they are effective in relieving all nasal symptoms of hay fever, including congestion. Both take some days to achieve optimum effect, and treatment should ideally be started at least two weeks before symptoms are expected.

Beclometasone

Beclometasone is presented as an aqueous non-aerosol spray, because pressurised sprays are thought to be more likely to cause local reactions. Absorption from the nasal mucosa is low, and at recommended doses systemic effects are very unlikely; any local reactions, such as stinging, burning or aftertaste, are mild and transient.

Patients should be advised that if symptoms are already present when treatment is started then it may be several days before an effect is noted and several weeks before full relief is obtained. Long-term use appears to be safe. Treatment may need to be maintained throughout the hay fever season, and repeated each year. The recommended adult dosage is two sprays twice a day.

Beclometasone is not licensed for use in children under 12 years, or in pregnant or lactating women. It should be avoided if there is infection in the nose or eye. There are otherwise no significant contraindications or interactions.

Sodium cromoglicate

This is available as nasal drops and an aqueous spray containing 4 per cent sodium cromoglicate (Rynacrom, Pantheon Healthcare) and also as an aqueous nasal spray containing 2 per cent sodium cromoglicate with 0.025 per cent xylometazoline hydrochloride (Rynacrom Compound, Pantheon Healthcare; Rynacrom Allergy Nasal Spray, Aventis Pharma). The strength of xylometazoline is one-quarter of that in topical nasal decongestants marketed for nasal congestion associated with colds, and the risk of rebound congestion with these products containing xylometazoline is claimed to be very low.

Sodium cromoglicate is a prophylactic agent. Treatment should be initiated before the pollen season starts and continued throughout. It is less effective at controlling nasal symptoms than corticosteroids, and has the disadvantage of requiring at least four times daily dosing. However, it is very safe and is suitable for children from five years old. There are no specific cautions or contraindications associated with its use, and it does not interact with other drugs.

Sympathomimetic decongestants

Drops and sprays containing sympathomimetic decongestants are used to relieve nasal congestion associated with hay fever, and may be useful to begin treatment when the nose is badly blocked. (For further details, see the section on colds.)

Antihistamines

Azelastine is a second-generation antihistamine. It is a potent long-acting anti-allergic compound with marked H_1-antagonist properties. It is marketed in the United Kingdom without prescription for intranasal use only (azelastine eye drops are POM), and at the doses administered has only local activity. It has been found to be as effective in controlling the symptoms of rhinitis as oral terfenadine or intranasal budesonide. Twice-daily use is recommended. Azelastine is not licensed for OTC sale for use in children, and caution is recommended for use in pregnant and breast-feeding women.

Levocabastine is a long-acting, potent antihistamine with a rapid onset of action which is licensed for use without prescription in both the nose and the eye. Clinical trials have shown it to be equally as or more effective in treating the symptoms of seasonal allergic rhinitis than sodium cromoglicate, but less effective than budesonide. There appear to be no three-way comparisons of efficacy between intranasal corticosteroids, sodium cromoglicate and antihistamines. There have been rare reports of sedation when levocabastine nasal spray and eye drops are used together, and the manufacturer recommends that these should only be used together concomitantly with an oral antihistamine under medical supervision. The recommended dose of levocabastine nasal spray is two sprays twice daily, although this can be increased if necessary to three or four times a day; the maximum recommended treatment period is one month. Levocabastine nasal spray is not recommended for use in children under 12 years, or during pregnancy.

Products

- Azelastine
  - — Rhinolast Allergy spray
    AHA Sales & Marketing

- Beclometasone
  - — Beconase Hayfever spray
    GlaxoSmithKline Consumer
  - — Nasobec Hayfever spray
    Norton Consumer
- Levocabastine
  - — Livostin Direct nasal spray
    Johnson & Johnson MSD
- Sodium cromoglicate
  - — Rynacrom 4% Nasal Spray
    Pantheon Healthcare
  - — Rynacrom Compound spray
    Pantheon Healthcare
  - — Rynacrom Allergy Nasal Spray
    Aventis Pharma

TREATMENT – EYE PREPARATIONS

Preparations for use in the eyes include sodium cromoglicate, levocabastine and combinations of antihistamine with a sympathomimetic.

Sodium cromoglicate

Most eye symptoms in hay fever sufferers will be controlled by oral antihistamines, but if symptoms are persistent or particularly troublesome, sodium cromoglicate 2 per cent eye drops are usually effective. Several proprietary brands are available. Sodium cromoglicate is especially useful if hay fever symptoms occur only in the eyes, where it rapidly exerts an action. It is used four times daily, and can be used in children.

Levocabastine

Comparative studies have shown levocabastine to be more effective in allergic conjunctivitis than sodium cromglicate and nedocromil, a related mast cell-stabilising anti-inflammatory. It requires only twice-daily application. It is not licensed for use in children under 12 years and is not recommended for use during pregnancy.

Antihistamine/decongestant combination

Otrivine-Antistin eye drops (Novartis Consumer Health) contain an antihistamine, antazoline sulphate 0.5 per cent and xylometazoline hydrochloride 0.05 per cent; the latter ingredient is used for its vasoconstrictor action as a conjunctival decongestant. This preparation can be used for the short-term treatment of hay fever symptoms; prolonged use may raise intraocular pressure and precipitate glaucoma. The drops are used twice or three times daily and are suitable for use in children from five years.

Sodium cromoglicate, levocabastine and Otrivine-Antistin eye drops contain benzalkonium chloride as preservative. This is absorbed into soft contact lenses and released on to the cornea during wear, causing inflammation and irritation. Contact lenses should therefore be removed while using these products.

Products

- Sodium cromoglicate
  - — Clarityn Allergy Eye drops
    Schering-Plough
  - — Hay-Crom Hay Fever Eye Drops
    Norton Consumer
  - — Opticrom Allergy Eye Drops
    Aventis Pharma
  - — Optrex Allergy Eye Drops
    Crookes Healthcare

- — Pollenase Allergy Eye Drops
  Peach Pharmaceuticals

- Levocabastine
  - — Livostin Direct eye drops
    Johnson & Johnson MSD

- Antihistamine/decongestant
  - — Otrivine-Antistin eye drops
    Novartis Consumer Health

PRODUCT SELECTION POINTS

- Oral antihistamines are the first-line treatment for mild or occasional hay fever, and are usually effective against all acute (early-phase) symptoms. Treatment is more effective if commenced when symptoms are expected rather than after they have started.
- All antihistamines, both first- and second-generation, are more or less equally effective, although response can vary between individuals.
- Second-generation antihistamines are usually the first choice for recommendation due to the low risk of sedation and anticholinergic side-effects. Of these, loratadine has the lowest potential for sedation.
- The degree of sedation caused by first-generation antihistamines varies between compounds; some cause relatively little, and some patients do not experience drowsiness at all. In addition, as first-generation antihistamines are generally cheaper than second-generation compounds, the former are often a suitable choice.
- Because of the anticholinergic side-effects of first-generation antihistamines and the need to avoid their use in patients with glaucoma and prostatic hypertrophy, they are best avoided in elderly patients generally. In any case, hay fever is unusual in the elderly, and patients with symptoms of this condition should be referred to their GP.

- Beclometasone nasal spray, plus a second-generation antihistamine if necessary, are the first choice for more persistent symptoms and nasal congestion. Oral combination products containing first-generation antihistamines and sympathomimetics are not the treatment of choice, due to the side-effects, cautions and contraindications associated with both classes of drugs, and because they should not be used long-term.
- Beclometasone is more effective for treating severe or persistent nasal symptoms of hay fever than sodium cromoglicate, but use is confined to individuals over 18 years. Sodium cromoglicate can be used in children from the age of five and is licensed for use in pregnancy. Both are safe to use throughout the hay fever season. Azelastine and levocabastine are also effective, and can be used in children from the age of 12 years.
- Sodium cromoglicate eye drops provide fast and effective relief for eye symptoms associated with hay fever, and are safe to use for prolonged periods. Levocabastine appears to be even more effective.

PRODUCT RECOMMENDATIONS

- Oral antihistamines
  - — Loratadine or cetirizine: second-generation, non-sedative, no reported interactions or side-effects, once-daily dosing
  - — Chlorphenamine (chlorpheniramine): first-generation, relatively little sedation, cheapest oral antihistamine
  - — Loratadine: for children from two years, non-sedating
- Nasal products (severe nasal symptoms and congestion)
  - — Adults: azelastine or beclometasone spray – equally effective and similar price
  - — Children: Rynacrom Allergy Nasal Spray

- Eye drops
  - For severe eye symptoms: levocabastine or sodium cromoglicate eye drops

Head lice

CAUSES

Head lice are small wingless insects (*Pediculus humanus capitis*) which live on and suck blood from the scalp. They leave tiny red spots which itch intensely. Scratching can lead to dermatitis and impetigo.

The female louse lays a daily batch of tiny pale eggs (nits) attached to the hairs close to the scalp. Adult lice may live for up to several weeks. Infection is spread by direct head-to-head contact, and possibly by transfer through contact with infected hairbrushes, hats, pillows, etc., although lice cannot survive for long away from the scalp. The condition is most common in children aged four to 11, and more common in girls than boys, but anybody can be infected. The length or state of cleanliness of the hair makes little difference to the likelihood of becoming infected.

TREATMENT

The insecticides (pediculocides) available without prescription for the treatment of head lice are:

- Malathion
- Permethrin
- Phenothrin

The last two are synthetic pyrethroids.

Several presentations are available, including aqueous and alcoholic lotions, a shampoo, a creme rinse and a mousse. All are licensed as P medicines. Some of these preparations are also licensed for the treatment of crab lice and scabies (see section on scabies). Products containing carbaryl were also P medicines until 1995, when they were reclassified as POM because it was found that carbaryl was carcinogenic when fed to laboratory animals at high doses over long periods. Benzyl benzoate in the form of Ascabiol lotion (Aventis Pharma) is also licensed for head lice treatment, but it is rarely used. A head lice repellent, piperonal, is also available.

Malathion

Mode of action

Also known as carbofos, malathion is an organophosphorus compound. It is a potent cholinesterase inhibitor which prevents the breakdown of acetylcholine and interferes with neuromuscular transmission in the head louse, paralysing it and preventing it from feeding. It is oil-soluble and absorbed by a process of passive diffusion through the lipid coat of both insect and egg; achieving a lethal dose depends on the concentration of the product and the length of contact.

Ovicidal activity of all pediculocides is increased by the incorporation of an alcohol in the base of the preparations. Malathion is poorly absorbed through human skin, and it is also much more efficiently detoxified by human metabolic processes than by those of insects. It is therefore safe for occasional or intermittent use at low concentrations as a pediculocide.

Administration

Aqueous solutions are rubbed gently into the scalp until all the hair and scalp is thoroughly moistened; application should extend to the neck area and behind the ears. Treatment failure is often due to the insecticide not reaching all of the scalp. The hair should be allowed to dry naturally as malathion is inactivated by heat. The solution is left on for 12 hours, usually overnight, and the hair is then shampooed in the normal way. While the hair is still wet it should be combed with a fine-toothed comb to remove dead and dying lice from the scalp and empty egg cases attached to the hair shafts.

Alcoholic lotions are applied in the same way as aqueous lotions, and it is important that no heat is applied to dry the hair due to the flammable nature of the vehicle. The room should be well ventilated with no naked flames or lighted objects. It is claimed that two hours' contact time is sufficient for alcoholic lotions to be effective, although the manufacturers recommend that they should be left on for 12 hours. The hair is then shampooed and combed while wet in the same way as for aqueous lotions.

A single application of an alcoholic or aqueous lotion, if used correctly, should be sufficient to eradicate infestation completely. However, a second application after seven days is now recommended to kill any lice emerging from eggs that may have survived the initial treatment.

The shampoo is much less effective than lotions. This is because, although it is more concentrated, it is diluted between 15 to 30 times with water when applied, it has a much shorter time in contact with the hair and scalp, and the insecticide may be inactivated by hot water. To apply, the hair should be thoroughly wetted and sufficient shampoo applied to work up a rich lather and cover the entire scalp and neck area. The shampoo is left on for at least five minutes, rinsed off and the process repeated. The hair is then wet-combed, as described above. The procedure must be carried out three times at three-day intervals. However, it has been shown in laboratory tests that shampoos do not kill all louse eggs, even after three applications.

Contraindications, cautions and side-effects

There are no contraindications to the use of malathion apart from known sensitivity. Preparations are not contraindicated in pregnant or lactating women, although manufacturers recommend caution. Alcoholic lotions should not be used for asthmatic patients and young children as isopropyl alcohol may precipitate bronchospasm. Nor should they be used for patients with eczema, as alcohol may cause inflammation and stinging.

All preparations may affect permed, coloured or bleached hair. The only reported side-effect of malathion preparations is very rare skin irritation.

Products

- Aqueous lotions (0.5 per cent)
  - — Derbac-M Liquid
    SSL International

— Quellada M Liquid
Stafford-Miller

- Alcoholic lotions (0.5 per cent in isopropyl alcohol)
  — Prioderm Lotion
  SSL International
  — Suleo-M Lotion
  SSL International

- Shampoo (1 per cent)
  — Prioderm Shampoo
  SSL International

All the above are licensed for use in patients of all ages from six months.

Permethrin and phenothrin

Mode of action

Natural pyrethrum, extracted from pyrethrum flowers (*Chrysanthemum cinerariaefolium*, Compositae), has been in use as a horticultural pesticide for many years. Pyrethrins are effective insecticides with low mammalian toxicity, but the naturally occurring compounds are unstable when exposed to light. In recent years photostable synthetic pyrethroids have been developed, and the first pyrethroid pediculocide product was introduced in the United Kingdom in 1990. Pyrethroids are rapidly absorbed across the insect cuticle and exert their action on the sodium channels of louse nerve axons, causing initial excitement and then paralysis.

Administration

Phenothrin (Full Marks, SSL International) is available as an alcoholic lotion, which is used in the same way as malathion alcoholic lotions.

It is also available as an aqueous liquid, used in the same way as malathion aqueous lotion, and as a mousse, which is left on the hair for 30 minutes and then washed off using an ordinary shampoo. Permethrin creme rinse (Lyclear, Warner Lambert) is applied following the final rinse after using an ordinary shampoo. The hair is towel-dried, and Lyclear is applied in sufficient quantity to coat the scalp and hair fully. After ten minutes the preparation is rinsed off and the hair is wet-combed.

Contraindications, cautions and side-effects

As for malathion, the manufacturers of Lyclear recommend that it be avoided in pregnancy and lactation.

Products

- Permethrin – Lyclear Creme Rinse (1 per cent in a creme rinse base with 20 per cent isopropyl alcohol)
  Warner Lambert
- Phenothrin – Full Marks Lotion (0.2 per cent in an alcoholic base)
  SSL International
- Phenothrin – Full Marks Mousse (0.5 per cent)
  SSL International

Piperonal

Mode of action

Piperonal is presented as an aqueous-alcoholic solution in a pump spray. Piperonal has a sweet floral odour resembling heliotrope and occurs naturally in the oils of some plants. It is widely used in foods and perfumery, and is classified as a safe product by the United States Food and Drug Administration. Its mechanism of action is unknown, but it is thought to provoke a negative response from the lice

antennae receptors, causing them to avoid movement into treated areas.

Piperonal has been shown to be effective by use of the Arena test, which is designed to compare repellent effects of different materials. The test is performed by placing the same number of lice on two filter paper discs, and half of one of the discs is treated with the test substance. Lice move around in a completely random manner and under normal conditions would be expected after a given time to be evenly distributed on the discs. The test showed a 93 per cent inhibition of lice on the half-disc treated with piperonal compared with the control disc. Piperonal has no insecticidal activity.

Administration

The product should only be used on heads that are clear of infestation. It is sprayed on to the hair once daily during periods when infection is likely. The normal precautions should be employed with persons who are asthmatic or have a sensitive skin, and use is not recommended for children under two years; otherwise, there are no restrictions. The main use of the product is to prevent inadvertent reinfestation after treatment with insecticides, before all cases have been traced and the lice eradicated. It is not intended to be used as a routine prophylactic.

Product

- Rappell
  Pfizer Consumer

Efficacy and resistance

There is no consensus as to which pediculocide is the most effective, and there is no conclusive evidence that any one is more effective than another. Several trials looking at the clinical efficacy of head lice treatment have been carried out, but there are relatively few that

have been well conducted. In a systematic analysis of seven trials considered to be relatively free from bias, conclusive evidence of effectiveness was only found for permethrin 1 per cent creme rinse. However, the way in which this analysis was carried out has itself been criticised. Another recent trial found malathion to be more effective than phenothrin, although the relative ineffectiveness of phenothrin was ascribed to emerging resistance. An *in vitro* study has shown that alcoholic lotions containing terpene fragrances (Suleo-M (malathion), Carylderm (carbaryl, prescription only)) have greater ovicidal activity than preparations without terpenes. The *British National Formulary* says that malathion, the pyrethroids and carbaryl are all effective, but that resistance has developed in some districts. Apparent treatment failure with pediculocides is quite frequent, and this is often suggested to be due to the ineffectiveness of the products. The more likely cause, however, is usually either incorrect use of products or rapid reinfestation following successful treatment. Contact tracing to prevent reinfestation, as described below, is therefore extremely important.

Concern about emerging resistance to pyrethroids and malathion began to be expressed in the mid-1990s. In the case of permethrin this may be due to its residual activity, which can persist for up to six weeks following a single application. Thus, while it may prevent reinfestation, permethrin may also permit resistant strains to evolve in its presence. Phenothrin does not have a residual effect. It has been suggested that resistance to this compound may have been due in part to the widespread use of a shampoo containing it, which was believed to be not very effective but was widely used between its launch in 1990 and withdrawal in 1992. Residual activity of malathion is uncertain. Little or no resistance appears to have developed to carbaryl, which would seem to justify its remaining as a prescription-only treatment of last resort.

Rotational policies to limit the development of resistance, whereby health authorities recommended a specific pediculocide to be used exclusively in an area for a period of usually three years, followed by other compounds in rotation for three years each, have now been abandoned and replaced by the mosaic method of treatment.

Here no particular pediculocide is recommended, but as patients come forward for treatment they are each given a different one in rotation. Two applications of insecticide one week apart are now recommended as standard treatment, and if one compound fails to effect a cure, a different one should be used for the next treatment.

Resistance is also encouraged by people, usually worried parents, trying to prevent reinfestation by prophylactic use of pediculocides, particularly shampoos, in the mistaken belief that routine use of these in place of ordinary shampoos will keep the family clear of lice. Another misconception is that if one family member is infested the entire family should be treated; however, there is no point in trying to eradicate lice unless their presence is confirmed, and unnecessary treatment merely contributes towards the possibility of resistance. Lice are almost always passed on from one person to another by close, personal head-to-head contact. The way to eradicate infestations and prevent recurrences is by tracing and checking everybody with whom an infested person is likely to have had such contact over the preceding few weeks, and to treat all those found to be infested.

'Bug busting'

'Bug busting' has been recommended as an alternative method for tackling the problem of head lice and resistance without the use of insecticides. The technique involves wet-combing the hair with a fine-tooth comb for about 30 minutes after shampooing and using conditioner, and if evidence of lice is found the process should be repeated twice weekly for two weeks to remove lice emerging from eggs before they can spread. However, a trial has shown this method to be much less effective than two applications of malathion lotion used seven days apart.

PRODUCT SELECTION POINTS

- There is no clear evidence that any one pediculocide is significantly more effective than the others. All should be effective if used correctly.
- Alcoholic lotions are considered to be more effective than aqueous lotions, but are not suitable for use in patients with asthma or eczema, or in young children.
- Two applications of pediculocide one week apart are now recommended as standard treatment.
- A mosaic policy should be used for selection of pediculocide.
- Shampoos are much less effective than lotions and are not recommended.
- Head lice products should not be used for prophylaxis, as they are usually not effective and their use in this way encourages the development of resistance. Tracing infested contacts and eliminating lice from them is the most effective way to prevent reinfestation.
- Piperonal spray can be used as a lice repellent to prevent reinfestation during outbreaks while contacts are being traced. It is not intended for routine prophylactic use.
- 'Bug busting' is an alternative method for identifying and eliminating head lice without the use of insecticides, but requires heavy commitment and is less effective than treatment with a pediculocide.

PRODUCT RECOMMENDATIONS

In the absence of contraindications, an alcohol-based malathion or pyrethroid preparation as first choice.

Indigestion

(continued . . .)

Indigestion and dyspepsia are names commonly used interchangeably to describe a range of somewhat vague symptoms in the upper gastrointestinal tract which are generally associated with the ingestion of food.

CAUSES

There are several possible causative factors, but whatever the cause, moderately raising stomach pH generally relieves symptoms. Treatment is therefore aimed either at neutralising gastric acid or suppressing its secretion. Antacids have traditionally been the main form of treatment, and some compounds additionally form a protective layer over the gastric mucosa. Indigestion medicines often contain ingredients to control associated symptoms such as wind, gastric reflux and colicky spasm. As with other categories of self-medication, indigestion remedies are usually formulations containing several constituents. H_2-receptor antagonists, which reduce gastric acid production, are also available for OTC treatment.

TREATMENT – ANTACIDS

Mode of action

Several alkali metal salts are used in the treatment of indigestion. These are weak bases which dissociate to form alkaline salts, thereby neutralising gastric acid. Antacids used in indigestion treatments have differing neutralising capacities, and the degree to which they are systemically absorbed also varies, influencing their duration of action. Soluble salts act quickly but are rapidly absorbed, so reducing their duration of action, while salts of divalent and trivalent metal ions are insoluble and have a less rapid but more prolonged action. The ideal antacid would be fast-acting, with a high neutralising capacity, not absorbed into the body and long-acting. No single compound possesses all these attributes, but combinations are formulated in an

attempt to produce medicines with most of the benefits and a minimum number of drawbacks. This means that antacid medicines are usually combinations of two or more compounds, each contributing towards the neutralising capacity of the product. The amount of each compound is therefore less than would be required to achieve neutralisation on its own.

Compounds used as antacids are:

- Sodium and potassium bicarbonates
- Calcium carbonate
- Aluminium hydroxide
- Magnesium and bismuth salts
- Magnesium/aluminium complexes

These compounds, together with their actions, uses, dosage, side-effects and cautions, are considered individually below. Because there are so many antacid products available, examples will be given in relation to each antacid compound rather than at the end of the section. Interactions for all antacids will be discussed as a separate topic at the end of the antacid section.

Sodium bicarbonate

Action, uses and dosage

This compound has been a traditional household standby for the treatment of indigestion because it is cheap, fast-acting and effective. It is also a standard ingredient in formulary preparations such as Magnesium Trisilicate Mixture BP, Magnesium Trisilicate Oral Powder BP and Aromatic Magnesium Carbonate Mixture BP.

Carbon dioxide is generated during neutralisation of acid with sodium bicarbonate, and excess gas escapes through eructation (belching). This helps to relieve the distension of the stomach that can contribute to the discomfort of dyspepsia. The antacid dose of sodium bicarbonate is 1 to 5 g.

Side-effects and cautions

The main disadvantage of sodium bicarbonate is that it is highly soluble and systemically absorbed, and prolonged use can lead to sodium overload and alkalosis. Excess sodium intake can lead to water retention, causing blood pressure to rise and increasing the load on the heart. Products containing significant amounts of sodium bicarbonate are therefore best avoided in patients with hypertension, cardiovascular or renal disease, by patients on a salt-restricted diet and also in pregnancy. In these individuals, while the occasional dose is unlikely to be harmful, regular use may cause problems, and there are many antacids available which either contain no sodium or contain insignificant amounts (less than 1 mmol sodium or 85 mg sodium bicarbonate per dose). Regular use of sodium bicarbonate may also cause 'acid rebound' in which there is an increase in stomach acid production.

Potassium bicarbonate

Potassium bicarbonate is used as an alternative to sodium bicarbonate. Hyperkalaemia is possible with prolonged regular use in patients taking potassium-sparing diuretics or ACE inhibitors; otherwise, there are no specific contraindications.

Potassium bicarbonate is included in two indigestion remedy brands, one of which, Algicon tablets (Aventis Pharma), has a high sugar content, which should be taken into account if recommending this product to a patient with diabetes.

Products

- Algicon Suspension and Tablets
  Aventis Pharma
- Gaviscon Advance Suspension
  Reckitt Benckiser

Calcium carbonate

Action, uses and dosage

Calcium carbonate has the greatest neutralising capacity of all antacids; it is also cheap and long-acting. It is a popular ingredient in proprietary products, both alone and in combination with other antacids. The antacid dose range is between 500 mg and 1 g.

Side-effects and cautions

Although calcium carbonate is safe in normal use, problems may arise with excessive usage. During stomach acid neutralisation, calcium chloride is formed; this salt is soluble and partially absorbed and can cause hypercalcaemia. Long-term use, especially if large quantities of milk and sodium bicarbonate (perhaps as an antacid ingredient) are also ingested, can give rise to a condition known as milk alkali syndrome, causing nausea, headache and possibly renal damage. Calcium carbonate is also associated with acid rebound, and can cause constipation. Regular use of antacids containing calcium carbonate should be avoided in patients taking thiazide diuretics, as these reduce calcium excretion and hypercalcaemia may result.

Product examples

As sole antacid constituent in:

- Rap-eze tablets
  Roche Consumer Health
- Remegel tablets
  SSL International
- Setlers Antacid Tablets
  Stafford-Miller
- Tums tablets
  GlaxoSmithKline Consumer Healthcare

Combined with other antacids in:

- De Witt's Antacid Powder and Tablets
  E C De Witt
- Bisodol Indigestion Relief Tablets
  Whitehall
- Moorland Tablets
  Torbet
- Opas Tablets
  Co-Pharma
- Rennie Tablets
  Roche Consumer Health

Aluminium hydroxide

Action, uses and dosage

Aluminium hydroxide reacts with gastric acid to form an insoluble colloid, which is not absorbed to a significant extent and is effective for much longer than a rapidly absorbed soluble salt. It also lines the gastric mucosa and acts as a mechanical barrier against excess acid. As an antacid, aluminium hydroxide is given in doses of up to 1 g.

Side-effects and cautions

Aluminium hydroxide is rarely used alone in antacid preparations for several reasons. Used on its own it can bind to phosphate in the gut, forming an insoluble complex which over a long period may interfere with phosphate and bone metabolism. This can give rise to bone and CNS problems, particularly in patients with renal disease. Products containing aluminium hydroxide as sole constituent are used to treat indigestion, but by virtue of their phosphate-binding action they are also used to treat hyperphosphataemia.

In recent years, a correlation has been shown between aluminium in water and Alzheimer's disease, but so far no link has been

demonstrated with aluminium-containing antacids. Aluminium hydroxide also tends to cause constipation, but this is often overcome by formulating it with a magnesium salt which has the opposite effect (see below).

The adsorptive capacity of aluminium hydroxide and its persistence in the gut can retard the absorption of vitamins and some drugs, including tetracyclines (see interactions below).

Product examples

Containing aluminium hydroxide as sole constituent:

- Aluminium Hydroxide Mixture and Aluminium Hydroxide Tablets
- Alu-Cap capsules
  3M Health Care
- Aludrox Liquid
  Pfizer Consumer Healthcare

Magnesium salts

Action and uses

The magnesium compounds utilised in antacid preparations are the trisilicate, hydroxide, oxide and carbonate. They possess similar properties to aluminium hydroxide, and in addition they tend to increase the tone of the gastro-oesophageal sphincter, and this is useful in treating gastric reflux.

Side-effects and cautions

Magnesium salts are absorbed to a greater extent than aluminium salts and excessive use, particularly in the presence of renal insufficiency, may lead to hypermagnesaemia with serious cardiovascular and neurological effects. Magnesium salts are osmotic laxatives and

some compounds are licensed for this use, e.g. magnesium hydroxide in Milk of Magnesia Liquid (GlaxoSmithKline). In general, however, diarrhoea is an undesirable side-effect in antacids, and is overcome by co-formulating magnesium salts with aluminium hydroxide. The dose of each component is lower than in sole-ingredient products, which minimises the possibility of adverse effects through absorption.

Magnesium trisilicate, found in Magnesium Trisilicate Mixture BP, was once the most popular of formulary antacids but is now less favoured. It is slower-acting and has less neutralising capacity than other magnesium salts. It has been reported to cause renal stones because of its silica content, and may also cause other renal damage with chronic use.

Product examples

Containing magnesium hydroxide as sole constituent:

- Milk of Magnesia Liquid and Tablets
  GlaxoSmithKline

Magnesium salts in combination:

- Aromatic Magnesium Carbonate Mixture BP
- Dijex Liquid
  SSL International
- Maalox Suspension
  Rhône-Poulenc Rorer
- Birley's Antacid Powder
  Torbet

Bismuth salts

Actions and uses

Bismuth salts have similar properties to aluminium and magnesium salts, neutralising acid and coating the gastric mucosa, thus protecting it against acid attack.

Side-effects and cautions

Long-term use may lead to absorption and neurological damage. Salicylate is absorbed following the administration of bismuth salicylate and may cause the same adverse effects as aspirin. The same precautions should therefore be applied to Pepto-Bismol (bismuth salicylate) as for aspirin, and it should be avoided by aspirin-sensitive individuals and in pregnancy. Bismuth salicylate may be converted to bismuth sulphide in the gut, causing blackening of the faeces and tongue.

Product example

- Pepto-Bismol (bismuth salicylate)
  Procter & Gamble (H&BC)

Aluminium/magnesium complexes

Aluminium and magnesium compounds have been combined in various ways in an attempt to achieve faster acid neutralisation, longer action and lower absorption. These include:

- Magaldrate, contained in Bisodol Heartburn Relief Tablets (aluminium magnesium hydroxide sulphate)
  Whitehall
- Hydrotalcite contained in Altacite Plus Suspension (aluminium magnesium carbonate hydroxide hydrate; it is claimed to maintain buffering in the optimum range of pH for over two hours)
  Peckforton Pharmaceuticals
- Aluminium hydroxide/magnesium carbonate co-dried gel, which is a co-precipitate of these two compounds dried to contain a proportion of water for antacid activity, is contained in:
  - Algicon Suspension and Tablets
    Aventis Pharma

— Dijex tablets
SSL International

- Alexitol contained in Actal Tablets (a sodium hydroxyaluminium carbonate–hexitol complex)
Merck Consumer Health

There appears to be little evidence to demonstrate an advantage for these products over straightforward aluminium/magnesium salt combinations.

Interactions

Antacids can interfere with the absorption of many drugs. They interact with tetracyclines, with the 4-quinolone antibacterials, e.g. ciprofloxacin, norfloxacin and ofloxacin, and also with penicillamine to form insoluble metal ion chelates. The absorption of tetracyclines as well as that of the antifungals, ketoconazole and itraconazole, is reduced in the presence of antacids as these drugs are less readily soluble in an alkaline than an acid medium. Other commonly prescribed drugs liable to reduced absorption in the presence of antacids include azithromycin, nitrofurantoin, rifampicin, phenytoin, chloroquine, phenothiazine antipsychotics and bisphosphonates.

Antacids also interact with enteric-coated tablets, capsules and granules. These products are formulated to resist gastric acid and dissolve in the more alkaline medium of the duodenum, releasing the drug there. Enteric coatings may be disrupted prematurely in the presence of antacids, causing unwanted release of the drug in the stomach. Because antacids can interfere with the absorption of so many drugs, patients might be best advised to leave at least a two-hour gap between taking a dose of an antacid and any other medicine.

Antacid preparations containing sodium bicarbonate should be avoided by patients on lithium therapy. Sodium ions are preferentially reabsorbed in the kidney, increasing lithium excretion and reducing plasma lithium concentrations.

Formulation and dosage

Liquids and powders generally provide faster relief and have greater neutralising capacity than tablets. This is because liquids and powders are very quickly mixed with the stomach contents and their small particle size provides a large contact surface area for neutralising activity.

Advantages of tablets over liquids include ease of portability and administration, and claims have been made for more prolonged action in some cases. Tablets are generally preferred to liquids by patients.

Tablets should not be swallowed whole, but should be chewed to initiate their disintegration or sucked to provide a relatively slow but sustained delivery of antacid to the stomach. The tabletting process can also influence the speed of action. Older formulary preparations, such as Magnesium Trisilicate Compound Tablets BP, may be relatively slow to disintegrate, but most proprietary tablets are formulated to optimise their disintegration and availability. Some novel formulations have been developed to improve both speed of action and palatability.

Timing of the dose also influences the effectiveness of antacids. Doses should not be taken before or immediately after meals, as peristalsis stimulated by the presence of food accelerates transit and reduces the length of contact of the antacid with the stomach contents. It has been shown that antacids exert the most prolonged effect when taken one hour after meals.

Antacid tablet formulations may contain large amounts of sugar in order to make them palatable, a factor to be considered especially when making recommendations to patients with diabetes.

Additional ingredients – alginates

Alginates used as additional ingredients with antacids are:

- Alginic acid
- Magnesium alginate
- Sodium alginate

Mode of action

Alginates act as reflux suppressants. Reflux of acidic stomach contents into the oesophagus is normally prevented by the lower oesophageal sphincter (LOS). This is situated at the junction of the oesophagus and stomach and acts as a non-return valve. Several factors can contribute to reducing the muscle tone of the LOS, allowing gastric contents back into the oesophagus. These include certain foods and drinks, alcohol, smoking, some drugs, obesity, pregnancy and anatomical abnormality. Unlike the stomach lining, the oesophageal mucosa has no protection against gastric acid and an irritant process ensues, giving rise to the characteristic symptoms of reflux oesophagitis – 'heartburn' and 'waterbrash'. Reflux oesophagitis is also known as gastric reflux, or simply reflux.

Alginates precipitate out in the acidic medium of the stomach to form a sponge-like polymer matrix of alginic acid. Carbon dioxide bubbles, generated by the reaction between stomach acid and the sodium or potassium bicarbonate which is included in alginate-containing preparations, become trapped in the matrix and make it buoyant so that it floats on top of the stomach contents like a raft, hence the name 'rafting agents' by which alginate-containing products are sometimes known. When peristalsis occurs, the stomach contents are pushed up against the diaphragm and the alginate raft, which is claimed to form a physical barrier against the reflux of stomach contents into the oesophagus, is forced towards the gastro-oesophageal junction. Aluminium and magnesium antacid salts are included in reflux-suppressant formulations because they help to neutralise stomach contents and any material that is refluxed through the LOS. Gastric alkalinisation is also thought to improve sphincter tone.

There is no indication that one alginate-containing product is more effective than another. Similar precautions apply as for antacid preparations generally.

Results of trials suggest that alginate/antacid combinations alleviate symptoms of reflux in about two-thirds of subjects, which makes them more effective than plain antacids. A recent study found that alginate/antacid combinations were more effective than antacids

alone for patients in an upright position, but not effective when patients were lying down. An H_2-antagonist may be a better choice for nocturnal heartburn; cimetidine is licensed for the treatment of this symptom (see below).

Alginate-containing products have been recommended to prescribers by the Medicines Resource Centre (MeReC) as the first-step treatment for gastric reflux. This may partly be on grounds of cost, but for OTC products there is little price differential between reflux suppressants and H_2-antagonists. However, alginate-containing products probably have the advantage of speed of action.

Products

- Alginic acid
  - — Asilone Heartburn Tablets
    SSL International
  - — Bisodol Heartburn Relief Tablets
    Whitehall
  - — Gastrocote Tablets
    SSL International
  - — Gaviscon 250 and 500 Tablets
    Reckitt Benckiser
  - — Topal tablets
    Ceuta Healthcare

- Magnesium alginate
  - — Algicon Suspension and Tablets
    Aventis Pharma

- Sodium alginate
  - — Acidex suspension
    Pinewood Healthcare International

— Asilone Heartburn Liquid
SSL International

— Gastrocote Liquid
SSL International

— Gaviscon Liquid
Reckitt Benckiser

— Gaviscon Advance suspension
Reckitt Benckiser

— Rennie DUO suspension
Roche Consumer Health

Additional ingredients – antiflatulents and carminatives

Compounds used as additional ingredients with antacids are:

- Simeticone (simethicone; activated dimeticone)
- Peppermint oil
- Aromatic cardamom tincture
- Capsicum tincture

Mode of action

Distension of the stomach caused by trapped gas often contributes to the discomfort of indigestion. Simeticone is a silicone-derivative surface active agent. Its surfactant activity helps to coalesce small gas bubbles into larger ones, which are then vented by eructation.

Peppermint and other volatile oils also have antifoaming (surfactant) properties, and they are used for this action and for the warming sensation that they produce in the stomach through mild local counterirritation. However, volatile oils are also smooth muscle relaxants and may aggravate gastric reflux by relaxing the LOS. Volatile oils and silicones have been shown to be effective in relieving gaseousness, but there is no clear evidence that they are more effective than antacids alone.

Products

- Simeticone
  - Actonorm Gel
    Wallace
  - Altacite Plus Suspension
    Peckforton Pharmaceuticals
  - Asilone Antacid Liquid and Tablets, Asilone Suspension
    SSL International
  - Asilone Windcheaters Capsules
    SSL International
  - Bisodol Wind Relief Tablets
    Whitehall
  - Kolanticon Gel
    Peckforton Pharmaceuticals
  - Maalox Plus Suspension and Tablets
    Rhône-Poulenc Rorer
  - Rennie Deflatine tablets
    Roche Consumer Health

All the above products contain antacid compounds, except Asilone Windcheaters Capsules, which contain only simeticone.

Aromatic Tincture of Cardamom BP is a constituent of Aromatic Magnesium Carbonate Mixture BP, and this and capsicum tincture are contained in Jackson's Indian Brandee (Anglian Pharma). Peppermint oil is used as a flavouring in many indigestion remedies.

Additional ingredients – antispasmodics

Compounds used as additional ingredients with antacids are:

- Atropine
- Homatropine methylbromide

- Hyoscine butylbromide
- Dicycloverine (dicyclomine)
- Mebeverine

Mode of action

Colicky spasm is sometimes a feature of dyspepsia, and antimuscarinic (anticholinergic) drugs are used in some indigestion remedies for their antispasmodic properties. These drugs exert a relaxant effect on gut smooth muscle and inhibit gastric secretion through competitive inhibition of acetylcholine at postganglionic parasympathetic effector sites. Antispasmodics are either naturally occurring alkaloids derived from solanaceous herbs, or chemically related synthetic compounds.

Antispasmodics used in indigestion remedies fall into two groups: tertiary amines, which are relatively lipid-soluble and cross the blood–brain barrier readily, and quaternary ammonium compounds, which are less lipid-soluble and less likely either to be absorbed or to cross the blood–brain barrier. The tertiary amines are therefore more liable to produce the undesirable centrally mediated side-effects associated with anticholinergic drugs, namely dry mouth, blurring of vision, urinary retention, constipation and confusion. The quaternary ammonium compounds may, however, still produce some side-effects, though less pronounced, through direct peripheral activity. Since they are smooth muscle relaxants, antimuscarinic antispasmodics may exacerbate gastric reflux.

Hyoscine butylbromide is a quaternary ammonium compound which is poorly absorbed, central effects are rare, and it is claimed that its action is confined to smooth gut muscle. The drug is claimed to relieve stomach and abdominal cramps.

Dicycloverine (dicyclomine) hydrochloride is a tertiary amine, with weaker anticholinergic activity than atropine but with a direct antispasmodic action on smooth muscle. It is included at a low dose (2.5 mg/5 ml) with antacids and simeticone in Kolanticon Gel (Peckforton Pharmaceuticals). Dicycloverine (dicyclomine) tablets and syrup (Merbentyl, Florizel) are not marketed for OTC sale but may

be supplied without prescription provided the maximum single dose is 10 mg and the maximum daily dose is 60 mg.

Mebeverine hydrocholoride is a non-antimuscarinic musculotropic antispasmodic. It is marketed as a 100-mg tablet (Colofac 100, Solvay Healthcare) for the relief of stomach cramps and colicky, abdominal pain. A 135-mg tablet is licensed for the treatment of irritable bowel syndrome. (For more detail on mebeverine, see section on irritable bowel syndrome.)

Contraindications and interactions

All products containing antimuscarinics are contraindicated in patients with glaucoma, and those containing tertiary amines should also be avoided in patients with prostatic hypertrophy, myasthenia gravis or thyrotoxicosis. It is probably advisable to avoid the use of products containing antimuscarinics in elderly patients generally. Indigestion preparations containing antimuscarinic antispasmodics, especially tertiary amines, should not be recommended to patients taking medicines which themselves exert antimuscarinic side-effects; these include tricyclic antidepressants and MAOIs, antihistamines and phenothiazine antipsychotics. The effects of sublingual tablets may also be reduced due to the reduction in salivary secretion caused by antimuscarinics. Antimuscarinics will also antagonise the effect of motility stimulants such as metoclopramide and domperidone, which are sometimes used to treat dyspepsia.

Products

- Atropine – Actonorm Powder
  Wallace
- Hyoscine butylbromide – Buscopan
  Boehringer Ingelheim
- Dicycloverine (dicyclomine) – Kolanticon Gel
  Peckforton Pharmaceuticals

- Mebeverine – Colofac 100
  Solvay Healthcare

(Actonorm and Kolanticon Gel are compound preparations containing antacids as well as an antispasmodic.)

TREATMENT – H_2-RECEPTOR ANTAGONISTS

Compounds available

Compounds available are:

- Famotidine
- Ranitidine

Mode of action

Histamine is thought to be the most important mediator of the secretion of gastric hydrochloric acid through activation of receptors on parietal cells. It stimulates the production of a protein kinase which in turn activates the parietal cell's proton pump, the enzyme H^+K^+-ATPase, to secrete hydrogen ions into the stomach. H_2-receptor antagonists interfere with this mechanism by occupying parietal cell receptor sites and blocking the action of histamine. H_1-antihistamines, used in the treatment of hay fever and allergic reactions, are of little use in controlling gastric acid secretion.

H_2-antagonists have been used extensively for around 25 years for the treatment of peptic ulcer and related conditions, and the evidence of research and trials running into thousands of published papers confirms their effectiveness and safety as prescription medicines. Much less information is available about H_2-antagonists as non-prescription products. Such trials as have been published indicate that H_2-antagonists are more effective than placebo and as effective as antacids.

H_2-antagonists exert their effect for longer than antacids as their action is not limited by their length of contact with the stomach

contents. Ranitidine reaches peak plasma levels about one hour after ingestion and the elimination half-life is around two to three hours. Peak plasma levels for famotidine are reached in about two hours and the half-life is up to four hours. With all drugs acid secretion is inhibited for much longer; famotidine will provide relief for up to nine hours after a dose, and its extended length of action is reflected in the twice-daily dosing schedule.

H_2-antagonists suffer the disadvantage in relation to antacids that they do not act quickly. For both rapid and extended relief, therefore, an antacid and an H_2-antagonist could be recommended to be taken together; the action of H_2-antagonists is not inhibited in the presence of antacids. A combination product containing calcium carbonate, magnesium hydroxide and famotidine (Pepcidtwo, Johnson & Johnson MSD) is available.

There is no indication that one H_2-antagonist is more effective than another at relieving symptoms of dyspepsia.

Uses

Since H_2-antagonists were first marketed as P medicines in 1994, the licensed indications have been widened to include both dyspepsia and indigestion; the original licensed indication was for dyspepsia only. This is important from a marketing point of view because the public perception of the term indigestion is likely to be that of a minor condition amenable to self-treatment, whereas dyspepsia is a less familiar and more medical-sounding term which people may interpret as a more serious disease that should be treated by a doctor. The licensed indications also now include prophylaxis of indigestion and its symptoms associated with food and drink, and the prevention of nocturnal symptoms.

H_2-antagonists are licensed for use for a maximum of two weeks. Although this is a requirement that has been introduced for these relatively recently licensed products, it reflects a principle that should be applied to all medicines sold for the treatment of indigestion. Patients should be referred to a doctor for further investigation if indigestion symptoms persist after two weeks' treatment with any OTC medicine.

Dosage

- Famotidine – 10 mg for symptomatic relief or one hour before consuming food or drink which causes symptoms; maximum dose 20 mg in 24 hours
- Ranitidine – 75 mg for symptomatic relief, followed by 75 mg one hour later if symptoms persist; maximum dose 300 mg in 24 hours

All products are restricted to use in adults and children over 16 years.

Nizatidine has been classified by the Medicines Control Agency (MCA) as a P medicine at a dose of 75 mg. The maximum dose would be 300 mg daily, and the maximum pack size four tablets. There is currently no 75 mg dosage form available.

Cautions and interactions

H_2-antagonists are well tolerated and the incidence of side-effects is low. They should not be sold to patients taking NSAIDs, as H_2-antagonists may mask the symptoms of developing peptic ulcer. They are not licensed for sale to pregnant or breast-feeding women.

The activity of drugs which require an acid medium for absorption may be reduced by H_2-antagonists, and both ketoconazole and itraconazole are known to be so affected.

Products

- Famotidine
  - — Pepcid AC Indigestion Tablets
    Johnson & Johnson MSD
  - — Pepcidtwo chewable tablets (also contains calcium carbonate and magnesium hydroxide)
    Johnson & Johnson MSD

- Ranitidine
  - — Ranzac tablets
    Eastern Pharmaceuticals
  - — Zantac 75 Relief tablets (6 and 12 tablets packs; GSL)
    GlaxoSmithKline Consumer Healthcare
  - — Zantac 75 tablets (24 tablet pack; P)

TREATMENT – DOMPERIDONE

Mode of action

Domperidone is a dopamine D_2-receptor antagonist with a mechanism of action and prokinetic and antiemetic properties similar to metoclopramide. Unlike metoclopramide, it does not cross the blood–brain barrier readily, and acts primarily on dopamine receptors in the gut. It has a high affinity for the tissues of the oesophagus, stomach and small intestine and acts upon them to enhance gastric and oesophageal sphincter tone, gastric emptying and propulsion of intestinal contents.

Uses

Domperidone is licensed for the treatment of dysmotility symptoms of dyspepsia, including sensations of fullness, bloating, 'heavy stomach', trapped wind, belching and nausea. A number of clinical studies have been conducted on the effectiveness of domperidone, which generally indicate that the drug is effective for the above symptoms in comparison with placebo.

Dosage

The recommended dose is one 10-mg tablet three times daily and at night, when required. The drug is licensed for use only in adults of 16 years and over.

Cautions and interactions

Domperidone is not recommended in pregnancy and breast-feeding. Use should also be avoided in patients with any underlying gastric pathology, with impaired hepatic or renal function or with prolactinoma. Risk of raised serum prolactin and central side-effects, such as extrapyramidal effects, are extremely low at OTC dosages, but pharmacists should advise patients against prolonged use.

There is theoretical potential for interaction between domperidone and several types of drug, although no problems appear to have occurred in practice. Opioid analgesics and antimuscarinic drugs may antagonise the effect of domperidone; paracetamol absorption may be enhanced; and the hypoprolactinaemic effects of bromocriptine and cabergoline may be antagonised.

Product

— Motilium 10 tablets
Johnson & Johnson MSD

PRODUCT SELECTION POINTS

- Despite the relatively recent introduction of histamine H_2-receptor antagonists as P medicines, antacids generally remain the first choice for treatment of indigestion. The evidence both of trials and of widespread use has shown antacids to be effective. They have the advantage of cheapness and rapid action, although their action is less prolonged than that of H_2-antagonists.
- Antacid preparations containing both aluminium and magnesium salts are a good choice as they are effective and long-acting, and are not absorbed to a significant extent. This combination also minimises potential adverse effects from either component and balances the constipating action of aluminium against the laxative effect of magnesium salts.

- Regular use of antacids containing significant amounts of sodium should be avoided in patients with hypertension and other cardiovascular problems, and by pregnant women.
- Many antacid preparations have a high sugar content, which should be considered when recommending products to patients with diabetes.
- Antacid preparations containing bismuth salicylate should not be recommended to patients who are sensitive to aspirin.
- Antacids are more effective if taken about one hour after eating. Due to interaction in the stomach between antacids and many other drugs, a two-hour gap should be left between a dose of an antacid and another medicine.
- Liquid antacid preparations are faster-acting and may be more effective than tablets, but tablets are more convenient.
- Preparations containing alginates are worth trying for symptoms associated with reflux oesophagitis if plain antacids are ineffective. H_2-antagonists may be more effective, particularly for night-time symptoms.
- Products containing antiflatulents can be tried if bloating or distension complicate indigestion, although there is no conclusive evidence that these combinations are more effective than antacids alone.
- Products containing antispasmodics may be worth trying to treat symptoms of colic or cramp associated with indigestion. But they should not be recommended to elderly patients, and the wide range of drugs with which they interact should be taken into account.
- H_2-antagonists are effective for treating indigestion, including heartburn, but are more expensive than antacids. They may be best reserved for patients whose symptoms are not adequately relieved by antacids. Cimetidine should not be sold to patients taking drugs with narrow therapeutic margins.
- Domperidone can be used for dysmotility symptoms.
- A patient who still has indigestion after two weeks' treatment with any indigestion medicine should be referred to a doctor.

PRODUCT RECOMMENDATIONS

- For indigestion uncomplicated by additional symptoms – a combination antacid containing magnesium and aluminium salts.
- To carry around for occasional use – tablets as above, or containing calcium carbonate.
- For heartburn, reflux oesophagitis unresponsive to simple antacids (but not for pregnant women, or elderly or hypertensive patients) – an H_2-antagonist or an alginate-containing antacid preparation.
- For pregnant women (usually last trimester), and elderly and hypertensive patients with heartburn – a sodium-free or low-sodium, antacid preparation containing an alginate.
- For indigestion not adequately relieved by antacids – an H_2-antagonist, with careful monitoring of the situation.

The above recommendations are made on the assumption that the possibility has been eliminated that the patient may have a potentially serious gastrointestinal condition.

Insect bites and stings

(continued . . .)

Insect bites and stings differ in the chemical composition of their constituents and in the type of reaction they provoke. Insect bites often go unnoticed at the time, and their effects may not be felt for some time afterwards but can then last for several days, whereas stings are felt immediately and the pain and discomfort they cause often subside within minutes or hours.

NATURE OF BITES AND STINGS

Bites

Insects usually bite in order to gain access to the victim's blood supply to feed on it. The skin is punctured and the insect's saliva is secreted into the dermis. The saliva usually contains enzymes or other agents to liquefy the blood in order to facilitate its flow back through the insect's feeding apparatus. It may also contain a local anaesthetic, so that the bite goes undetected by the victim and allows the insect to feed undisturbed. The reaction produced by the bite is essentially an irritant dermatitis provoked by the insect's saliva.

Stings

Insect stings are primarily weapons, either of attack when used to incapacitate prey, or of defence when a threat is perceived, and their effect is intended to be immediate. The pain and inflammation of a bee or wasp sting is caused by the direct pharmacological effects of its constituents. These include: histamine and other biogenic amines; toxic polypeptides, including melittin which has a haemolytic effect, apamin, which is neurotoxic, and mast cell-degranulating peptide, which causes further release of histamine; and enzymes such as hyaluronidase and phospholipase, which break down intercellular tissue cement and assist penetration of the venom into the tissues.

TREATMENT

Preparations marketed for the treatment of bites and stings contain:

- Antihistamines
- Local anaesthetics
- Astringents
- Soothing constituents

Preparations are generally intended to suppress cutaneous sensory receptors. Hydrocortisone is also licensed for the treatment of insect bites.

Antihistamines

As one of the principal components of insect stings is histamine, and as histamine is also one of the principal mediators of the inflammatory response to bites, treatment with antihistamines, which competitively block histamine H_1-receptor sites, would seem logical. Several topical products containing antihistamines are licensed for treatment of the pain, itching and inflammation associated with bites and stings. However, topical antihistamines have been criticised as not being very effective. They are also liable to cause sensitisation, and for this reason their use is restricted to a maximum of two or three applications per day for no longer than three days.

Oral antihistamines are more likely to bring sustained and effective relief than topical preparations, although their disadvantage is that they do not act immediately. Non-sedating compounds are preferable, as they are as effective for peripherally mediated reactions as the older antihistamines but are not associated with their central sedating and antimuscarinic side-effects. There appear to be no clear differences in efficacy for the treatment of bites and stings between oral antihistamines and compounds used topically. (For further information on antihistamines, see the section on hay fever.)

Some patients develop an allergic sensitivity to bites and suffer quite severe local reactions. They should be advised to keep with them a supply of antihistamines ready to take in case they are bitten, as well as taking precautions against being bitten. A few individuals develop severe anaphylaxis to stings; they may be prescribed adrenaline (epinephrine) 1:1000 injection to keep at hand for intramuscular or subcutaneous use if they are stung.

Products

- Antazoline
  - — R.B.C. Cream
    Co-Pharma
  - — Wasp-Eze Ointment
    SSL International

- Diphenhydramine
  - — Benadryl Skin Allergy Relief Cream and Lotion
    Warner Lambert Consumer Healthcare
  - — Histergan cream
    Norma Chemicals

- Mepyramine
  - — Anthisan cream
    Aventis Pharma
  - — Anthisan Plus Sting Relief Spray
    Aventis Pharma
  - — Wasp-Eze Spray
    SSL International

All the above products are also licensed for the treatment of allergic skin reactions.

Crotamiton

Crotamiton is not an antihistamine but has antipruritic properties and can be used for bites and stings; it is claimed to have a prolonged action of six to ten hours following application. (Crotamiton is also licensed for the treatment of allergic skin reactions.)

Products

- Eurax Cream and Lotion
  Novartis Consumer Health
- Eurax Hc Cream (also contains hydrocortisone)
  Novartis Consumer Health

Local anaesthetics

The effectiveness of local anaesthetics in the treatment of bites and stings is debatable. A United States Food and Drug Administration advisory panel concluded that products containing them are safe and effective, but claims have also been made that the concentrations found in non-prescription products are insufficient to produce adequate pain relief. Sensitisation on prolonged usage is an acknowledged problem and licensing restrictions on the length of use take account of this.

Spray formulations may be more effective than creams or lotions as they contain higher concentrations of local anaesthetic. They are likely to be most useful immediately after a bite or sting because they will produce relief, although short-lived, when the pain is most intense. The cooling effect produced by the evaporation of the propellant will also contribute to the pain relief. (For further information on local anaesthetics, see section on haemorrhoids.)

Products

- Benzocaine
  - — Anthisan Plus Sting Relief Spray
    Aventis Pharma
  - — Lanacane cream
    Combe International
  - — Solarcaine Cream, Lotion and Spray
    Schering-Plough
  - — Wasp-Eze Spray
    SSL International
- Lidocaine (lignocaine)
  - — Dermidex cream
    SSL International
  - — Solarcaine Gel
    Schering-Plough
- Tetracaine (amethocaine)
  - — Anethaine cream
    Torbet

Hydrocortisone

The usefulness of hydrocortisone cream for bites may be limited by being restricted to two applications daily, as more frequent application may be necessary to sustain relief. It is also not licensed for use in children under 10 years of age.

Products

For products, see under irritant and allergic dermatitis.

Calamine, zinc oxide

Calamine is naturally occurring basic zinc carbonate with ferric oxide, which imparts the characteristic pink colour. It is mildly astringent and its soothing, antipruritic action is due to the large surface area and porous nature of its particles, which promote the evaporation of water from the preparations in which it is formulated, with a consequent cooling effect. Calamine Lotion BP also contains phenol 0.5 per cent as a preservative, which has an incidental local anaesthetic action and contributes to its effectiveness. It is a popular preparation for treating urticaria and pruritus from many causes, including insect bites. It is cheap and there are few restrictions on its use. Zinc oxide has similar properties to calamine.

Products

- Calamine
  - — Calamine Cream, Aqueous BP
  - — Calamine Lotion BP
  - — Lacto Calamine Creme and Lotion
    Schering-Plough
  - — R.B.C. Cream
    Co-Pharma
- Zinc oxide
  - — Benadryl Skin Allergy Relief Cream and Lotion
    Pfizer Consumer Healthcare
  - — Lacto Calamine Cream and Lotion
    Schering-Plough

Aluminium sulphate

Aluminium sulphate is a powerful astringent. A 20 per cent solution has been used for the treatment of stings by insects and marine organisms. It is thought that it may cause precipitation of proteins within the venom and reduce local toxicity.

Product

There is only one product:

- Stingose spray
  Ayrton Saunders

Ammonia solution

Ammonia has been claimed to have a neutralising effect on bites and stings, but a United States Food and Drug Administration advisory panel found that submitted data did not substantiate this claim. However, there is a documented report of the successful use of Aromatic Ammonia Spirit to treat bathers who had been stung by Portuguese men-of-war jelly fish.

Product

There is only one product:

- After Bite applicator pen
  E C De Witt

PRODUCT SELECTION POINTS

- Although hydrocortisone cream and ointment are licensed for the treatment of insect bite reactions, their effectiveness may be

limited by the restrictions on frequency of application. The same applies to topical antihistamines, the efficacy of which is in any case in doubt. Calamine lotion may be the best topical treatment for bites as it is an effective antipruritic, can be applied as frequently as required and is cheap.

- For bites, oral antihistamines are likely to provide more effective and prolonged relief than either topical hydrocortisone or topical antihistamines, although their action is not immediate. Non-sedating compounds should be as effective as the older, sedating ones but are not associated with their side-effects. The best overall approach may be use of a topical preparation immediately plus an oral antihistamine to maintain relief.
- A spray presentation containing a local anaesthetic may be the best initial treatment for stings, but early application is essential for optimum response. There is some evidence that aluminium sulphate and ammonia solution may be effective in treating stings. Continued relief can be provided as for bites.

PRODUCT RECOMMENDATIONS

For insect bites – hydrocortisone cream or ointment or calamine lotion, and an oral antihistamine if necessary.

For stings – a spray containing a local anaesthetic used promptly, and an oral antihistamine if necessary.

Irritable bowel syndrome

Irritable bowel syndrome (IBS) is a chronic motility disorder of the colon.

CAUSES

There is no demonstrable organic cause for IBS. It is characterised by a range of symptoms which may include abdominal pain (either colicky or dull and aching), diarrhoea or constipation (or both alternately), abdominal distension and flatulence, and non-intestinal symptoms such as headache and fatigue. Symptoms are often exacerbated by stress, anxiety or depression. As the cause cannot be determined, treatment is symptomatic.

TREATMENT

A number of preparations are believed to have a direct relaxant effect on intestinal smooth muscle, are available without prescription, and specifically licensed for the treatment of IBS:

- Alverine
- Hyoscine butylbromide
- Mebeverine
- Peppermint oil

Alverine citrate

Alverine is a non-antimuscarinic selective antispasmodic acting directly on smooth muscle used for the treatment of pain and smooth muscle spasm in IBS. There have been few reported side-effects during the 30 years it has been available as a prescription medicine, and there are no known interactions.

The recommended dose for adults and children over 12 years is one or two 60-mg capsules up to three times daily. It is not contraindicated in pregnancy and lactation, but caution is advised in the first

trimester of pregnancy. The manufacturer recommends that the drug should be supplied only to patients who have had IBS diagnosed by a doctor.

Products

- Relaxyl capsules
  SSL International
- Spasmonal Fibre granules
  Norgine

The second of these contains alverine citrate and also sterculia, a bulk-forming laxative indicated in the treatment of IBS. However, its price (around £22 per 500-g pack) probably rules out OTC sales.

Hyoscine butylbromide

Hyoscine butylbromide is an antimuscarinic antispasmodic which is poorly absorbed from the gut and claimed to act directly upon it. It is a hydrophilic quaternary ammonium compound, and any drug which is absorbed does not readily cross the blood–brain barrier. Nevertheless, antimuscarinic side-effects have been very occasionally reported and hyoscine butylbromide is contraindicated in patients with glaucoma. Caution is also advised with use in patients with prostate problems, the elderly and pregnant women. The recommended dosage is from three to eight 10-mg tablets daily, in divided doses, for adults, and 30 mg daily for children between six and 12 years. Hyoscine butylbromide is also licensed to relieve stomach cramps and for cramping that occurs with period pains.

Product

There is only one product:

- Buscopan
  Windsor

Mebeverine hydrochloride

Mebeverine is a musculotropic antispasmodic which is claimed to act directly on the smooth muscle of the intestine without affecting normal gut motility. Like alverine, it has no antimuscarinic side-effects and no contraindications or interactions with other drugs. Mebeverine hydrochloride is licensed for use in adults and children over ten years; it should be used in pregnancy only under medical supervision. The dose is 135 mg up to three times daily, taken 20 minutes before meals.

Products

- Colofac IBS tablets
  Solvay Healthcare
- Equilon tablets
  Chefaro Proprietaries

Peppermint oil

Menthol, the principal constituent of peppermint oil, has been shown to have a relaxant action on smooth muscle similar to that of calcium-channel antagonists. The oil acts directly on the colon, although conflicting evidence has been presented as to its effectiveness in treating IBS.

Peppermint oil is available as enteric-coated capsules containing 0.2 ml of the oil. The recommended dosage for adults is one or two capsules three times a day, preferably before food; it may be taken after food, but not immediately after. The capsules should not be chewed, as peppermint oil can cause irritation to the mouth and

oesophagus, in addition to which the drug would be dispersed before it reaches the colon. Heartburn sufferers may, in any case, experience an exacerbation of symptoms even when the capsules are correctly taken. Peppermint oil capsules are not contraindicated in pregnancy or lactation, although the usual precautions should be observed.

Products

- Colpermin capsules
  Pharmacia
- Mintec capsules
  Shire Pharmaceuticals

PRODUCT SELECTION POINTS

- All four of the above drugs have a history of prescription use for IBS, but convincing clinical trial evidence of their efficacy is lacking.
- In view of the general absence of side-effects, interactions, cautions or contraindications in relation to alverine or mebeverine, they may be the safest choices for recommendation.
- As psychological factors may be a contributory factor of IBS in many cases a placebo effect could play a large part in the perceived effectiveness of any treatment.

PRODUCT RECOMMENDATIONS

Alverine citrate or mebeverine hydrochloride, although the pharmacist should first ensure that the patient has been diagnosed by a doctor as suffering from IBS.

Irritant and allergic dermatitis and mild eczema

Dermatitis and eczema are used interchangeably by dermatologists to describe a range of inflammatory skin conditions of which the principal symptoms are dryness, erythema and itch, often with weeping and crusting. However, it has become conventional to apply the term eczema to conditions with an endogenous cause in atopic individuals and dermatitis to reactions to external agents.

CAUSES

Atopic eczema

Atopic eczema is a chronic fluctuating inflammatory condition of the skin with no known cause, although there is often a genetic link and a family history of allergic sensitivity. It affects 5 to 15 per cent of schoolchildren and 2 to 10 per cent of adults. It usually resolves spontaneously by 30 years of age, although the skin may remain sensitive to irritant agents. The rash of atopic eczema usually starts on the face and then spreads to the hands and flexural sites around the body; the exact pattern of distribution depends on age.

Irritant dermatitis

Irritant dermatitis results from contact with substances which cause direct chemical damage to the skin, and can occur on the first exposure to a strong irritant or on repeated exposure to a milder one. It is commonly associated with occupational use. Examples of irritant agents include: detergents and household cleaning materials; hair tinting and perming products; acids, alkalis, industrial solvents, oils and plastics used by textile workers, car mechanics, woodworkers, decorators and builders; and fertilisers and soil with which florists and agricultural workers come into contact. The reaction is confined to the area of contact with the causative agent.

Allergic contact dermatitis

Allergic contact dermatitis is due to hypersensitivity to a sensitising agent, which can occur after just a couple of exposures or may take many years of repeated exposure to develop. The rash may appear at, or away from, the site of contact. Once established, sensitivity generally remains for life. Sensitising agents include: rubber in household gloves and footwear; nickel in costume jewellery, zips, bra clips, belt buckles and coins; resins used in glues; ingredients of cosmetics and topical medications; plants, particularly primula and chrysanthemum; and chromates in paints and cement.

TREATMENT – HYDROCORTISONE CREAM AND OINTMENT

In atopic eczema the principal problems are skin dryness and itch over widespread areas, and the mainstays of treatment are hydrating agents and soothing emollients. Topical corticosteroids are used to treat severe flare-ups, and systemic sedative antihistamines may be given to alleviate itching, particularly at night. Atopic eczema should be treated under medical supervision, although hydrocortisone cream is licensed for the treatment of mild to moderate eczema (see below), and most antihistamines are available without prescription.

Community pharmacists are likely to be asked to provide advice and treatment for irritation caused by contact dermatitis, the standard treatment for which is hydrocortisone cream or ointment. (For treatment of eczema, see also under dry skin.)

Mode of action

(For the mechanism of the local anti-inflammatory action of corticosteroids, see under mouth ulcers.)

In creams and ointments for non-prescription use, only hydrocortisone as the free alcohol and hydrocortisone-21-acetate are permitted. These compounds have only mild potency, a short duration of activity, weak side-effects and a greater safety profile in comparison

with other topical corticosteroids. Also, unlike more potent corticosteroids, hydrocortisone does not affect protein synthesis of human skin and is therefore unlikely to cause antiproliferative side-effects such as thinning of the skin and telangiectasis (the dilatation of superficial blood capillaries).

Indications

In 1987, hydrocortisone cream and ointment, up to a concentration of 1 per cent, was licensed for sale without prescription from pharmacies for the treatment of inflammation and pruritus associated with irritant and allergic contact dermatitis and insect bite reactions, but not for atopic eczema, for which hydrocortisone remained prescription-only. These restricted indications caused difficulties for pharmacists with patients who could not understand why they could buy hydrocortisone for contact dermatitis but not for eczema, even when their doctor had recommended purchase.

When hydrocortisone was first reclassified, there was considerable opposition from some medical quarters, with concern expressed over safety once it was freed from prescription control. One of the major fears was that abuse might lead to systemic absorption sufficient to cause adrenal suppression. However, experience has proved hydrocortisone to be very safe as a non-prescription medicine, and in 1995 the licensed indications were extended to include mild to moderate eczema.

Hydrocortisone has also since been licensed in combination products with crotamiton, an antipruritic, and with the antifungals clotrimazole and miconazole, with indications further extended to athlete's foot and candidal intertrigo in the latter combination. Haemorrhoidal preparations containing hydrocortisone are also now licensed as P medicines.

Use, cautions and restrictions

Hydrocortisone cream and ointment should be applied sparingly once or twice daily for a maximum of seven days. The licensing conditions

restrict application to a 'small area', presumably in order to limit the potential for widespread application in atopic eczema and any possible risk of skin damage or systemic absorption.

Preparations should not be used on the eyes or face, although they may be applied to the ear lobes, which are often the site of allergic contact dermatitis caused by nickel in costume jewellery ear-rings. Use on anogenital areas is not permitted, although haemorrhoidal preparations containing hydrocortisone are licensed for rectal use.

Hydrocortisone cream or ointment should not be applied to any infections of the skin, including athlete's foot (although clotrimazole and miconazole with hydrocortisone cream are licensed for this indication), acne or cold sores, as symptoms may be masked while the infection is allowed to progress and natural immune reactions may be suppressed by the steroid. Preparations should not be applied to ulcerated, broken or weeping skin, or used with occlusive dressings, because of the risk of absorption.

In addition to the restrictions relating to application, hydrocortisone cream and ointment is not licensed for use in children under ten years, or during pregnancy or lactation.

Products

The following products contain 1 per cent hydrocortisone or hydrocortisone acetate and are licensed for sale without prescription:

- Hc45 cream
  Crookes Healthcare
- Lanacort Cream and Ointment
  Coombe International
- Zenoxone cream
  Biorex
- Dermacort Cream (0.1 per cent hydrocortisone in a formulation designed to provide equivalent activity to 1 per cent hydrocortisone cream BP)
  Sankyo Pharma

- Eurax Hc cream (0.25 per cent hydrocortisone with 10 per cent crotamiton)
  Novartis Consumer Health

Note that packs of hydrocortisone cream and ointment (1 per cent) licensed as POMs may not be sold without prescription as they do not comply with the labelling requirements for OTC sale.

TREATMENT – CLOBETASONE BUTYRATE CREAM

Clobetasone butyrate 0.05% cream was reclassified as a P medicine in 2001. Clobetasone butyrate is a moderately potent corticosteroid, and is licensed for the short-term treatment and control of patches of eczema and dermatitis, including atopic eczema and primary irritant and allergic dermatitis. It is more effective than hydrocortisone for flare-ups of eczema, and will generally break the 'itch–scratch cycle' before it takes hold. The licensing conditions and restrictions are generally as for hydrocortisone cream, but the product may be used for children under 12 on the advice of a doctor. Clobetasone butyrate cream should not be used on the same area of skin for more than two one-week treatment periods within three months, or for the treatment of psoriasis or seborrhoeic eczema.

Product

- Eumovate Eczema and Dermatitis Cream
  GlaxoSmithKline Consumer

PRODUCT SELECTION POINTS

- Hydrocortisone cream and ointment are licensed for sale without prescription for irritant and allergic dermatitis. They are safe and effective when used in accordance with the licensing restrictions.

- Hydrocortisone is also licensed for sale without prescription for mild to moderate eczema. However, licensing restrictions limit application to small areas only and prevent its use on the face and in children under ten years, precluding most of its uses in atopic eczema. The condition should be treated wherever possible with emollients (see under dry skin).
- Clobetasone butyrate cream is now available for flare-ups of atopic eczema.

PRODUCT RECOMMENDATIONS

For contact and allergic dermatitis – hydrocortisone cream or ointment.

For flare-ups of atopic eczema – clobetasone butyrate cream.

Minor eye conditions

(continued . . .)

Minor eye conditions for which non-prescription medication is available are: bacterial and allergic conjunctivitis and styes; sore and 'tired' eyes; dry eyes; and blepharitis. For preparations for allergic conjunctivitis, see under hay fever.

BACTERIAL CONJUNCTIVITIS AND STYES

Causes and treatment

Bacterial conjunctivitis is an infectious condition affecting one or both eyes, in which the conjunctiva become inflamed. The infecting organism is most often *Staphylococcus aureus*, but several other bacteria may also be responsible. The main symptoms are a feeling of itchiness or grittiness, and there is often also a discharge. There is no pain, and vision is not affected, except for blurring caused by the discharge. A stye (external hordeolum) is an infection of the lash follicle of the eyelid, producing pustules. The most common infecting agent is *Staph. aureus*.

The only non-prescription antimicrobial compounds available for the treatment of these infections are:

- Propamidine isetionate
- Dibromopropamidine isetionate

Propamidine isetionate and dibromopropamidine isetionate

These compounds are aromatic diamidine antiseptics. They are bactericidal against Gram-positive organisms, but less active against Gram-negative bacteria. The first successful treatment with propamidine isetionate of bacterial conjunctivitis was reported in 1944. Since then there appears to have been no clinical research or trials of any kind in relation to bacterial eye infections, although there have been some recent clinical reports on the use of propamidine isetionate in the treatment of acanthamoeba keratitis, a condition beyond the

scope of this book. Current clinical opinion is that chloramphenicol is the drug of choice for superficial bacterial eye infections, and the *British National Formulary* regards propamidine and dibromopropamidine as of little value.

Eye drops are formulated with propamidine isetionate 0.1 per cent and eye ointment with dibromopropamidine isetionate 0.15 per cent. Both may be used for adults and children. The ointment persists longer on the corneal surface and needs to be applied only twice daily, but can cause stickiness and blurring of vision. It is suitable for the treatment of both conjunctivitis and styes. The drops need to be used four times daily, and are not suitable for styes. Probably the best regimen for conjunctivitis is to use drops during the day, and ointment at night. In both conditions treatment should be continued for 24 hours after symptoms have cleared. If symptoms do not significantly improve within 48 hours, treatment should be discontinued and the patient referred for medical advice.

Cautions

Both formulations may cause slight stinging when applied. Contact lenses should not be worn when either preparation is being used and, as with all ophthalmic preparations, they should be discarded one month after opening.

Products

As ointment and drops:

- Brolene
  Rhône-Poulenc Rorer
- Golden Eye
  Typharm

SORE AND 'TIRED' EYES

Causes and treatment

Redness and mild irritation in the eyes can be caused by activities such as driving and close work, and environmental pollutants.

Several products, based mainly on astringents and vasoconstrictors, are available.

Witch hazel

Several products contain distilled witch hazel, which contains flavonoids and tannins. Witch hazel has astringent and anti-inflammatory properties, but there appears to be no evidence concerning its efficacy in ophthalmic preparations. Distilled witch hazel is the sole constituent of Optrex eye lotion and drops (Crookes Healthcare), and is also a constituent of Optrex Clear Eyes drops.

Vasoconstrictors

Mode of action

Decongestant vasoconstrictors are included in some ophthalmic preparations to shrink the dilated blood vessels which cause redness. Naphazoline is a sympathomimetic agent with marked alpha-adrenergic activity, with a rapid and prolonged action when applied topically. It is documented as being effective in constricting conjunctival blood vessels, and in reducing discomfort associated with ocular inflammation. It is included with distilled witch hazel in Eye Dew and Optrex Clear Eyes drops (both Crookes Healthcare), and is the sole active constituent of Murine (Abbott). Phenylephrine, another alpha-adrenergic agonist, is contained in Isopto Frin drops (Alcon).

Cautions, contraindications and interactions

A hazard of long-term use of decongestant eye drops is rebound congestion (hyperaemia), and a paper has recently been published documenting a large number of cases of conjunctival inflammation following long-term use. Purchasers should therefore be advised not to use these products continuously.

Phenylephrine may interfere with the action of antihypertensive agents, and MAOIs and tricyclic antidepressants can exacerbate its systemic effects. Decongestants may slightly dilate the pupils, so their use should be avoided in patients with glaucoma. Because of the slight risk that these sympathomimetic ophthalmic decongestants may raise blood pressure, and interfere with carbohydrate metabolism and thyroid function, patients with high blood pressure, heart disease, diabetes or hyperthyroidism should consult their doctor before using these products.

DRY EYES

Causes and treatment

Dry eye (keratoconjunctivitis sicca) is, as its name implies, a chronic condition characterised by dryness of the surface of the eye. It is caused either by a deficiency of conjunctival mucus, due to the absence or significant impairment of the mucin-producing goblet cells of the conjunctiva, or to tear deficiency; the latter is often associated with rheumatoid arthritis.

Treatment of dry-eye conditions is usually with tear substitutes ('artificial tears'), and there are several products available which take slightly different approaches to the problem. The main goal of formulation is to prolong the action of products and reduce the frequency of application required.

The compounds used are:

- Hypromellose
- Polyvinyl alcohol

- Carbomer 940
- Hydrophobic ocular lubricants

There is little information available on the relative efficacy of tear substitutes. Knowledge of the cause of a patient's dry eye should help with selection of a suitable preparation, but choice is often a matter of patient preference arrived at by a process of trial and error.

Hypromellose

Hypromellose is the only tear substitute compound available in non-proprietary form. It is a mixed cellulose ether with viscosity-enhancing properties, which prolongs the persistence of the water in the drops containing it on the surface of the eye. It is most useful for dry eye caused by tear deficiency, e.g. Sjögren's syndrome associated with rheumatoid arthritis. Viscosity of hypromellose solutions increases with concentration, and it has been suggested that the 0.3 per cent concentration of the official formulation may be too low. On the other hand, too high a concentration can lead to blurring and crusting. The optimum range appears to be between 0.5 and 1 per cent. Dextran 70 0.1 per cent is included with hypromellose 0.3 per cent in Tears Naturale (Alcon) as a fluid volume expander. pH also seems to be an important factor in relation to the comfort of the drops in the eye, and slightly alkaline formulations are thought to be preferable; the official preparation has a pH of 8.5.

Products

- Hypromellose Eye Drops BP (0.3 per cent)
- Isopto Alkaline (1 per cent)
  Alcon Laboratories
- Isopto Plain (0.5 per cent)
  Alcon Laboratories

- Moisture-eyes (0.3 per cent)
  Co-Pharma
- Tears Naturale (0.3 per cent)
  Alcon Laboratories

Polyvinyl alcohol (PVA)

This is a viscosity enhancer, usually used at a concentration of 1.4 per cent. It also promotes wetting of the ocular surface, and is useful to help spread the water content of the drops over the eye when the mucus layer is deficient and tear film distribution is patchy. Like hypromellose, it enhances stability of the tear film without causing ocular irritation or toxicity. Liquifilm Tears Preservative-Free (Allergan) and Refresh (Allergan) also contain povidone, which is thought to mimic the action of natural conjunctival mucin.

Products

PVA 1.4 per cent unless otherwise stated:

- Hypotears (1 per cent)
  Novartis Ophthalmics
- Liquifilm Tears
  Allergan
- Liquifilm Tears Preservative-Free
  Allergan
- Refresh (single-use vials)
  Allergan
- SnoTears
  Chauvin Pharmaceuticals

Carbomer 940

This is an acrylic acid polymer which is formulated as a liquid gel for the treatment of dry eye. Its claimed advantages include ease of application and prolonged contact with the corneal surface, requiring application only three or four times a day. In one trial a carbomer 940 gel-based product was found to remain on the cornea for seven times longer than a conventional PVA-based formulation.

Products

- GelTears
  Chauvin Pharmaceuticals
- Viscotears Liquid Gel
  Novartis Ophthalmics

Hydrophobic ocular lubricants

These are sterilised ointments containing liquid and soft paraffins and wool fat or a similar, non-lanolin derivative. They mimic the lipid layer of human tear film and are intended mainly for night-time use to protect and lubricate the cornea during sleep.

Products

- Simple Eye Ointment
- Lacri-lube
  Allergan
- Lubri-Tears
  Alcon Laboratories

BLEPHARITIS

Blepharitis is inflammation of the margins of the eyelids, often accompanied by crusting. In many cases the cause is unknown, but it is sometimes associated with seborrhoea of the scalp. In these cases treatment of the scalp with an antidandruff shampoo containing pyrithione zinc, selenium sulphide or ketoconazole may resolve the condition (see section on dandruff and seborrhoeic dermatitis). The hydrophobic ocular lubricants discussed above can be used to soften crusts.

ADMINISTRATION OF EYE DROPS AND OINTMENT

The following techniques are recommended for the most effective use of eye drops and ointment.

- Wash hands thoroughly.
- Tilt head backward.
- Gently grasp lower outer eyelid just below the lashes and pull the eyelid away from the eye.
- Place the dropper or ointment tube directly over the eye by looking directly at it.
- With drops:
  - — just before applying a drop, look upwards
  - — after applying a single drop, look downward for several seconds
  - — release the eyelid slowly
  - — keep eyes closed for one to two minutes
  - — with a finger, gently press over the opening of the tear duct in the inner corner of the eye
  - — blot excess liquid from around the eye.

- With ointment:
  - with a sweeping motion, insert 1 to 2 cm of ointment inside the lower lid
  - release the eyelid slowly
  - keep eyes closed for one to two minutes
  - blot excess ointment from around the eye.

PRODUCT SELECTION POINTS

- Propamidine and dibromopropamidine isetionates are the only antibacterial compounds licensed for the non-prescription treatment of conjunctivitis and styes. There is little evidence supporting the efficacy of these compounds, but they have been used for many years.
- Naphazoline appears to be an effective ocular decongestant for the treatment of sore and 'tired' eyes due to trivial causes, but prolonged, continuous use should be avoided.
- There are several tear substitute products, based on three main active constituents, available for the treatment of dry eye conditions. Choice is often a matter of patient preference.

PRODUCT RECOMMENDATIONS

- For bacterial conjunctivitis – propamidine isetionate eye drops or dibromopropamidine isetionate eye ointment.
- For styes – dibromopropamidine isetionate eye ointment.
- For sore and 'tired' eyes due to mild ocular congestion – eye drops containing naphazoline.
- For dry eye conditions – choice often dependent on patient preference.

Motion sickness

Motion sickness is a term covering all forms of travel sickness, by any type of transport – air, sea or land.

CAUSES

Motion sickness is a form of vertigo in which autonomic symptoms predominate. It may include, in addition to nausea and vomiting, increased salivation, general malaise, pallor, sweating, yawning and hyperventilation. Gastric motility is reduced and digestion impaired. Two main theories have been put forward to account for motion sickness: overstimulation of the vestibular apparatus of the inner ear caused by unaccustomed types of movement, and a conflict between stimuli received in the brain from the vestibular system, the eyes and other non-vestibular spatial receptors.

Vomiting is a complex process involving both the CNS and the gastrointestinal system. It is mediated by the vomiting centre in the medulla of the brain. The vomiting centre receives stimuli from peripheral areas, such as the gastric mucosa, and from within the CNS. The chemoreceptor trigger zone in the brain operates in close association with the vomiting centre; it is stimulated by many drugs and by certain metabolic disturbances, and it activates the vomiting centre.

The vomiting centre is also activated by impulses from the gastrointestinal tract and the vestibular apparatus of the inner ear, the activity of the latter being involved in the causation of motion sickness. Once activated, the vomiting centre transmits stimuli via a cranial nerve to the abdominal musculature, stomach and oesophagus to initiate vomiting.

TREATMENT

First-generation antihistamines and hyoscine (scopolamine) are used in non-prescription medicines for the prophylaxis and treatment of motion sickness.

Antihistamines

Compounds available

Compounds available are:

- Cinnarizine
- Meclozine hydrocholoride
- Promethazine hydrochloride
- Promethazine teoclate

Mode of action, dosage and products

In addition to their anti-allergic, antipruritic, antitussive and antimuscarinic effects, first-generation H_1-antagonists, in varying degrees, also have antiemetic properties, and some are used exclusively for these actions. Their effectiveness for this indication may be due to their antimuscarinic activity, but it has also been proposed that their antiemetic activity results from blockade of dopamine D_2-receptors in the brain.

Second-generation antihistamines, having much lower lipid solubility than first-generation compounds, do not cross the blood–brain barrier to a significant extent and exert little or no central activity. Tests have shown them to be of no value as hypnotics or as prophylaxis for motion sickness.

The compounds used against motion sickness are selected primarily for their antiemetic properties, but factors such as length of action and side-effects are also taken into account. All the above compounds are thought to be of similar efficacy, although there appears to be no evidence from comparative trials. All motion sickness preparations are intended for prophylactic use, and are less effective once nausea or vomiting has begun; apart from the risk of their being vomited up, the drugs will be more slowly absorbed in such cases because gastric motility is decreased.

- **Cinnarizine**

  Cinnarizine is a piperazine derivative and compounds in this group generally possess antiemetic properties. Cinnarizine causes some drowsiness, but antimuscarinic side-effects do not appear to be a problem. Peak plasma concentrations occur two to four hours after administration, and the half-life is three to six hours. A recent trial found cinnarizine 25 mg to be no more effective than placebo in rough seas, although 50 mg was more effective.

  For adults, a loading dose of 30 mg is recommended two hours before the start of a journey, followed by one 15 mg tablet eight-hourly throughout the journey. Half this dose may be given to children between the ages of 5 and 12 years, but cinnarizine is not licensed for use in younger children.

- **Meclozine hydrochloride**

  Meclozine is a piperazine and is considered to be among the least sedating compounds in this group and to have low anti-muscarinic activity. It is long-acting.

  The adult dose is two 12.5 mg tablets of meclozine hydrochloride taken the night before or one hour prior to travelling, repeated once every 24 hours if necessary. The dose for children between 6 and 12 years is half the adult dose, and for children from two to six years one-quarter the adult dose.

- **Promethazine teoclate and promethazine hydrochloride**

  Promethazine teoclate and hydrochloride are phenothiazines. They have marked antimotion sickness activity, but also marked antimuscarinic properties and sedation is common. Both compounds have been widely used for the treatment of nausea, vomiting and vertigo. The sedative effect of promethazine hydrochloride is sometimes considered to be an advantage in young children on long journeys. (Promethazine hydrochloride has other non-prescription uses: see the sections on cough, hay fever and temporary sleep disturbance.)

Promethazine teoclate is long-acting, with an initial dose for an adult or child over ten years of one 25 mg tablet, taken two hours before a short journey or the night before a long journey, with further 25 mg doses every 24 hours if required. Half the adult dose can be given to children between five and ten years old. Promethazine hydrochloride is also long-acting, and it is licensed for use in children from the age of two years. It has the advantage of being available as tablets in two strengths (10 mg and 25 mg) and as an elixir (5 mg/5 ml). Dosage schedules are as for promethazine teoclate, but one 10-mg tablet is recommended for five- to 10-year-olds, and a 5-mg dose of the elixir for children between two and five years.

Hyoscine hydrobromide

Mode of action and dosage

Hyoscine (scopolamine) hydrobromide is a naturally occurring alkaloid which competitively inhibits the actions of acetylcholine at the muscarinic receptors of autonomic effector sites innervated by parasympathetic nerves. It has a central as well as a peripheral action, as it is lipid-soluble and crosses the blood–brain barrier.

Hyoscine is probably the most effective drug for prevention of motion sickness, although it is relatively short-acting and has more pronounced antimuscarinic side-effects than antihistamines. A recent double-blind trial showed that hyoscine was more effective against seasickness than cinnarizine, although the latter was better tolerated in having less marked side-effects. As motion severity increased, comparative tolerability of hyoscine improved. Hyoscine is available as a transdermal patch (on prescription only), and this formulation has been shown in placebo-controlled trials to be more effective than either oral meclozine or dimenhydrinate for prophylaxis of motion sickness for periods of less than eight hours.

Doses vary slightly between products, but the *British National Formulary* recommends, for adults, hyoscine hydrobromide 0.3 mg 30 minutes before travelling, followed by 0.3 mg every six hours if

required, to a maximum of three doses in 24 hours; the recommended dose for children over 10 years is 0.15 to 0.3 mg and for children four to 10 years 75 to 150 μg (0.075 to 0.15 mg). Kwells Junior (Roche) and Joy-Rides (Stafford-Miller) are licensed for use in children from age three years.

ANTIHISTAMINES AND HYOSCINE

Adverse effects, cautions and contraindications

Antihistamines and hyoscine possess peripheral and central antimuscarinic activity and have similar adverse effects, including sedation, dry mouth, blurred vision, urinary retention and constipation. However, at the low doses used over short periods these do not normally cause problems.

Antihistamines and hyoscine should be avoided in patients suffering from glaucoma or prostatic hypertrophy, and should be used with caution generally in the elderly, and in patients with epilepsy or cardiac or cardiovascular disease. Paradoxical CNS stimulation may occur with antihistamines in children, resulting in insomnia and excitement and, rarely, nightmares, hallucinations and even convulsions. Photosensitivity reactions have been reported with promethazine. Alcohol should be avoided when taking any antimotion sickness preparations.

In pregnancy, use under medical supervision is advised for antihistamine travel sickness products, due to fears regarding possible congenital malformations. Antihistamines were at one time routinely prescribed for morning sickness, but concerns arose over a product containing the antihistamine doxylamine and it was withdrawn from the market in 1983. Although no firm causal link was established between this product or other antihistamines and congenital abnormalities, antihistamines have since been used with caution in pregnancy. Similar fears have not been expressed about hyoscine products and no warnings have been issued against their use in pregnancy. However, it is prudent to avoid any medication in pregnancy, if possible, and certainly in the first trimester.

Interactions

Antihistamines and hyoscine interact with other drugs that cause sedation or have antimuscarinic effects, including tricyclic antidepressants, MAOIs, phenothiazines, hypnotics, nefopam, amantadine and disopyramide. Dry mouth caused by the antimuscarinic effects of antihistamines and hyoscine may reduce the effect of sublingual nitrates.

Products

- Cinnarizine
  - — Stugeron tablets
    Johnson & Johnson MSD
- Meclozine hydrochloride
  - — Sea-legs tablets
    SSL International
- Promethazine hydrochloride
  - — Phenergan Tablets (25 mg and 10 mg) and Elixir
    Aventis Pharma
- Promethazine teoclate
  - — Avomine tablets
    Manx Pharma
- Hyoscine hydrobromide
  - — Joy-rides raspberry-flavoured chewable tablets (0.15 mg)
    Stafford-Miller
  - — Kwells tablets (0.3 mg)
    Roche Consumer Health
  - — Kwells Junior tablets (0.15 mg)
    Roche Consumer Health

PRODUCT SELECTION POINTS

- All the available products appear to be effective for the prophylaxis of motion sickness, but hyoscine hydrobromide is probably the most effective, especially for sea travel.
- The antimuscarinic side-effects of hyoscine are generally more pronounced than those of the antihistamines.
- Meclozine combines the advantages of relatively low side-effects with prolonged action.
- Promethazine hydrochloride can be used for children from the age of two years.

PRODUCT RECOMMENDATIONS

Adults and older children for short journeys – hyoscine hydrobromide; for long journeys – meclozine.

Children between two and five years – promethazine hydrochloride.

Mouth ulcers

Mouth ulcers (recurrent aphthous stomatitis) are a very common condition of the oral mucosa. Estimates of the proportion of the population affected vary from 5 to 20 per cent. About 75 per cent of cases are minor aphthous ulcers which are self-limiting and usually treated by sufferers without recourse to a doctor.

CAUSES

Aphthous ulcers are painful, shallow ulcers up to 5 mm in diameter, occurring singly or in groups of up to five lesions on the tongue and the mucosal surfaces of the lips and cheeks. They usually appear suddenly, although some patients experience sensitivity and tingling beforehand, and disappear just as abruptly – usually within seven to 14 days. Both adults and children can be affected. Patients who have ulcers which are significantly larger, persist longer or are relatively painless should not be treated but referred immediately to a doctor.

The cause of aphthous stomatitis remains unknown. Several causes have been suggested with some degree of justification, including stress, trauma of the oral mucosa, infection, vitamin B or iron deficiency, hormonal changes and heredity, but none has been conclusively proven. Several drugs also appear to induce mouth ulcers. As the cause is unknown, treatment can only be symptomatic; anti-inflammatories (including corticosteroids) seem to be the most effective, but a wide range of products containing local anaesthetics, antiseptics and astringents is also available.

TREATMENT

Corticosteroids

Compounds available

Compounds available are:

- Hydrocortisone sodium succinate
- Triamcinolone acetonide

Mode of action

Hydrocortisone is a naturally occurring glucocorticoid secreted by the adrenal cortex. Chemically it is a C21-steroid containing a 17α-hydroxy group. Esterification of glucocorticoids at the 17 or 21 position with fatty acids generally increases topical activity; hydrocortisone sodium succinate is esterified at the 21 position. Fluorination and the formation of cyclic acetonides at the 16 and 17 positions of glucocorticoids, both of which are features of the chemical structure of triamcinolone acetonide, further increase topical anti-inflammatory activity.

Corticosteroids are widely used as topical anti-inflammatory agents. Their action is thought to be exerted through two mechanisms: firstly, the stabilisation of lysosomal membranes resulting in a reduction in the release of inflammatory lytic enzymes, and secondly, the inhibition of phospholipase A. The latter effect reduces the release of arachidonic acid from phospholipids in cell membranes with a consequent inhibition of prostaglandin synthesis.

Mouth ulcer tissue is intensely inflamed and corticosteroids would therefore be expected to be helpful. Few, if any, clinical trials have been conducted but there have been many published attestations by clinicians over a period of nearly 40 years to the effectiveness of both hydrocortisone sodium succinate and triamcinolone acetonide in the treatment of aphthous stomatitis.

Administration and use

Hydrocortisone sodium succinate is presented as small white pellets. One should be placed in the mouth in close proximity to the ulcer(s) and allowed to dissolve slowly four times a day for a maximum of five days. Pellets are useful when ulcers are situated between the gum and cheek or beneath the tongue, but may be difficult to maintain in position elsewhere in the mouth.

Triamcinolone acetonide is presented in carmellose (carboxymethylcellulose) gelatin paste, which is insoluble in saliva and adheres to the oral mucosa to form a thick layer. (Carmellose gelatin paste can be used alone for the mechanical protection of oral lesions.)

The preparation is applied to the ulcer with a finger, at bedtime and two or three times a day, up to four times daily for a maximum of five days. The area of application should be dry to ensure that the preparation adheres, and some manual dexterity is required to get the paste into areas of difficult access.

Cautions and contraindications

There are no significant side-effects with either product. Both can be used for children and elderly patients with the normal precautions, but should not be used in pregnancy as high topical doses in experimental animals have caused fetal abnormalities. Patients with a history of hypersensitivity to product components, and those with tuberculous or viral lesions (patients presenting with both mouth ulcers and cold sores should be referred) should not use these products. Another contraindication is the presence of fungal or bacterial infection without the use of additional antimicrobial therapy.

Products

- Corlan pellets (hydrocortisone 2.5 mg, as the sodium succinate) *Medeva Pharma*
- Adcortyl in Orabase (triamcinolone acetonide 0.1 per cent) *Bristol-Myers Squibb Pharmaceuticals*

Benzydamine hydrochloride

Benzydamine hydrochloride is a non-steroidal anti-inflammatory and analgesic drug, available for the treatment of mouth ulcers as an oral rinse and spray both containing 0.15 per cent. The oral rinse has been shown to be effective in the treatment of some oral inflammatory conditions, but there is poor evidence of its effectiveness against mouth ulcers. Its principal advantage may be that as a solution it can reach areas inaccessible to other mouth ulcer treatments.

For adults, 15 ml of the rinse or four to eight puffs of the spray are used every one-and-a-half to three hours for up to seven days; if stinging occurs, the solution may be diluted with water. The rinse is not suitable for children under 12 years, but one to four puffs of the spray, depending on age, may be used for children from the age of six.

Product

There is only one product:

- Difflam Oral Rinse and Spray
  3M Health Care

Other mouth ulcer treatments

A wide range of products in the form of gels, paints, pastilles and mouthwashes is available, most of which contain combinations of anaesthetic, analgesic, antimicrobial and astringent ingredients. The rationale for the use of these ingredients appears to be similar to that for cold sore products (see section on cold sores).

The inclusion of local analgesic and anaesthetic agents seems reasonable as they should be useful in reducing pain and discomfort until lesions resolve. Many formulations are, however, aqueous or aqueous/alcoholic liquids or gels which tend to be fairly rapidly diluted and washed away from the site of application by saliva, requiring frequent re-application. The use of pastilles or sore throat lozenges containing local anaesthetic placed close up against lesions and allowed to dissolve slowly may produce a more prolonged effect. Some lozenges containing higher concentrations of local anaesthetic are unsuitable for children. The Committee on Safety of Medicines (CSM) warning against aspirin for use in children does not extend to topical products containing salicylates. However, excessive use of products containing choline salicylate or salicylic acid may itself lead to ulceration and salicylate poisoning.

There is no evidence that antiseptics or astringents have any effect on mouth ulcers, although the former may help prevent secondary infections.

Product examples (with main constituents)

- Compound Thymol Glycerin BP 1988
- Anbesol Liquid (lidocaine (lignocaine) hydrochloride, chlorocresol, cetylpyridinium chloride)
  SSL International
- Anbesol Adult Strength Gel (lidocaine (lignocaine) 2 per cent)
  SSL International
- Bansor paint (cetrimide)
  Thornton & Ross
- Bonjela Antiseptic Pain Relieving Gel (choline salicylate, cetalkonium chloride)
  Reckitt Benckiser
- Corsodyl mouthwash (chlorhexidine gluconate)
  GlaxoSmithKline Consumer
- Frador paint (menthol, chlorbutanol, prepared storax, benzoin)
  Trinity Sales and Marketing
- Medijel Gel and Pastilles (lidocaine (lignocaine) hydrochloride, aminoacridine hydrochloride)
  DDD
- Pyralvex paint (anthraquinone glycosides, salicylic acid)
  Norgine
- Rinstead Adult Gel (benzocaine, chloroxylenol)
  Schering-Plough
- Rinstead Sugar-free Pastilles (menthol, chloroxylenol)
  Schering-Plough

- Several lozenges marketed for sore throat also contain combinations of local anaesthetic and antimicrobial agents, and could be used for mouth ulcers.

PRODUCT SELECTION POINTS

- Although there is little clinical trial evidence relating to mouth ulcer treatments, hydrocortisone pellets and triamcinolone in carmellose paste have a long record of clinical endorsement and would seem to be the products of choice. The mechanical protective effect of carmellose paste may itself contribute to the relief of discomfort.
- Products containing local anaesthetic or analgesic agents should provide symptomatic relief; pastilles or lozenges may have a more prolonged effect than liquids or aqueous gels.

PRODUCT RECOMMENDATIONS

First choice – triamcinolone acetonide in carmellose paste or hydrocortisone pellets.

Second choice – pastilles or lozenges containing local anaesthetic or analgesic constituents.

Napkin rash

Napkin (nappy) rash is a form of irritant dermatitis.

CAUSES

The causes are not known with certainty, but faecal enzymes and ammonia from urine are likely contributory agents, acting on skin damaged by prolonged exposure to moisture and occlusion under napkins. Further irritants are residual detergents and disinfectants left in cotton nappies after washing.

The condition can be complicated by bacterial and fungal infection, and some nappy rash products contain antiseptics to inhibit bacterial growth and reduce the likelihood of infection. Weeping or crusting of the rash indicates that bacterial infection is present, when referral to a doctor is necessary. Secondary fungal infection (candidiasis) can be identified by the presence of small, red papules at the edge of the rash, and can be treated without prescription with clotrimazole 1 per cent cream (see under athlete's foot).

TREATMENT

Hydrocortisone may be used by doctors to treat severe napkin rash, but this option is not available to pharmacists, as topical hydrocortisone is not licensed for non-prescription use in children under ten years.

OTC medicine treatment of napkin rash is based upon soothing and rehydrating damaged skin, providing a physical barrier between the skin and irritant agents, and reducing the possibility of bacterial infection. The main constituents of preparations are emollients, skin protectants, antiseptics and silicone barrier agents. There is considerable variation in the formulae and approach to treatment between preparations marketed for this indication, as a brief review of the most popular will illustrate.

Products

- **Zinc and Castor Oil Ointment BP**

  This has been a popular treatment for several generations. It contains zinc oxide in a greasy emollient base. Zinc oxide is claimed to have antiseptic, astringent, soothing and protective properties. The main effect of this formulation is to provide a hydrophobic and mechanical protective barrier on the skin.

- **Conotrane Cream**
  Yamanouchi Pharma

  This product contains benzalkonium chloride and dimeticone in an emollient cream base. Benzalkonium is one of two antiseptic compounds used in napkin rash preparations, cetrimide being the other. Both are quaternary ammonium surfactant compounds with activity against a wide range of Gram-positive and some Gram-negative bacteria. Their detergent properties are useful in loosening debris and dead tissue from the skin. They do not generally cause irritation and are widely used as skin antiseptics. Dimeticone is a water-repellent fluid silicone, used as a topical barrier to protect skin against water-soluble irritants.

- **Drapolene Cream**
  Pfizer Consumer Healthcare

  This is an antiseptic and emollient product containing benzalkonium chloride and cetrimide in a water-miscible cream base.

- **Hewletts Cream**
  Kestrel Healthcare

  This product contains zinc oxide in an emollient cream base.

- **Metanium Ointment**
  Roche Consumer Health

  Metanium ointment contains titanium salts, which have an action on the skin similar to zinc oxide, in a silicone-paraffin base. The overall effect is that of a mechanical barrier and occlusive emollient. Titanium salts may stain clothing and bedclothes.

- **Morhulin Ointment**
  SSL International

  This product contains cod liver oil and zinc oxide in an ointment base. Cod liver oil has been claimed to promote wound healing, but the evidence does not support this, and in this preparation it has no special properties beyond its water-resistant and emollient effects.

- **Sudocrem Antiseptic Healing Cream**
  Tosara

  Sudocrem contains zinc oxide in an emollient cream base.

Application and practical points

All nappy rash preparations should be applied after each nappy change until the rash has cleared, and the following advice may be given to reduce future occurrences:

- Change nappies frequently to avoid prolonged contact of moisture and excretion products with the skin.
- Clean the nappy area thoroughly at each nappy change, and dry thoroughly afterwards. Talcum powder can be helpful – a light dusting should be applied to dry skin.
- Nappies should be left off as much as possible, to allow air to circulate and help dry the skin.
- If terry nappies are used they should be thoroughly rinsed after being washed and disinfected, as any residual detergent or bleach can act as an irritant.

PRODUCT SELECTION POINTS

- Preparations for napkin rash are based on emollients, agents that act as physical barriers between the skin and irritants, and antiseptics, with individual products containing different combinations of these. Choice is usually based on personal preference.
- A good nappy-changing routine can reduce the occurrence of napkin rash.

PRODUCT RECOMMENDATIONS

Choice according to personal preference. For napkin rash complicated with candidiasis – clotrimazole 1 per cent cream.

Oral thrush

Oral thrush appears as creamy white patches on the oral mucosa which may be mistaken for milk curds, but they are difficult to remove and if scraped away reveal inflamed patches which may bleed.

CAUSES

Oral thrush (oral candidiasis) is an infection caused by a yeast-like fungus, *Candida albicans*, the same organism that causes vaginal candidiasis and may complicate napkin rash. It is common in newborn babies, because they pick up the organism on their way through an infected birth canal. It can also be contracted by users of inhaled corticosteroids or following antibiotic treatment, but in these cases patients should be referred as infection may indicate reduced immune status. Oral candidiasis can also be a problem in patients with dentures (this condition is called denture stomatitis); such patients should also be referred.

TREATMENT

The standard treatment in infants is miconazole oral gel, which can be recommended by pharmacists. Adult patients may be referred back from the GP to the pharmacist for treatment as the product costs less than an NHS prescription charge. Only the 15 g pack is classified as a P medicine; the 80 g pack is POM.

Mode of action

See under athlete's foot.

Dosage and administration

Babies and children, birth to six years – apply a small amount of the gel to the affected area with a clean finger twice daily; children from six years and adults – apply four times daily. The gel should be retained in the mouth for as long as possible.

Interactions and contraindications

Miconazole potentiates the activity of anticoagulants, antiepileptics and hypoglycaemic drugs. The gel is absorbed from the oral mucosa, and at least part of a dose will be swallowed and absorbed systemically. Pharmacists should consult with the doctor if patients are receiving any of the above drugs.

Miconazole has been shown to be fetotoxic, although not teratogenic, in animal studies, and the oral gel is not licensed for use in pregnant women without prescription.

Product

There is only one product:

- Daktarin Oral Gel (24 mg/ml)
  Johnson & Johnson MSD

Pain

(continued . . .)

Pain can be treated by non-prescription oral or topical analgesics.

Oral analgesics are based on three compounds – aspirin, ibuprofen and paracetamol. Aspirin and ibuprofen are non-steroidal anti-inflammatory drugs (NSAIDs), have similar pharmacologies and will be considered together. Paracetamol is not an NSAID. All are used to treat a wide variety of aches and pains, including headache, migraine, toothache, period pain, and muscular and rheumatic pain. They also have antipyretic activity and are used to alleviate cold and flu symptoms. One compound may be more suitable than another for particular indications and situations, due to its mode of action, side-effect profile, etc.

Topical analgesics are applied externally to relieve a variety of painful conditions. Products have traditionally been based on rubefacients and local anaesthetics, but since 1991 preparations containing NSAIDs have been added to the range as a result of POM to P reclassification.

TREATMENT WITH ASPIRIN AND IBUPROFEN

Mode of action

Aspirin and ibuprofen exert their therapeutic action by interfering with the biosynthesis of prostaglandins, which are major contributors to inflammation and pain. NSAIDs act by blocking the enzyme cyclooxygenase, thereby preventing the formation of prostaglandin endoperoxides from arachidonic acid produced when tissue is damaged. The action of NSAIDs is therefore local at the site of tissue damage, in contrast to the central effect of opioids which influence the recognition of pain within the brain.

Products of arachidonic acid also have a role in platelet aggregation. Aspirin interferes with their synthesis, producing a net anticoagulant effect through inhibiting platelet aggregation. In large doses aspirin also competitively inhibits vitamin K in the synthesis of clotting factors. Ibuprofen has much less antiplatelet activity.

NSAIDs also inhibit production of cytoprotective prostaglandins in the gastric mucosa, which accounts in part for their tendency to

cause gastrointestinal irritation, although the incidence is much lower with ibuprofen than aspirin. Prostaglandin inhibition also explains the antipyretic activity of ibuprofen and aspirin, as prostaglandins are released in the brain during fever and have a potent pyrogenic effect on the temperature-regulating region of the hypothalamus.

Uses

Both aspirin and ibuprofen are licensed for treatment of mild and moderate pain from a wide variety of causes, including dental and musculoskeletal pain and dysmenorrhoea, where their anti-inflammatory activity is particularly useful, and as antipyretics. In clinical trials ibuprofen has been found to be more effective than aspirin for dysmenorrhoea and dental pain.

Side-effects, cautions and contraindications

Aspirin and ibuprofen share the same range of NSAID side-effects, although they are generally less pronounced with ibuprofen. The most common side-effect is gastric irritation and bleeding. This is more severe with aspirin as it has a direct effect on the gastric mucosa (leading to back-diffusion of acid from the gastric lumen to mucosal tissue) as well as its effect on gastric prostaglandin synthesis. Both drugs should be avoided in patients with ulcers or a history of gastric problems. Minor gastric side-effects can be reduced by taking the drugs with or after food, and by use of soluble formulations.

Hypersensitivity reactions to aspirin are much more likely to occur in patients with asthma or allergic problems than in the normal population. One in ten patients with asthma may be hypersensitive and suffer severe bronchospasm. Other reactions are urticaria, angioedema and rhinitis. The incidence of hypersensitivity to ibuprofen is much lower, but the drug should be avoided in asthmatics and patients sensitive to aspirin unless they have taken it before without problems.

Aspirin and ibuprofen should not be recommended to patients with renal, cardiac or hepatic disease, as NSAIDs may impair both

liver and kidney function. As renal function tends to decline with age, and also because the elderly tend to be particularly vulnerable to gastric side-effects, aspirin and ibuprofen should be used with caution in this group.

Aspirin and ibuprofen should be avoided in the third trimester of pregnancy, as they may delay the onset of labour and have adverse effects on late-stage developments in the fetus. Aspirin also increases the risk of haemorrhage during labour. There have been some reports of toxicity in animal studies with NSAIDs during the early stages of pregnancy, so it may be prudent not to recommend the use of aspirin or ibuprofen at all during pregnancy.

Aspirin has been associated with the incidence of Reye's syndrome, a rare but potentially fatal encephalopathy of infants and children. Nursing mothers should therefore avoid aspirin. Aspirin is no longer licensed for use in children under 12 years. Ibuprofen is safe to take as there is no evidence of association with Reye's syndrome.

Interactions

Aspirin potentiates the anticoagulant effect of warfarin because of its inhibitory effect on platelet aggregation and its inhibition of vitamin K synthesis of clotting factors. A daily dose of only 600 mg can significantly increase blood clotting time, so patients on anticoagulant therapy must avoid OTC aspirin products. Low doses are sometimes intentionally prescribed in conjunction with warfarin, particularly to prevent thrombus formation on prosthetic heart valves; it is safe to do so as long as prothrombin time is monitored regularly.

Aspirin also reduces excretion of methotrexate, and can cause life-threatening rises in serum levels of the drug. As all NSAIDs interfere with renal prostaglandin production, inhibiting perfusion and clearance of methotrexate by the kidney, concurrent administration of ibuprofen should also be avoided.

Ibuprofen reduces the excretion of lithium and can raise plasma concentrations to toxic levels. The drug may also antagonise the diuretic and antihypertensive effect of diuretics, and should not be recommended to patients taking these drugs.

Dosage

Aspirin

Adults and children over 12 – 300 to 900 mg every four to six hours when required; maximum daily dose 3600 mg.

Ibuprofen

Infants six to 12 months – 50 mg three or four times in 24 hours. Children (all doses are to a maximum of three times in 24 hours): one to three years – 100 mg; four to six years – 150 mg; seven to nine years – 200 mg; ten to 12 years – 300 mg. Adults and children over 12 – 200 to 400 mg every four hours, up to a maximum of 1200 mg daily. (Children's doses can be given accurately using ibuprofen suspension – see below.)

Formulation factors

Aspirin is a weak acid, and peak plasma concentrations are achieved one to two hours after administration. Ionisation can be increased by formulation with alkaline salts, speeding absorption and reducing gastrointestinal side-effects. Some effervescent preparations (e.g. Alka-Seltzer, Bayer Consumer) use sodium bicarbonate as a buffer, but the amounts required are high and their use may be inadvisable in patients with high blood pressure or on antihypertensive medication. Calcium carbonate, which does not present this problem, is used in Soluble Aspirin Tablets BP and in Disprin (Reckitt Benckiser). Soluble formulations of ibuprofen are also available. Soluble preparations are useful in the treatment of migraine, as the rate of gastric emptying slows in this condition, delaying absorption and increasing the possibility of gastrointestinal side-effects.

Another method of increasing absorption is to render the drug dispersible by formulating with an amino acid. Nurofen Advance (Crookes Healthcare) contains ibuprofen lysine, which the manufacturer claims reaches peak plasma levels nearly three times faster than ibuprofen. Disprin Direct (Reckitt & Colman) contains aspirin with glycine.

Enteric coating has been suggested as a solution to the problem of gastric irritation, and absorption of aspirin from the lower gastrointestinal tract is efficient. However, there is a delay in absorption while the tablet passes through the stomach, and gastric irritation by aspirin has been shown to be due to both systemic and local effects. This formulation may be useful for patients taking aspirin regularly as an anti-inflammatory, but its slow onset of action makes it unsuitable for general analgesic OTC indications. (Due to pack size restrictions on aspirin introduced in 1998 there is no presentation of enteric-coated aspirin tablets licensed for sale without prescription.)

Product examples

Aspirin

- Aspirin Tablets BP
- Alka-Seltzer effervescent tablets
  Bayer Consumer
- Aspro Tablets
  Roche
- Disprin soluble tablets
  Reckitt & Colman

Ibuprofen

- Ibuprofen 200 mg and 400 mg tablets (non-proprietary)
- Advil (200 mg) and Advil Extra Strength (400 mg) tablets
  Whitehall
- Cuprofen Tablets (200 mg)
  SSL International
- Librofem (200 mg tablets)
  Eastern Pharmaceuticals
- Nurofen (200 mg tablets)
  Crookes Healthcare

- Nurofen Long Lasting (300 mg sustained-release capsules)
  Crookes Healthcare
- Nurofen Advance (200 mg ibuprofen lysine tablets)
  (Crookes Healthcare)
- Nurofen for Children suspension (licensed for use in babies and children from six months of age)
  Crookes
- Relcofen 200 mg and Relcofen 400 mg tablets
  Cox

TREATMENT WITH PARACETAMOL

Paracetamol, unlike aspirin and ibuprofen, is not an NSAID and so is considered separately.

Mode of action

The mechanism of action of paracetamol is not well understood. It has little anti-inflammatory activity but is an effective analgesic and antipyretic. It is postulated that its activity may be due to selective inhibition of cyclo-oxygenase in the CNS rather than in peripheral tissues. However, there is evidence that paracetamol also acts peripherally at pain chemoreceptors.

Side-effects and cautions

Paracetamol is a very safe drug at normal therapeutic dosages, and its only major drawback is its hepatotoxicity in overdose. Paracetamol is metabolised in the liver where it is converted to a highly reactive toxic intermediate, which is normally detoxified by conjugation with glutathione. In overdose, this detoxification mechanism is overwhelmed. The free toxic metabolite then combines with hepatic macromolecules causing hepatitis and necrosis, which often prove fatal.

Paracetamol poisoning is particularly dangerous as the toxic level need not be greatly above the therapeutic level, and symptoms of overdose may not appear for two days or more. This allows unwitting overdosage to be continued, and there have been several fatalities in patients who were taking large doses, or two or more preparations containing paracetamol, for a minor ailment such as a cold. It is therefore extremely important to ensure that patients do not exceed the recommended dosage or use more than one product at a time containing paracetamol.

Methionine is an effective antidote in paracetamol poisoning if used early enough, and there is a proprietary product (Paradote tablets, Penn Pharmaceuticals) containing paracetamol co-formulated with methionine.

Dosage

Adults: 0.5 to 1 g every four to six hours, to a maximum of 4 g daily. Children three months to one year, 60 to 120 mg; one to five years 120 to 250 mg; 6 to 12 years, 250 to 500 mg, all four- to six-hourly when necessary to a maximum of four doses in 24 hours.

Product examples

- Paracetamol Tablets BP
- Alvedon suppositories (60 mg, 125 mg, 250 mg: their price makes them prohibitively expensive for OTC sale)
  Novex Pharma
- Calpol Infant Suspension
  Pfizer Consumer Healthcare
- Calpol 6 Plus Suspension
  Pfizer Consumer Healthcare
- Disprol Soluble Paracetamol Tablets (120 mg)
  Reckitt Benckiser

- Hedex tablets
  GlaxoSmithKline Consumer
- Infadrops (100 mg/ml)
  Ceuta Healthcare
- Panadol tablets
  GlaxoSmithKline Consumer
- Paracets Capsules
  Sussex
- Tixymol suspension
  Novartis Consumer Health

Restriction of pack sizes of aspirin- and paracetamol-containing medicines

In 1998, in order to reduce the incidence of poisoning incidents with aspirin and paracetamol, the government introduced legislation to reduce pack sizes and the total quantity of these drugs that could be supplied. The maximum pack size of aspirin and paracetamol products (with the exception of soluble formulations, which remain unrestricted) available from pharmacies is now 32, with a total of three packs being allowed to be sold at the discretion of the pharmacist. In other outlets the maximum pack size is 16, although there is no restriction on the number of packs that can be supplied. There is evidence that these measures have reduced admissions to hospitals and deaths due to overdose.

TREATMENT WITH COMBINATION PRODUCTS

The majority of proprietary oral analgesics are not simple formulations of aspirin, ibuprofen or paracetamol but combination products containing these. The theory behind combination products is that they will be more effective than one drug used alone, and that the dose of each drug can be reduced, thus reducing the possibility of adverse effects. Pain relief is only modestly increased by raising the dose of

aspirin and paracetamol, so it is postulated that the effect may be increased by including another analgesic, especially if it has a different mechanism of action. Further additional components are sometimes added to treat symptoms associated with the pain. Leading medical opinion does not generally favour combined analgesics, claiming that low doses of additional ingredients may reduce the severity but increase the range of side-effects, without producing significant extra pain relief. Some products (e.g. Anadin Extra, Whitehall; Disprin Extra, Reckitt Benckiser) are combinations of aspirin and paracetamol, but the main additional analgesic ingredient used is codeine.

Codeine as additional ingredient

Codeine may be combined with aspirin, paracetamol, aspirin and paracetamol, or ibuprofen. Codeine is a member of the opioid group of analgesics acting directly on opiate receptors in the brain, producing analgesia, respiratory depression, euphoria and sedation. It is a weak narcotic analgesic useful for the treatment of mild to moderate pain. Its major side-effect at non-prescription dosage levels is constipation.

The combination of codeine with one of the other OTC analgesics is logical from the point of view that they have different mechanisms of action. But it is argued that at the dosages at which it is normally included (8 mg per tablet with a two-tablet maximum dose) there is no significant added analgesic efficacy. In addition several of the indications given by manufacturers for these combinations, such as dysmenorrhoea, and dental and rheumatic pain, are not opioid-sensitive. Some more recently marketed products contain higher doses of codeine. Dihydrocodeine, which is about as effective as codeine, is combined with paracetamol in one product.

Product examples

- Aspirin and codeine
  - — Co-codaprin tablets and soluble tablets
  - — Codis 500 soluble tablets
    Reckitt Benckiser

- Paracetamol and codeine
  - — Co-codamol tablets and soluble tablets
  - — Paracodol Capsules and Soluble tablets
    Roche Consumer Health
  - — Solpadeine Max tablets
    GlaxoSmithKline Consumer Healthcare

- Aspirin, paracetamol and codeine
  - — Veganin tablets
    Pfizer Consumer Healthcare

- Ibuprofen and codeine
  - — Nurofen Plus tablets
    Crookes Healthcare
  - — Solpaflex tablets
    GlaxoSmithKline Consumer Healthcare

- Containing higher dose of codeine
  - — Nurofen Plus (12.5 mg/tablet)
    Crookes Healthcare
  - — Panadol Ultra (12.8 mg/tablet)
    GlaxoSmithKline Consumer Healthcare
  - — Solpadeine Max tablets (12.8 mg/ tablet)
    GlaxoSmithKline Consumer Healthcare
  - — Solpaflex tablets (12.8 mg/tablet)
    GlaxoSmithKline Consumer Healthcare

- Paracetamol and dihydrocodeine
  - — Paramol Tablets (7.5 mg dihydrocodeine per tablet)
    Seton

Co-dydramol tablets (non-proprietary) contain 10 mg dihydrocodeine per tablet and are POM.

Aloxiprin as additional ingredient

Aloxiprin, a polymeric condensation product of aspirin and aluminium oxide, is co-formulated with aspirin in one product. It is less liable to cause gastric irritation than aspirin, as it is mainly hydrolysed and absorbed in the duodenum, but is more slowly absorbed and included at such a low dose as to make its contribution doubtful.

Product

There is only one product:

- Askit Powders
  Askit

Caffeine as additional ingredient

A large number of OTC analgesics contain caffeine, the rationale being that as a CNS stimulant it will alleviate the depression often associated with pain. However, most preparations contain less caffeine than would be obtained from a cup of tea and half of that from a cup of coffee. In addition caffeine increases the irritant effect of aspirin on the gastric mucosa.

Product examples

- Anadin, Anadin Maximum Strength, Anadin Extra, Anadin Extra Soluble tablets
  Whitehall
- Propain tablets
  Sankyo Pharma
- Solpadeine Capsules, Tablets and Solpadeine Soluble tablets
  GlaxoSmithKline Consumer Healthcare

Antihistamines as additional ingredients

Antihistamines are included in some products marketed for the treatment of migraine to counteract the nausea with which it is often associated.

Buclizine is included with paracetamol and codeine in Migraleve Pink tablets (Warner Lambert Consumer Healthcare).

Doxylamine is present at a very low dose with paracetamol, codeine and caffeine in Syndol tablets (SSL International), promoted for tension headache. It is claimed to have a muscle relaxant and sedative effect.

Diphenhydramine is included at a similarly low dose in Propain tablets (Sankyo Pharma), presumably for the same reasons.

Hyoscine as additional ingredient

Hyoscine is an ingredient of Feminax (Roche Consumer Health), marketed for the treatment of period pain. It is included as an antispasmodic to reduce cramping, but appears to be present at a subtherapeutic dose. Hyoscine and the other components of the product – paracetamol, codeine and caffeine – would seem not to accord with the current view on the causes and treatment of dysmenorrhoea. It has been shown that period pain coincides with raised intrauterine

prostaglandin levels around the start of menstruation, and that NSAIDs are the analgesics of choice. However, as community pharmacists will know, Feminax users seem to be satisfied with the product as it sells well with regular repeat purchases. This illustrates the very subjective nature of pain treatment, and the importance of marketing.

Isometheptene mucate as additional ingredient

Isometheptene is a sympathomimetic, used for its vasoconstrictor effect in the treatment of migraine and throbbing headache, in combination with paracetamol in Midrid capsules (Manx Pharma). The cautions, contraindications and interactions relating to sympathomimetics described in the section on cough apply to this product.

PROCHLORPERAZINE FOR NAUSEA AND VOMITING IN MIGRAINE

Mode of action and use

Prochlorperazine is a phenothiazine derivative, closely related chemically to antihistamines such as promethazine and antipsychotics such as chlorpromazine and trifluoperazine. Although it has been used as an antipsychotic, it is generally used at lower doses for the treatment of vertigo and the prevention of nausea and vomiting, for which it has a long history of use as a prescription medicine. Comparative studies have shown prochlorperazine to be more effective than either metoclopramide or domperidone when given parenterally as an emergency treatment for headache and nausea in migraine. In November 2001, prochlorperazine maleate buccal tablets were licensed as a P medicine for the treatment of nausea and vomiting associated with migraine. Absorpton via the buccal route is directly into the circulation, avoiding first-pass hepatic metabolism and delayed absorption from the stomach due to gastric stasis which often accompanies migraine. The drug can therefore be supplied at a lower dose that via the oral route.

Restrictions and contraindications

The licensing conditions only permit supply if migraine has already been diagnosed by a doctor. Use is restricted to persons of 18 years and over, and contraindicated in pregnancy and in breastfeeding women. It is also contraindicated in patients with impaired hepatic function, narrow-angle glaucoma, prostatic hypertrophy, epilepsy and Parkinson's disease.

Side-effects and interactions

These are typical of phenothiazines and are as described for antihistamines in the sections on motion sickness and cough. Postural hypotension is also possible, particularly in volume-depleted patients. Extrapyramidal side-effects are also a possibility, but are highly unlikely at the licensed dosage.

Dosage

Buccal tablets are placed in the buccal cavity, high up between the upper lip and gum, and allowed to dissolve there. One or two tablets may be taken twice daily for up to two days if necessary.

Product

- Buccastem M
  Reckitt Benekiser

PRODUCT SELECTION POINTS FOR ORAL ANALGESICS

- The selection of appropriate non-prescription analgesics is complicated by the fact that the perception of pain is highly subjective, and the choice of drug often depends on personal preference.

- The three principal compounds – aspirin, ibuprofen and paracetamol – are all effective for mild to moderate pain, although theoretically the first two are better where pain is due to local inflammation, such as musculoskeletal, dental and dysmenorrhoea pain.
- Aspirin and ibuprofen have similar indications, but ibuprofen appears to be more effective with a lower profile of adverse and side-effects.
- Paracetamol is a good alternative in situations where aspirin and ibuprofen should be avoided. It is therefore safe for the elderly, children under 12 years and pregnant women, and patients with a history of asthma and gastrointestinal problems.
- Aspirin must be avoided by patients taking warfarin and methotrexate, and ibuprofen by those on lithium. Patients with cardiovascular problems should also avoid ibuprofen.
- It may be wise for patients taking medicines liable to interactions to avoid both aspirin and ibuprofen, due to the possibility of cross-sensitivity between NSAIDs.
- Soluble formulations have the advantage of faster action and, in the case of aspirin, reduced gastric irritation. They are particularly useful in migraine as gastric emptying is slowed during attacks, delaying absorption of the analgesic.
- Combination products containing codeine are worth trying when single-ingredient products are not effective. Constipation is a possible side-effect.
- Antihistamines are useful additional components in migraine products for patients who suffer nausea during attacks. In some analgesic products additional constituents may be present at doses too low to be expected to exert an effect.

PRODUCT RECOMMENDATIONS FOR ORAL ANALGESICS

- Ask the patients; they will often know what works for them, even though their choice may not accord with what may be best in theory.

- If asked for a recommendation – first choice, ibuprofen. For patients in whom ibuprofen is contraindicated – paracetamol.
- Worth trying if a single analgesic product is not effective – a combination product containing ibuprofen or paracetamol with codeine.

TREATMENT WITH TOPICAL ANALGESICS

Products in this group are applied externally to relieve a variety of painful conditions, including muscular and rheumatic pain, fibrositis, sciatica, lumbago, sprains, strains, bruises, etc.

NSAIDs

Compounds available

Compounds available are:

- Benzydamine
- Felbinac
- Ibuprofen
- Ketoprofen
- Piroxicam
- Salicylic acid

Mode of action

Mode of action is as described above, under ibuprofen and aspirin. Recommendation of the use of topical NSAIDs is based on the premise that the drug acts directly at the affected site, thereby avoiding the systemic adverse effects and side-effects that can result from oral administration. This argument depends on the drug being absorbed sufficiently into local tissue to exert an effect, but not entering the systemic circulation. The skin presents a barrier to absorption and only a small proportion (20 to 25 per cent in tests conducted on

ibuprofen and benzydamine) penetrates. Once absorbed, NSAIDs show a strong affinity for tissues, although there is evidence that they may be absorbed systemically first and then into the target tissue.

Topical NSAIDs have been tested against other topical analgesic preparations and placebos and have been found to be effective, although a large placebo effect has been demonstrated. No comparisons of their effectiveness against that of non-prescription oral NSAIDs appear to have been carried out, but trials conducted on felbinac foam and on piroxicam gel found them to be as effective as oral ibuprofen, with no difference in the incidence of side-effects.

Uses

Topical NSAIDs are licensed for the treatment of backache, rheumatic and muscular pain, sprains and strains, including sports injuries, and for pain relief in non-serious arthritic conditions.

Side-effects, cautions and contraindications

Topical NSAIDs are generally well tolerated; occasional local reactions have been reported, but these resolve on withdrawal of treatment. Products should not be applied to broken skin, lips or near the eyes. Hands should be washed after application. Topical NSAIDs should not be used with occlusive dressings.

Systemic side-effects produced by oral NSAIDs can occur with topical agents; the risk is increased with application of large amounts. Topical NSAIDs (except benzydamine) are contraindicated in patients in whom aspirin and other NSAIDs induce sensitivity reactions. They are not recommended for use in pregnant or nursing mothers, or for children under 14 years.

Interactions

Serum levels of NSAIDs after topical administration are low and clinically significant drug interactions are unlikely.

Dosage

Creams and gels – a ribbon of between 3 and 10 cm applied in a thin layer and massaged in, up to three times a day.

Sprays – 1 to 2 ml (five to ten sprays) three or four times a day.

Product examples

- Benzydamine
  - — Difflam-P Cream
    3M Health Care
- Felbinac
  - — Traxam Pain Relief Gel
    Goldshield Healthcare
- Ibuprofen (there are at least 12 brands and about 20 variants available)
  - — Ibuleve Gel, Mousse, Spray and Sports Gel
    (5 per cent ibuprofen)
    Dendron
  - — Ibuleve Maximum Strength Gel (10 per cent ibuprofen)
  - — Mentholatum Ibuprofen Gel (5 per cent ibuprofen)
    Mentholatum
  - — Nurofen Maximum Strength Gel (10 per cent ibuprofen)
    Crookes Healthcare
  - — Proflex Pain Relief Cream (5 per cent ibuprofen)
    Novartis Consumer Health
- Ketoprofen
  - — Oruvail Gel
    Aventis Pharma

- Piroxicam
  - — Feldene P Gel
    Pfizer Consumer Healthcare

- Salicylic acid
  - — Movelat Relief Gel and Cream (also contains heparinoid which is said to help disperse oedema from damaged tissue)
    Sankyo Pharma

Rubefacients (counterirritants)

Mode of action

Rubefacients are compounds that produce local vasodilation and create a sensation of warmth, exerting an analgesic effect by masking the perception of pain. Massaging greatly enhances this effect by increasing the penetration of the rubefacient into the skin and by stimulating nerve fibres which feed back messages to the brain, overriding painful stimuli. The pressure created also helps to disperse local tissue mediators of pain. Massaging is therefore an important component of the action of topical analgesics, including NSAIDs. Placebo effects also play a significant part.

Most proprietary rubefacient preparations are mixtures of several ingredients, including salicylates, nicotinates and counterirritant substances from natural sources.

Salicylates – product examples

Methyl salicylate, diethylamine salicylate and glycol salicylate are ingredients of many topical analgesic products. As well as being counterirritants, they are hydrolysed in the skin to salicylic acid and have an anti-inflammatory action. Products containing salicylates should therefore be avoided by people sensitive to aspirin.

Product examples are:

- Algesal cream
  Solvay Healthcare

- Radian-B Muscle Lotion and Heat Spray
  Roche Consumer Health

- Deep Heat Maximum Strength cream
  Mentholatum

- Ralgex Heat Spray and Stick
  SSL International

Nicotinates – product examples

Nicotinates are other popular components of topical analgesics, producing vasodilatation and raised skin temperature. There is some evidence that salicylates may reduce the activity of nicotinates, but the popularity of products which contain combinations of these esters indicates that this is not a problem as far as users are concerned.

Product examples are:

- Algipan cream
  Whitehall

- Cremalgin cream
  Co-Pharma

- Transvasin Heat Rub
  SSL International

Capsicum – product examples

Capsicum oleoresin, and capsaicin which is obtained from it, are included in several topical analgesics and produce a burning sensation on the skin which is not accompanied by vasodilatation. Capsaicin works directly on nerve endings, depleting them of substance P, a pain-inducing peptide.

Product examples are:

- Fiery Jack Ointment and Cream
  Pickles
- Ralgex Cream
  SSL International

Other constituents – product examples

Other rubefacient ingredients of analgesic preparations include turpentine oil, camphor and menthol. The last produces a sensation of coolness rather than warmth.

Product examples are:

- Balmosa Cream
  Pharmax
- Deep Freeze Cold Gel
  Mentholatum
- Tiger Balm
  SSL International

Local anaesthetics

Local anaesthetics prevent pain by causing a reversible block of conduction along nerve fibres. They are not normally used for the treatment of inflammatory pain, although Intralgin Gel (3M Health Care) contains benzocaine in combination with salicylamide. Ointments and gels are sometimes used to ease pain associated with defecation in cases of haemorrhoids and anal fissure.

Freeze sprays contain pressurised liquids that evaporate at low temperature when sprayed on to the skin, producing a loss of sensation until the nerve endings warm up again. They are most useful for treating the sharp, but short-lived pain caused by minor knocks and sports injuries.

Product examples

- Intralgin Gel
  3M Health Care
- Deep Freeze spray
  Mentholatum
- Ralgex Freeze Spray
  SSL International

Cautions for topical analgesics

All topical analgesic products should be kept well away from the eyes, mouth and mucous membranes, and should not be applied to broken skin. The hands should always be washed after use. Topical analgesics should not be used on young children, whose skin is more sensitive than adults' and in whom reactions are therefore more likely.

PRODUCT SELECTION POINTS FOR TOPICAL ANALGESICS

- The action of massaging contributes significantly to the effectiveness of topical analgesics, and may be as important as the product chosen. Placebo effect is also an important factor.
- NSAID topical analgesics have been shown to be effective, but can produce the same adverse and side-effects as oral NSAIDs. They should therefore not be used by people sensitive to aspirin and other NSAIDs. Rubefacients containing salicylates are also contraindicated.
- NSAID topical analgesics are unlikely to interact with other drugs.

PRODUCT RECOMMENDATIONS FOR TOPICAL ANALGESICS

Either rubefacients (they are generally cheaper than NSAID preparations and, from an objective viewpoint, are no less likely to be effective) or NSAIDs (probably at least as effective as rubefacients, but contraindicated in some patients).

Note that oral analgesics are at least as effective as topical analgesics, but may lack the placebo effect of something applied directly to the site of the pain.

Pattern baldness

Pattern baldness (alopecia androgenetica) is a natural loss of hair associated with advancing age, usually developing in middle age, although the process can begin soon after puberty.

CAUSES

The precise biochemical mechanism is unknown, although it is believed to be a response to androgenic stimulation. The condition usually affects men, but women may suffer too.

TREATMENT – MINOXIDIL

Minoxidil 2 per cent and 5 per cent solutions are available without prescription for the treatment of pattern baldness.

Mode of action

Minoxidil is a potent, direct-acting peripheral vasodilator used in the treatment of hypertension. However, its use is limited by adverse effects, one of which is the encouragement of hair growth (hypertrichosis), and it is this property which is exploited to treat baldness. The mechanism of action is unknown, but regular application of minoxidil 2 per cent solution causes some hair regrowth in about 40 per cent of individuals within 12 months. For the 5 per cent solution the manufacturer claims that it can produce over 40 per cent more hair growth over a 12-month period than the 2 per cent solution. It also claims that in some cases it produces visible hair growth at eight weeks compared with 16 weeks for the regular strength.

Administration

For both strengths, 1 ml of the solution is applied to the affected area twice daily at 12-hourly intervals. The hair should not be washed for at least one hour following an application. The manufacturer claims that it is most likely to be effective in patients who have been losing

their hair for less than ten years and where the balding area is less than 10 cm diameter, and that it works in up to two-thirds of patients.

Reduction of hair loss is not visible for at least four to six weeks, and regrowth cannot be expected for at least four months with the 2 per cent solution, but these periods may be reduced by as much as half with the 5 per cent solution. New hair is soft and downy at first but will eventually become a normal thick growth in about one-third of the patients who are responding to the treatment. Regrowth will only be maintained while the product is being used, and any regrown hair may be lost within three to four months of stopping treatment. The manufacturer recommends that treatment should be discontinued if there is no hair regrowth after one year. The cost of treatment, before the abolition of resale price maintenance on medicines, was £25 per month for the 2 per cent strength and £30 for the 5 per cent (or a pack of three bottles for £60).

Contraindications, cautions and side-effects

The only contraindication to use is known sensitivity to minoxidil, or to ethanol or propylene glycol, which are used in the vehicle. Minoxidil is minimally absorbed through the scalp and topical application is unlikely to affect blood pressure, although patients with cardiovascular disease are advised to check with their doctor before starting to use the product.

Use by pregnant or breast-feeding women is not advised, and the 5 per cent solution should not be used at all by women. Side-effects in all body systems have been found to be equivalent to those of placebo, except for the skin, where more reactions such as local irritation, dryness and hair colour changes have been reported.

Products

- Regaine Regular Strength (2 per cent)
  Pharmacia Consumer Healthcare
- Regaine Extra Strength (5 per cent)
  Pharmacia Consumer Healthcare

PRODUCT SELECTION POINT

Minoxidil 2 per cent solution is the only licensed product available. Some people may consider it worth paying up to around £300 a year for its possible cosmetic benefits.

Premenstrual syndrome

Premenstrual syndrome (PMS) is associated with a wide range of physical and psychological symptoms, including fluid retention and oedema, breast tenderness, tension, anxiety and depression, all of which may appear up to 14 days before the start of a period and subside once menstruation commences. Symptoms vary between sufferers and even from cycle to cycle in the same individual.

CAUSES

The causes of the condition are still not known with certainty, but it is probably due to a range of metabolic factors influenced by hormones.

TREATMENT

Some OTC treatments are marketed for PMS, for both specific and generalised symptoms. Thus, ammonium chloride and caffeine are contained in a tablet marketed for water retention, pyridoxine is indicated for psychological and emotional symptoms, and evening primrose oil (EPO) for breast pain (cyclical mastalgia). However, in a condition with such broad symptoms and ill-defined causes, placebo effect is likely to play a large part in the perceived effectiveness of medication.

Ammonium chloride

Mode of action

Aqua Ban tablets (Ceuta Healthcare) contain ammonium chloride 325 mg and caffeine 100 mg, and the product is marketed as a mild diuretic for premenstrual water retention. Ammonium chloride is absorbed from the gastrointestinal tract and in the liver is converted into urea, which has the effect of acidifying the urine and producing transient diuresis. The caffeine content is equivalent to that in a cup of coffee; it has mild diuretic activity and is presumably also included

as a stimulant to lift mood. Reducing sodium and water intake for a few days before a period may achieve a reduction in fluid retention as effectively as OTC medication.

Dosage, cautions and contraindications

The recommended dose is two tablets three times daily for four or five days before a period, stopping when menstruation starts. Ammonium chloride is irritant to the stomach, and to overcome this Aqua Ban tablets are enteric-coated and it is recommended that they are taken after food. The product is contraindicated in patients with renal or hepatic impairment. Because it acidifies the urine, ammonium chloride may cause bladder inflammation, and excessive use may result in metabolic acidosis.

Pyridoxine (vitamin B_6)

Mode of action

Pyridoxine is a co-enzyme in the final step of the biosynthesis of serotonin, a substance which is known to have potent effects on mood. It has been theorised that a contributory cause of depressive symptoms in PMS may be a deficiency of pyridoxine, and the vitamin has been found to relieve depression caused by oral contraceptives in some patients. Clinical trials have produced conflicting evidence of effectiveness, but a meta-analysis published in 1999 concluded that pyridoxine was better than placebo at treating premenstrual depression.

There has been some controversy over the safety of pyridoxine. Pyridoxine is classified as GSL, but high doses (2000 to 7000 mg daily) have been associated with peripheral neuropathies, which are generally reversible on discontinuation of the drug. In 1997, as a result over concerns about toxicity (based apparently on the evidence of a single, self-report study conducted in 1987), the United Kingdom government, through its Committee on Toxicity of Chemicals in Foods, Consumer Products and the Environment, proposed the

following restrictions on the availability and dosage of pyridoxine: preparations providing a daily dose of 50 mg and above to be classified as POMs, those providing between 11 mg and 49 mg to be P medicines, while preparations containing up to 10 mg would be GSL medicines. In the United States the daily maximum dose for preparations available without prescription has been set at 100 mg. The United Kingdom government was due to make a final decision in July of 1998; up to the end of 2001 it had not done so, but was advising that people wanting to take a daily dose greater than 10 mg should do so only on medical advice. The Royal Pharmaceutical Society has left it to pharmacists to decide for themselves whether to sell higher strengths of vitamin B_6 as GSL or P, or to treat them as POMs. As a result of the controversy and indecision, all proprietary licensed medicines containing more than 10 mg pyridoxine have been withdrawn, although 20 mg and 50 mg non-proprietary tablets remain available.

Dosage

The recommended dose is either 100 to 200 mg daily for three days before the onset of symptoms until two days after the commencement of menstruation, or 50 to 100 mg daily throughout the month. If no benefit is perceived within three months, treatment should be discontinued.

Products

- Pyridoxine Tablets (10, 20 and 50 mg)

Evening primrose oil (EPO)

Mode of action

EPO is a rich source of gamma-linolenic acid (GLA), a precursor of prostaglandin E_1, which is believed to be important in moderating responses to hormones associated with the menstrual cycle. One of the

theories put forward to explain some of the symptoms of PMS is that sufferers have low levels of GLA. This deficiency is believed to be responsible for breast pain, as prostaglandin E is depleted and not available to down-regulate the response to prolactin, the hormone primarily responsible for lactation, but which in non-pregnant women causes the breast engorgement and tenderness which some suffer before a period.

EPO has been shown to improve the symptoms of cyclical mastalgia in about 50 per cent of cases, although a recent systematic review concluded that its benefit is unproven. It is licensed for this use and is allowable on NHS prescription. The prescribable preparation (Efamast, Searle) is licensed as a POM but is the same strength (40 mg GLA per 500 mg capsule) as many OTC EPO products. The *British National Formulary* recommends a dose of 240 to 320 mg GLA daily for up to three months, continuing thereafter at a lower maintenance dose if necessary. OTC treatment at this dosage would work out to be expensive (around £20 per month).

EPO has been promoted for treatment of generalised symptoms of PMS, but the results of trials have not been encouraging.

Dosage

The recommended dose for EPO products specifically promoted for treatment of PMS is equivalent to about 180 mg daily for ten days before a period. There is some doubt as to whether this level of dosage would be effective.

Cautions and contraindications

EPO has few adverse effects. These include mild gastrointestinal effects (indigestion, nausea and diarrhoea have been occasionally reported) and headache. EPO has induced seizures in schizophrenics being treated with epileptogenic phenothiazine antipsychotics. It has also induced seizures in patients with an initial diagnosis of schizophrenia, and being treated with phenothiazines, who were then diagnosed as epileptics. It is therefore advisable not to recommend EPO to patients with a history of epilepsy or who are taking phenothiazines.

Product examples

OTC EPO products are classified as food supplements, not licensed medicines. They are therefore not subject to restriction on dosage, or on any other conditions of use.

- Efamol capsules (500 and 1000 mg)
  Efamol
- Seven Seas Pure Evening Primrose Oil capsules (500 and 1000 mg)
  Seven Seas

Agnus castus (chaste tree) fruit extract

The fruits of *Vitex agnus-castus* (Verbenaceae) have traditionally been used to relieve the symptoms of premenstrual syndrome and other menstrual problems. Compounds similar in structure to the sex hormones have been isolated from some parts of the plant, and the effects of agnus castus have been described as similar to those of the corpus luteum. A prospective, randomised, placebo-controlled study published in 2001 found it to be considerably more effective than placebo across a wide range of PMS symptoms, at a dose standardised to 20 mg casticin daily. Few adverse effects were reported. There is no preparation of agnus castus available as a licensed medicine, although products marketed as food supplements are available.

PRODUCT SELECTION POINTS

- There is some evidence of efficacy for vitamin B_6 (pyridoxine) in premenstrual depression and EPO in cyclical mastalgia.
- Agnus castus fruit extract has traditionally been used in the treatment of PMS, and a recent placebo-controlled study found it effective against a wide range of symptoms.

PRODUCT RECOMMENDATIONS

- For premenstrual depression – vitamin B_6 (pyridoxine) 100 to 200 mg daily on a cyclical basis for a few days around a period, or 50 to 100 mg daily continuously.
- For cyclical mastalgia – EPO equivalent to the *British National Formulary* dose of 240 to 320 mg GLA daily.
- For fluid retention and bloating – reduce sodium and fluid intake for a few days around a period; if this is unsuccessful and the problem is particularly troublesome, seek medical advice.
- For generalised symptoms – agnus castus is worth trying. It is only available as a food supplement, not a licensed medicine.

Scabies

Scabies is a contagious skin infestation caused by a mite.

CAUSES

The female scabies mite (*Sarcoptes scabei* var. *hominis*) burrows through the stratum corneum of the skin and lays its eggs just above the boundary between the epidermis and dermis. Sites of burrowing are mainly the finger webs and wrists, but can also be the palms of the hands, soles of the feet, external genitalia of both sexes and women's breasts. Mite burrows can sometimes be identified as slightly raised greyish 'pencil' lines, but they are not easy to spot. The principal symptom of infection is severe itching; this is caused by mite faeces or saliva containing water-soluble glycopeptides and which eventually provoke an allergic response, although this takes several weeks to develop.

The areas of itching are not necessarily the same as the sites of infection but can be diffuse and widespread, and are often distributed symmetrically on both sides of the body. Symptoms are often as much a manifestation of damage done to the skin and secondary infection caused by scratching, as of the infestation itself, and can be confused with excoriated eczema.

Skin contact for several minutes is necessary for transmission of infection from one person to another and often occurs through holding hands. Individuals may unwittingly spread infection for several weeks before symptoms develop, so treatment of all close contacts is therefore necessary once infestation has been identified. The scabies mite cannot survive for long outside the human body and infection is not transferred through bedclothes or clothing, so they do not require more than normal laundering.

TREATMENT

Scabicidal preparations available without prescription contain one of the following:

- Malathion
- Permethrin
- Benzyl benzoate
- Crotamiton

Antipruritic topical preparations, including those containing calamine and crotamiton, and systemic antihistamines can be used to treat the itching. Clinical trial evidence for the efficacy of scabicides is sparse, but such as there is indicates that permethrin and malathion are more effective following a single application than benzyl benzoate or crotamiton. Permethrin is also reported to produce less skin irritation and fewer eczematous reactions than benzyl benzoate.

Malathion and permethrin do not appear to have been directly compared for effectiveness. The *British National Formulary* recommends both as first-choice treatments for scabies.

Malathion

Mode of action, contraindications, cautions and side-effects

See under head lice.

Administration

The same lotion preparations are licensed for the treatment of scabies as for head lice, but the method of administration is different. Products are licensed for use without prescription from the age of six months. They may also be used in pregnancy, but treatment under medical supervision is advisable. Use of the alcohol-based lotion on skin damaged by scratching should be avoided, as it can cause stinging.

The lotion should be applied with the hand, cotton wool, a small sponge or an 8-cm paintbrush to cool, dry and clean skin. Traditional advice to have a hot bath before application has now been discounted as this does not increase the effectiveness of the scabicide, and may in fact decrease it by enhancing absorption into the blood stream and

away from the site of action on the skin. The lotion should be applied to the entire body surface from the soles of the feet to the hairline, including the groin, axillae and skin folds, between fingers and toes, and under finger and toe nails. Lotion should be re-applied to the hands if they are washed after application.

Traditional advice that the head and neck do not need to be treated is incorrect, as mites can be present on the face and ears, particularly in the elderly and young children, and missing out these areas can lead to treatment failure. About 100 ml of malathion lotion is needed for a single application for an average adult. Mites are usually killed within minutes, but the aqueous lotion should be left on for 24 hours and the alcoholic lotion for 12 hours, to ensure complete eradication. A single application is normally sufficient to eliminate infestation if properly applied, but itching may persist for up to two to three weeks until the allergenic mite material is cleared from the skin, and should not be regarded as a sign of treatment failure. Patients should therefore be reassured and symptomatic relief offered, if necessary.

Treatment failure may have occurred if itching has not ceased after three weeks, or if new areas of itching are continuing to appear seven to ten days after treatment. In these situations, patients should be referred to their GP for confirmation of the diagnosis, in which case a second application of scabicide may be advised. If treatment fails for a second time, patients should be referred to a dermatologist.

Products

- Aqueous solutions (0.5 per cent)
  - — Derbac-M Liquid
    SSL International
  - — Quellada M Liquid
    Stafford-Miller

- Alcoholic solution (0.5 per cent)
  - — Prioderm Lotion
    SSL International

Permethrin

Mode of action, contraindications, cautions and side-effects

See under head lice.

Administration

The product is presented as a cream. It is not licensed for use without prescription in children under two years, and treatment under medical supervision is advised for patients over 70 years and pregnant women.

Application is as for malathion, but the preparation need only be left on the skin for 8 to 12 hours before being washed off. For a single application of the cream, which should be sufficient to eliminate infestation, between 7.5 g for a two-year-old child and 60 g for a large adult is required.

Product

There is only one product:

- Lyclear Dermal Cream
  Kestrel Healthcare

Benzyl benzoate

Benzyl Benzoate Application BP, a 25 per cent emulsion, was at one time the first-choice treatment for scabies, but it can be unpleasant to use and has now been superseded by more effective products. At least two, and sometimes three, 24-hour applications of benzyl benzoate

application may be necessary to eradicate mite infestations. In addition, it has an unpleasant smell, is irritant, can cause itching, burning and stinging, and may cause skin rashes. It should not be used on patients with skin excoriated through scratching.

For children, it has been suggested that the emulsion can be diluted to reduce adverse effects, but this also reduces efficacy. The *British National Formulary* recommends that benzyl benzoate should not be used at all for children.

Products

- Benzyl Benzoate Application BP
- Ascabiol emulsion
  Aventis Pharma

Crotamiton

Crotamiton has antipruritic and weak scabicidal activity. However, up to five 24-hour applications at daily intervals are necessary for complete eradication of infections. It is recommended for controlling residual itching after treatment with a more effective scabicide. It appears to have a relatively long duration of activity of six to ten hours, requiring application only two or three times a day. There appears to be no objective proof of the antipruritic activity of crotamiton, and one double-blind clinical trial found it to be no more effective than its vehicle.

Product

There is only one product:

- Eurax Cream and Lotion (10 per cent)
  Novartis Consumer Health

PRODUCT SELECTION POINTS

- Malathion and permethrin both appear to be effective as scabicides with a single application, and are the treatments of choice. There is no firm evidence that one is more effective than the other.
- Permethrin cream is three to four times more expensive per treatment than malathion preparations.
- Unlike the case with head lice, all close contacts of a person infected with scabies should be treated.
- Residual itch following treatment is not necessarily a sign of treatment failure. Symptomatic treatment can be recommended; systemic antihistamines are probably most effective, although topical application of calamine lotion or crotamiton cream or lotion may also be helpful.

PRODUCT RECOMMENDATIONS

First choice for eradication of infection – malathion preparations or permethrin cream.

For treatment of residual pruritus – a systemic antihistamine, with additional application of calamine lotion or crotamiton cream or lotion, if desired.

Smoking cessation products

Smoking of cigarettes, and to a lesser extent cigar and pipe smoking, are not in themselves diseases. But the consequences of smoking, in terms of mortality, suffering and financial costs, are comparable to any pandemic. Persuading and helping smokers to give up is one of the greatest challenges facing health-care professionals, but pharmacists, with their ready accessibility to the public and a range of effective smoking cessation aids available without prescription, are ideally placed to meet it.

ADVERSE EFFECTS OF TOBACCO SMOKE

The constituents of tobacco smoke include nicotine, and about 4000 pyrolysis products including tar components (aliphatic and aromatic hydrocarbons, phenols and other compounds), alcohols, amines, nitrosamines, ammonia, nitrogen oxides and carbon monoxide.

Nicotine

Nicotine is the addictive component of tobacco smoke. It is readily absorbed through the oral mucosa and the lungs, and peak blood concentrations are very rapidly achieved – within 30 seconds of a puff of a cigarette. The drug acts on the CNS, causing transient euphoria, a feeling of relaxation, improved concentration and memory, and reduced appetite. Nicotine is highly addictive, producing withdrawal symptoms of anxiety, difficulty in concentrating and irritability, which are relieved by the next cigarette. Eventually smokers establish a steady blood level of nicotine through a regular smoking pattern to prevent withdrawal cravings.

Psychological and behavioural components contribute toward dependence on smoking in approximately equal measure to physiological addiction, and are of two types: associations which reinforce the habit, which can be positive (e.g. social drinking and following meals) or negative (e.g. stressful situations), and ritual behaviour associated with lighting, holding and inhaling a cigarette, which the smoker associates with the reward of a measure of nicotine.

Other effects of nicotine include stimulation of the autonomic nervous system, which increases heart rate, raises blood pressure and causes vasoconstriction. It also increases the stickiness of blood platelets, leading to increased risk of clotting. It raises the levels of serotonin, catecholamines, pituitary hormones and vasopressin in the blood and brain. And it increases gastric acid secretion, which may lead to peptic ulceration.

Tar

Tobacco tar is a complex mixture of compounds, many of which are carcinogenic. Tar is largely unabsorbed and most becomes trapped in the lungs, causing carcinomas; the increased risk of bronchial carcinomas compared with non-smokers ranges from 15-fold for someone regularly smoking less than ten cigarettes a day to 60-fold for someone smoking more than 40 a day. The risk of cancer of the buccal cavity, larynx and oesophagus is also much higher than for the population as a whole. Some tar constituents enter the blood stream and pass through the kidneys, bladder and liver and can be responsible for cancer in these organs.

Carbon monoxide

Carbon monoxide binds tightly to haemoglobin, forming carboxyhaemoglobin, decreasing the availability of oxygen in the blood supply to the tissues, including the myocardium. Carbon monoxide acts together with nicotine to increase the risk of ischaemic heart disease significantly. Circulatory problems can also lead to intermittent claudication, which can lead to gangrene and result in limb amputation.

Other effects

Tobacco smoke irritates the upper airways and inhibits the protective actions of the ciliary epithelium and the production of mucus by glandular cells. This leads to chronic pharyngitis, laryngitis and particularly bronchitis. Eventual destruction of bronchial and alveolar tissues often results, leading to bronchiectasis and emphysema, irreversible conditions which progressively restrict gaseous interchange in the lungs and cause increasing respiratory distress.

Smoking can also impair the retina and optic nerve, increase blood sugar and lipid levels, have teratogenic effects in both men and women, increasing the possibility of congenital malformations in babies, increase premature births and decrease birth weight.

TREATMENT – NICOTINE REPLACEMENT THERAPY

Giving up smoking is essentially a matter of self-motivation and determination and most ex-smokers have stopped without using drugs or any kind of assistance, but products which have been shown to be helpful are available for those who feel unable to give up unaided. The effectiveness of smoking cessation products is in part due to an attention-placebo effect, because almost any treatment which provides positive expectations, structure and encouragement will have some success. Nevertheless, smoking cessation products do have a real effect, as is borne out by the results of placebo-controlled trials (see below).

In the past, products available included some which used an aversion therapy approach, but they were found to be little better than placebos and have been discontinued. Today, nearly all smoking cessation products licensed as medicines are forms of nicotine replacement therapy (NRT). Presentations include chewing gum, transdermal patches, a cigarette-shaped inhaler, a sublingual tablet, a lozenge and a nasal spray. A product which claims to alleviate the unpleasant effects of stopping smoking is also available.

Mode of action

NRT assists smokers to give up by providing nicotine, although at a lower level than is obtained through smoking, to help prevent withdrawal symptoms and cravings. After a period at a steady state, nicotine intake is progressively reduced to zero over two to three months. Nicotine is absorbed efficiently through the buccal and nasal mucosae, the skin and the lungs, all of which are employed for NRT products.

NRT delivery systems

- **Transdermal patches**

  There are two types of transdermal patch, both of which are changed daily: one is left on for 24 hours, and the other is used for 16 hours daily during waking hours only and removed on going to bed. The former provides a residual nicotine level the next morning, and may be better for smokers who crave a cigarette as soon as they wake up. However, nicotine levels maintained overnight can produce sleep disturbances: use of the 16-hour patch should avoid this. Three brands of patch are available, all providing three patch strengths, which are intended to allow for a smooth reduction in nicotine intake. With both 16- and 24-hour patches nicotine plasma concentrations are about half of those obtained from smoking the average number of cigarettes per day.

- **Chewing gum**

  Nicotine is absorbed from chewing gum through the buccal mucosa; peak blood concentrations are reached within about two minutes and the contents of a piece of gum are intended to be released over about 30 minutes. A piece of gum is chewed whenever the urge to smoke is felt, and the method mimics the pattern of nicotine intake obtained by smoking, but blood level peaks are lower and steady-state nicotine concentrations are

about 30 per cent of that obtained from cigarettes. The method is also useful because putting a piece of gum in the mouth and chewing provides some of the same kind of behavioural involvement as smoking.

- **Inhaler**

  The inhaler is intended to address both the physical and behavioural components of smoking cessation, as it involves putting the inhaler to the mouth and inhaling as in smoking, and may be particularly useful for the highly behaviour-dependent smoker. Nicotine is contained in an impregnated porous polyethylene plug inside a plastic tube, and is used in the same way as a cigarette, with 'puffs' being inhaled as desired. Users can inhale by deep pulmonary inhalation or shallow buccal 'puffing'. Nicotine intake is slightly higher with the former method, but both types produce comparable steady-state plasma concentrations equivalent to those achieved with nicotine gum.

- **Sublingual tablets**

  This presentation provides an unobtrusive method of nicotine replacement. One sublingual tablet is bioequivalent to one piece of nicotine 2 mg chewing gum, and the recommended dosage is comparable. Like lozenges (see below), it may be a useful method for smokers who do not like or have difficulty in chewing gum.

- **Nasal spray**

  This presentation was developed to provide a fast-acting and flexible method of nicotine delivery for highly dependent smokers. A 50 µl metered spray administered to each nostril delivers a dose of 1 mg nicotine. Nicotine is rapidly absorbed from the nasal mucosa, reaching maximum plasma levels in 10 to 15 minutes; about half the dose is absorbed. Side-effects include nose and throat irritation, watering eyes and coughing, and are fairly common, especially in the first couple of weeks of treatment.

- **Lozenges**

  As with chewing gum, nicotine is absorbed from lozenges through the buccal mucosa and they are used in much the same way. Lozenges provide a more discreet means of nicotine replacement than chewing gum, and also may be preferred by those who do not like or have difficulty in chewing gum. There are two brands available. Nicotinell Mint 1 mg Lozenges (Novartis Consumer Health) contain 1 mg nicotine, and are more or less bioequivalent to 2 mg gum, as some nicotine remains bound to the ion exchange resin in the latter and is not released. NiQuitin CQ Lozenges (GlaxoSmithKline Consumer) are available in 2 mg and 4 mg strengths.

Efficacy

NRT is one of the few categories of non-prescription medicines for which claimed effectiveness is supported by a large body of clinical trial evidence. Many trials and some meta-analyses have been published, and the overall opinion is that NRT is significant in helping smokers give up. Some interesting points have emerged from these researches, which pharmacists could use to provide advice and encouragement to smokers wanting to give up, and may also help them to select the best method for particular clients. These include:

- A review of 20 systematic reviews in the Cochrane Library concluded that all forms of nicotine replacement are effective, increasing the quit rate by about one-and-a-half to two times compared with placebo. There appears to be little difference in efficacy between one method and another.
- In one large-scale (1700 patients) double-blind, placebo-controlled trial using patches it was found that they were more effective than placebo, and that abstinence from smoking for one week was a strong predictor of long-term abstinence in both patch- and placebo-using groups. A week's trial of patches may

therefore be a useful indicator of smokers who are likely to be able to give up permanently.

- A trial using chewing gum showed that one-third of heavy smokers were still not smoking two years after a course of the 4-mg strength, and that for moderate and low nicotine-dependent smokers, the 2-mg strength produced comparable results.
- A meta-analysis of 28 randomised trials of gum and patches has confirmed this finding, and concluded that for lower-dependency smokers there is little difference in efficacy between gum and patches. The 4-mg gum has been found to be most effective for high-dependency smokers. The paper concludes overall that NRT could assist about 15 per cent of smokers who seek help to give up the habit.
- Another meta-analysis found no difference in effectiveness between the 16- and 24-hour patches.
- One meta-analysis, in examining trials of gum, demonstrated that motivation is an extremely important factor in giving up. For low-dependency, highly motivated smokers motivation alone appeared to be as successful as active treatment, as the same proportion of subjects using placebo as using active treatment (about 50 per cent in each case) were still stopped after one year. However, active treatment was more successful than placebo in well-motivated, highly nicotine-dependent smokers.

Several clinical trials have been carried out on the nicotine inhaler, although most of these have been conducted by the manufacturer. All were double-blind and placebo-controlled and show success rates comparable to gum and patches, so long as at least four cartridges of nicotine are used per day to ensure suppression of withdrawal symptoms. Results have also shown that the inhaler is likely to be most successful for moderate-dependency smokers who smoke between about 10 and 20 cigarettes daily. Two small-scale trials have been carried out to determine the effects of the inhaler on craving, and both found the device to be significantly better than placebo. One meta-analysis includes a single trial on the inhaler, and the authors report

that it appears promising, although not enough data are available to determine whether it is more effective than gum or patch.

Dosage and administration

Subjects must stop smoking completely while using any NRT product, and different presentations should not be used together.

- **Transdermal patches**

  Transdermal patches have the advantage of the convenience of a once-daily application and may be the most suitable form of NRT for people in whom the behavioural aspects of smoking dependency play a relatively unimportant role. All of the three brands available (Nicorette, Pharmacia; Nicotinell TTS, Novartis Consumer Health; NiQuitin CQ, Glaxo SmithKline Consumer) are supplied in three strengths. The three strengths of Nicotinell TTS and NiQuitin CQ each provide 7, 14 and 21 mg nicotine respectively over 24 hours. Nicorette patches deliver 5, 10 and 15 mg over the 16 hours daily for which they are intended to be applied, and overnight plasma nicotine levels should be insignificant.

  The recommended starting strength for the three strength brands is generally the highest, except for light smokers (defined as less than ten cigarettes per day for NiQuitin CQ, and less than 20 for Nicotinell TTS), when the medium strength should be used first. The recommended treatment period and the length of time on each strength varies between brands, but the overall strategy is a stabilisation period on the high strength for between four and eight weeks, followed by a progressive stepping-down of strength over a further two to eight weeks, before stopping altogether. The total maximum recommended course for Nicorette and Nicotinell TTS is 12 weeks, and for NiQuitin CQ 10 weeks.

  Transdermal patches should be applied daily to a clean, dry, non-hairy area of the trunk or upper arm. Nicorette patches

should be removed at bedtime, and a fresh one applied next morning. To minimise the possibility of localised skin reaction a new site of application should be chosen each day, and several days should be allowed to elapse before a patch is re-applied to the same area. Used patches should be folded in half with the adhesive side inwards and disposed of carefully, because they still contain significant amounts of nicotine, certainly sufficient to cause poisoning in children.

- **Chewing gum**

Use of nicotine chewing gum mimics the pattern of peaks and troughs of nicotine provided by smoking, although blood levels achieved are much lower. Because a piece of gum can be chewed whenever the urge to smoke is felt, the method may be most suitable for the smoker who finds cigarette cravings difficult to resist. It may also provide a greater sense of control over curbing the habit, and the chewing activity also acts as a behavioural substitute for smoking.

Nicotine gum is available in two brands (Nicorette, Pharmacia; and Nicotinell, Novartis Consumer Health), both in two strengths: 2 mg and 4 mg. Recommended dosages and maxima differ slightly for the two brands. For Nicorette, heavier smokers (more than 20 cigarettes per day) and those who crave a cigarette within 20 minutes of waking up are recommended to start on the higher strength. Less heavy smokers should start with the lower strength, and transfer to the higher if they need more than 15 pieces per day. A piece may be chewed whenever the urge to smoke is felt. Recommended daily maxima are 15 pieces per day for both strengths. For Nicotinell, for both strengths, one piece of gum is to be chewed when the urge to smoke is felt. The normal requirement is 8 to 12 pieces daily, but up to a maximum of 25 pieces daily may be used. The higher strength is recommended if particularly strong withdrawal symptoms are experienced. For both brands the recommended course of chewing gum is about three months of

ad libitum use, after which it is gradually withdrawn over a few weeks.

Correct chewing technique maximises buccal absorption of nicotine from the gum and reduces adverse effects from swallowing the drug in saliva. The gum is chewed slowly to release nicotine, until the taste becomes strong and 'peppery'. Chewing is then stopped and the gum is rested between the gum and cheek until the taste fades. The process is repeated until the gum has lost its flavour, which should take about 30 minutes.

- **Inhaler**

Because the device (Nicorette Inhalator, Pharmacia) is held like a cigarette and the nicotine is inhaled by puffing, the nicotine inhaler provides a close approximation to the hand-to-mouth activity and inhaling associated with smoking which reinforce the nicotine addiction. This presentation is therefore recommended for highly behavioural-dependent smokers. On demand, *ad libitum* usage also helps to alleviate cravings and provide a sense of control.

The device consists of a two-part plastic mouthpiece and holder, into which is inserted a cartridge containing a polyethylene porous plug impregnated with nicotine. Each plug contains 10 mg, of which 5 mg is available for inhalation. Each puff delivers about 13 μg of nicotine, which is only between one-twelfth and one-twenty-fifth of that obtained per puff of a cigarette. However, a plug will last much longer than a cigarette because the available nicotine content is designed to be released over about 20 minutes of active continuous puffing but, as in smoking, puffs are only taken intermittently. In this way nicotine intake is not only reduced compared to cigarettes, but the concentration peaks are flattened. The plug is flavoured with menthol, and the disappearance of the flavour indicates that the nicotine is exhausted.

Between six and 12 cartridges should be used per day. The inhaler is intended to be used freely for three months, following

which the daily dosage should be reduced over a further six to eight weeks. Treatment should be completed within six months.

- **Sublingual tablets (Nicorette Microtab, Pharmacia)**

  A tablet is placed under the tongue, where it slowly disintegrates in about 30 minutes. One tablet is used per hour (eight to 12 tablets per day), or two per hour (16 to 24 tablets per day) for heavy smokers (more than 20 cigarettes per day). The dose may be increased to two per hour if one seems inadequate to control craving, or if the individual feels that relapse is likely. The absolute maximum dosage is 40 tablets per day. The full dosage should be maintained for three months, and then gradually tapered off to zero within the next three months.

- **Nasal spray (Nicorette Nasal Spray, Pharmacia)**

  One metered spray is inhaled into each nostril when necessary to relieve craving, with a maximum rate of two doses per hour and 64 sprays (32 into each nostril) in 24 hours. *Ad libitum* dosage can be maintained for up to eight weeks, after which the dosage should be reduced by half over the next two weeks, and down to zero over the following two weeks.

- **Lozenges (Nicotinell Mint 1 mg Lozenge, Novartis Consumer Health; NiQuitin CQ 2 mg and 4 mg Lozenge, GlaxoSmithKline Consumer)**

  The dosage schedule for Nicotinell lozenges is much the same as for Nicotinell Gum: one lozenge every one to two hours, when the urge to smoke is felt. The recommended daily dosage is eight to 12 lozenges, but a maximum of 25 may be used. The sucking technique is similar to that for nicotine chewing gum: a lozenge is sucked slowly until the taste becomes strong; it is then 'parked' between the cheek and gum until the taste has faded, and the process continued until the lozenge has gone. One lozenge should last for about half an hour.

For NiQuitin CQ Lozenges the strength is determined by the time between waking and the first cigarette, rather than by the number of cigarettes smoked per day as for other NRT products. The 4 mg lozenge is recommended for those who smoke within 30 minutes of waking, and the 2 mg strength for those who are less dependent and can go longer before smoking their first cigarette of the day. Users stay on the same strength of lozenge throughout the course, stepping down the frequency of use rather than the strength of the preparation. The total length of treatment is up to 24 weeks, starting with one lozenge every one to two hours, to a maximum of 15 lozenges per day, for the first six weeks. For the next two three-week periods the frequency is reduced to one lozenge every two to four hours, then to one every four to eight hours. Thereafter, one or two lozenges may be sucked when the urge to smoke is strong, and use should have ceased altogether within a further 12 weeks.

Cautions, contraindications and adverse effects

NRT products provide much lower doses of nicotine than are obtained by smoking, and the adverse effects are not complicated by the additional toxic effects of tar and carbon monoxide generated in tobacco smoke. Nevertheless, due to the cardiovascular effects of nicotine, caution is advised with the use of NRT products in patients with a history of angina, recent myocardial infarction or cerebrovascular accident, cardiac arrhythmias, hypertension or peripheral vascular disease. Because of the effects of nicotine on metabolism, caution is also advised in patients with diabetes, hyperthyroidism and phaeochromocytoma.

With the use of patches there is a possibility of localised skin reactions, and they should be avoided in patients with any chronic or serious skin condition. Although nicotine can exacerbate symptoms in patients with peptic ulcers or gastritis, the possibility is greater with gum than other NRT products, as nicotine may be swallowed and enter the stomach directly. Denture wearers may also have difficulty in chewing gum. Patients with chronic bronchitis or severe asthma may find inhalation from the inhaler difficult, and should therefore avoid this product.

In addition to the potential adverse effects mentioned, NRT products may produce the same range of side-effects as nicotine from smoking and these include hiccups, sore throat, headache, nausea and dizziness. However these are less likely to occur than with smoking, and clinical trials have shown most to be comparable to those caused by placebo. Nicotine withdrawal symptoms such as somnolence, impaired concentration and mood swings, fatigue, hunger, productive cough, bowel disturbances and paraesthesia are also possible.

Although NRT products are less harmful than smoking, they are not licensed for sale to pregnant and breast-feeding women, and should not be sold to individuals under 18 years of age. However, they may be supplied following authorisation by a doctor, as the doctor would then assume clinical responsibility for its use. Patient group directions may also authorise supply to individuals who are outside of the licensing conditions for non-prescription sale.

Transfer of dependence from smoking to NRT products is unlikely, but possible.

Interactions

NRT products do not interact with other medication. However, tobacco smoke reduces serum levels of a wide range of drugs, and adjustment of dosage may be necessary when smokers have given up. The *British National Formulary* specifically cites theophylline, but beta-blockers and adrenergic agonists, nifedipine, tricyclic antidepressants, phenothiazines, benzodiazepines and insulin may also require dose adjustment.

TREATMENT – OTHER PRODUCT

Product

- **Nicobrevin**

  Nicobrevin (Cedar Health) is a 28-day course of gelatin capsules containing menthyl valerate, quinine, camphor and eucalyptus

oil. The rationale given by the original manufacturer for the formulation was that quinine helps to alleviate the effects of smoking withdrawal on tobacco craving and metabolism, camphor helps to alleviate the undesirable effects of smoking on the respiratory system, menthyl valerate is a mild sedative and helps to relieve the irritability experienced by persons giving up smoking, and oil of eucalyptus helps to relieve the accumulation of mucus which occurs during smoking withdrawal. These claimed actions remain to be substantiated, but the complex dosage regimen is likely to enhance the product's attention-placebo effect. One small-scale, placebo-controlled, double-blind trial has been carried out on Nicobrevin, which reported that it was significantly superior to placebo as an aid to stopping smoking, and that the product was rated by subjects as 'very effective'.

PRODUCT SELECTION POINTS

- Motivation is the most important factor in giving up smoking, but NRT has been clinically proven to be an effective aid.
- Low-dependency smokers who are highly motivated to give up probably do not need any kind of antismoking aid. However, lozenges provide the lowest dose of nicotine of all NRT products and may be useful for light smokers who feel they need some pharmacological as well as psychological support.
- There is little difference in efficacy overall between the various forms of NRT, but a particular form or strength may be best suited to a particular type of smoker.
- Patches are convenient to use, but may not be suitable for smokers with a high behavioural component to their dependence.
- The 24-hour patch is better for smokers who crave a cigarette within 20 minutes of waking up in the morning, otherwise the 16-hour and 24-hour patches are equally suitable and effective. The 16-hour patch should be used if sleep disturbances occur with the 24-hour patch.

- Gum of 4-mg strength is probably the best approach for heavy smokers with high behavioural dependence: the 2-mg strength is suitable for moderate and relatively light smokers.
- The nicotine inhaler might be most useful for moderate smokers with high behavioural dependency.
- The nasal spray may be the most effective form of NRT for very heavily dependent smokers.
- There is insufficient trial evidence to confirm the effectiveness of Nicobrevin, but it is in any case likely to have some placebo effect.

PRODUCT RECOMMENDATIONS

NRT is the antismoking treatment of choice. The following recommendations are made for specific types of smoker:

- Low dependency (less than ten cigarettes/day), high motivation – encouragement and advice only.
- Low dependency – lozenges, sublingual tablets or 2-mg gum.
- Moderate dependency (ten to 20 cigarettes/day), with low behavioural component and normal or heavy build – patch, starting with highest strength.
- Moderate dependency, low behavioural component, slight build – patch, starting with middle strength.
- Moderate dependency, high behavioural component – inhaler, sublingual tablets or 2-mg gum (switch to 4 mg if necessary).
- High dependency (more than 20 cigarettes/day) – 4-mg gum or lozenges or nasal spray.
- Very high dependency – nasal spray.

Sore throat

Sore throat OTC treatment for sore throat as a symptom of the common cold is based on one or more of the following approaches: stimulation of saliva production, use of antimicrobials and local anaesthesia.

CAUSES

Although many products for sore throat contain antibacterial compounds, causative infections are normally viral and not susceptible to them.

TREATMENT – PASTILLES AND LOZENGES

The action of sucking anything produces saliva, which lubricates and soothes inflamed tissues and washes infecting organisms off them. All lozenges and pastilles, regardless of ingredients, produce this action and much, if not all, of their effectiveness is due to this.

Demulcents

Non-medicated glycogelatin-based demulcent pastilles, such as glycerin, lemon and honey pastilles, or boiled sweets, may be as effective as anything for soothing a sore throat, for the reasons stated above. Because they contain no medicament they can be taken as often as necessary to stop the throat feeling dry, thereby relieving discomfort. Some products contain ingredients with volatile constituents, particularly eucalyptus oil and menthol. These produce a sensation of clearing blocked nasal and upper respiratory passages, and can be useful in relieving associated symptoms of upper respiratory tract infections which often accompany sore throat. The main disadvantage of demulcent throat lozenges and pastilles is their high sugar content.

Product examples

- Glycerin, Lemon and Honey Pastilles
- Meggezones
  Schering-Plough
- Potter's Glycerin and Thymol Sore Throat Pastilles
  Ernest Jackson
- Zubes
  Ernest Jackson

Antibacterials

The compounds used in sore throat lozenges are mainly cationic surfactants and phenolic antiseptics. They are bactericidal and have varying degrees of antifungal activity. They possess activity against lipophilic viruses, but rhinoviruses which are largely responsible for the common cold are hydrophilic. A sore throat complicated by a secondary bacterial infection would normally be treated with a systemic antibiotic. Several sugar-free antibacterial throat lozenges are available.

Product examples

- Benzalkonium chloride
  - Bradosol Sugar-Free Lozenges
    Novartis Consumer Health
- Dequalinium chloride
  - Dequadin
    Crookes Healthcare
  - Labosept Pastilles (sugar-free)
    Laboratories for Applied Biology

- — Mac Sugar Free
  Ernest Jackson

- Cetylpyridinium chloride
  - — Merocets
    SSL International
  - — De Witt Throat Lozenges (also contains benzocaine)
    E.C. De Witt

- Domiphen bromide
  - — Bradosol Plus (Sugar-free)
    Novartis Consumer Health

- Amylmetacresol
  - — Strepsils
    Crookes Healthcare

- Hexylresorcinol
  - — Lemsip Sore Throat Antibacterial Lozenges
    Reckitt Benckiser
  - — TCP Sore Throat Lozenges
    Warner Lambert Consumer Healthcare

- Tyrothricin
  - — Tyrozets
    Johnson & Johnson MSD

Local anaesthetics

Local anaesthetics are included in many products and may be helpful if the patient finds swallowing uncomfortable.

Benzocaine and lidocaine (lignocaine) are the local anaesthetics

used in throat lozenges. Concentrations vary between 5 and 10 mg per lozenge, which is within the therapeutic dosage range. They are effective when applied to the oral mucosa, and may provide additional relief for patients with more seriously inflamed throats that make swallowing painful. Local anaesthetics can cause sensitisation in some individuals with prolonged use, so usage should be limited to five days. They should not be used at all by children or the elderly.

Product examples

- Benzocaine
  - — Dequacaine
    Crookes Healthcare
  - — Merocaine
    SSL International
  - — Tyrozets
    Johnson & Johnson MSD
- Lidocaine (lignocaine)
  - — Bradosol Plus (Sugar Free)
    Novartis Consumer Health
  - — Strepsils Pain Relief Plus
    Crookes Healthcare

TREATMENT – GARGLES

Gargles mainly contain antiseptic ingredients, often the same as those in throat lozenges, with the same drawback in so far as most have no proven antiviral activity. In addition, contact time with infected tissue is extremely short. The main action of gargles is the mechanical removal of microbes from the pharynx, but tests have shown that levels of contamination are restored within about an hour.

Product examples

- Oraldene (contains hexetidine)
  Pfizer Consumer Healthcare
- TCP Liquid Antiseptic (contains phenol and halogenated phenols)
  Pfizer Consumer Healthcare
- Difflam Sore Throat Rinse (contains benzydamine, an anti-inflammatory)
  3M Healthcare
- Betadine Gargle and Mouthwash (contains povidone-iodine 1 per cent – its iodine content renders it unsuitable for use in patients with thyroid problems or those on lithium therapy, and in pregnant and breast-feeding women)
  SSL International

TREATMENT – SPRAYS

AAA Mouth and Throat Spray (Manx Pharma) and Vicks Ultra Chloraseptic Sore Throat Spray (Prestige Brands) both contain benzocaine (3 mg per recommended adult dose), and may be used for children of six years and over.

Strepsils Pain Relief Spray (Crookes Healthcare) contains lidocaine (lignocaine); it is not licensed for use in children under 12 years. Eludril Spray (Ceuta Healthcare) contains chlorhexidine and tetracaine (amethocaine); it is recommended for adult use only.

NEW PRODUCT – FLURBIPROFEN LOZENGES

Flurbiprofen is a non-steroidal anti-inflammatory drug which has been available as a lozenge formulation (Strefen, Crookes) for the relief of sore throat as a POM since 1999. In July 2001, the MCA proposed to reclassify this preparation to P, with a maximum daily dose of five 8.75 mg lozenges and a maximum pack size of 16. The product is likely to become available early in 2002.

PRODUCT SELECTION POINTS

- The greatest beneficial effect of throat lozenges is due to the salivation produced by sucking them; the active ingredients are less important.
- Antiseptic constituents of throat lozenges probably have little impact on the causative organisms of sore throat.
- Gargles probably have little effect beyond that of placebo.
- Anaesthetic constituents of lozenges and sprays relieve discomfort but can cause sensitisation.

PRODUCT RECOMMENDATIONS

For a sore, 'tickly' throat – demulcent pastilles, e.g. glycerin, lemon and honey.

For a sore throat with discomfort on swallowing – lozenges containing benzocaine or lidocaine (lignocaine).

Temporary sleep disturbance

Temporary sleep disturbance (insomnia) is reported by nearly one-third of the adult population and there is a high demand from the public for hypnotics. However, prescribing of hypnotics, particularly benzodiazepines, has declined in recent years following discouragement by the CSM after it became apparent that widespread and long-term use was leading to problems of tolerance and dependence. The expansion of the non-prescription hypnotic market, with the launch of several new antihistamine brands, appeared to coincide with the reduction in prescribed hypnotics. Although non-prescription sleep aids are quite safe when used for limited periods according to manufacturers' directions, there is still the danger of tolerance and psychological dependency developing if they are relied on as a long-term solution to an insomnia problem which may have underlying organic or psychological causes. OTC hypnotics should only be recommended when the normal sleep pattern has been disturbed for an identifiable reason, e.g. long-haul air travel, a change in shift-working patterns or a stressful situation of short duration.

TREATMENT – ANTIHISTAMINES

Compounds available

Compounds available are:

- Diphenhydramine hydrochloride
- Promethazine hydrochloride

Mode of action and efficacy

The relevant actions of antihistamines are described in the section on cough. Their effectiveness as hypnotics may be due to their antimuscarinic actions, but it has also been proposed that sedation is due to the blockade of central H_1-receptors.

Diphenhydramine hydrochloride

Diphenhydramine is a potent antihistamine of the ethanolamine group with a high incidence of sedation and antimuscarinic effects. Maximum sedation is achieved one to three hours after administration, and duration of sedation is between three and six hours. From psychomotor tests it appears that mental alertness and cognitive ability are not impaired beyond the length of time that drowsiness lasts. The optimum dose appears to be 50 mg; higher doses do not increase efficacy but do increase the potential for side-effects.

Trials generally show that diphenhydramine is more effective than placebo, although in some cases only moderately so. In one trial, it was found that patients who had never used a sleep aid before tended to respond better to diphenhydramine than individuals who had.

Another trial showed that the patient groups who found the drug most useful were younger subjects with low levels of anxiety, and those who had significant difficulties in falling asleep. In a telephone survey carried out in the United States, consumers of OTC sleep aids reported them to be less effective than benzodiazepines. Diphenhydramine seems to be less effective in Asian than in Caucasian individuals, as in one trial the former required a dose up to 1.7 times higher than the latter to experience sedation. Tolerance to diphenhydramine appears to develop with repeated use. Use should be restricted to seven to ten consecutive nights at most.

Dosage

Adults over 16 years – 50 mg at bedtime.

Products

- Dreemon Tablets (25 mg)
  Peach Pharmaceuticals
- Nightcalm tablets (25 mg)
  Galpharm International

- Nytol tablets (25 mg)
  Stafford-Miller
- Nytol One-A-Night tablets (50 mg)
  Stafford-Miller
- Paxidorm tablets (25 mg)
  Norma Chemical
- Panadol Night tablets (diphenhydramine 25 mg and paracetamol 500 mg)
  GlaxoSmithKline Consumer

Promethazine hydrochloride

Promethazine hydrochloride is a phenothiazine derivative with marked sedative properties. It is long-acting, with action reported to last between four and 12 hours. Residual drowsiness the next morning therefore seems more likely than with diphenhydramine. Unlike diphenhydramine, promethazine is not licensed in the United States for non-prescription sale and little work appears to have been carried out on its effectiveness as a hypnotic, although it has been used for many years in the United Kingdom for night-time sedation in children as well as adults. One study has reported that promethazine increased the duration and quality of sleep in volunteer poor sleepers.

Dosage

Adults over 16 years – 20 or 25 mg, depending on brand, at bedtime.

Promethazine Oral Solution BP (Phenergan Elixir) is licensed as a P medicine with a sedative dosage for children as follows: two to five years, 15 to 20 mg, five to ten years, 20 to 25 mg, as a single night-time dose. The preparation can only be given to children between one and two years of age under medical supervision. Promethazine Oral Solution is not recommended for children under one year, as it is thought that giving any sedative drug, including phenothiazines, to an infant may increase the risk of sudden infant death syndrome.

Products

- Phenergan Elixir (5 mg/5 ml)
  Aventis Pharma
- Phenergan Nightime tablets (25 mg)
  Aventis Pharma
- Sominex tablets (20 mg)
  SSL International
- Ziz tablets (10 mg)
  Chatfield Laboratories
- Ziz Forte tablets (25 mg)
  Chatfield Laboratories

Adverse effects, interactions and cautions

See section on motion sickness.

TREATMENT – HERBAL SLEEP AID PRODUCTS

A number of herbal products are licensed as GSL medicines for the relief of restlessness and for promotion of relaxation and sleep. As is generally the case with herbal medicines, most are mixtures of several constituents. The constituents occurring most frequently are discussed below.

Herbal constituents

- **Hops**

  The compound 2-methyl-3-buten-2-ol extracted from hops (*Humulus lupulus*, Cannabinaceae) has been shown to possess narcotic properties in mice, and the plant is reported to exhibit hypnotic and sedative actions in humans. Hops have been

claimed to improve sleep disturbance when taken in association with valerian. Hops are thought to be non-toxic in small doses, but their sedative action may potentiate the effects of other sedative therapy and alcohol.

- **Valerian**

  Valerian (*Valeriana officinalis*, Valerianaceae) contains valerenic acid, which has been shown to inhibit the enzyme system responsible for the metabolism of gamma-aminobutyric acid (GABA). Increased levels of GABA are associated with a decrease in CNS activity, and CNS depression has been observed in mice after injection of a valerian extract. Several studies have documented the sedative effect of valerian in humans, with beneficial effects on several subjective sleep parameters, although not on objective measures of sleep. Other constituents of valerian are also thought to contribute to its sedative effect. Valerian appears to be safe in use.

- **Passionflower**

  Passionflower (*Passiflora incarnata*, Passifloraceae) contains maltol and ethylmaltol, which have been shown to cause sedation and to increase the length of sleeping induced by hexobarbital. Passionflower also contains constituents which cause CNS stimulation, but the sedative effects appear to predominate. No adverse effects of the herb have been reported.

- **Jamaica dogwood**

  Studies with Jamaica dogwood (*Piscidia erythrina*, Leguminosae) in animals have shown weak cannabinoid and sedative properties, but no trials in humans appear to have been conducted. In *in vitro* and *in vivo* animal studies Jamaica dogwood has been reported to depress strongly the activity of uterine muscle; use during pregnancy and lactation is therefore not recommended.

- **Wild lettuce**

  Wild lettuce (*Lactuca virosa*, Asteraceae/Compositae) has been reported to have mild sedative, analgesic and hypnotic properties, but this has not been scientifically demonstrated in humans.

Dosage

Recommended dosage varies from product to product, some being taken at bedtime, others in the early evening and at bedtime, and some others three times daily.

Product examples

- Heath and Heather Quiet Night tablets
  Peter Black Healthcare
- Natrasleep tablets
  Peter Black Healthcare
- Nodoff Passiflora tablets
  Potter's
- Nodoff Mixture
  Potter's
- Nytol Herbal tablets
  Stafford-Miller
- Slumber Tablets
  Seven Seas
- Valerina Night-Time tablets
  Chemist Brokers

PRACTICAL ADVICE

A good night's sleep can often be achieved without resort to drugs, and practical advice can be offered to patients by the pharmacist. Wherever possible, the underlying cause of insomnia, such as pain or anxiety, should be identified and addressed, and appropriate referrals made where necessary. Sleep aids should only be recommended to help re-establish a regular pattern of sleep, and should be used for only a short period – ten days at most.

Advice that can be given to aid sleep without the use of drugs includes:

- Wind down and relax towards the end of the evening. Do not do anything mentally stimulating within 90 minutes of bedtime. Gentle exercise, such as a short walk, just before bedtime, often helps.
- Do not sleep or doze during the evening. Do not go to bed until you feel tired and ready for sleep.
- Do not eat a large meal or have tea or coffee before bedtime. Do not drink alcohol; it may cause drowsiness but its effect is short-lived. A milky drink is often relaxing.
- Make sure that the bedroom and bed are warm and comfortable.
- Once in bed, put out the light immediately; do not read or watch television.
- Once the light is out, just relax, perhaps thinking of something pleasant and relaxing. Try to put any worries aside. Do not try to force yourself to sleep, let it come naturally.
- Aim to get up at the same time every day until a sleep pattern is restored.
- If you have not fallen asleep after 20 minutes get up and do something relaxing and go back to bed when you feel sleepy. Do the same if you wake in the middle of the night and cannot get back to sleep.
- Remember that if you have naps during the day you will need to sleep less at night.
- Many people need much less than eight hours sleep per night.

PRODUCT SELECTION POINTS

- Non-drug strategies should be used for dealing with chronic insomnia where no specific cause can be identified.
- Diphenhydramine and promethazine appear to be effective in promoting sleep. 'Hangover' drowsiness the following morning may be a problem, particularly with promethazine.
- There is some evidence that herbal sleep aids are effective, but the same potential problem of psychological dependence exists for herbal products as for other hypnotics.
- Promethazine elixir is licensed for non-prescription use in children over two years, but should only be used as a last resort, when a cause has been clearly identified, and for a short period.
- OTC hypnotic products should only be recommended for occasional short periods and when a clear cause of stress can be identified. For sleeplessness due to any other reason, the cause should be identified and treated.

PRODUCT RECOMMENDATIONS

Temporary sleep disturbance associated with an identified change in sleeping pattern or short-term stress-related cause – diphenhydramine or a herbal sleep aid product.

Threadworm and roundworm

Threadworm, also known as pinworm, causes enterobiasis, the only commonly occurring helminth infection in the United Kingdom. Roundworm infections have a much lower incidence, and are likely to have been contracted abroad rather than in the United Kingdom.

CAUSES

Threadworm

Threadworm, *Enterobius vermicularis*, is estimated to have affected up to 40 per cent of children by the time they are ten years old and is also contracted by adults, but the incidence is lower. The condition can often be diagnosed by the pharmacist and suitable non-prescription treatment recommended.

Threadworms are initially acquired through swallowing eggs, which hatch and mature in the small intestine. After copulating the males die, and the females migrate to the caecum and anus at night to lay their eggs in the perianal area, attaching them to the skin with a sticky, highly irritant fluid. Some eggs hatch there and return to the rectum to mature. The intense itching caused by the sticky secretion provokes scratching by the host, and eggs are transferred on to the fingers.

Infection is passed on or perpetuated through picking up eggs on the fingers followed by ingestion. Infection is transmitted either by direct contact between individuals or from contaminated surfaces or objects, as under suitable conditions eggs can remain viable for several weeks outside the human host. Infection is recognised by sighting the whitish worms, about 10 mm in length, on the stools after defecation and sometimes around the anus, and also from the intense perianal itching that they cause. Enterobiasis is treated with mebendazole or piperazine, both of which are available without prescription.

Roundworm

Roundworm infections (ascariasis) have a much lower incidence, and are likely to have been contracted abroad rather than in the United Kingdom. The consequences of infection are potentially much more serious than enterobiasis and, if suspected, the patient should be referred to a doctor. The condition is included here because the same products are used to treat threadworms and roundworms, and as they cost less than an NHS prescription charge, patients may be recommended by their doctor to buy roundworm treatments over the counter.

Roundworm infection is much less easy to identify than threadworm, and is potentially serious. Eggs of the common roundworm (*Ascaris lumbricoides*) are ingested in faeces-contaminated food and water and hatch in the intestine. The larvae pass into the blood stream and lymphatic system and migrate via the lung, liver, trachea and oesophagus back to the intestine. Light infections are usually symptomless, but heavy infections produce serious gastrointestinal symptoms and are sometimes fatal. The condition is rare in the United Kingdom and specialised medical expertise may be necessary to diagnose it.

Piperazine is licensed for non-prescription sale for the treatment of roundworm infections, but mebendazole may only be used on prescription.

TREATMENT

Mebendazole

Mode of action

Mebendazole is a benzimidazole derivative which disrupts parasite energy metabolism by causing selective destruction of cytoplasmic microtubules in tegumental and intestinal cells; it irreversibly inhibits glucose uptake and causes immobilisation and death of the parasite within three days of administration. It also binds to tubulin, a protein required by the parasite for the uptake of nutrients.

Mebendazole is effective against both threadworms and roundworms, but is licensed for non-prescription use only for the former. It is poorly absorbed from the human gastrointestinal tract, and the small proportion of a dose that is absorbed is almost entirely eliminated from the body following first-pass metabolism in the liver. Mebendazole has been in use for 25 years and is an established treatment throughout the world, and in clinical trials it has been shown to be highly effective.

Dosage

For adults and children over two years, a single dose of one 100-mg tablet. Treatment failures are rare, but reinfection is possible, in which case a second dose should be given after two to three weeks. Mebendazole is not recommended for children under two years.

Adverse effects and cautions

Side-effects are unlikely at the dosage used for threadworm infection; transient diarrhoea and abdominal pain have been rarely reported in patients with heavy infections. Hypersensitivity reactions also occur rarely.

Mebendazole has shown embryotoxic and teratogenic activity in rats, but not in other species. When it has been used in pregnant women, even during the first trimester, there has been no greater incidence of malformations or spontaneous abortion than in the general population. However, the drug is not licensed for use in pregnancy or breast-feeding when sold without prescription.

Interactions

Cimetidine inhibits the metabolism of mebendazole in the liver, increasing blood plasma concentrations. Phenytoin and carbamazepine induce enzyme metabolism and have been found to reduce serum mebendazole levels. However, since mebendazole exerts its effect directly within the gut, and the drug is poorly absorbed, these interactions are unlikely to have any clinical significance.

Products

- Ovex tablets
  Johnson & Johnson MSD
- Pripsen Mebendazole Tablets
  SSL International

Both products are 100-mg orange-flavoured, chewable tablets.

Piperazine

Mode of action

Piperazine has been in use for more than 45 years, and its efficacy appears to have been established without clinical trial evidence. Until 1989, when mebendazole was reclassified from POM to P status, piperazine was the only anthelmintic available without prescription. However, mebendazole is now usually the first-choice treatment. Piperazine is active against both threadworms and roundworms, and can be sold without prescription for infections caused by either.

Piperazine acts by blocking the response of worm muscle to acetylcholine, and by interfering with the permeability of cell membranes to ions which regulate cell resting potential. Flaccid paralysis results, and the paralysed worms are then expelled from the gut by peristalsis. Piperazine is readily absorbed from the gastrointestinal tract, but is almost completely metabolised and excreted through the kidney within 24 hours.

Dosage

Several salts of piperazine are used as anthelmintics, but only the phosphate is available in the United Kingdom.

Piperazine phosphate is presented as a powder in sachets containing 4 g, together with standardised senna which acts as a laxative to facilitate the expulsion of the paralysed worms.

Dose for threadworms – adults and children over six years, one sachet; children one to six years – two-thirds of a sachet; infants three months to one year (treatment only on medical advice) – one-third of a sachet. The dose should be stirred into a small glass of water or milk and drunk immediately. Because the life cycle of the threadworm is about 30 days and some worms may be in the larval stage when the first dose is taken, the manufacturer recommends that a second dose be taken after 14 days to eliminate the possibility of reinfection.

Dose for roundworms – the initial dose as for threadworms; follow-up doses every month for three months may be advised to prevent the risk of reinfection.

Adverse effects and cautions

At dosages within normal therapeutic ranges, adverse effects are rare. Allergic-type symptoms in some sensitive individuals and mild gastrointestinal disturbances have been reported. Neurotoxic reactions resulting in convulsions have occasionally occurred in patients with neurological or renal abnormalities, and piperazine should not be used in patients with severe renal or hepatic dysfunction or a history of epilepsy.

The drug is not contraindicated in pregnancy, but isolated instances of congenital malformations have been reported in babies whose mothers had taken piperazine while pregnant, although no causal relationship has been established. Manufacturers advise that piperazine should be taken in pregnancy only if strictly necessary and under medical supervision, and should be avoided altogether in the first trimester. The drug is excreted in breast milk, although no untoward effects in infants have been reported. However, it is recommended that mothers taking piperazine should not breast-feed their babies for at least eight hours following a dose.

Interactions

Caution is advised in administering piperazine to patients taking phenothiazines or tricyclic antidepressants; this is based on a single

reported case of an interaction causing convulsions, and also on studies in animals.

Product

- Pripsen Piperazine Phosphate Powder (with senna)
  SSL International

PRACTICAL ADVICE

In addition to use of an anthelmintic, whether mebendazole or piperazine, pharmacists should advise patients of the following measures to take to prevent reinfection and transmission of threadworms:

- When infection is detected in any member of a family, the whole family should be treated with an anthelmintic, as other members may be in the early stages of infection, although asymptomatic.
- As infection is easily passed on through contact, scrupulous hygiene should be observed. All members of the family should wash their hands thoroughly before preparing, handling and eating food. As eggs can be harboured under the finger nails, they should be kept short and scrubbed with a nailbrush when the hands are washed.
- Children with threadworms should wear underpants under pyjamas at night to prevent them transferring eggs to their fingers if they scratch during sleep.
- Infected individuals should have a bath or shower on getting up each morning, to wash away any eggs laid overnight.

PRODUCT SELECTION POINTS

- Mebendazole is the treatment of choice for threadworms. It is suitable for all patients over two years old with the same single

dose for all ages. It is almost completely free from adverse effects, and apart from pregnancy there are no contraindications.

- Mebendazole is not licensed for non-prescription use in children under two years, but piperazine can be used from the age of one year. Children under one year should only be treated under medical supervision.
- Neither mebendazole nor piperazine can be supplied without prescription to pregnant women.
- Piperazine, but not mebendazole, is available without prescription for the treatment of roundworms, but it should only be supplied following medical diagnosis.
- Stringent hygiene precautions should be taken to prevent reinfection and transmission of threadworms.

PRODUCT RECOMMENDATIONS

For threadworms the first choice for adults and children over two years – mebendazole. For children one to two years – piperazine phosphate sachets.

Piperazine may be sold without prescription for roundworm infections, but supply should only be made following medical diagnosis.

Vaginal candidiasis

Vaginal candidiasis (thrush) is the most common vaginal infection, with about half of all women between the ages of 16 and 60 suffering an attack at some time and more than one-third having at least one attack each year. However, it can be successfully treated with azole preparations which are available without prescription. Products based on iodine are also available, but they are less effective and more inconvenient to use.

CAUSE

Vaginal candidiasis is caused by a yeast, *Candida albicans*, usually a harmless inhabitant of the gastrointestinal tract, skin and vagina, which overgrows opportunistically to cause infections when conditions allow.

All vaginal infections other than candidiasis require treatment under medical supervision.

TREATMENT - AZOLES

Compounds available

Compounds available are:

- Imidazoles
  - — Clotrimazole
  - — Econazole
- Triazole
  - — Fluconazole

Mode of action

Azoles are synthetic antimycotic agents which act by inhibiting replication of the yeast cells through interfering with the synthesis of

ergosterol, the main sterol in the yeast cell membrane. As a further consequence, the transformation of candidal yeast cells into hyphae, the invasive and pathogenic form of the organism, is also inhibited. Preparations of clotrimazole and econazole are applied locally; fluconazole is taken orally.

Imidazoles for local application are weak bases and have to remain in the non-ionised form in order to be active; they therefore work best in an alkaline medium and should not be used in the presence of acidifying agents. The use of live yoghurt is sometimes advocated as a 'natural' treatment for vaginal candidiasis. This advice has a rational basis, as lactobacilli in the yoghurt convert glycogen present in the vagina into lactic acid, which reduces the adherence of the yeast cells to the walls of the vagina and inhibits their growth. However, by creating an acid medium the use of yoghurt would reduce the effectiveness of imidazoles, so the two should not be administered together. Yoghurt may sometimes be helpful for vaginal candidiasis, but it is much less effective than treatment with imidazoles and is messier to use.

The imidazole compounds for local application appear to be equally effective at the recommended doses. Preparations are formulated as creams, pessaries or vaginal tablets and courses of treatment range from a single dose to six applications. Creams are also available for application to the vulva to treat irritation. In addition, some medical authorities consider that application of such a cream to the male partner's penis is useful in preventing reinfection, although there is no consensus on this. Systemic absorption of the locally applied imidazoles is slight, with wide intersubject variation. However, there is no evidence of problems occurring due to absorption following the short courses used for non-prescription treatment. Trials have indicated that single-dose formulations are as effective as longer courses, and they are preferred by patients on grounds of convenience.

Fluconazole is presented as a single-dose oral capsule. It is well absorbed when taken by mouth, reaching peak serum concentrations within one to two hours of administration; the elimination half-life is about 30 hours.

Administration and dosage

Night-time use is recommended for intravaginal preparations as the patient will be lying down for several hours, thus allowing the drug a chance to act and avoiding the problems of seepage and loss that would occur if the patient were upright and moving around. Oral fluconazole is more convenient from this point of view and can be taken at any time of day.

- Clotrimazole
  - — Vaginal cream (10 per cent: 5 g at night as a single dose)
  - — Pessaries (1 × 500 mg as a single dose at night, 1 × 200 mg nightly for three nights or 1 × 100 mg nightly for six nights)
  - — Topical cream (1 per cent and 2 per cent: apply to the anogenital area two to three times a day)
- Econazole
  - — Pessaries (150 mg formulated for single-dose therapy, one at night as a single dose; standard formulation, 1 × 150 mg nightly for three nights)
  - — Topical cream (1 per cent: apply to the anogenital area twice daily)
- Fluconazole
  - — Oral capsule (150 mg – one as a single dose)

Adverse effects, cautions and contraindications

Burning and irritation may occur with the topical imidazoles, and contact dermatitis has been reported. However, it is thought that the amount of these drugs absorbed from the short courses used to treat vaginal candidiasis is insufficient to cause adverse systemic effects. The bases used in some preparations damage latex condoms and diaphragms; package inserts provide information.

Adverse effects associated with oral fluconazole are mainly

gastrointestinal, including abdominal pain, diarrhoea, nausea and vomiting and flatulence. Teratogenicity has occurred in animals with high doses of fluconazole, and the drug is also excreted in breast milk. However, the licensing conditions for all non-prescription azoles prohibit their use in pregnant and breast-feeding women. Fluconazole should also be used with caution in patients with impaired renal or hepatic function.

In order to minimise any risk of adverse effects or inappropriate use, the MCA has imposed a number of conditions and prohibitions on the supply of azoles without prescription, which include the following:

- They should only be supplied to women who have had vaginal candidiasis diagnosed previously by a doctor. This is to exclude the possibility that a patient may be suffering from another type of vaginal infection, which will have to be treated with drugs available only on prescription. If a woman has had a previous diagnosis of candidiasis, she will know what the symptoms should be.
- They should not be supplied to patients who have had more than two attacks of candidiasis in the previous six months, as this could indicate an underlying cause, such as diabetes, which needs to be investigated.
- They should not be supplied to women under 16 or over 60 years of age. Vaginal candidiasis is rare in these age groups, as the oestrogen necessary to create the conditions which favour the growth of *C. albicans* is lacking. However, lack of oestrogen increases susceptibility to other vaginal infections.
- They should not be supplied to pregnant or breast-feeding women. Teratogenicity has occurred in animals with high doses of fluconazole and other systemic imidazoles, and although there is no evidence of such an effect with locally administered preparations or a single oral dose, the MCA has decided that the potential risks should be considered by a patient's doctor before a supply is made.
- They should not be supplied to patients reporting symptoms

such as vaginal bleeding, dysuria, pain in the lower abdomen or sores or blisters in the genital area, which might indicate more serious conditions than candidiasis.

- They should not be supplied to patients with a previous history of sexually transmitted disease or who have been in contact with a partner with such a history, as other infections apart from candidiasis may be present.

Interactions

Fluconazole interacts with a number of drugs, including those that are metabolised by cytochrome P450 enzymes. It can increase plasma concentrations of several drugs that have narrow therapeutic margins such as warfarin, theophylline and phenytoin. It also increases plasma concentrations of sulphonylureas, tacrolimus and ciclosporin. Rifampicin increases the metabolism of fluconazole, resulting in reduced plasma concentrations. These interactions are unlikely to be clinically significant with a single dose of fluconazole.

Products

- Clotrimazole
  - — Candiden Cream (topical: 1 per cent)
    Akita Pharmaceuticals
  - — Candiden Vaginal Tablets (500 mg)
    Akita Pharmaceuticals
  - — Canesten Cream (topical: 1 per cent)
    Bayer Consumer Care
  - — Canesten Thrush Cream (topical: 2 per cent)
    Bayer Consumer Care
  - — Canesten Once (vaginal cream: 10 per cent)
    Bayer Consumer Care
  - — Canesten Pessaries (100 mg, 200 mg, 500 mg)
    Bayer Consumer Care

- — Canesten Combi (500 mg pessary and topical cream 2 per cent)
  Bayer Consumer Care
- — Pivacom (500 mg pessary)
  Typharm

- Econazole
  - — Ecostatin Cream (topical: 1 per cent)
    Bristol-Myers Squibb Pharmaceuticals
  - — Gyno-Pevaryl Cream (vaginal and topical: 1 per cent)
    Janssen-Cilag
  - — Gyno-Pevaryl Pessaries (150 mg, triple application)
    Janssen-Cilag
  - — Gyno-Pevaryl 1 Pessary (150 mg, single application)
    Janssen-Cilag
  - — Gyno-Pevaryl Combipack (150 mg pessaries, triple application and topical cream)
    Janssen-Cilag
  - — Gyno-Pevaryl CP (150 mg pessary, single application and topical cream)
    Janssen-Cilag
  - — Pevaryl Cream (topical: 1 per cent)
    Janssen-Cilag

- Fluconazole
  - — Diflucan One oral capsule (150 mg)
    Pfizer Consumer Healthcare

TREATMENT – POVIDONE-IODINE

Mode of action

Povidone-iodine is an iodophore in which povidone, a vinyl polymer, acts as a carrier for iodine allowing its gradual release for antimicrobial

and antiseptic effect. It is less potent than preparations containing free iodine but is also less toxic. It has activity against a wide range of micro-organisms, including fungi, but is less effective than the azoles and requires twice-daily administration for up to 14 days. It should not be used in pregnancy or if breast-feeding, due to the risk of iodine interfering with infant thyroid function.

Products and dosage

- Betadine Vaginal Pessaries (200 mg – one inserted twice daily)
  SSL International
- Betadine VC vaginal cleansing kit (10 per cent solution with a special bottle and vaginal applicator – for daily use diluted as a douche)
  SSL International
- Betadine Vaginal Gel (10 per cent – 5 g daily in association with pessaries or douche)
  SSL International

PRODUCT SELECTION POINTS

- All imidazole compounds for local application appear to be equally effective.
- Single-dose topical formulations are as effective as longer courses and obviate compliance problems.
- Single-dose oral fluconazole is as effective as preparations for local use and is generally preferred by patients. Possible disadvantages are the higher price and the slightly higher risk of adverse effects due to greater systemic absorption.

PRODUCT RECOMMENDATIONS

A single-dose imidazole pessary, vaginal tablet or vaginal cream, or fluconazole oral capsule (best avoided in patients taking medication with which it interacts).

A topical cream for use on the external genitalia, if necessary.

Vaginitis and vaginal dryness

Vaginitis and vaginal dryness are due to atrophic changes which reduce secretions and alter their pH, increasing susceptibility to infection, and sexual intercourse can become painful.

CAUSES

Vaginitis and vaginal dryness can be caused by oestrogen deficiency following the menopause.

TREATMENT

For many women these problems are avoided or remedied by use of hormone replacement therapy or intravaginal oestrogen preparations, which are available on prescription. However, hormonal therapy is unsuitable for some women and others choose not to use it, and non-prescription products are available to counteract problems of vaginal dryness and reduction in acidity.

Products, actions and use

Products available are inert aqueous gels.

K-Y Jelly (Johnson & Johnson MSD) provides short-acting lubrication and can be applied immediately before sexual intercourse.

Replens (Anglian Pharma) is a bioadhesive product containing polycarbophil, a polymer which holds up to 60 times its weight in water, and has the ability to adhere to vaginal epithelial cells. The manufacturer claims that an application stays in place for up to 72 hours, until the cells to which it adheres are naturally discarded, and that, as well as lubricating, the product moisturises the vaginal walls by driving water into the underlying cells. Polycarbophil is acidic and reduces vaginal pH to premenopausal levels, thereby increasing resistance to infection. Replens can be used three times a week continuously. (Feminesse is an identical product marketed by the same company.)

Aci-Jel (Janssen-Cilag) contains acetic acid in an aqueous base buffered to pH 4, which is about the premenopausal level of acidity of the vagina; it is used daily.

Verrucas

(continued . . .)

Verrucas (plantar warts) are benign infections of the epidermis on the sole of the foot.

CAUSES

Verrucas are caused by the human papillomavirus and result in hyperkeratinisation. A verruca is simply a wart which has been compressed by the weight put upon it, and is painful because of pressure exerted on the nerve endings. Verrucas are most common in children, and although they resolve spontaneously they are usually actively treated as resolution can take from months to years.

TREATMENT

Treatment is by gradual removal of the hyperkeratotic skin layers and the viral core by keratolytic agents.

Several products are marketed for the removal of corns and calluses and also for warts and verrucas. Compounds used include:

- Salicylic acid
- Lactic acid
- Podophyllum resin
- Formaldehyde
- Glutaraldehyde
- Silver nitrate

Salicylic acid

Mode of action

When used in the treatment of warts and verrucas, salicylic acid reduces viral numbers by mechanical removal of infected tissue; it also stimulates production of protective antibodies in response to the mildly irritant effect of the acid. Salicylic acid is a constituent of many

wart and verruca treatments, both alone and in combination with other ingredients. Some products are the same as those marketed for corns and calluses.

Product examples

- Salicylic Acid Collodion BP (12 per cent: see section on corns and calluses)
- Bazuka Extra Strength (26 per cent in a film-forming gel)
  Dendron
- Occlusal (26 per cent in a polyacrylic vehicle)
  DermaPharm
- Scholl Verruca Removal System (medicated discs containing 40 per cent)
  SSL International
- Verrugon Complete (ointment containing 50 per cent)
  Pickles

Lactic acid

Mode of action

Lactic acid has corrosive properties and is included with salicylic acid in several verruca products. It is claimed to enhance the effects of salicylic acid but a United States Food and Drug Administration advisory panel found insufficient evidence to demonstrate this. Care must be taken that preparations do not spread on to unaffected skin.

Product examples

- Containing 16.7 per cent lactic acid, with salicylic acid 16.7 per cent in a collodion base

— Duofilm
Stiefel

— Salactol Wart Paint
Dermal

- Containing 4 per cent lactic acid, with salicylic acid 11 to 12 per cent in a film-forming gel

— Bazuka
Dendron

— Cuplex Gel
Smith & Nephew

— Salatac Gel
Dermal

Podophyllum resin

Mode of action and adverse effects

Podophyllum resin (podophyllin) is obtained from the dried rhizome of the May-apple (*Podophyllum peltatum*). It has a potent corrosive action, and for non-prescription use it is solely indicated for plantar warts. It is cytotoxic and a caustic and powerful skin irritant, and care must be taken to confine its application to the verruca only. There have also been reports of teratogenicity and it is contraindicated in pregnancy.

Product

There is only one product:

- Posalfilin ointment (podophyllum resin 20 per cent, plus salicylic acid 25 per cent)
Norgine

Formaldehyde

Mode of action

Formaldehyde has antiviral activity; it also has a direct anhidrotic action, drying the verruca and surrounding skin.

Products

- Veracur Gel (formaldehyde 0.75 per cent in an aqueous gel base – a disadvantage is that it must be used twice daily)
  Typharm
- Solution of formaldehyde (3 per cent – can be used for daily foot soaks if there are a large number of verrucas, although care must be taken to protect unaffected skin)

Glutaraldehyde

Mode of action

Glutaraldehyde has similar properties to formaldehyde. However, it appears to have no advantage over formaldehyde and may be a more potent skin sensitiser. It stains skin brown, but this fades once treatment is discontinued.

Product

There is only one product:

- Glutarol Wart Paint (10 per cent)
  Dermal

Silver nitrate

Mode of action

Silver nitrate is a caustic agent; it is used in the form of a stick or pencil (95% toughened with 5% potassium nitrate) to destroy warts, verrucas and other skin growths. Unlike other treatments for verrucas, silver nitrate pencil is used for only a short period; the manufacturer of the only commercially available product claims that three daily applications are sufficient, but that a maximum of six may be made.

Product

There is only one product:

- AVOCA Wart and Verruca Set
  Bray Health and Leisure

Application and use

Removal of verrucas is achieved by a process of gradual abrading of the infected tissue, and the same basic method is used for all preparations. The following are points of advice that should be given to patients:

- Before application, gently rub away the top layer of skin with a file, emery board or pumice stone.
- Apply the preparation directly to the top of the verruca, taking precautions to confine it to that area.
- Cover the verruca with a plaster to encourage maceration and improve penetration of the medicament.
- Remove the plaster after 24 hours and file away the dead tissue on top of the verruca.
- Repeat the process daily until all trace of the verruca has been

removed; this may take up to three months (except for silver nitrate – see above) but the verruca may regrow if all infected tissue has not been removed.

PRODUCT SELECTION POINTS

- Collodion-based paints containing 12 to 16 per cent salicylic acid are considered to be the best form of treatment.
- There is little evidence that the inclusion of lactic acid in preparations adds to the effectiveness of salicylic acid.
- Other verruca preparations have little to commend them in comparison to salicylic acid.

PRODUCT RECOMMENDATIONS

Salicylic Acid Collodion BP or similar preparation.

Warts

Warts are benign growths which occur most frequently on the hands and fingers, and less commonly on the elbows and knees.

CAUSE

Like verrucas, warts are caused by the human papillomavirus and apart from their location, and the fact that they are usually painless because they are not compressed, they are identical to verrucas (see section on verrucas).

TREATMENT

Treatment is essentially the same as for verrucas and nearly all the products available are licensed for both warts and verrucas.

Of the products listed under verrucas, most are licensed for treatment of both common and plantar warts. Some are licensed exclusively for the latter because they are presented as kits containing plasters or pads to relieve pain resulting from pressure exerted by body weight on plantar warts. Only Posalfilin (Norgine) is restricted to treatment of plantar warts by virtue of one its constituents – podophyllum resin.

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