

Essential Drugs

Diseases of the skin (continued)*

The infectious dermatoses and other skin conditions that are particularly prevalent in developing countries were discussed in the previous issue of this journal. The following account is concerned with the more diverse spectrum of dermatological diseases which occur worldwide and which, in many instances, result from immunological disturbances in predisposed individuals. The coverage is not comprehensive. Emphasis is given to those conditions which can be managed largely on an outpatient basis. Drug induced eruptions and chronic diseases, in which skin lesions are a manifestation of generalized systemic disease, will be covered in a separate account.

Acne vulgaris

Acne is an inflammatory disease of the pilosebaceous units in the skin of the face, neck, chest and upper back. Typically, it first appears during puberty when androgenic stimulation triggers excessive production of sebum. This results in abnormal follicular keratinization, colonization by a Gram-positive bacterium — *Propionibacterium acnes* — and local inflammation. It is possible, but not proven, that *P. acnes* promotes inflammation by hydrolysing lipid esters to irritant fatty acids.

Clinically, the disease varies in intensity from a trivial condition, in which a few comedones (dilated pilosebaceous cysts containing sebum, cornified epithelium, bacteria and saprophytic yeasts) leave small atrophic scars, to a severe disfiguring disease in which cysts, nodules and sinuses form in areas of intense inflammatory reaction. Scarring is sometimes followed by keloid formation, particularly among Africans. The disease has been claimed to be less common among vegetarians, but there is no evidence that the course of the disease can be influenced by dietary manipulation.

Occasionally, systemic or topical exposure to specific chemicals is implicated. These include:

- orally-administered drugs, notably corticosteroids, isoniazid, lithium carbonate, phenytoin and halogen-containing sedatives and expectorants;

* The first part appeared in *WHO Drug Information*, 6(2): 60-74 (1992)

- topical exposure to irritant oils or cosmetics;
- environmental exposure, even in minute amounts, to dioxin or halogenated phenolic compounds.

Management

Exposure to agents suspected of causing or aggravating the condition should be avoided or minimized.

The aims of drug therapy are to reduce secretion of sebum and follicular keratinization, and to inhibit infection and inflammation. Mild cases usually respond satisfactorily to topical therapy alone. Systemic use of antibiotics, estrogens, anti-androgens or retinoids should be reserved for severe and unresponsive cases.

Systemic treatment must be invariably sustained for several months before a response can be anticipated. During this time topical preparations should be applied concomitantly to affected areas to prevent new lesions from developing.

Topical therapy

Benzoyl peroxide, which promotes desquamation and has a potent bactericidal action, is most widely used. Gel formulations are claimed to be more effective than creams or ointments, but they are also more irritant. Treatment is usually started with a 2.5 % preparation applied every other day. The strength and frequency of application is later increased as the irritant reaction subsides.

Preparations containing sulfur — which also has a bactericidal action and promotes desquamation — continue to be used, often in formulations containing salicylic acid as a keratolytic agent.

Retinoic acid is claimed to be more effective than benzoyl peroxide when applied topically, but it is considerably more expensive. It reduces follicular hyperkeratosis by stimulating turnover of epithelial cells. A variable degree of irritation is induced which is aggravated by exposure to ultraviolet light. The required dosage can be reduced by concomitant treatment with topical or systemic antibiotics or with topical benzoyl peroxide.

Topical antibiotics, although widely used when signs of inflammation are prominent, hold a disputed place in the treatment of acne. Erythromycin, tetracycline and clindamycin are widely used. Treatment must be maintained for 2 to 3 months before any benefit is obtained and this prolonged treatment carries risks of sensitization, of folliculitis due to invasion of resistant Gram-negative bacteria, and of selection and spread of antibiotic-resistant organisms.

Systemic therapy

Systemic administration of antibiotics, estrogens, antiandrogens or retinoids should be considered only when topical treatment fails or when severe cystic acne threatens to result in substantial scarring.

The clinical response to systemically administered antibiotics is probably not directly dependent upon the antimicrobial action. Penicillins, for instance, are likely to be effective only in cases of Gram-negative folliculitis, even though they are bactericidal to *P. acnes*. Low doses of tetracycline (0.5 to 1.0 gram daily) are most widely used and, when they are contraindicated, erythromycin is commonly substituted. To be effective, treatment has to be maintained for at least 6 months, during which time *P. acnes* can become resistant to tetracyclines and the normal bowel flora may be overgrown by *Clostridium difficile*, exposing the patient to a remote but potentially fatal risk of pseudomembranous colitis.

Estrogens and antiandrogens, which produce clinical remission by reducing secretion of sebum, can be used only in women because of their feminizing action. Combined oral contraceptives are often effective when administered at normal dosages. Products containing norethisterone are favoured because, by raising circulating concentrations of sex-hormone binding globulin, they reduce plasma concentrations of free testosterone. The antiandrogen, cyproterone acetate — administered in combination with the estrogen, ethinylestradiol, to assure a contraceptive action — has been claimed to be more effective.

The oral retinoic acid derivative, isotretinoin, which is a more potent inhibitor of sebum production, is the most effective treatment available for severe cystic acne. However, it is very expensive; it often induces signs of hypervitaminosis A, including cheilitis, dry eyes, generalized xerosis, pruritus and paronychia; and, most problematic of all, it is a proven and potent human teratogen. Even where the most rigorous precautions have been exercised

both by the manufacturer and by prescribers to exclude pregnancy before treatment is instituted, and to ensure that effective contraception is practised throughout treatment and for at least three months after its withdrawal, congenital abnormalities attributed to intrauterine exposure to the drug are still occasionally reported.

Pruritus

Itching is thought to result from the release of histamine from mast cells in the dermis. It is a persistent and distressing symptom of many skin disorders, but it also occurs in apparently healthy people, and particularly among adults living in tropical climates.

Non-specific pruritus, unaccompanied by other evidence of skin disease, is commonly diffuse and can be aggravated by restrictive clothing. In temperate climates, it is often exacerbated by warm weather. Elderly patients, in particular, should be carefully examined to exclude specific skin conditions, incipient jaundice and other systemic causes of pruritus.

Management

Frequent applications of calamine lotion often provide useful relief. Hydrocortisone applied sparingly and intermittently in low concentrations sometimes provides additional relief when the sensation remains troublesome. Systemic antihistamines are justified only in severe, refractory cases.

Urticaria

Urticaria (hives) is a non-specific vascular response to a wide variety of stimuli. It is determined by genetic, immunologic and other largely unknown factors and it is triggered by chemical and physical stimuli including cholinergic activity, sunlight, localized pressure, heat and cold. As many as 20% of persons probably experience the condition at some time in their lives. It is characterized by cutaneous weals — erythematous pruritic papules — that blanch on pressure. Angioedema is a variant that predominantly affects the mucous membranes. Most episodes are transient but, particularly in patients with autoimmune thyroid disorders, lesions may persist for many months.

Hereditary angioedema is an autosomal dominant trait. Weals typically spread in annular fashion in response to trauma. A similar disorder sometimes occurs in patients with lymphoproliferative diseases; lymphosarcoma and chronic lymphocytic leukemia.

Cholinergic urticaria is common in young adults after vigorous exercise or emotional stress. It is often accompanied by other signs of cholinergic activation including abdominal cramps, dizziness and wheezing. The lesions are usually confined to the trunk. Most regress within 30-60 minutes but occasionally they are more persistent and tend to coalesce.

Solar urticaria develops within minutes of exposure to direct sunlight and resolves completely within an hour of withdrawing. Some persons are even sensitive to light that has been filtered through window glass.

Dermographism, in which weals are induced by scratching or rubbing of the skin is probably genetically determined. However, an allergic mechanism seems to be involved, since it has been transferred passively by intradermal injection of serum from affected patients.

Cold urticaria is often, but not invariably, familial. Localized pruritus, erythema, and swelling develop rapidly in response to a cold stimulus. Predisposed individuals risk shock, loss of consciousness and even death from drowning if they plunge into cold water.

Urticarial vasculitis, which is sometimes associated with systemic lupus erythematosus, shares the clinical features of other causes of urticaria but it is a totally different condition resulting from necrotizing vasculitis which is probably caused by deposition of immune complex. It cannot be managed symptomatically. It must be treated as a manifestation of systemic lupus.

Management

Urticaria, even in its more chronic forms, is usually self-limiting. Identification and avoidance of causative stimuli is the only practicable approach to prevention in most instances. Patients with any form of urticaria are often sensitive to acetylsalicylic acid and to specific foods including meats, shellfish, tomatoes, chocolate and fresh berries.

Selective desensitization, which may be directed to physical as well as chemical stimuli, is sometimes effective. Frequent hot baths for patients with cholinergic urticaria and controlled graduated exposure to UV light for those with solar urticaria sometimes induce a useful measure of tolerance.

The aim of symptomatic treatment is to deplete stores of histamine or to inhibit its release from mast cells, or to block either agonist drugs or receptor sites competitively. Antihistamines that are

claimed to be non-sedating possibly hold advantage and they should be given regularly until all signs have been suppressed for at least 2 to 3 days. Patients resistant to antihistamines sometimes respond to cromoglycate sodium, which inhibits histamine release by stabilizing mast cell membranes.

Psoriasis

Psoriasis, which affects people of all ages in every country, is one of the commonest of the chronic dermatoses. It is estimated, overall, to affect about 2% of the population of the United States and northern Europe. Considerable local variations in its prevalence have been variously attributed to climatic, nutritional and ecological factors. It is recognized to be genetically determined, but the precise mode of inheritance is unknown. Various biological events may trigger its expression, including streptococcal or viral infection, an emotional crisis or pregnancy. Other cases appear to be related to the administration of specific drugs including lithium, chloroquine and beta-adrenergic blocking agents.

Psoriasis vulgaris, the most common form of the disease, is characterized by erythematous, scaly plaques of varying size. These are usually confined to the scalp, elbows and knees, although disabling widespread extension, described as **erythrodermic or exfoliative psoriasis**, frequently occurs. Histologically, the lesions show intense proliferation and incomplete differentiation of the epidermal keratinocytes, abnormal endothelial changes in the dermal blood vessels, and infiltration of activated neutrophils and T lymphocytes into the dermis and epidermis. Acute inflammatory exacerbations characterized by a severe febrile reaction and pustule formation are commonly a consequence of inappropriate treatment. About 10 % of patients develop a destructive peripheral inflammatory arthritis of the hands and feet which is sometimes associated with ankylosing spondylitis. Psoriasisiform skin lesions are also seen in some patients with Reiter's syndrome and subacute cutaneous lupus erythematosus.

Guttate psoriasis, which occurs mainly in children, is characterized by the sudden appearance of smaller but widespread lesions. The condition sometimes resolves spontaneously, but most cases ultimately transform into psoriasis vulgaris.

Management

Many different approaches to treatment are used. Each has advantages and shortcomings and none reliably assures remission from relapse.

Topical applications

Localized psoriasis vulgaris can frequently be cleared, sometimes for many months, by daily applications of dithranol cream for 2 to 4 weeks. A "short contact" method in which each application is rinsed off within 30 to 60 minutes causes slight, if any, irritation or staining of normal skin. This is particularly useful for outpatient management although there is a risk of severe conjunctivitis if the paste accidentally enters the eye.

Topical corticosteroids should be reserved for short-term treatment of active lesions on the scalp, face, palms and soles. More extensive applications are inappropriate. They neither induce remission nor are they effective in clearing plaques and there is always a danger of rebound after withdrawal, resulting in a more unstable form of psoriasis. Systemic corticosteroids should not be used under any circumstance. They are not reliably effective and their withdrawal frequently induces a severe exacerbation of the disease.

Resistant lesions need to be treated in hospital either with prolonged applications of dithranol in increasing concentrations or, when lesions are widespread as in erythrodermic and guttate psoriasis, with coal tar. The latter has a wider margin of safety, but patients need to be highly motivated to tolerate the mess and smell of coal tar dressings in the home. Both liquid tar and crude coal tar are available in various solutions and ointments, some of which also contain salicylic acid as a keratolytic. Better results are often obtained when daily applications or baths are combined with ultraviolet irradiation. Preliminary results, which have yet to be confirmed, suggest that calcipotriol, a vitamin D₃ analogue, which promotes the differentiation of epidermal keratinocytes, offers promise as an effective and acceptable form of topical therapy.

Systemic treatment

Several options exist for the systemic treatment of patients unresponsive to topical therapy. Each, however, is associated with hazards. It is prudent, when treating patients who require extended systemic treatment, to change the drug regimen from time to time to reduce the risk of cumulative toxicity associated with any one agent.

Most lesions can be cleared by combining oral administration of a psoralen, methoxsalen, with 12 to 24 sessions of long-wave ultraviolet A irradiation (PUVA therapy). Light of this wave-length promotes an interaction between the psoralen and DNA in the basal cells of psoriatic plaques with the result that

growth is slowed to normal. The psoralen is taken 2 hours before each session of irradiation. Clearance of lesions can be expected within 5-6 weeks when standard incremental exposure to irradiation is arranged 3 times weekly. This therapy has not been associated with serious systemic complications, although nausea, pruritus and unwanted phototoxic reactions can be troublesome. Any risk of non-melanomatous skin cancer is thought to be negligible if the aggregate life-time therapeutic exposure is no greater than 400 J/cm² UVA and it is possible that the risk may be further diminished by administering each course in fewer, more powerful doses.

In the past, reliance has been placed in the antimetabolite, methotrexate, as a treatment of last resort for patients with recalcitrant and severe cutaneous or arthritic lesions. In some cases it was highly effective, but treatment was sometimes compromised by oral ulceration and gastrointestinal intolerance. Regular monitoring of the blood count was necessary because of the risk of bone marrow suppression and serial liver biopsies were recommended for patients on long-term therapy as the only means of detecting early drug-induced cirrhotic changes. Treatment was contraindicated in patients with pre-existing liver disease or an alcoholic tendency. Several other antimetabolites and immunosuppressive agents, including hydroxycarbamide and azathioprine, have been similarly employed. However, each has been associated with systemic toxicity and, in general, they are considered to be less effective than methotrexate.

More recently, highly impressive short-term results have been reported with the immunosuppressant, ciclosporin, administered for 4 months at daily doses as low as 5 mg/kg. Ciclosporin is vasoactive to the extent that it is contraindicated in hypertensive patients and, even at these low doses, it substantially — but reversibly — reduces glomerular filtration rates. In the short term, this dose does not appear to increase the risk of incidental infection, nor does it seriously derange other physiologically important immunological responses. However, more must be known about the speed and rate of relapse after discontinuation of treatment and the possible toxicity of longer term therapy — including any risk of lymphoma or non-melanomatous skin cancer — before the use of ciclosporin can be regarded as established in the routine management of psoriasis. Those patients that are selected for ciclosporin therapy are probably best transferred back to one of the longer

established treatments for maintenance therapy. Extensive clinical experience has also confirmed that systemic administration of the synthetic retinoid, etretinate, is highly effective in many patients with severe forms of psoriasis. Its mechanism of action remains unknown, but it rapidly attenuates both inflammation and scaling and restores normal histological architecture throughout all skin layers. Most lesions clear within 8 to 12 weeks of continuous daily therapy but plaque-like lesions respond better when etretinate is used in conjunction with PUVA therapy. Etretinate is well tolerated by most patients. However, dryness of skin and mucous membranes can be troublesome, while its association with cases of hepatotoxicity and raised blood lipids render it unsuitable in some patients. Of more general concern is the drug's proven teratogenic potential. No woman of childbearing age should receive etretinate until pregnancy has been positively excluded and — having regard to its prolonged sequestration in fatty tissues — until she has agreed to use an effective method of contraception throughout the period of treatment and for at least 2 years after the last dose is taken.

Seborrhoeic dermatitis

Dandruff, an erythematous, greasy scaling eruption primarily involving the scalp, is the mildest form of seborrhoeic dermatitis and one of the most common of the chronic skin diseases. In its more florid forms, the lesions are more extensive and the inflammatory reaction is more intense.

Pityrosporum yeasts are presumed to play at least a facultative, and possibly a causative role in the development of seborrhoeic dermatitis. Androgens may also be involved since men are more frequently affected. Other factors, including fatigue, stress and infection are claimed to trigger some cases. An association has been established with other diseases, including Parkinson's disease, epilepsy, cardiac failure, zinc deficiency and phenylketonuria.

Management

Application of keratolytic shampoos and exposure to ultraviolet light reduce both the inflammation and scaling.

Shampoos should be massaged into the scalp, immediately rinsed off and reapplied until a foam is produced. The last application should remain in contact with the scalp for at least 5 minutes.

Selenium sulfide is widely used as a keratolytic agent in many proprietary shampoos. A combination of sulfur and salicylic acid, which has an additional antimicrobial action, is also active.

Topical applications of the fungicidal agent, ketoconazole, are also reported to be effective. Because of the associated risk of hepatotoxicity, systemic administration of ketoconazole is not justified in the management of a benign condition that is likely to recur within a short period of time.

Alopecia areata

Alopecia areata is relatively common everywhere. It is characterized by patchy hair loss, usually on the scalp but sometimes elsewhere, within circumscribed oedematous areas of skin. "Exclamation point" hairs can be plucked out at the margins. Diffuse thinning of hair sometimes occurs in the early stages and, in severe cases, the lesions may extend and ultimately result in total hair loss. The lymphocytic T-cells, which are reduced in number in the peripheral circulation, appear to be involved in the cytotoxic process that destroys the hair follicles.

The condition can occur at any age but, typically, it first appears in early adult life, rather more frequently in men than in women. In some patients there is an apparent hereditary predisposition and it is often associated with other diseases: one quarter of the patients have atopic syndrome and less pronounced associations have been described with vitiligo, Down's syndrome, and various autoimmune conditions including thyroid disease and polyglandular syndromes, lupus erythematosus and lichen ruber. In two-thirds of the cases, partial or complete regrowth of hair occurs within five years. After this time spontaneous recovery is unusual.

Management

The response to drug therapy is generally disappointing. The prospect for improvement is uncertain and beneficial results are often short-lasting. Localized regrowth of hair is sometimes stimulated by application of topical corticosteroids or of irritants such as dithranol and retinoic acid. In more severe cases systemic corticosteroids have been used but, given the dangers of this treatment and the uncertain response, even at high doses, it can rarely, if ever, be justified.

Patchy hair loss is sometimes a secondary manifestation of systemic disease. It is vital, particularly before corticosteroids are administered, to exclude autoimmune disorders and infectious diseases,

including syphilis. In general, drug therapy is not warranted in children and adolescents, nor in any patient in whom the condition is stable and the likelihood of spontaneous recovery is relatively high. In most cases, a wig or other cosmetic aid provides a more satisfactory solution.

Pityriasis rosea

Pityriasis rosea is a common self-limiting dermatosis that is presumed to be infective in origin. A prodromal episode of malaise, headache and sore throat often precedes the appearance of the characteristic annular erythematous herald plaque on the trunk, neck or upper limb. Within a few days, a symmetric rash commonly indistinguishable from that of secondary syphilis, becomes apparent, usually on the back. In Caucasians this rash rarely lasts for more than a few weeks, but in more deeply pigmented persons it may be more persistent and more extensive, often involving the face and distal extremities. In these cases scaling of the active lesions and post-inflammatory pigmentary changes can be particularly prominent.

Management

Specific treatment is neither available nor necessary but a serological test to exclude the possibility of syphilis should be undertaken whenever the diagnosis is in doubt. Calamine lotion effectively relieves pruritus in most cases, but topical application of hydrocortisone acetate in a concentration not exceeding 1% is occasionally justified in severe cases.

Photodermatoses

Exposure of skin to solar ultraviolet irradiation is beneficial in moderation since it is vital to the synthesis of vitamin D and hence to satisfactory skeletal development. Excessive exposure, however, is hazardous, particularly in light-skinned persons who tan poorly, and in patients with pathological sensitivity to sunlight.

The damage is most immediately evident as acute sunburn or, in the longer term, as premature aging of the skin. However, excessive exposure is also a predisposing factor in the development of malignant and pre-malignant skin lesions including solar keratosis, squamous cell carcinoma, basal cell carcinoma and malignant melanoma.

The incidence of these neoplastic conditions is particularly high among light-skinned persons living in hot sunny climates. Many cases could be

prevented by persuading parents and those directly at risk of the importance of avoiding sunburn and reducing their exposure to solar radiation. The use of protective clothing — tightly woven fabrics, wide-brimmed hats, long sleeves and long trousers — is highly effective. When this is not practicable or acceptable, it is important to encourage regular use of sunscreen products with a protection factor rating of at least 15.

Pathological photodermatoses

Some patients react idiosyncratically to sunlight, either as a result of genetic predisposition or metabolic disease, or following exposure to specific drugs or chemicals.

Solar urticaria, which is probably immunologically mediated, is characterized by transient weals lasting from a few minutes to one hour. These may be single or multiple, and they develop within minutes or even seconds of exposure to strong sunlight. Antihistamines are of limited value, but long-term administration of chloroquine is claimed to increase the tolerance of the skin to sunlight.

Polymorphic light eruptions occur in vulnerable individuals within hours or days of exposure to sunlight and usually persist for several days. Irritating papules, which may coalesce into plaques, occur on exposed sites. The lesions, which frequently become excoriated, usually subside within 2–5 days if further exposure is avoided. Systemic use of antimalarials, which were once widely used to suppress intense inflammation, has now been largely superseded by topically-applied corticosteroids. Systemic corticosteroids are sometimes needed to treat severe and widespread eruptions.

Actinic prurigo, which occurs among people of American and Asian descent, is probably genetically determined. It first appears during childhood, and it regresses progressively and completely during adolescence and early adult life. Recurrent patchy oedematous erythema results in the formation of persistent excoriated plaques, papules and nodules. Cheilitis is a common feature, particularly during the early phases of the disease. Vesicles and small pitted scars sometimes develop on the face, while chronic conjunctivitis and pterygium formation are common among affected children in South America. Sunscreens, when used regularly, provide a useful measure of protection. The cutaneous signs are suppressed by thalidomide and, to a lesser extent, topical corticosteroids, but they recur within a few weeks of discontinuation of treatment.

Hydroa vacciniforme is a disease of childhood which becomes apparent toward the end of the first ten years of life and regresses spontaneously during adolescence. It is sometimes associated with atopy and, while several members of the same family are often affected, it has no clear genetic basis. Tense necrotic blisters and papules form where exposure to intense sunlight has induced oedematous erythema. This is followed by crusting and eventually by varioliform scars. These changes occur at intervals throughout periods of exposure and, over a period of several years, they become less intense and eventually cease. Chloroquine and beta carotene are reputed to be of value in suppressing the reaction but no comparative clinical trials have been undertaken.

Chemical photodermatoses are phototoxic reactions caused by sensitization to a systemically or topically administered inducing agent. Sulfonamides, salicylanilides, phenothiazines, quinoxaline dioxide, tar products, dyes, psoralens, plant constituents, fragrances, animal feeding stuffs, and topical sunscreens are most frequently responsible. Following sensitization, exposure to sunlight or other sources of ultraviolet radiation results in erythema, sometimes with oedema. All exposed skin areas may be affected if the sensitizing agent is ingested. Lesions resulting from topical application are usually limited to sites of chemical contact and blistering may be extensive. Symptomatic treatment with systemic antihistamines and acetylsalicylic acid can alleviate discomfort, pruritus and erythema. Prevention is dependent upon avoidance of contact with presumed causative agents.

Ichthyosis

Various factors, both hereditary and acquired, are determinants of ichthyosis, which is characterized by defective desquamation of the skin.

Ichthyosis vulgaris, an autosomal dominant disease which occurs worldwide, is the most common of the hereditary varieties. Small, rough, dry, whitish scales, which are most apparent on the extensor surfaces of the arms and legs, and to a lesser extent on the back, typically first appear during the first few years of life and tend to regress with age. About half the patients also have atopic dermatitis and other signs of atopy. The course of the disease is largely unpredictable, but it is often exacerbated by environmental factors and particularly by cold. In severe cases the cornified layer of the epidermis is greatly thickened, but the underlying

granular layer is often thinned and sometimes absent.

Sex-linked ichthyosis, which is a recessive disorder, becomes apparent during infancy. It differs histologically and clinically from ichthyosis vulgaris. Larger, brownish scales thicken the cornified layer, but the granular layer remains essentially normal. With the exception of the central areas of the face, the palms and the soles, virtually all skin surfaces, including flexural regions, are affected and the front of the trunk tends to be more severely involved than the back. Corneal opacities frequently develop during adulthood, but they rarely impair visual acuity.

Acquired ichthyosis is most prevalent in tropical climates where it is associated with nutritional deficiency disorders, long-standing lepromatous leprosy and other debilitating infectious diseases. Clinically, it resembles ichthyosis vulgaris, but it develops later in life as a secondary manifestation of other diseases, and there is no evidence of familial predisposition.

Treatment

Simple precautionary measures are important. Detergents and other degreasing agents should be avoided. Baths should be tepid rather than hot, and soap should be used sparingly. Adequate protective clothing should be worn in cold weather and centrally-heated premises should be humidified.

An emollient such as propylene glycol should be applied weekly, or daily in more severe cases, to affected skin. The addition of a keratolytic, such as 5% salicylic acid or lactic acid can be helpful. Occlusion therapy using 60% propylene glycol in water is more effective in less responsive patients where circumstances permit. However, it is inappropriate where the climate is hot or conditions are unhygienic and; because of the risk of secondary infection, it should always be employed sparingly. In adverse conditions, a cream containing 10% urea, which is claimed to have moisturizing, keratolytic and antimicrobial properties, may prove more effective than an emollient. Sodium chloride is sometimes added to augment the moisturizing effect.

Topical or systemic administration of retinoids, which have an antiproliferative action, are unlikely to be of value except in rare forms of ichthyosis in which hyperkeratosis is a consequence of hyperproliferation rather than defective desquamation.

Bullous dermatoses

These diseases, which are characterized by the formation of multiple blisters in the epidermis and mucous membranes, result from localized destruction of intercellular cement. This process of acantholysis, which ultimately results in failure of the barrier function of the skin, is mediated by autoantibodies directed against the cell surfaces of keratinocytes. The most prevalent clinical forms, which differ in their severity and prognosis, are pemphigus and dermatitis herpetiformis.

Pemphigus

Pemphigus vulgaris and a less severe variant, pemphigus foliaceus, in which the blisters are more superficial and mucous membranes are spared, are the most common variants of this condition. Occasionally, particularly after exposure to sunlight, the lesions become confluent and give rise to a form of exfoliative dermatitis.

Pemphigus vulgaris is typically a disease of middle age. It is most prevalent in eastern India, in south-east Asia and among patients of Jewish descent. Elsewhere, it is rare. Occasional cases follow exposure to penicillamine or captopril and associations have also been described with thymoma, myasthenia gravis and other immunopathic conditions. Painful erosions in the mouth often precede skin lesions by several months. Fragile flaccid blisters develop in the deeper layers of the cutaneous epidermis in non-inflamed skin, typically on the scalp, chest and intertriginous areas. They extend readily on digital pressure and they often rupture giving rise to large areas of weeping denuded skin. Ulceration of mucosal surfaces is common and can be extensive. Untreated, most patients die within 5 years from secondary sepsis, electrolyte imbalance and emaciation.

Pemphigus vegetans is a clinically distinct variant of the disease in which skin lesions are largely limited to intertriginous areas and the scalp, and appear as crusted papillomatous lesions. In time, most cases progress to pemphigus vulgaris.

Treatment

The removal of skin debris from blistered areas is facilitated and the risk of secondary infection is reduced by regular four-hourly application of compresses soaked in either 5% aluminium diacetate or 0.1% potassium permanganate.

Corticosteroids, which must be administered systemically at high dosage, offer the only means of holding the disease in check. Once the condition becomes stabilized, the dose is gradually attenuated to the minimum necessary to maintain quiescence. Commonly, prednisolone is administered orally at an initial dose of 500 mg daily. Once improvement is apparent the dose can usually be reduced rapidly to some 50 mg daily. Further cautious tapering of the dose over several months is often possible. Decrements should not exceed 5–10 mg within any 7-day period. Treatment needs to be maintained until the pemphigus antibody is no longer detectable in the blood and the initial dose should be reinstated immediately should reactivation occur.

Concomitant use of immunosuppressive agents, such as azathioprine or cyclophosphamide, can be of value when the maintenance steroid requirement cannot otherwise be reduced to acceptable levels. The steroid sparing effect develops gradually and is rarely perceptible within 4 to 6 weeks. Corticosteroids should be withdrawn before the immunosuppressive agent is discontinued.

A high-calorie, high-protein diet is required for as long as the disease remains active. Fluid and electrolyte balance should be carefully monitored. Systemic antibiotics may be needed to treat secondary infections.

Bullous pemphigoid, which occurs in elderly patients, is less common and generally less severe than pemphigus. Spontaneous remission can occur and not all patients require systemic treatment. Tense blisters, which tend to heal spontaneously, form in inflamed skin in the axillary and inguinal folds. Their rupture does not result in large denuded areas of skin.

Treatment

Patients who need systemic therapy often respond to dapsone alone. In more severe cases corticosteroids are additionally required. As in the case of pemphigus, treatment should be continued until serum is clear of detectable antibody and then withdrawn gradually.

Dermatitis herpetiformis is a chronic, relatively benign disease that typically first appears in early adulthood and is characterized by alternating phases of activity and remission. Pruritic papular vesicles develop symmetrically on the buttocks and the extensor surfaces of the knees and elbows. The condition is often associated with gluten-sensitive

enteropathy and, in some cases at least, the disease appears to be an expression of sensitivity to dietary gluten or iodine.

Treatment

All patients require life-long treatment. Many respond adequately to a gluten-free diet alone, but others require long-term anti-inflammatory therapy. Most experience has been gained with dapsone which has been claimed to block the release of chemotactic factors from neutrophils. Used at an initial dose of 100 mg daily, it suppresses the formation of new lesions within 24-48 hours and dramatically reduces pruritus. However, its use is justified only when the quality of the patient's life is compromised since prolonged administration invariably induces a degree of haemolytic anaemia and methaemoglobinaemia. Dosage should be adjusted to the minimum that will suppress symptoms. In some cases the daily requirement is as high as 400 mg daily. Others remain in prolonged remission on as little as 25 mg daily.

BENZOYL PEROXIDE

cream or lotion 2.5%, 5%, 10%

Benzoyl peroxide is a keratolytic agent with bacteriostatic activity against *Propionibacterium acnes*.

It is absorbed to some extent by the skin after topical application and metabolized to benzoic acid.

Uses

Topical treatment of mild to moderate acne vulgaris and as an adjunct to therapy in more severe cases.

Dosage and administration

Apply to clean skin initially once daily, gradually increasing to twice daily as tolerance develops. It should not be applied to inflamed or broken skin.

Contraindications

Known hypersensitivity.

Precautions

Avoid contact with the eyes and mucous membranes.

Adverse effects

Irritation to the skin is common after topical application but subsides with continued treatment.

Rarely, contact sensitivity has been reported.

Storage

Benzoyl peroxide should be stored in well-closed containers and should not be allowed to freeze.

CALAMINE LOTION

Calamine is a basic zinc oxide or carbonate coloured with ferric oxide. It has a mild astringent action on the skin.

Uses

Symptomatic topical treatment of mild pruritus.

Dosage and administration

Apply to affected skin 3-4 times daily.

Contraindications

Known hypersensitivity

Precautions

Avoid contact with the eyes and the mucous membranes of the mouth, nose, and genito-anal region.

Storage

Calamine lotion should be stored in well-closed containers in a cool place.

CHLORPHENAMINE

tablet 4 mg (as hydrogen maleate)

Chlorphenamine is a propylamine-derivative antihistamine. It reversibly and competitively inhibits the binding of histamine to H_1 receptors. It is well absorbed following oral administration and it is widely distributed throughout the body including the central nervous system. Plasma concentrations peak after 2-3 hours. It is metabolized in the liver and excreted in the urine, largely as metabolites.

Uses

Symptomatic treatment of urticaria. Severe and intractable pruritus.

Dosage and administration

Dosage of chlorphenamine should be adjusted according to the patient's response and tolerance. *Adults and children over 12 years:* 4 mg every 6 hours.

Children under 12 years: 0.35 mg/kg daily administered in 4 divided doses.

Contraindications

Antihistamines should not be administered to neonates.

Precautions

The anticholinergic effects of chlorphenamine can cause drowsiness, dizziness, blurred vision and

psychomotor impairment. These effects can seriously impair the patient's ability to drive and use machinery.

Use in pregnancy

Safe use in pregnancy has not been established. Chlorphenamine should be used only when the need of the mother outweighs any possible harm to the fetus.

Adverse effects

The most common adverse effect is sedation which can vary from mild drowsiness to deep sleep but patients rapidly develop tolerance. Other unwanted central effects include dizziness, lassitude, incoordination and blurred vision. Paradoxical excitation in children and confusional states in the elderly have been reported.

Newer H₁ antagonists which do not cross the blood-brain barrier rarely produce these effects.

Gastrointestinal symptoms including anorexia, nausea, vomiting, epigastric distress, and constipation or diarrhoea are also common.

Drug interactions

Alcohol and other drugs acting on the central nervous system have an additive sedative effect. Phenytoin toxicity has resulted from inhibition of its metabolism. Monoamine oxidase inhibitors intensify the anticholinergic effects.

Overdosage

Drowsiness, dizziness and ataxia are the most common symptoms of acute overdosage. Anticholinergic effects including flushing, dilated pupils and hyperthermia occur within 2 hours of ingestion. In serious cases, seizures are followed by respiratory and cardiovascular depression.

Emesis or gastric lavage followed by administration of activated charcoal is of value within a few hours of ingestion. Treatment is otherwise symptomatic and is directed to maintenance of respiration and treatment of seizures and cardiovascular abnormalities.

Storage

Tablets should be stored in well-closed containers, protected from light.

DAPSONE

tablet 50 mg, 100 mg

Dapsone, a sulfone, which is of prime importance in the treatment of leprosy is also used in the treatment of certain bullous dermatoses. The mecha-

nism of action is unknown but it is claimed to block the release of chemotactic factors from neutrophils and may act as an immunomodulator.

Following its absorption from the gastrointestinal tract dapsone is distributed widely in body tissues and it is subsequently retained selectively in skin, muscle, liver and kidneys. It is partially acetylated or conjugated in the liver and ultimately excreted in the urine as metabolites. A dose of 100 mg produces a peak serum concentration of approximately 2 micrograms/ml which declines with a half-life ranging from 1–2 days.

Uses

Treatment of bullous pemphigoid and dermatitis herpetiformis.

Dosage and administration

Adults: 100 mg daily increased, as necessary, up to 400 mg daily until signs of remission are apparent. Continuous maintenance therapy, which is required in some cases, should be administered at the lowest dosage which prevents recurrence (25 mg daily).

Contraindications

Hypersensitivity to sulfones.
Pre-existing untreated severe anaemia should be treated first.

Precautions

Dapsone can induce haemolysis of varying degree, particularly in patients with glucose-6-phosphate dehydrogenase deficiency. Dose-dependent methaemoglobinaemia may supervene during the second week of treatment. Pre-existing anaemia should be corrected and the blood count must be closely monitored in susceptible patients during the first weeks of treatment.

Use in pregnancy

Safe use in pregnancy has not been established. Dapsone should be used in the treatment of dermatological disorders only when the need of the mother outweighs the potential risk to the fetus.

Adverse effects

Dapsone is generally well tolerated at recommended dosages, but symptoms of gastrointestinal irritation occasionally occur. Other, less common reactions include headache, nervousness and insomnia.

Blurred vision, paraesthesiae, reversible peripheral neuropathy, drug fever, skin rashes and psychoses have also been reported. Hepatitis, Herxheimer reactions and agranulocytosis may rarely occur.

Storage

Dapsone tablets should be kept in well-closed containers protected from light.

DITHRANOL

ointment 0.1 to 2%

Dithranol slows epidermal cell division and inhibits excessive proliferation and keratinization in patients with psoriasis. It is not significantly absorbed through the skin.

Uses

Topical management of moderately severe psoriasis.

Dosage and administration

Treatment should be started with the 0.1% ointment. After one week, the concentration may be increased to 0.25% and subsequently doubled, if necessary, at weekly intervals to a maximum strength of 2%. After application, the ointment should be left in place for up to 30 minutes.

Contraindications

Ointment should not be used on the face, on acute eruptions or excessively inflamed areas.

Precautions

If the initial treatment produces excessive soreness, or if the lesions spread, the frequency of application should be reduced, and in extreme cases discontinued.

Patients should be warned that staining of the skin and hair may occur and that some fabrics may be permanently stained.

Use in pregnancy

Safe use in pregnancy has not been established but no adverse effects have been reported.

Adverse effects

Contact with the eyes may cause conjunctivitis. Irritation is common.

Excessive erythema may occur on adjacent normal skin.

Storage

Dithranol ointment should be stored in tightly-closed containers protected from light.

ERYTHROMYCIN

*enteric coated tablets 250 mg
(as stearate or ethylsuccinate)*

Erythromycin is a macrolide antibiotic produced by *Streptomyces erythreus*. It has a broad spectrum of bacteriostatic activity. *Inter alia*, it is active against *Propionibacterium acnes*.

Because it is inactivated by gastric juices, oral formulations are enteric-coated. It diffuses rapidly into all tissues except the brain and cerebrospinal fluid, and readily crosses the placental barrier. The plasma half-life is approximately 90 minutes. It is partially demethylated in the liver and is excreted largely via the bile and faeces.

Uses

Moderate to severe acne in patients in whom tetracyclines are contraindicated.

Dosage and administration

Adults: Initially 250 mg four times daily for 2 weeks followed by 250 mg twice daily until improvement occurs. Treatment may need to be continued for up to 6 months.

Contraindications

Known hypersensitivity.

Precautions

Hepatic function should be monitored in patients with a previous history of liver disease.

Cholestatic hepatitis, which may present with symptoms suggestive of acute cholecystitis, occasionally complicates prolonged courses of treatment. Symptoms resolve rapidly when the drug is withdrawn.

Anaphylaxis and other hypersensitivity reactions are rare.

Drug interactions

Erythromycin, chloramphenicol, and clindamycin, which have similar bacteriostatic actions tend to be mutually antagonistic when administered together. Erythromycin decreases the rate of metabolism of carbamazepine and warfarin in the liver to a degree that can warrant readjustment of dosage.

Overdosage

Symptoms of overdosage include severe nausea, vomiting, diarrhoea and hearing loss. Induction of emesis or gastric lavage may be of value if undertaken within a few hours of ingestion.

Storage

Capsules and tablets should be stored in tightly-closed containers.

ETRETINATE

capsules 10 mg

Etretinate is a synthetic, aromatic derivative of retinoic acid which inhibits keratinization, proliferation and differentiation of epithelial cells. It is especially effective in the treatment of severe forms of psoriasis, and severe congenital ichthyosis.

It is incompletely absorbed from the gastrointestinal tract after oral administration and is excreted in the urine largely as inactive metabolites. Both etretinate and its active metabolite, acitretin, have half-lives of about 100 days. They accumulate in fat and plasma after continuous administration and they have been detected in plasma 3 years after discontinuation of treatment.

Uses

Severe extensive psoriasis resistant to other forms of therapy.

Severe congenital ichthyosis.

Dosage and Administration

Because of its teratogenic potential and its prolonged sequestration, use of etretinate should only be considered for women of childbearing potential when all other treatments have been found to be ineffective.

Adults: 0.75 mg/kg daily in divided doses for 2–4 weeks. The dose may subsequently be increased, as necessary, up to 1 mg/kg. The total daily dose should never exceed 75 mg. Once signs of remission are apparent the dose should be reduced to 0.5 mg/kg daily in divided doses for a further 6–8 weeks.

Subsequent exacerbations may be treated intermittently, as necessary. Continuous maintenance therapy, which is required in some cases, should be administered at the lowest dosage which prevents recurrence (0.25–0.5 mg/kg daily).

Children: The same dosage recommendations as for adults apply but long-term maintenance therapy is not recommended.

Contraindications

Pregnancy and lactation.
Patients with hepatic or renal impairment.

Precautions

Women of childbearing potential must be informed and carefully counselled about the potentially teratogenic effects of etretinate. An effective method of contraception must be used continuously for a period extending from 2 months prior to treatment until at least 2 years after discontinuation. Liver function tests and blood lipids should be measured at the start of treatment and at 3-monthly intervals thereafter.

Diabetic patients may become unstable. Blood sugar concentrations should be checked frequently particularly at the start of therapy.

Adverse effects

Dryness of the mucous membranes, sometimes with erosion commonly involve the mouth, lips conjunctivae and nasal mucosa. Dryness of the skin may be associated with scaling, thinning, erythema and pruritus.

Reversible rises in serum levels of liver enzymes occur frequently and may necessitate dosage reduction or discontinuation of therapy. Acute hepatitis is a rare complication.

Blood lipids rise in about half the patients. Reduction of the dosage or discontinuation of therapy is often necessary in patients with other cardiovascular risk factors.

Skeletal hyperostosis and extraosseous calcification has been reported following long-term administration.

Overdosage

Symptoms of overdosage include severe headache, nausea, vomiting, drowsiness, irritability and pruritus. Emesis or gastric lavage is of value within a few hours of ingestion.

Storage

Capsules should be stored in well-closed containers, protected from light.

HYDROCORTISONE

ointment or cream 1% (acetate)

At this dosage hydrocortisone provides a topical corticosteroid preparation of low potency. Its therapeutic effects result from vasoconstriction, reduction of membrane permeability, and suppression of mitotic activity and the immune response.

Uses

Topical treatment of contact dermatitis, atopic dermatitis, lichen planus and intractable pruritus.

Phototoxic reactions, including polymorphous light eruptions and actinic prurigo.

Short-term treatment of psoriasis of the face, scalp, palms and soles.

Dosage and administration

A thin film should be applied to the affected area 1–4 times daily. When a favourable response is apparent, the frequency of application should be reduced to the minimum necessary to maintain control and avoid relapse. Treatment should be discontinued at the earliest opportunity.

The cream is suitable for most dermatoses, but ointments are often used for dry, scaly lesions. Occlusive dressings should be reserved for severe or resistant lesions; they should never be applied to weeping surfaces.

Contraindications

Known hypersensitivity.

Infections (bacterial, fungal or viral) at the intended site of application.

Precautions

Hydrocortisone is the least potent of the corticosteroids. Only when treatment with this preparation fails should the use of preparations containing more potent corticosteroids be considered.

The use of occlusive dressings facilitates penetration into keratinized lesions. Occlusion should be maintained for no longer than two days, and preferably at night only.

If secondary infection occurs the corticosteroid should be withdrawn and appropriate antimicrobial therapy should be given.

Use in pregnancy

Topical corticosteroids should not be used in large amounts or for prolonged periods during pregnancy.

Adverse effects

Corticosteroids exacerbate untreated infections. Prolonged use can induce skin atrophy, particularly on the face and in skinfolds. This is characterized by thinning of the dermis, depigmentation, dilatation of superficial blood vessels and formation of striae. Glaucoma may result after accidental contact with the eye.

Infants and young children are particularly susceptible to the local and systemic effects of topical corticosteroids. Prolonged use can result in hypercorticism and suppression of the hypothalamic-pituitary-adrenal axis.

Storage

Cream and ointment should be stored in well-closed containers.

METHOXSALEN

capsule 10 mg

Methoxsalen is a psoralen derivative which occurs naturally in many plants but is prepared synthetically for therapeutic use. When exposed to ultraviolet A irradiation it forms photochemical conjugates with nucleic acid that inhibit DNA replication.

It is readily absorbed after oral administration and photosensitivity peaks 1–2 hours after ingestion. The drug is rapidly and extensively metabolized and is excreted in the urine.

Uses

Treatment of severe psoriasis refractory to topical therapy in conjunction with controlled exposure to UVA radiation (PUVA therapy).

Dosage and administration

Adults: 0.3–0.4 mg/kg administered 2 hours before exposure to UVA radiation. Twelve to twenty four sessions are usually necessary.

Contraindications

Hypersensitivity to psoralens.
Patients with diseases associated with photosensitivity including porphyria, acute systemic lupus erythematosus and hydroa vacciniforme.
Pregnancy.

Precautions

Treatment should be administered only under the supervision of a physician with special training in photochemotherapy.

Protective sunglasses should be worn during therapy and for the following 24 hours in order to avoid the risk of cataract formation.

Patients must be advised to avoid exposure to sunlight for at least 8 hours after therapy.

Adverse effects

Gastric discomfort occasionally occurs.

Cheilitis and transient loss of muscle coordination has been reported.

PUVA therapy carries an increased risk of cutaneous carcinoma in patients with predisposing factors.

Overdosage

Overdosage of methoxsalen or overexposure to ultraviolet light following methoxsalen administration can result in severe burning and blistering of the skin. The patient should be placed in a darkened room for at least 24 hours or until the cutaneous reaction has subsided, and supportive measures for the treatment of burns should be initiated. Emesis or gastric lavage is of value within a few hours of ingestion.

Storage

Capsules should be stored in well-closed containers, protected from light.

PREDNISOLONE

tablet 5 mg

injection 5 mg (as sodium phosphate or succinate) in vial

Prednisolone is a synthetic glucocorticoid with weak mineralocorticoid properties. Its therapeutic effect results from inhibition of macrophage accumulation, suppression of capillary wall permeability and oedema formation, and reduction of fibroblast proliferation and collagen deposition. It is readily absorbed from the gastrointestinal tract, is extensively protein-bound and has a plasma half-life of about 8 hours.

Uses

Bullous dermatoses.
Atopic and contact dermatitis
Lichen planus
Photodermatoses pruritus

Dosage and administration

The lowest dosage to produce an acceptable clinical response should be used. Dosage is dependent upon the disease, its severity and the response to treatment.

In life-threatening conditions such as bullous dermatoses, dosage should start at 1 mg/kg daily and be raised progressively to about 5 mg/kg if a prompt response is not obtained.

In many other conditions dosages of 10–30 mg daily suffice.

During prolonged therapy, dosage may need to be incremented temporarily during periods of stress or in exacerbation of illness.

Withdrawal of treatment must be gradual to avoid adrenal insufficiency. Following prolonged treatment, decrements of as little as 1 mg monthly may be necessary.

Contraindications

Known hypersensitivity.
Prednisolone should not be used, except in life-threatening situations, in patients with active bacterial, viral or fungal infections.

Precautions

Patients must understand the importance of following dosage instructions rigorously.

Patients on long-term treatment must remain under close medical supervision. Weight, blood pressure, fluid and electrolyte balance and blood sugar should be monitored for as long as treatment is continued. Bone pain, and particularly backache, may be indicative of osteoporosis.

The response of the pituitary-adrenal axis to stress is reduced and may remain depressed for many months after withdrawal. Dosage may need to be doubled or reinstated temporarily during this period if infection occurs.

Should a patient receiving, or having recently received long-term corticosteroid therapy require emergency surgery, parenteral hydrocortisone should be administered as follows:

- 200 mg i.m. with premedication;
- 100 mg infused i.v. in 500 ml saline during the procedure;
- 100 mg i.m. six-hourly for 72 hours.

Minor surgical procedures should be covered by 100 mg i.m. shortly before and after the intervention.

Corticosteroids should be used only for serious conditions in patients with diabetes, tuberculosis, peptic ulcer, hypertension, heart failure, epilepsy, a history of mental disorder or psoriasis. Patients with a history of tuberculosis should receive prophylactic chemotherapy during prolonged therapy.

Children on steroid therapy should receive a course of gamma globulin if they are exposed to a childhood virus infection to which they have no acquired immunity. They should not receive live virus vaccines.

Intermittent dosage regimens reduce the risk of stunted growth in children when steroid therapy is prolonged for more than six months.

Use in pregnancy

Corticosteroids should not be administered during pregnancy unless the need outweighs any possible risk of harm to the fetus. Adrenal development may be impaired and an association with cleft palate and other abnormalities has been described, particularly in the case of fluorinated compounds. Dosage should be kept as low as possible, but requirements may be raised slightly in replacement therapy as a result of increased binding of steroids to plasma proteins during pregnancy.

Corticosteroids are secreted into breast milk and breast-feeding should be avoided.

Adverse effects

Doses in excess of prednisolone 20 mg daily are immunosuppressive. Infections contracted during therapy can be overwhelming in the absence of effective treatment. Quiescent tuberculosis may be reactivated.

Continuous dosage in excess of normal physiological requirements (approximately 10 mg daily) is liable to result in:

- stunting of growth in children, which may be averted by giving corticotrophin and selecting alternate day dosage schedules;
- features of hypercorticism, including moonface, hirsutism, acne, bruising, striae, redistribution of fat, muscle wasting, hypertension;
- spinal osteoporosis and vertebral collapse, which may be retarded by calcium supplements and small doses of vitamin D;
- aseptic osteonecrosis, particularly of the femoral head;
- subcapsular cataracts, glaucoma;
- development or aggravation of peptic ulcer;
- diabetes mellitus;
- depression and psychosis, with risk of suicide;
- raised intracranial pressure and convulsions, particularly in children;
- increased coagulability of blood;
- delayed tissue healing;

- myopathy characterized by weakness of proximal musculature of arms and legs.

Fluid retention is not characteristic of prednisolone therapy since it has little mineralocorticoid activity.

Psoriasis may be seriously exacerbated on sudden withdrawal of corticosteroid therapy.

Drug interactions

Hepatic enzyme inducers including phenobarbitone, phenytoin and rifampicin may accelerate the metabolism of prednisolone.

The response to oral anticoagulants may be altered. Inhibition is characteristic, but isolated reports of potentiation are on record.

The incidence of gastrointestinal ulceration may increase when acetylsalicylic acid or nonsteroidal anti-inflammatory drugs are administered concomitantly.

The risk of hypokalaemia is increased when corticosteroids are taken concomitantly with potassium-losing diuretics.

Overdosage

A single large overdosage is unlikely to result in dangerous sequelae.

Symptomatic treatment is vital in the management of the adverse effects described above when they result from chronic poisoning.

Storage

Tablets should be stored in well-closed containers. Prednisolone sodium phosphate injection should be protected from light and freezing should be avoided.

SELENIUM SULFIDE

lotion 2.5%

Selenium sulfide is a topical antimicrobial agent with antibacterial and mild antifungal activity. It is not absorbed following application to intact skin, but it is readily absorbed from damaged skin.

Uses

Topical treatment of seborrhoeic dermatitis.

Dosage

Seborrhoeic dermatitis:

5-10 ml of the lotion is massaged into the wet scalp and left for 2-3 minutes before rinsing off. This should be repeated twice weekly for 2 weeks.

Contraindications

Known hypersensitivity to selenium sulfide.
Children under 2 years.

Precautions

Selenium sulfide lotion should not be applied to damaged skin because of the risk of systemic toxicity.

Treatment should be discontinued if cutaneous sensitization occurs.

Contact with the eye should be avoided.

Use in pregnancy

Safe use in pregnancy has not been established.
Treatment is best deferred until after delivery.

Adverse effects

Prolonged contact with the skin may cause local irritation.

Topical application to damaged skin can cause systemic toxicity characterized by tremors, weakness, lethargy, pain in the lower abdomen and occasional vomiting. These effects may be expected to resolve within 10 days of discontinuing treatment.

Storage

Selenium sulfide lotion should be stored in tightly closed containers in a cool place.

SUNSCREENS

(para-aminobenzoic acid, benzophenones)
skin protection factor 15
creams, lotions, gels

Sunscreens protect the cells of the skin by absorbing and reflecting solar radiation. They include para-aminobenzoic acid which absorbs UVB radiation only and benzophenones which absorb both UVB and some UVA radiation. The efficacy of a particular preparation is usually described as its sun protection factor (SPF). This is a ratio of the time required to produce minimal erythema with the sunscreen compared to the time without protection.

Uses

To prevent sunburn, actinic keratosis, premature ageing of the skin and skin cancer (basal and squamous cell carcinomas).

They may also provide some protection in photosensitive disorders.

Dosage and administration

Cream, lotion or gel should be applied generously, initially, to all exposed areas at least 1 hour before exposure to sunlight. It should be reapplied after swimming or profuse sweating.

Precautions

Contact sensitivity and photosensitivity may occur.

Storage

Store in well-closed containers protected from light.

TAR PRODUCTS

solution 5%

ointment 1%

Tar suppresses epidermal cell DNA synthesis and mitotic activity and restores a normal rate of proliferation.

A variety of tars, most commonly coal tar, is used to treat chronic skin disease.

Uses

Treatment of widespread, erythrodermic and guttate psoriasis either alone or in combination with ultraviolet light.

Dosage and administration

Tar baths: 100 ml of solution should be thoroughly mixed with bath water and the patient should soak for 10-20 minutes.

This may be repeated once every 3 days for at least 10 baths.

At least 24 hours should elapse before phototherapy is started and the tar preparation should be entirely removed from the skin.

Contraindications

Known hypersensitivity.
Tar preparations should not be applied to inflamed, broken or infected skin.

Precautions

Exposure to direct sunlight should be avoided for at least 24 hours after application because of the risk of photosensitivity reactions.

Although a potential carcinogen, there is no evidence that in the doses used therapeutically, coal tar preparations increase the risk of skin cancer.

Use in pregnancy

Safe use in pregnancy has not been demonstrated. Treatment should be deferred until after delivery whenever possible.

Adverse effects

Tar preparations are irritant and may rarely cause allergic sensitization.

Coal tar preparations produce photosensitivity reactions.

They frequently stain the skin and hair and consequently may not be well accepted by the patient.

Storage

Tar preparations should be stored in tightly closed containers, and protected from light. Freezing should be avoided.

TETRACYCLINE

capsule or tablet, 250 mg (hydrochloride)
topical solution 2%

Tetracycline is a broad-spectrum antibiotic derived from a species of *Streptomyces*. It is selectively concentrated by susceptible bacteria and induces bacteriostasis by inhibiting protein synthesis.

Absorption from the gastrointestinal tract is always incomplete and can be further impaired by alkaline substances and chelating agents and particularly by milk and milk products, aluminium, calcium, magnesium and iron salts. Following topical application, the drug is absorbed to some extent. Peak plasma concentrations occur within 4 hours and decay with a half-life of about 8 hours. Excretion is effected primarily by glomerular filtration into the urine. Enterohepatic circulation gives rise to high concentrations in the liver and bile.

Tetracycline crosses the placenta and is excreted into breast milk.

Uses

Topical and systemic treatment of moderate to severe acne.

Dosage

Topical: Solution should be applied generously to clean affected skin twice daily.

Systemic: 250 mg four times daily for the first two weeks thereafter reducing the dose to 250 mg twice daily until the lesions are cleared. Treatment may have to be continued for up to 6 months.

As much as 2 g daily may be necessary for severe, recalcitrant acne.

Contraindications

Known hypersensitivity.
Pre-existing severe hepatic or renal damage.
Children under 8 years of age.

Precautions

Oesophagitis which can be troublesome, may be averted if the patient remains upright while the tablets are swallowed, and if they are always washed down immediately with a glass of water.

Tetracycline should be withdrawn if infective diarrhoea occurs.

Suprainfection of the bowel with resistant organisms can result in potentially fatal staphylococcal enteritis and pseudomembranous colitis.

Time-expired tetracycline capsules or tablets should be discarded. Degraded tetracycline has been reported to induce renal dysfunction indistinguishable from the Fanconi syndrome and skin lesions similar to those of systemic lupus erythematosus.

Use in pregnancy

Tetracycline is generally contraindicated in pregnancy. It impairs skeletal calcification in the fetus and can result in abnormal osteogenesis and hypoplasia of dental enamel. There is no evidence of teratogenicity with topical tetracycline, but it should be applied during pregnancy only when the need outweighs any possible harm to the fetus.

Adverse effects

Tetracycline is well tolerated following topical application. Local irritation may occur initially but subsides with continued treatment.

Following oral therapy, gastrointestinal irritation is common. So, also, is depletion of the normal bowel flora permitting overgrowth of resistant organisms. Irritative diarrhoea should be differentiated from enteritis due to suprainfection, particularly with positive staphylococci and pseudomembranous colitis due to *Clostridium difficile*.

Phototoxic reactions occasionally result in porphyria-like skin changes and pigmentation of the nails.

Pre-existing renal insufficiency may be aggravated. Acute renal failure and transient diabetes insipidus have been reported.

Skeletal deposition is a potential hazard to bone and tooth development during fetal life and childhood. Depression of bone growth is substantial, but readily reversible following short periods of exposure. Discoloration of teeth and enamel hypoplasia is permanent.

Hypersensitivity reactions are rare. Morbilliform rashes, urticaria, fixed drug eruptions, exfoliative dermatitis, cheilosis, glossitis, pruritus and vaginitis are described. Angioedema, anaphylaxis and pseudotumour cerebri have been reported.

Drug interactions

The action of oral anticoagulants may be potentiated. Severe renal failure has been reported in patients who have received a halogenated anaesthetic agent while receiving a tetracycline.

Storage

Tetracycline capsules, tablets or topical solution should be kept in well-closed containers, protected from light.