

# Treatment of skin diseases: recent trends

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RESEARCH IN THE FIELD of dermatology has made substantial contribution to the understanding of the pathogenesis of many skin disorders. Though cosmetic improvement with reduction in the morbidity of various disorders has been the main aim of advances in the treatment, permanent cure of some disorders does not seem to be far off. Recent trends in the treatment of some common disorders are reviewed in this article.

## **Psoriasis and Methotrexate**

The normal epidermal cells divide approximately every 19 days whereas the psoriatic epidermal cell does it much rapidly, completing the germinative cell cycle every 37 hours (Weinstein and Frost, 1968). Methotrexate prevents DNA synthesis at the S phase of the cell cycle, thus cell replication is stopped. The actively dividing psoria-

tic epidermis should be selectively more sensitive to methotrexate than other tissues, e.g. normal epidermis. The duration of inhibition of DNA synthesis in psoriatic epidermis following administration of a single dose has been determined to be 12 to 16 hours (Weinstein et al., 1970).

Various regimes of methotrexate has been used for the treatment of psoriasis but Weinstein and Frost (1971) proposed the administration of low-dose methotrexate in three divided doses over the life cycle of the psoriatic cell population. During the 36-hour period, most of the psoriatic cells would, as they enter the S phase, be prevented from completing the germinative cycle, whereas only a relatively small proportion of other actively dividing tissues of the body, such as hair follicle, bone marrow, normal epidermis and the mucous membrane of the gastrointestinal tract, would be

affected with minimal toxic effects. The irreversible damage to the liver on prolonged therapy with this drug is a serious menace which one must bear in mind when we are dealing with a disease which itself is not fatal.

Patients who have had a fair trial of various topical therapy, with no history of past or present liver disease, with intact renal function and women beyond the reproductive age can be considered suitable for methotrexate therapy. They must have pre-therapy liver biopsy, regular blood counts and liver functions tests during the regime. The low dosage regime mentioned above might prove to be more tolerable to patients.

### Vitiligo

Development of vitiligo, especially on the exposed part of the body, has both cosmetic and social significance, the latter because of the mistaken belief that it is leprosy. In spite of the specific therapy, available cover-up cosmetics have still a place when the distribution of vitiligo is limited.

To induce repigmentation of the vitiliginous skin both meladinine and 8-methoxypsoralen were used but they were not very effective. A new synthetic compound, furocoumarin derivative, 4, 5', 8-trimethylpsoralen is now used. This is more potent than the previously available preparations in its photosensitising effect and the results of the therapy suggest that it may prove to be a more effective therapeutic agent (Bleehen, 1972).

Two hours after taking the drug, the patient must expose all the affected areas to sunlight, gradually increasing the exposure time depending on the severity of the erythema the vitiliginous skin develops. The effect of the therapy is noticeable after using the drug for a minimum of six months.

The mode of action is not well understood but the observation of perifollicular repigmentation at the initial stages of improvement led to the suggestion that treatment with this substance might induce colonisation of the depigmented skin by the melanocytes originating from the pigmented hair bulbs (Pegum, 1955). However, repigmentation of the mucosa and the genitalia, which is seen with this therapy, is not dependent on the above mechanism. Psoralens with a mitotic effect on the melanocytes (Clark et al., 1968) may activate those found on the border of the vitiliginous spot. Whether the effect produced by this drug is permanent or it has systematic toxic effects is unknown at present.

### Acne Vulgaris and Topical Vitamin A

Comedones and seborrhoea are the two chief

factors which contribute to the development of acne vulgaris. It is believed that comedone formation is dependent on the production of horny cells which tend to adhere together forming a plug at the follicular opening. In normal person these cells desquamate invisibly at the follicular orifice, as they are loose and non-adherent.

Short of reducing the sebum secretion by anti-androgen, cyproterone, (Cunliffe et al., 1969), which is still in the experimental stage, dislodging the comedones already present or preventing its formation seems an attractive method for treatment of acne vulgaris. The conventional anti-acne agents irritate the surface of the skin to remove the comedones. Vitamin A acid is not only the most potent irritant substance but is also believed to act on the epithelium lining the sebaceous follicle and it inhibits the formation of comedones by increased production of non-adherent horny scales which readily slough and are cast off by desquamation of skin (Kligman et. al. 1969).

On application of Vitamin A topically the skin becomes inflamed, desquamates and crusts. The patient must be warned of this initial effect or he may be frightened and discard the treatment. As with any other anti-acne therapy, continuous treatment for a period of six months is necessary before assessing the results of the therapy.

### Urea Cream for the Skin

The degree of hydration keratin decides the softness of the skin and its cosmetic appearance. In ichthyosis and xeroderma, the skin contains much less water than the normal skin and the disorder becomes particularly noticeable on the exposed part of the skin, now that we spend a large part of the day in a low humid air-conditioned atmosphere. Water content of the keratin can be increased first by moistening the skin, then applying grease to the surface to prevent evaporation, or cosmetic improvement can be obtained by keratolytic agents which disperse the scales on the surface. None of these treatments has proved very effective.

Urea binds water and thus it is able to rehydrate the ichthyotic scales (Swanbeck, 1968). It is bactericidal and does not sensitise the skin. However, it is unstable in aqueous mixture. A ten per cent concentration of the substance in a stable emulsified base has proved cosmetically acceptable and has long shelf life (Martin Beare, 1971; Swanbeck, 1968). This is to be applied more than once a day and especially before exposure to the low humidity atmosphere.

**Bullous Disorders and Methotrexate**

Available evidence indicates that both pemphigus and pemphigoid are autoimmune diseases (Beutner et al., 1968). The bulla, which is the pathologic marker of both diseases, is intraepidermal in pemphigus and is at the dermo-epidermal junction in pemphigoid. It can be demonstrated that localisation of antibodies corresponds to the site of the pathology and the titre of antibody is proportional to the severity of the disease. Use of immunosuppressive therapy in the form of methotrexate has been found useful in the treatment of both disorders (Lever and Hashimoto, 1969).

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Prednisolone was the drug of choice for both disorders but as a lifelong therapy for pemphigus with all its consequent dangers left much to be desired. Methotrexate is a useful alternative for all patients except those with very active disease in whom prednisolone is given initially till the disease is under control and then changed to methotrexate. The mode of action is through both suppression of antibody formation and anti-inflammatory action.

**Acknowledgement**

I wish to thank Miss Kwan for typing this manuscript.