ABSTRACTS FROM CURRENT LITERATURE

Persistence of antifolate activity in skin of rats following systemic administration of methotrexate, Zimmerman CL, Franz TJ and Slattery JT : J Invest Dermatol, 1984; 82 : 57-61.

For more than 20 years, methotrexate has been used in the management of severe psoriasis. The weekly dose regimen is based on the 36-hour duration of the S-phase of the psoriatic cells and duration of action of methotrexate following a single dose.Polar active metabolite, the poly γ - glutamyl conjugates of methotrexate have been found to be retained in the cultured human fibroblasts. The authors carried out the study to evaluate the hypothesis that formation and retention of poly- γ - glutamyl conjugates of methotrexate in the skin after systemic administration will result in prolongation of methotrexate effects in skin. Several skin and plasma samples were observed over 48 hours after varying doses of methotrexate. Pharmacokinetic parameter values and skin to plasma ratios were not significantly different between different doses. The terminal half life of methotrexate in plasma was 20.3 ± 9.2 hours. At early times, methotrexate activity in skin was less than plasma, but at later times, the activity in skin was an order of magnitude greater than that in plasma. The persistent activity in the skin was associated with the presence of poly- γ -glutamyl conjugate of methotrexate. It appears that methotrexate is sequestered in the skin, released slowly to the blood and then eliminated.A metabolite mono γ - glutamate methotrexate is equipotent to methotrexate in terms of inhibition of dihydrofolate reductase. The present study has shown the presence of active concentrations of poly- γ - glutamate conjugate of methotrexate in skin 24 hours after the dose. The formation of long acting methotrexate conjugates in skin that bind effectively to dihydrofolate reductase and share many of the cytotoxic activities of methotrexate may have implications for therapy of psoriasis. Because of this retention of conjugates in the epidermal cells, subsequent doses of methotrexate may have a much longer duration of action than the first.

Bhushan Kumar

Dermographism (mechanical urticaria) mediated by IgM, Horiko T and Aoki T : Brit J Dermatol, 1984; 111 : 545-550.

The pathogenesis of dermographism is not well understood. Successful transfer of dermographism has been already described in which the transfer substance was either IgA or IgE. Here the authors describe the weal-producing IgM in the sera of dermographic patients. Sera of 3 patients with symptomatic mechanical urticaria caused an immediate weal and flare reaction when injected intradermally into related recipients and serum of one patient caused the same reaction in his own skin. An immunoabsorption study using anti-IgM serum identified this weal-producing substance as IgM. This study opens new possibilities in the pathogenesis of mechanical urticaria. IgM may be a substance that makes mast cells fragile, perhaps acting via the supposed IgM receptor, so that stroking the skin can directly cause wealing without the involvement of the antigens. Secondly, it may be an antibody to the mast cells, so that it can disrupt the cells after leakage through the skin capillaries in the Lewis' triple response caused by skin stroking.

K. Pavithran

Coudability—A new physical sign of alopecia areata, (correspondence), Suster S : Brit J Dermatol, 1984; 111 : 629-631.

A new sign is described in the hairs of alopecia areata. The sign is of a normal-looking hair which can easily be made to kink when bent or pushed inward, the kink corresponds to the shaft defect produced by the episode of alopecia areata. Often such kinks occur 5-10 mm above the scalp, presumably because the follicle is no longer active and the stationary shaft defect has not yet revealed itself by snapping. Less commonly, it is because the follicle has recovered but the hair has not yet grown out sufficiently to localise a fracture. When irregularity of the shape or vagueness in the outline of the lesion causes diagnostic doubt, inward movement of the hair will invariably produce a sharp kink, usually several millimeters from the scalp which reveals the sight of affection of hairs caught by alopecia areata. The follicles of such hairs can be removed with a forceps applied below the kink and usually show the characteristic anagen atrophy. Author comments that he has not seen such hairs in other diseases. The appearance of the kink gives the hair the shape of a coude catheter. For this reason and because the adjective kinky has already been applied to the hair in copper deficiency, coudability would be an appropriate term for this sign of the hairs in alopecia areata.

K. Pavithrau

Atypical psoriasis of the face and hands after PUVA treatment, Verhagen AR, Van Der Wiel AG and Wuite GG : Brit J Dermatol, 1984; 111 : 615-618.

Recent reports show lack of response in psoriasis to prolonged PUVA therapy. Psoriasis is usually less prominent in areas exposed to sunlight. After repeated PUVA courses with a relatively high total dose, many patients tend to develop recalcitrant lesions in superimposed areas, especially in the butterfly area of the face and dorsa of hands. In 60 patients with psoriasis, 2 types of lesions developed after repeated and prolonged courses of PUVA radiation. In 16 patients, the new lesions on the face resembled seborrhoeic dermatitis or SLE, but antinuclear factor in the serum was negative. Thirteen patients developed thick plaques on the dorsa of the hands and the development of this lesion was dose related. The appearance of recalcitrant psoriasis on the face and hands appears to be a complication of PUVA treatment. In patients who were treated subsequently with methotrexate or etretinate, the authors observed beneficial effect on the PUVA-induced lesions.

K. Pavithran

Low dose oral chloroquine in the treatment of porphyria cutanea tarda, Ashton RE, Hawk JLM and Magnus IA : Brit J Dermatol, 1984; 111 : 609-613.

Low dose oral chloroquine therapy in PCT apparently acts by releasing tissue-bound hepatic porphyrin and facilitating its excretion in the urine. Seven patients with PCT received a total of 10 courses of low dose oral chloroquine therapy (125 mg chloroquine phosphate twice weekly). They were treated for a mean 14.9 months during which time all of them went into clinical and biochemical remission. Relapse occurred in 4 patients. There were no adverse side effects from the treatment. Other methods of treatment of PCT include, strict alcohol abstention and repeated venesection. The drawbacks of venesection are, that (1) it is sometimes difficult for the therapist as in drug addicts with thrombosed veins, and (2) it requires regular haematological monitoring. Low dose oral chloroquine therapy alone is easy. Though in severe PCT with marked liver damage, venesection is still preferred. In patients with a mild disease, a few signs of liver damage, reliable personalities, and stable social backgrounds, low dose oral chloroquine now appears to be the treatment of choice.

K. Pavithran

The response of seborrhoeic dermatitis to ketoconazole, Ford GP, Farr PM, Ive FA et al : Brit J Dermatol, 1984; 111 : 603-607.

The role of pityrosporum yeasts in the aetiology of seborrhoeic dermatitis is controversial. The availability of ketoconazole, an orally administered imidazole derivative which is active against pityrosporum yeasts, both in vivo and in vitro, allowed the authors to put these controversial views to the test. A double-blind, randomized, controlled trial of ketoconazole in seborrhoeic dermatitis was carried out. Nineteen patients (10 males and 9 females) with seborrhoeic dermatitis were given ketoconazole 200 mg daily. The response to treatment was assessed by the clinician and the patients independently using a linear analogue scale. The clinical signs and symptoms of dermatitis regressed considerably and significantly with this drug in all but 5 patients, 3 of whom subsequently responded to a higher dose. Three patients with dandruff alone also responded to ketoconazole. It is concluded that pityrosporum yeast infection is the immediate cause of seborrhoeic dermatitis and that dandruff is its mildest manifestation. One patient developed a transient widespread erythematous rash after 7 days of treamtent with ketoconazole. The present study was done to provide aetiological evidence and not to establish a practical therapy. Since seborrhoeic dermatitis rapidly relapsed when ketoconazole was stopped, and since ketoconazole is hepatotoxic, and it interferes with testosterone metabolism, the drug is not suitable for prolonged treatment of seborrhoeic dermatitis and dandruff. It is to be hoped that an equally effective topical preparation or derivative will be developed.

K. Pavithran