ABSTRACTS FROM CURRENT LITERATURE

Apoptosis in primary cutaneous amyloidosis. Change YJ, Wong CK, Chow KC, et al. Br J Dermatol 1999;140:210-215.

Primary cutaneous amyloidosis is a chronic pruritic skin disorder characterised histologically by deposition of amyloid in the papillary dermis. The exact pathogenesis is not known. Hashimoto and co-workers have proposed filamentous degeneration theory which suggests that the degenerating keratinocytes are discharged into the dermis and converted to amyloid. The mechanism of keratinocyte death is uncertain. The authors investigated the role of apoptosis in its pathogenesis. The apoptotic cells were detected by the TUNEL method. It was seen in the granular layer in normal skin, but in 11 out of 20 cases of primary cutaneous amyloidosis also in basal and spinous layers. Other conditions in which apoptosis is involved in the pathogenesis are sunburn, regression of neoplasms, psoriasis, alopecia areata, Stevens Johnson syndrome, vesicular skin lesions with zinc deficiency and interface dermatitis including lichen planus and graft versus host disease. It remains unclear what kind of factors initiate apoptosis in amyloidosis and transform cytokeratin to amyloid. Prolonged friction, scratching, UV light or viral infection might induce apoptosis and lead to primary cutaneous amyloidosis in susceptible individuals.

Anoop UC

Patch testing with natural rubber latex (N R L). Waklin S H, Jenkins R E, Mc Fadden JP. Contact Dermatitis 1999:

Natural rubber latex is a frequent cause of immediate type hypersensitivity with symptoms ranging from contact urticaria to anaphylaxis. Serveral important allergic proteins have been identified and characterised and at risk groups have been defined. As some latex allergic individuals present with chronic eczema, a delayed type hypersensitivity to latex proteins confirmed by prick testing rather than patch testing can occur. The aims of the study were to investigate the prevalance of positive reactions to different formulations of natural latex among a patch tested population.

During an eight month period, consecutive adult patients for suspected contact dermatitis were patch tested. Both wet and dry patches of high ammonia latex and low ammonia latex were used. Readings were carried out on days 2 and 4,2 and 5 or 3 and 5.

Six hundred and eight patients of mean age 41 years were patch tested. Patch test reactions were observed in 24 patients. No strongly positive reaction was observed. No patients showed allergic reaction to all four latex patches. Dry H A latex elicited the lowest number of reactions.

The risks of developing immediate type hypersensitivity to latex proteins are significantly and firmly established. Delayed type hypersensitivity reaction to a wide range of rubber additives is also well recognized. In the vast majority of patients with rubber gloves contact dermatitis, allergy to an additive can be identified. In this study no strong allergic reaction was observed. Majority of reactions were weak or doubtful. None of the patients showed allergic reactions to all four patches. It is therefore likely that these reactions were caused by the additives rather than by N R L itself.

Ashraf Ali

Study of immunity to varicella in doctors. Solomon BA, Kaporis A, Glass AT, et al. J Am Acad Dermatol 1998; 38: 763-765.

Primary infection with varicella zoster virus (VZV) occurs most often during childhood. Reactivation of VZV within dorsal ganglion cells results in herpes zoster (HZ). Cell mediated immunity is responsible for viral latency. A decline in CMI is associated with reactivation of latent VZV. Reexposure to VZV results in increased CMI to VZV and may suppress reactivation of latent VZV. Repeated reexposure to VZV is encountered by physicians who treat patients with varicella.

A study was conducted to find out the incidence of herpes zoster among doctors. A total of 9000 questionnaires were sent to equal numbers of three doctor groups: paediatricians, dermatologists and psychiatrists. Pediatricians were selected because primary varicella is predominantly a childhood disease resulting in higher exposure to VZV. Psychiatrists were selected as a negative control because they rarely treat patients with varicella. Dermatologists were selected because the number of patients examined with active VZV infection would fall somewhere between the number contacted by pediatricians and psychiatrists. The questionnaires focussed on past medical history of chicken pox and the numbers of patients with VZV infection seen annually.

A total of 3555 responses were returned from the 9000 questionnaires. Responses were obtained from 1109 paediatricians of whom 62% reported direct response to VZV during treatment of more than 25 VZV infected patients annually. The incidence of herpes zoster in this group was 5.95%. Responses were obtained from 1984 dermatologists of whom 76% reported examining less than 25 patients with VZV annually. The incidence of HZ in this group was 9.27%. Responses were obtained from 462 psychiatrists of whom 90% reported contact with zero to 5 patients with VZV annually. The incidence of herpes zoster in this group was 10.82%.

The study demonstrated that the incidence of herpes zoster varied significantly between pediatric, dermatology and psychiatry speciality groups. Exposure rates of physicians to patients with VZV differed significantly. Pediatricians who had the maximum contact with patients with VZV annually had the lowest incidence of herpes zoster. In contrast psychiatrists treated the fewest patients with VZV and had the highest incidence of herpes zoster.

It was concluded that exogenous reexposure to VZV may confer additional immunity against VZV and subsequently a decreased incidence of herpes zoster.

Salim PK

Pulse dosing of thioguanine in recalcitrant psoriasis. Silvis NG, Levine N. Arch Dermatol 1999; 135 : 433 - 436.

Recalcitrant psoriasis is a resistant form of psoriasis which does not respond to the usual conventional treatment. Thioguanine is a purine alogue which acts by inhibiting DNA synthesis. Daily dose thioguanine had been used previously but with inevitable bone marrow suppression . Thus, pulse dosing of thioguanine was tried to reduce the toxicity of thioguanine.

This is a two year study of fourteen patients with recalcitrant psoriasis for whom previous therapy had failed or had not been tolerated. Patients were initially treated with 80 -100 mg of thioguanine twice a week and the dosage was increased by 20 -40 mg every 2 -4 weeks. A determination was made as to when improvement was first noted with regard to scaling, pruritus, thickness of plaques or number of pustules and was defined as INITIAL RESPONSE. Eleven out of fourteen patients showed improvements with a duration of treatment ranging from fourteen to forty three weeks. Three patients ie., 25% failed to show any response after thirteen weeks of treatment. Mean dose duration for initial response was 80 mg at 7.4 weeks. Adverse effects were minimal

thrombocytopenia in one patient, hyperglycemia in a diabetic patient, pruritus in two patients, dry mouth in one patient and inital worsening of psoriasis in two patients.

Thioguanine is a purine analogue that interferes with DNA synthesis. Thioguanine is converted into thioguanine ribose monophosphate which is diphosphorylated and triphosphorylated and then incorporated into DNA and RNA. Since it interferes with DNA synthesis, it is possible that decreased keratinocyte proliferation is the major effect that produces clinical resolution. It may also act by affecting the trafficking of inflammatory cells, resulting in decreased movement into psoriatic lesions. Most common adverse effects of thioguanine is myelosuppression ie., leukopenia, anemia and thrombocytopenia. Other side effects include increase in liver enzyme levels which return to normal six months after cessation of treatment ; hepatitis, cholestasis and veno occlusive disease at 320 mg/day dosage.

Thus, pulse dosing of thioguanine therapy appears to be an effective treatment for recalcitrant psoriasis with minimal toxicity.

Rahima S

Erosive mucosal lichen planus : Response to topical treatment with tacrolimus. Vente C, Reich K, Rupprecht R, et al. Br J Dermatol 1999; 140: 338-342.

Erosive mucosal lichen planus, a painful and disabling inflammatory skin disease is highly resistant to topical treatment. Tacrolimus (FK 506), a potent immunosuppressant, that prevents rejection of organ transplants inhibits proliferation and activation of T-lymphocytes and hence may be effective in lichen planus.

This is a case report on six patients with severe recalcitrant histologically proven erosive mucosal lichen planus who benefitted from topical tacrolimus ointment. Three patients had oral lesions only, two suffered from erosive lichen planus of vulva and introitus vaginae and one had both oral and genital affection. All topical and systemic medications were stopped two weeks prior and tacrolimus at a concentration of 0-1% in a hydrophilic petroleum ointment containing bleached beeswax, stearyl alcohol, cholesterol and white petroleum was applied twice daily for four weeks. Photographing of representative lesions, assessment of subjective symptoms as burning and soreness and measurement of blood levels of tacrolimus were done at each weekly visit. After four weeks of topical tacrolimus, complete resolution occurred in three cases, while prolonged treatment resulted in further improvement or healing in the other three cases.

In lichen planus, there is a vacuolar interface dermatitis with a dense band-like lymphocytic infiltrate in the dermis and liquefactive degeneration of basal cell caused by cell-mediated immune reaction involving T-lymphocytes, Langerhan cells and macrophages. The present case study asserts the efficacy of topical tacrolimus in erosive mucosal lichen planus. Relapse of lesions in five out of six patients after cessation treatment further supports the assumption that tacrolimus ointment had controlled the disease. No serious adverse effects were noted except for a slight burning which ceased after healing of erosions.

Successful treatment of erosive mucosal lichen planus with cyclosporin A mouthwash is attributed to systemic blood levels from swallowed mouthwash, since cyclosporin A has high molecular weight and hence penetration into skin and mucosa is insufficient. Tacrolimus is a macrolide antibiotic with high immunosuppressant potential which inhibits T-lymphocyte activation at hundred times lower concentration than cyclosporin-A. It is a small molecule and has better penetration. Since activated T-lymphocytes are involved in the immunopathogenesis of lichen planus, topical tacrolimus appears highly effective. The present study thus brings to focus the efficacy of topical tacrolimus in the treatment of

recalcitrant erosive mucosal lichen planus.

E J Prameela

Langerhans cells in benign, premalignant and malignant skin lesions of renal tranplant recipients and the effect of retinoid therapy. Gibson GE, O'Grady A, Kay EW, et al. J Eur Acad Dermatol Venereol 1998; 10 : 130-136.

The authors investigated cutaneous Langerhans cell densities in fifteen renal transplant recipients, of which eleven patients were receiving low dose etretinate as chemoprophylaxis for recurrent skin cancer.

The tumours studied were twenty nine squamous cell carcinomas, sixteen of which developed following institution of etretinate therapy, five basal cell carcinomas, four Bowen's disease, eight actinic keratoses and three viral warts. Normal skin from renal transplant recipients and controls were also studied.

The Langerhans cells in frozen tissue were stained with the antihuman Leu 6 monoclonal antibody and immunolabelling was performed using avidin-biotin complex immunoperoxidase method. The number of Langerhans cells was calculated per square millimeter epidermal section surface and also, per thousand keratinocytes. The number and appearance of dendrites attached were also noted.

There was no significant difference in Langerhans cell numbers between normal skin from renal transplant and those from controls. There was a statistically significant reduction in Langerhans cell density for the tumours, compared with normal skin. The Langerhans cells in tumours were more rounded and had shorter, thicker and plumper dendrites compared to those in normal skin. There was a trend for an increase in Langerhans cell density in squamous cell carcinoma which developed during etretinate therapy, compared with pre-etretinate, but the difference was not statistically significant.

The marked depletion of Langerhans cells in skin cancers, precursor lesions and viral warts suggests a central role for them, in skin cancer promotion in renal transplant recepients.

Lekha T