ABSTRACTS FROM CURRENT LITERATURE

Topical and intralesional cidofovir: A review of pharmacology and therapeutic effects Zabawski EJ, Cockerell. J Am Acad Dermatol 1998; 39: 741-745.

Cidofovir (HPMPC), an acyclic nucleoside phosphonate, belongs to a new class of DNA polymerase inhibitors independent of thymidine kinase for initial phosphorylation. It is a nucleoside analogue of deoxycytidine monophosphate and has activity against several DNA viruses like human papilloma virus, herpes viruses (including acyclovir and foscarnet resistant strains), molluscum contagiosum and Kaposis sarcoma associated herpesvirus. It has no activity against RNA viruses. In the host cell, it undergoes a 2 stage phosphorylation to yield cidofovir diphosphate - the active metabolite which acts by competitive inhibition and gets incorporated into the DNA strand thus blocking further viral DNA synthesis. The activity lasts beyond the half life of 17-65 hours of the active metabolite as human DNA polymerase is unable to excise incorporated cidofovir diphosphate from viral DNA. It binds more avidly to viral DNA polymerase than the human DNA polymerase.

After intravenous administration, 90% is excreted in urine in 24 hours. Elimination is both by filtration and tubular secretion. Based on studies in rabbits, topical cidofovir has a bioavailability of 0.2 - 2.1% on intact skin which can be enhanced in vehicles containing propylene glycol. On abraded skin the bioavailability was increased upto 41%. Negligible systemic exposure occurred following topical application provided the epidermis was intact.

Side effects include nephrotoxicity, neutropenia and metabolic acidosis. It is embryotoxic in rats and rabbits and is to be avoided in pregnancy.

Several reports have shown intralesional cidofovir to be effective in florid laryngeal papillomatosis unresponsive to other modalities and no adverse effects have been reported except in one. Topical cidofovir 1% is effective in relapsing genital warts in both immunocompetent and immunosuppressed patients. In extensive verrucae vulgaris resistant to conventional therapies, cidofovir cream 3% cleared the lesions with no residual lesions on follow up after 9 months.

Extensive molluscum contagiosum resistant to conventional therapy in an HIV patient was found to clear up following intravenous cidofovir for CMV retinitis. Topical cidofovir 3% also resulted in clearing after 2 weeks. Cidofovir 3% gel is effective in clearing lesions in patients with acyclovir and foscarnet resistant genital herpes. Two consecutive courses of topical cidofovir also resulted in emergence of an acyclovir susceptible strain which could be treated. Many of the disorders caused by the

viruses do not have satisfactory therapy and given the efficacy of cidofovir in treating many of these conditions, it holds great promise.

C Lakshmi

Sparing of tuberculoid leprosy patch in a patient with dapsone hypersensitivity syndrome. Pei-Lin Ng P, Goh CL. J Am Acad Dermatol 1998;39:646 - 648.

The authors describe a case of dapsone hypersensitivity syndrome in a patient with tuberculoid leprosy who had sparing of his tuberculoid lesions despite a generalized eruption. A twenty - five year old patient presented with hypoaesthetic plaques on his right forearm of 1 year duration. He was diagnosed to have tuberculoid leprosy and treated with dapsone 100mg daily and rifampicin 600mg once a month. Seven weeks after starting treatment, patient developed pruritic erythematous papules, urticarial and purpuric plaques on his limbs with conspicuous sparing of the tuberculoid leprosy plaques on the right forearm. This was associated with jaundice, generaiised lymphadenopathy and mild hepato-splenomegaly. Biopsy from the erythematous urticarial, slightly purpuric plaque showed focal exocytosis with superficial perivascular lymphocytic infiltrate. Direct immunofluorescence showed fibrinogen deposits in the walls of blood vessels in the dermis. Dapsone hypersensitivity was diagnosed, dapsone stopped and patient was given oral prednisolone 40mg daily which was gradually reduced. The eruption cleared and hepatitis abated. The patient was restarted on treatment with rifampicin and clofazimine. The immunologic mechanism behind dapsone hypersensitivity syndrome is thought to be a combination of type I, type IV and perhaps type III Gell and Coomb's hypersensitivity reaction. It is also suggested that dapsone syndrome is modified graft - versus - host disease type reaction mediated by activated T cells. In leprosy, damage to nerves supplying the microvasculature of skin causes impairment of flare response to histamine which may explain the absent or milder eruption. In tuberculoid leprosy, the damaged nerves may possibly cause some degree of down regulation of mast cell activity which may contribute to lack of response in affected skin. Vasoactive amines that act on microvasculature are released by mast cells in type III and type IV reactions. This being a neurogenic reflex, lack of neuropeptides will affect the expression of drug reaction. Neuropeptides, such as substance P, are also involved in immunostimulation and cellular proliferation. They have been found to enhance T-cell proliferation, immunoglobulin and cytokine production and monocyte chemotaxis. Nerve damage in leprosy affects microvasculature as well as the other arms of local immune response and hence, expression of a hypersensitivity reaction.

V Bindu

Is there a microbiological rationale for single dose treatment of leprosy. Editorial, Lepr Rev 1998; 69:2-5.

Though the three drugs used in the ROM regimen, rifampicin, ofloxacin and minocycline, have reasonably high bactericidal activity against *Mycobacterium leprae*, they kill only the metabolically active M.leprae. Leprosy lesions are not synchronous cultures of

bacteria which can be instantaneously killed. It is inappropriate to consider all single lesion cases as low bacillated paucibacillary cases with their M. leprae actively multiplying and easily killed when drugs are extremely difficult to generate and sustain even in artificial test tube conditions. The experience with MDT regimes in the past in multibacillary and paucibacillary cases clearly shows that we are not dealing with synchronous actively multiplying organisms. Number of pulses required cannot be predicted with certainity. Though single lesion cases are paucibacillary cases with good immunity and low bacterial load, M.leprae may be multiplying in internal organs and actual load may be higher. Therapy cannot be based on the killing observed in mouse foot pad, ignoring the presence of viable M.leprae demonstrated by the same technique. Hence ROM regimen has poor microbiological rationale which cannot be theoretically defended as evidenced by the slower response seen in trials.

S Prasanna Kumar

Brachioradial pruritus: A recurrent solar dermopathy. Wallengren J. J Am Acad Dermatol 1998;39:803 - 806.

Brachioradial pruritus (BRP) is a localized itch in the skin of the lateral aspects of the arms and was first described by Waisman in 1968. BRP is often refractory to treatment with topical or oral corticosteroids and antihistamines. This article reports 13 cases of BRP from the south of Sweden who were treated with capsaicin in a randomized, double blind, placebo - controlled trial.

Thirteen patients with symmetric, bilateral symptoms seen in the summer and autumn of 1995 were enrolled in this study. None of the patients had been taking any phototoxic medication when the itch occured. Patients were given 0.025% capsaicin cream and placebo containing only the vehicle cream and were instructed to apply the creams locally to itchy or painful areas (on the right side and left side respectively) 5 times daily during the first week and 3 times daily during the following four weeks. The result of two treatments were compared after 5 to 6 weeks. The patients were contacted for follow-up 1 year later in autumn 1996.

All patients but 1 reported improvement of the condition during the test period. Capsaicin treatment reduced the itch by 63.1% where as placebo reduced the itch by 65.5%; there was no significant difference. At follow-up in 1996, all but 2 patients reported recurrence in the following summer.

Normally scratching relieves an itch. According to the 'gate theory' of Melzak and Wall, an impulse flow in the A-S fibres tends to shut off the firing of C-fibres through a negative feed back pathway. Paradoxically, the stimulation of A-S fibres in BRP by scratching seems to potentiate the sensation of pain and itch transmitted via the C-fibres. The normal feed back mechanism of interneurons in the dorsal horn of the spinal cord may be dysfunctional and stimulatory interneurons induce stimulation of the C-fibre input.

The C-fibres contain the neuropeptides. The rationale for capsaicin treatment is its ability to deplete C-fibres of sensory neuropeptides. In this study, capsaicin was not more effective than placebo. In severe BRP, without skin inflammation, treatment with capsaicin should be considered.

K Jyothi