
Leucopenia after gold and sulphasalazine treatment

Sir: I read the interesting report by Bliddal and colleagues of three patients who developed leucopenia after both gold and sulphasalazine treatment.1 HLA-DR3 as a marker for toxic reactions after treatment with gold or d-penicillamine could not be shown. Patient 1, however, was apparently a carrier of HLA-B7. It is well known that female patients with rheumatoid arthritis, who are HLA-B27 positive, have a significantly higher risk for drug induced agranulocytosis, not only after treatment with levamisole2,3 but also with other antirheumatic drugs.4 Thus under these conditions the possibility should be considered that in this patient, in the absence of HLA-D3, HLA-B27 may be the risk indicator for her relapsing leucopenia.

K L SCHMIDT
Department of Rheumatology and Physical Medicine
University of Giessen
Ludwigstrasse 57-59
D 6350 Bad Nauheim
West Germany

3 Vey E M, Mielants H, Verbruggen A. Leva-

Low incidence of antinuclear antibodies in dermatomyositis with malignancy

Sir: In 1958 Walton and Adams first classified ‘polymyositis/dermatomyositis with malignancy’ as a distinct subset of polymyositis. Recent prospective controlled studies, however, cast doubt upon the increased incidence of malignancy in polymyositis/dermatomyo-

Letters to the editor

Sir: The observation on our treatment patients with rheumatoid arthritis, was leucopenia after D3, which was not accompanied by toxicity or other side effects. Further, in the group of 12 patients with dermatomyositis with malignancy (nine definite and three probable dermatomyositis) and 24 patients with dermatomyositis without malignancy (16 definite and eight probable dermatomyositis), there were no cases of leucopenia among patients with dermatomyositis which overlapped with other connective tissue diseases were excluded from this analysis. Existence of malignancies was proved histologically by biopsy or necropsy, or both. Antinuclear antibodies were tested by indirect immunofluorescence with HEp2 cells (Kallstad, Chaska, MN, USA) as substrates. Serum samples giving apparent fluorescence at a dilution of 1:40 were considered positive. The χ2 test was used for the statistical analysis.

Positive antinuclear antibodies were found in 13/24 (54%) patients with dermatomyositis with malignancy, but they were found in only 2/17 (12%) of those with malignancy (p<0.03). The low incidence of antinuclear antibodies in dermatomyositis with malignancy suggests the presence of a different serological background from that in the dermatomyositis without malignancy. This conclusion supports the view that a distinct subset of dermatomyositis exists—dermatomyositis with malignancy.

MASHIKO NISHIKAI
AKIO SATO
Department of Internal Medicine
Second Tokyo National Hospital
Tokyo
Japan

Sir: Thank you for your interesting comments on our article about HLA types of patients with leucopenia.

Our patients all had classical rheumatoid arthritis and none was positive for antinuclear antibodies. The observation in a small group of patients of HLA-B27 in just one case does not justify further conclusions.

Like many others we no longer use leva-

Destructive spine lesions in ankylosing spondylitis

Sir: We read with interest the article by Aufdermaur entitled ‘Pathogenesis of square bodies in ankylosing spondylitis’.1 In this case report of a patient with ankylosing spondylitis the author provided histopathological evidence to suggest a primary acute and chronic inflammatory lesion, resulting in destruction of the vertebral bodies, followed by new bone formation.

It might be interesting to recall our case of destructive cervical vertebral lesions showing ankylosing spondylitis in a 19 year old woman.2 During her disease of 18 months’ duration she had inflammatory pain of the lumbar spine, sacroiliac joints, knees, and heels; radiographs showed bilateral sacroiliitis; HLA typing was A3, B7, 12 and erythrocyte sedimentation rate 60 mm/1st h. From the start of her disease she had had inflammatory pain of the cervical spine. Radiographs showed severe destructive lesions of the 6th cervical vertebra without discal lesions or cervical ankylosis, and a milder anterosuperior spondylitis of the 5th cervical vertebra (figure). There was no history of trauma. Surgical biopsy excluded a tumourous or infectious process. Spinal fusion (C4-7) was performed, and cervical pain disappeared with non-steroidal anti-inflammatory drugs. Histopathological examination of the 6th cervical vertebra biopsy specimen showed the absence of any inflammatory cells and the presence of spongiosa surrounded by fibrous tissue. These findings are consistent with those of Aufdermaur; the inflammatory cervical pain, which was noted as an early symptom of the disease in our patient, might have been due to the inflammatory lesion of the vertebral body, and the present histopathological findings might represent the reparative stage with scar and new bone formation. It is noteworthy that this severe destructive cervical lesion was the first manifestation of ankylosing spondylitis in this patient.

A KAHAN
C J MENKES
Service de Rhumatologie A
Hôpital Cochin
27 rue du Faubourg Saint-Jacques
75014 Paris, France

Inhibition of xanthine oxidase by allopurinol: its lack of effect on models of inflammation

Sir: In response to an article published in the Annals, entitled ‘Inhibition of xanthine oxidase by allopurinol: A therapeutic option for ischaemia induced pathological processes’?,1 we wish to report our findings on the effect of xanthine oxidase inhibition in models of joint


and soft tissue inflammation. Recent evidence shows that endothelial cells subjected to immunological stimuli and ischemia-reperfusion injury stimuli produce reactive oxygen species, that allopurinol and oxypurinol may be effective in reducing radical production and concomitant cell damage. As xanthine oxidase is considered to be one of the sources of these radicals its contribution to the pathogenesis of injury requires clarification.

As the potential contribution of xanthine oxidase lies both in endothelial cell activation and in ischemia-reperfusion injury we used mice as a model in which an ischemia-reperfusion injury component had not previously been invoked (carrageenan induced air pouch inflammation and foot pad inflammation in the rat) and, in addition, a model of chronic persistent synovitis (adjuvant arthritis) in which the joint movement may lead to ischemia-reperfusion injury as suggested by Blake et al.

Allopurinol (18 mg/kg daily for five days before killing) drinking water had no effect on acute inflammation induced by the subplantar injection of carrageenan in the rat paw. Similarly, allopurinol injected directly into rat air pouches (10-250 mg/kg daily for three days and that resulted in no effect on the acute (24 hour) or chronic (seven day) phases of carrageenan induced inflammation in this model as measured by total white cell count. Possibly, the use of a low molecular weight inhibitor such as allopurinol with relatively fast renal clearance, resulted in incomplete inhibition of the enzyme for at least part of the duration of the experiment.

We therefore used a more direct method to test the role of xanthine oxidase in inflammation by preventing the synthesis of active enzyme.

Tungsten mediated inhibition of molybdenum cofactor synthesis results in a profound inhibition in the activity of the enzyme xanthine oxidase, one of only three molybdenum dependent enzymes found in rats. We found that rats fed a diet low in molybdenum and supplemented with tungsten showed no change in the progress of carrageenan induced paw oedema when compared with rats fed a matched diet without tungsten supplementation and with defined molybdenum content. Similarly, there was no change in the progress of, or extent of, Mycobacterium buycrurn induced adjuvant arthritis (disease assessed by a joint scoring system and total body weight variation).

In conclusion, it seems unlikely that xanthine oxidase system plays a significant part in these models of inflammation.

We have previously proposed that the arthritic component of adjuvant disease may be exacerbated by episodes of ischemia-reperfusion injury and that this may be a feature of chronic synovitis in humans. Although these experiments do not support that hypothesis, they do not exclude other ischemia-reperfusion mediated sources of injury or the effectiveness of trace amounts of residual xanthine oxidase. The immunological component of adjuvant disease is so powerful a drive in the progress of the arthritis that this is probably not the most sensitive of models for testing the contribution of a non-immunological variable. Ischaemia-reperfusion injury has not been proposed as a contributory factor in the other models of inflammation we used, but the involvement of endothelial cells in acute inflammation is well known and the aim of these experiments was to assess the contribution of xanthine oxidase in the endothelial cell response. Allopurinol is apparently ineffective in these models either because xanthine oxidase inhibition is unimportant or because a greater degree of inhibition is required.

Correspondence to: Professor Blake.


Genitourinary tract infections in women: the role of Trichomonas vaginalis infection in our patient, and appropriate cultures were all negative. She was treated with metronidazole to cover possible anaerobic infection.

Sukhraj Krvavic
Women’s Health Institute and Medical Center
Sarajevo, Yugoslavia

Sir: There was no evidence of Trichomonas vaginalis infection in our patient and appropriate cultures were all negative. She was treated with metronidazole to cover possible anaerobic infection.

Rheumatological journals

Sir: With the expansion of rheumatology over the past 50 years and the establishment of many new rheumatology centers in the United Kingdom, Europe, and elsewhere there must be a demand for back numbers and volumes of journals covering this exciting period, but I find it difficult to dispose of the following either for a nominal charge or for carriage:

Annals of the Rheumatic Diseases (1945-1982), all bound
Arthritis and Rheumatism (1958-1988)
Rheumatology (1981 to date)
British Journal of Rheumatology (1973 onwards), unbound

It seems unlikely that I shall need them after this current year and I would welcome any offers from new centres in the United Kingdom or abroad. They take up a lot of shelving but it seems a pity to discard them, together with the other journals, the Journal of the Royal Society of Medicine, the Journal of the Royal Society of Medicine, and the Annals of Internal Medicine, if there is any current need for them.
Inhibition of xanthine oxidase by allopurinol: its lack of effect on models of inflammation.

R E Allen, A W Claxson, D R Blake and C J Morris

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