Alternatives to allopurinol

Sir. In their letter to the Annals Kelsey et al state that there is ‘no available alternative to allopurinol with its unique mode of action’.1 There are at least two alternatives:1–4 isopurine (1H-pyrazolo[3,4-d]pyrimidine-4-thiol (C_{4}H_{4}N_{4}S)) and oxypurinol (1H-pyrazolo[3,4-d]pyrimidine-4,6-diol(C_{4}H_{4}N_{4}O_{2})). Neither are available in the United Kingdom.

In the treatment of gout, isopurine has been shown to reduce effectively both the plasma and urinary uric acid levels of hyperexcretors, but plasma levels only of normal excretors.5–7 These effects were shown without a concomitant increase in urinary hypoxanthine and xanthine excretion.8,9 Isopurine is only one tenth as active as allopurinol (1H-pyrazolo[3,4-d]pyrimidin-4-ol(C_{4}H_{4}N_{4}O)) as a xanthine oxidase inhibitor in vitro,2 and is ineffective in lowering uric acid levels in gout associated with a partial deficiency of the enzyme hypoxanthine guanine phosphoribosyl transferase.10,11 Therefore, isopurine reduces uric acid concentrations by interfering with the early stages of its synthesis, thus avoiding increased blood concentrations of hypoxanthine and xanthine. There is no evidence that there is a cross reactivity between isopurine and allopurinol. The dose range is from 200 to 400 mg daily.

Oxypurinol is the active metabolite of allopurinol in vivo. Its half life is about eightfold longer than that of allopurinol.8 Allopurinol is the more effective administered orally in view of the relatively poor absorption of oxypurinol from the gastrointestinal tract.9 Although several patients with a history of untoward reactions to allopurinol have received oxypurinol without cross reactivity,11 others do cross react, and in some cases may have an immunological basis.11

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References


Hyper-responsiveness to EBV in ankylosing spondylitis

Sir. Recently, Drs Robinson and Panayi reported a deficient control of in vitro Epstein-Barr virus (EBV) infection in patients with ankylosing spondylitis (AS).1 Under blind study control, using peripheral blood mononuclear cells from B27+ spondylitic patients, we have observed a similar hyper-responsiveness to EBV. Cultures were set up in quadruplicate in 96-well, flat bottomed microtitre plates. Virus supernatant, obtained from a 10 day culture of B95–8 marmoset cells, was titrated and mononuclear cells were added to each well to give a final concentration of 5 x 10^5 cells/ml. Fig. 1 shows the minimum virus concentration required to immortalise the blood B cells of patients with either clinically active AS or rheumatoid arthritis (RA). In these experiments, cells from 90% (9 of 10) of the spondylitic patients and 69% (11 of 16) of the rheumatoid patients formed permanent cell lines and the range of minimum concentrations was similar; the results are based on six week cultures. Since we have shown previously an increased responsiveness to EBV of rheumatoid blood B cells2 we extended the experiments further to evaluate the role of the spondylitic B cell in this observed hyper-responsiveness. Non-T cells, negatively selected using 2-aminoethyls- thiourea bromide hydrobromide (AET) treated sheep erythrocytes, were infected with EBV supernatant at a dilution of 1/10. Work from our laboratory has previously shown this dose to be effective in the measurement of hyper-responsiveness in RA.2 Infected and uninfected cells were set up in 24-well, flat bottomed plates at a concentration of 5 x 10^5 cells/ml. The results of six week cultures are shown in Table 1. In this study no healthy individuals were used and the number of rheumatoid patients was small. The results for the rheumatoid patients, however, were in agreement with our previous data from a larger study.2 There, we reported that no B cells from healthy controls spontaneously grew into cell lines as compared with 22% of the B cell samples from rheumatoid patients and only 40% of infected healthy B cells were maintained in culture for six weeks; some of the 'normal' controls carried the