Conclusions

COLIN G BARNES AND JOHN L DECKER

The problem of adequately suppressing disease activity in rheumatoid arthritis remains with us, and it is acknowledged that currently available drugs are only effective in a proportion of patients. These drugs do not eradicate the disease, their effect in some patients may only be modest and all are potentially toxic.

The immunological basis for the use of the immunosuppressive agents is well known and the rationale for their use has been reviewed in these proceedings by Dr Hitchings and Dr Denman, both of whom envisage substantial developments in this form of treatment in the future.

Again, the clinical efficacy of gold and azathioprine has been reviewed, indicating long-term effect of these drugs in suppressing rheumatoid inflammatory activity. The point has been stressed, however, that to hope to obtain lasting benefit for the patient, suppressive medication must be continued for many months or years. Increasing benefit to the patient may continue for one or more years after the drug has been started, and thus, in a chronic progressive disease, short courses of drugs which may modify the disease process are unlikely to prove effective in modifying the long-term progress of the disease. It is difficult to achieve suitable radiological comparison groups over extended time periods, but azathioprine over 18 months has been associated with less x-ray deterioration than that observed with gold.³⁸

In view of the potential toxicity of this form of treatment, and the need to continue treatment long-term, much of the discussion has concentrated on toxic effects. Of these, gastrointestinal intolerance to oral medications and bone marrow suppression, the latter virtually always reversed by dose reduction, are

well known. These have again been reported in a substantial proportion of cases. However, the possible potential for the 'immunosuppressive agents' to induce neoplasia has been reviewed in as much detail as is presently available. The results remain inconclusive with sporadic reports of commonly occurring solid tumours developing in patients while receiving azathioprine or other antimitotic agents. Uncertainties as to the incidence of cancer in rheumatoid patients who have not received cytotoxic drugs are sufficiently great, and the incidence in azathioprine treated rheumatoids is so low, as to necessitate further controlled analysis of the problem. There has not been any substantial incidence of lymphoreticular tumours reported as is known to occur in patients receiving these drugs after renal transplantation.

Thus, this workshop has served to review the current knowledge on the effect and toxicity of drugs aimed at suppressing rheumatoid disease, with the conclusion that all of these drugs—gold salts, penicillamine and immunosuppressives (azathioprine and cyclophosphamide in particular)—may be partially effective but toxic. Although the immunosuppressives still require further evaluation regarding oncogenesis and studies are continuing, there do not seem to be any notable differences in frequency or severity of toxic reactions when one drug is compared with another. The alkylating agents may present a slightly increased risk. Until more effective and less toxic drugs are developed to suppress rheumatoid disease in our patients, we continue to have to use available agents to improve their clinical situation, realising the need for careful supervision during long-term treatment.