CONCLUSION

The introduction of a therapeutic agent capable of producing selective inhibition of xanthine oxidase has been an event of considerable pharmacological significance. For this reason investigators from various countries were invited to participate in the symposium on allopurinol. A useful interchange of experience took place and the collected papers, discussion, and bibliography give a comprehensive account of current ideas on the subject.

The drug is clearly capable of producing effective and sustained suppression of uric acid formation and its theoretical uses are being substantiated in clinical practice. While the level of uric acid in many patients with gout can be adequately reduced with uricosuric drugs, there are certain situations, such as severe chronic tophaceous disease or advanced renal failure, where these are not effective or only partially so, and where allopurinol brings special advantages. It seems likely that allopurinol will eventually become the treatment of choice in all patients in whom it is desired to lower the serum uric acid, though further experience will be necessary to establish this. The management of patients with uric acid stones has been radically changed by allopurinol and it is now possible to prevent the serious complication of acute uric acid nephropathy which can occur during the treatment of leukaemia and malignant disease with cytotoxic drugs.

Toxic effects do not appear to be a major problem, skin rashes being the most troublesome though not very common. There is the possibility of other more serious hazards, such as disorders of iron metabolism, liver damage, and xanthine stone formation: these were fully discussed by several speakers in the symposium but none of these hypothetical complications has yet been encountered clinically.

It is also likely that these recent developments will have a bearing on long-term research into gout and abnormalities of purine metabolism. It is true that the reaction mediated by xanthine oxidase and inhibited by allopurinol—oxidation of the oxypurines xanthine and hypoxanthine to uric acid—is the final step of purine metabolism in Man, and that abnormalities responsible for uric acid overproduction lie at earlier stages. But it is clear that stimuli have been provided for further work, for example, investigation into the reduction in overall purine excretion which so often and unaccountably accompanies the use of allopurinol. Indeed, knowledge of underlying mechanisms in gout has always lagged behind therapeutic ability. We possess several drugs which effectively terminate or prevent the acute gouty attack—and one of them, colchicine, has been known for centuries—but we have little idea of the actual processes concerned despite a good deal of interesting work and speculation now going on. Similarly, we can manipulate a patient’s serum uric acid level by different methods to his obvious benefit, but the ease and degree of control which we can achieve seem almost presumptuous when one considers how ill-defined remains our concept of hyperuricaemia and its causes.

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