Studies with Allopurinol (HPP) in Patients with Tophaceous Gout

By CHARLEY J. SMYTH, M.D.

University of Colorado School of Medicine

We elected to use HPP in four of our most stubborn patients and studied them on a metabolic ward. The pattern of the experiment is illustrated in Figure 131.

The patients all had advanced tophaceous disease. Each of these patients was removed from all his previous urate diuretic therapy during a control period and was then given HPP in a dose of 800 mg. per day. Following another control period each patient was given both HPP and Anturane together.

The serum urate levels have followed the patterns that others have described and this needs no repetition. The amount of urinary output in this patient remained remarkably unchanged. An acute attack of gout occurred while receiving HPP. We also have found that acute attacks of gout are very frequent and in each of the four patients that we have studied there has been an acute exacerbation of acute gouty arthritis either during HPP therapy or immediately after it. Our interest was to follow the serum urate concentration upon withdrawal of HPP and upon resumption of the drug. The urate levels rose to the pretreatment level and when exhibiting the drug again, the serum urate immediately came down. When we gave the patient a combination of Zyloprim and Anturane, a very satisfactory and sustained urinary excretion of urate occurred, and a sustained suppression of the serum urate below normal level was attained. The patient is now on about the 130th day of the study and is receiving both drugs as an outpatient with very satisfactory control and without any further acute attacks (Fig. 131).

The second patient exhibited a little different response as far as the urinary excretion of uric acid is concerned. There was a very significant drop in the amount of urinary uric acid output. When the HPP was stopped, the amount of urinary uric acid in the urine returned to the pretreatment level. The serum urate returned toward normal and when the drug was again exhibited it came down again. When the two drugs, HPP and Anturane, were given together, the urinary uric acid excretion increased. An acute attack occurred which was treated with Butazolidin and a very satisfactory result was observed. As others have observed, a rash occurred. Because of this we reduced the amount of HPP from 800 mg. per day to 400 mg. per day. The rash did not recur. It would appear that 200 mg. HPP was not adequate to bring the serum urate to 6 mg. per cent or below (Fig. 132).

The third patient is one who had six years of therapy with sulfinpyrazone. The finger which was normal six years before had gone on to this destructive

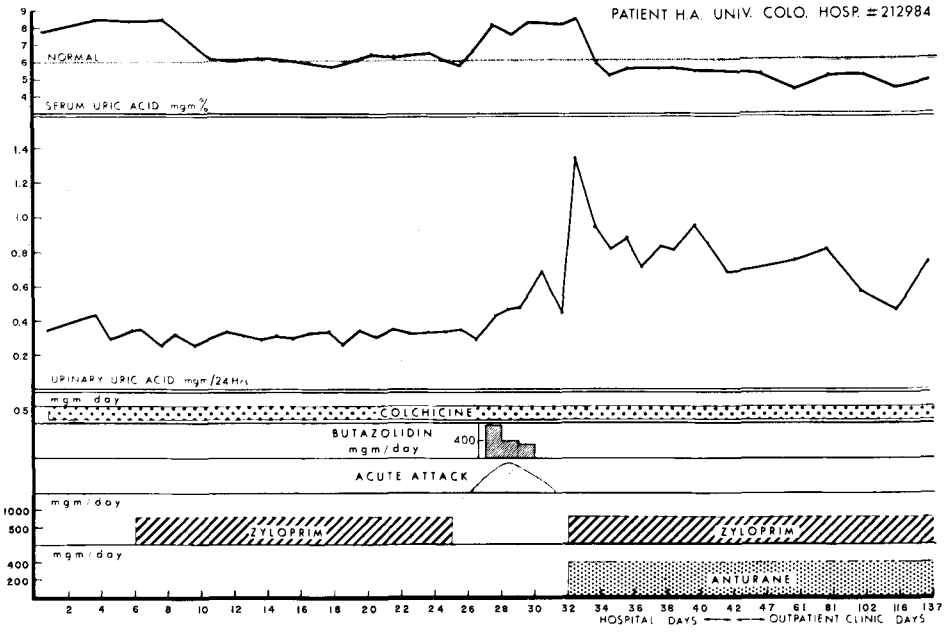

Fig. 131.

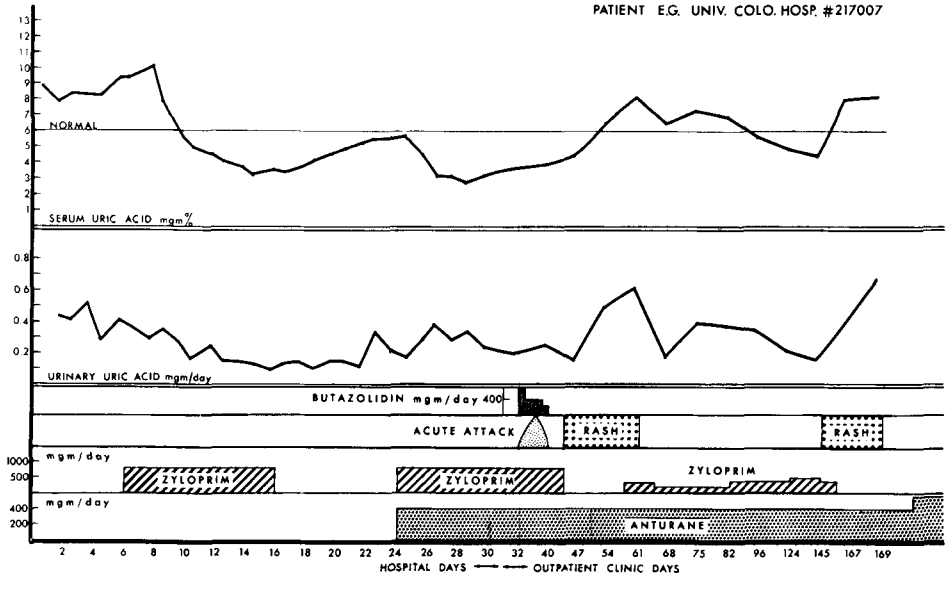

Fig. 132.

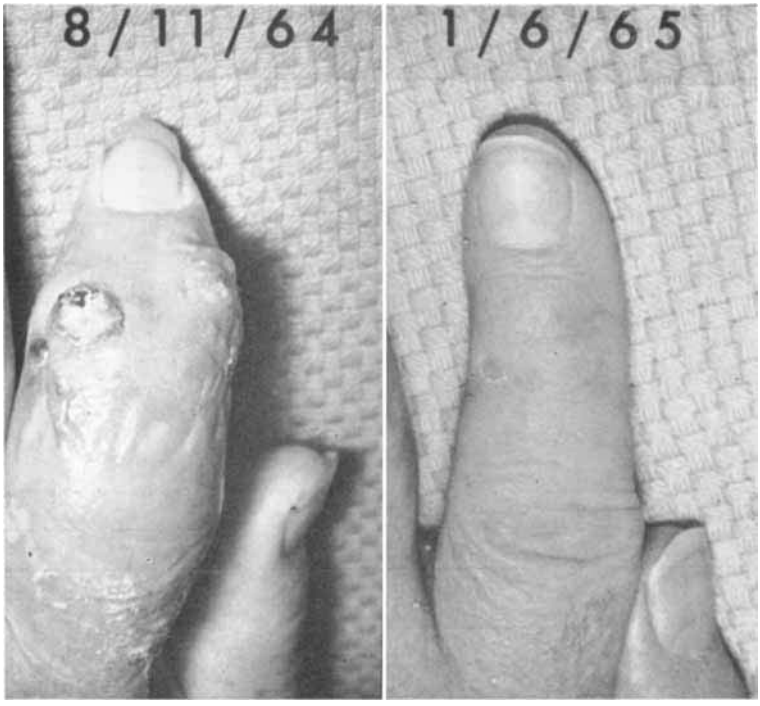

Fig. 133.—(Left): Left index finger patient, F. D. (Case III) at the beginning of allopurinol therapy (8/11/64) showing draining and infected tophus overlying distal interphalangeal joint. (Right): Same finger 4½ months later (1/6/65) with marked reduction in the size of the finger and healing of the ulcerated tophus.

stage of the disease, with the development of ulcerated tophi as shown in Figure 133. This patient showed a different pattern of urinary excretion with HPP although the serum urate pattern is identical with that of the three previous patients. The serum urate came down and stayed down. When the drugs were discontinued, it came up again, and when the combination of HPP and Anturane was given the serum urate came down. This patient is now on about the 50th day of the study. The urinary uric acid excretion swings widely and I think he illustrates another type of urinary excretion pattern (Fig. 134).

In these three patients with advanced tophaceous disease and with renal disease, there has been a different urinary pattern excretion and the urinary uric acid excretion will probably vary from those who do not have advanced tophaceous disease.

We think that this new drug, HPP, has an exciting potential for therapy. There is no interference with urate diuretic therapy and we can attack the overproduction of uric acid with the xanthine oxidase inhibitor, HPP, and increase the urinary output wtih the currently available drugs. With this dual attack we may be able to improve the management of the difficult cases of gout which we all encounter.

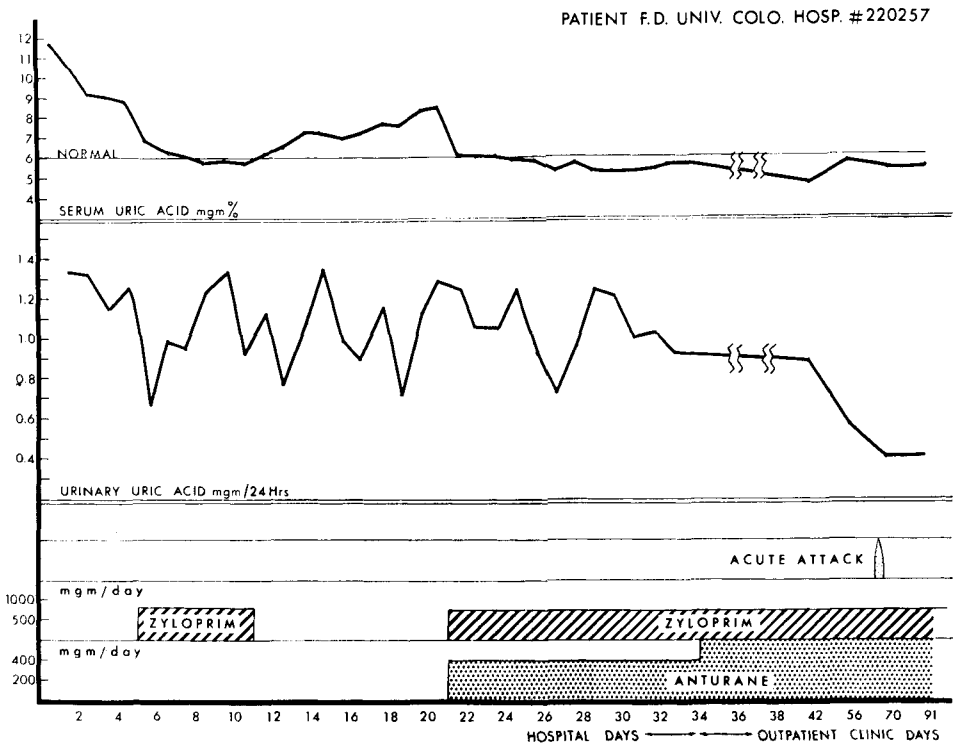

Fig. 134.

I turn the meeting back to Dr. Gutman and say for our participants that we deeply appreciate your efforts.

DR. GUTMAN: This Conference has been a most inspirational experience, I think, for all of us. The credit does not go to me but to Dr. Lamont-Havers and his staff. I want to express to them our appreciation of their wonderful arrangements for the meeting, and also our thanks to the supporting agencies. I want to thank the participants again for their interest and indulgence.