because we are missing the diagnosis. You did not comment on two particular diagnostic features. One is the menstrual irregularities affecting women, and the second is tenosynovitis especially around the wrist and ankle.

**DR. SEIFERT** Three of the patients had tenosynovitis in the region of the wrist. Seven patients presented with symptoms within a few days of a menstrual period, and one was pregnant.

**PROF. E. G. L. BYWATERS (London)** I seem to remember crystals had fibrosis, tubular permanent were concomitant.

**Discussion**

**PROF. E. G. L. BYWATERS (London)** I seem to remember that I had two reprints from the 19th century on spontaneous guanine gout in pigs (Ewing, 1895). Have you actually excluded guanine in these deposits? The second point is that the kidneys you showed looked very much like the kidneys I have described in crush syndrome, in haemoglobinuric nephropathy in sulphonamide crystal deposition, or in hydronephrosis. Have you seen any of the tubular venous aneurysms found in those conditions? I have not observed them in the rather analogous acute kidney that you see in secondary gout when there is a great deal of urate excretion.

**DR. HATFIELD** The leg weakness which occurs in pigs has been attributed to guanine gout, as the pig was thought to lack the enzyme guanase. The kidney deposits did not contain guanine, in spite of the large doses of guanine we used in conjunction with the allopurinol to block xanthine oxidase. The pig can obviously metabolize guanine easily and does not get guanine gout. We did not see any aneurysms in the affected kidneys.

**DR. D. I. HASLOCK (Leeds)** Allopurinol treatment in man has been associated with crystal deposition in muscle. Did you find any crystal deposition in muscle or elsewhere in your pigs?

**DR. HATFIELD** We looked for crystal deposition in muscle and in other tissues but only found it in the kidney.

**DR. M. L. SNAITH (Oxford)** This very large dose of allopurinol is totally outside the normal range and one cannot be certain that you are mimicking the human situation. Since you are blocking xanthine oxidase so completely, a high proportion of oxypurinol would be produced and excreted by the kidney. Were there any crystals of this being formed? Because you blocked xanthine oxidase so effectively presumably the ratio of xanthine to hypoxanthine is rather different from usual, so again this would not be a very similar model of the human situation.

**DR. HATFIELD** We had to use this large dose of allopurinol to produce the crystals in the tube. As I said the dose is 70 times greater than had been given to man. The crystals did contain oxypurinol, they were a mixture of xanthine and oxypurinol in the ratio of 2:1 so there were large quantities of oxypurinol being formed. The experiment was designed to produce a crystal nephropathy not to test the toxic affects of allopurinol. We did show however that allopurinol alone, even in these high doses, had no effect on kidney histology or function.

**Reference**

Acute intratubular crystal deposition causing permanent renal damage in the pig.
P J Hatfield, H A Simmonds, D A Farebrother and A S Jones

Ann Rheum Dis 1973 32: 393
doi: 10.1136/ard.32.4.393

Updated information and services can be found at:
http://ard.bmj.com/content/32/4/393.citation

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/