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*) The histology of the skin lesions is very much like that of an Osler's node taken in the acute stage.

References

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Acute Intratubular Crystal Deposition causing Permanent Renal Damage in the Pig. By P. J. HATFIELD, and H. A. SIMMONDS (*Guy's Hospital Medical School*), D. A. FAREBROTHER (*Wellcome Research Laboratories*) and A. S. JONES (*The Rowett Research Institute*).

Irreversible renal damage has been produced experimentally in pigs by dietary loading with guanine (150 mg./kg.) and the xanthine oxidase inhibitor allopurinol (300 mg./kg.) for a 3-week period. These experiments may provide an animal model for gouty nephropathy.

Twelve pigs weighing approximately 25 kg. at the beginning of the experiment were studied for a period of 8 weeks. Four pigs were used as controls, four were killed during the 3-week loading period, and four were killed 4 weeks after they had been returned to a normal diet.

Animals killed during the 3-week loading period had grossly enlarged kidneys with intratubular crystal deposition, accompanied by an interstitial nephritis and a concomitant fall in renal function. The animals which were subsequently maintained on a normal diet showed a return towards normal renal function as judged by blood urea and creatinine clearances. However, the kidneys of these animals were shrunken and scarred and although the crystals had dissolved there were large areas of interstitial fibrosis, tubular degeneration and glomerulosclerosis.

These experiments demonstrate that intratubular crystal deposition for even short periods may produce permanent renal damage in the pig.

Discussion

PROF. E. G. L. BYWATERS (*London*) I seem to remember that I had two reprints from the 19th century on spon-

taneous 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 tubule. 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

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