Discussion

PROF. D. L. GARDNER (*Belfast*) There is some indirect evidence which supports Dr. Russell's interesting hypothesis. We have recently examined the kidneys from two cases of infectious mononucleosis nephritis and there is a striking similarity in the microscopical findings and those pictures shown today. A further situation which supports your general hypothesis is Aleutian disease of blue mink. I wonder whether you would like to comment on the possible relationships between N.Z.B. disease, Aleutian disease of blue mink, and the infectious mononucleosis nephritis in terms of virus nephritis.

DR. RUSSELL We are also looking at the Aleutian mink disease, which again shows a marked vascular infiltration of superficially the same type, but in fact the cells are largely plasma cells. Infectious mononucleosis has also depression of T-cell controlling factors and they show depression in the PHA and PPD responses. So again this may be a similar type of mechanism. There is also the possibility that it is an immune complex nephritis which may be generated in the classical way or perhaps again by autoantigens, because patients with infectious mononucleosis develop nuclear antibodies.

DR. W. C. DICK (*Glasgow*) Do your experimental methods exclude the possibility of complement-mediated killing or of B-cell killing? I am interested by your ratio of lymphocytes to target cells which seem to me very similar to that of the Hellströms. Why do we need so many cells to kill one target cell?

DR. RUSSELL I think these target cells can rapidly resynthesize the lesions in the cell membranes and that is why you have to hit them in several places at once. There is no overt complement in this system; the question is whether complement is synthesized by the cells that are present. I think this is irrelevant, because we know that lymphocytes do contain some complement components, C'9 for example, and maybe the lesions are mediated by a C'9 but this is nevertheless cell-mediated toxicity. They did not synthesize all the components of complement so it is not conventional cytotoxicity.

DR. L. E. GLYNN (*Taplow*) The proportion of sensitized cells amongst the number you put into the tube is probably very low. In the *in vivo* system, the whole body content of the sensitized cells becomes available to make the necessary contacts. So you would need a very much higher proportion of static cells for the right number of sensitized ones to make contact.

Benign Gonococcal Arthritis with Cutaneous Lesions. By M. H. SEIFERT, A. C. MILLER, and A. P. WARIN (*Departments of Rheumatology, Venereology, and Dermatology, St. Thomas' Hospital, London, S.E.1*).

The association of cutaneous lesions and arthralgia with gonorrhoea was noted for the first time for 20 years in the English medical literature by Abu-Nasser, Hill, Fred, and Yow (1963).

Since then a number of papers from the United States and Scandinavia have appeared, but, apart from three patients reported by Wolff, Goodman, and Vahrman (1970), there has been no other series from a British source.

Fifteen patients with benign gonococcal arthritis accompanied by cutaneous lesions were seen over a period of 18 months.

The diagnosis was suspected when patients presented with joint pain and swelling usually associated with typical cutaneous lesions and pyrexia. Confirmation required the isolation of *Neisseria gonorrhoeae* from the genital tract, blood, or synovial fluid.

The age range of the patients was 17 to 43 years; all except three were females, and the series included a married couple.

On clinical examination all fifteen patients had an inflammatory arthropathy that was asymmetrical, sometimes migrating, predominantly of the larger joints, and in thirteen accompanied by pyrexia.

Typical cutaneous lesions appeared in thirteen patients a few days after the arthralgia. These were initially erythematous macules which became maculopapular, vesiculopustular, and usually haemorrhagic. They were distributed over the limbs and were found on the trunk in only two patients. Skin biopsy in three patients showed no evidence of focal sepsis.

None of the patients complained of urogenital symptoms and no evidence of salpingitis was found in the females.

All patients responded dramatically to antibiotics within 24 to 48 hours of treatment.

Benign gonococcal arthritis with cutaneous lesions has been found to be less rare than has been previously thought (Boyle and Buchanan, 1971). In fact, nine of these patients presented within a period of 5 months.

The findings indicate that a diagnosis of benign gonococcal arthritis with cutaneous lesions must be considered in any patient with a combination of fever, polyarthritis, and vesiculopustular or haemorrhagic skin lesions.

Discussion

DR. F. DUDLEY HART (*London*) This condition is rather more common nowadays. For years I never saw gonococcal arthritis at all and Reiter's syndrome dominated the scene. The problem is not so much one of the individual but of the social group and family.

DR. A. S. RUSSELL (*Canada*) Did the three men have urethral discharge or was it rectal gonorrhoea that they contracted? For the joint fluid cultures, did you use regular media or the hyperosmolar media to try to culture the L forms?

DR. SEIFERT The three men denied having urogenital symptoms, though they did have urethral discharge on examination; they did not have rectal gonorrhoea. I am not aware of the cultural techniques used by the bacteriology department.

DR. R. GRAHAME (*London*) Does the gonococcal complement-fixation test help in the diagnosis of this condition?

DR. SEIFERT In eleven cases we performed the gonococcal complement-fixation test and only four of these were positive.

DR. G. V. HUGHES (*London*) I noticed a marked difference in the prevalence of gonococcal arthritis between America and the United Kingdom and I do not think it is

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

- Ewing, J. (1895) *Proc. N. Y. path. Soc.*, 1894, p. 107