## Experimental Nephritis in Histamine- or 5-Hydroxytryptamine-depleted Rats

SIR,—Masugi (1933) evolved an experimental method for producing nephritis, by injecting specific nephrotoxic serum. Nephritis produced in this way appeared closely akin to human glomerulonephritis, in its clinical course and pathologic lesions (Seegal and Bevans, 1957). Sometimes symptoms resembling anaphylactic shock have also been produced (Baxter and Goodman, 1956). Preferential depletion of histamine and of 5-hydroxytryptamine (5-HT) from the rat, according to the method of Parratt and West (1957) did not affect the production of fatal anaphylactic shock (Sanyal and West, 1958), though contrary viewpoints regarding the role of histamine in anaphylaxis in this species have been reported (Mota, 1957). We have therefore been interested to discover whether the production of experimental nephritis could be influenced by previous depletion of histamine or 5-HT.

Kidneys from rats were perfused in saline to remove all traces of blood before being homogenised with saline to give about 1 g./ml. After the injection i.p. on 6–12 occasions at intervals of 1–2 days in rabbits, an antibody titre of serum was produced which was not less than 1 in 32, but usually between 1 in 64 to 1 in 128, as determined by a complement fixation test. Intravenous injection of 1 ml. of such sera per 100 g. of weight per rat was sufficient to produce histologically detectable changes.

The changes which were present in more than three-quarters of the animals, and appeared 24 hr. after treatment, consisted of swelling of epithelium of collecting tubules, distal and proximal convoluted tubules, almost blocking the lumen; dilatation of glomerular capillaries and oedema of interstital tissues. At 48 hr., the lesions were more marked, proliferation of glomerular tufts, adhesions between tufts and capsules were also present. In some animals epithelial crescents were seen.

Groups of 10–12 rats of either sex weighing about 100 g. obtained from local dealers were used for the main study. Animals were fed with "Anidiet" the composition of which has been previously described (Dhar and Sanyal, 1962). Water was allowed *ad lib.* One group of animals served as control, while one group received injections of polymyxin B to deplete tissue histamine, a third group received injections of reserpine to deplete 5-HT (Parratt and West, 1957).

Each of the animals then received an intravenous injection of the same batch of nephrotoxic serum. In the control group approximately 60 per cent of animals developed changes of nephritis; in the rest lesions, though present, were minimal.

In animals depleted of histamine by polymyxin injections, and then given nephrotoxic serum, kidney changes were insignificant in almost all animals.

Results obtained in animals depleted of 5-HT by injections of reserpine, were quite severe and of two types. In about half the animals, areas of coagulative necrosis were present. The lining epithelial cells of the convoluted tubules showed granular acidophilic cytoplasm with pyknotic or no nucleus. In other animals, granular material was seen in the glomerular spaces; those animals which showed considerable exudation had shrunken glomerular tufts: all stages of distintegration of glomerular tufts could be demonstrated.

Repeated injections of histamine, 5-HT or polymyxin did not produce significant histological changes in kidneys of rats.

Injections of reserpine in several species (rat, dog, guinea-pig, rabbit and mouse) failed to produce histological renal lesions. This is of significance,

since reserpine given before the nephrotoxic serum produced aggravated lesions.

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## REFERENCES

Baxter, J. H. and Goodman, H. C. (1958). *J. exp. Med.*, **104**, 467–485.
Dhar, H. L. and Sanyal, R. K. (1962). *Int. Arch. Allargy*, **21**, 172–178.
Masugi, M. (1933). *Beitr. path. Anat*, **91**, 82–112.
Mota, I. (1957). *Brit. J. Pharmacol.*, **12**, 453–456.
Parratt, J. R. and West, G. B. (1957). *J. Physiol.*, **137**, 179–192.
Sanyal, R. K. and West, G. B. (1958). *Ibid.*, **144**, 525–531.
Seegal, B. C. and Bevans, M. (1957). *J. chron. Dis.*, **5**, 153–172.