# PANCREATIC, HEPATIC AND VASCULAR CHANGES FOLLOWING LOWER-NEPHRON NEPHROSIS IN RATS *

J. A. H. CAMPBELL, M.MED. (PATH.) (CAPE TOWN), *Department of Pathology, University of Cape Town*

The speaker presented his findings in 26 male albino rats given subcutaneous glycerol and intravenous bile-salts in the form of deoxycholate. The dose of glycerol used was large enough to ensure severe intravascular haemolysis and consequent acute tubular necrosis (lower-nephron nephrosis) which, in the rat, is associated with a great number of other lesions of which only the pancreatic, hepatic and vascular were further described. Not all three lesions occurred in every animal and they varied in severity in affected rats.

The pancreas showed interstitial oedema, haemorrhage and polymorph exudate with duct changes and, in the later stages, a fibroblastic response around atrophic acini. Disseminated necrosis of abdominal fat occurred after 48 hours. Vascular changes seen microscopically were blood sludging in capillaries, hyaline swelling of arterioles, and loss of mural structure in muscular arteries. The commonest hepatic lesion was focal coagulative haemorrhagic necrosis, but a few rats showed great swelling of cell cytoplasm and nucleus without true necrosis of cells.

The pathogenesis of the syndrome of changes resolved itself roughly into answers to the following questions: Are the changes the result of a specific toxic effect of glycerol or the result of some unknown non-specific action common to glycerol and other agents, or is the kidney damage the primary event with all others simply a consequence of the uraemic state? Of the accepted views on the pathogenesis of the lower-nephron nephrosis, none appeared to provide an explanation of the other organ changes seen in the glycerol-treated rats, though capillary sludging remained an intriguing possibility. A comparison was then made with other morphologically similar experimental lesions in an attempt to obtain indirect evidence of the pathogenesis of the glycerol lesions, many of the examples being chosen deliberately on provocative grounds alone. Comparison was first made with the acute vascular change in rats suffering malignant hypertension or uraemia following nephrectomy, and with the proliferative so-called polyarteritis nodosa lesions reported after renal infarction in rats. In particular the apparent scarcity of these lesions in all experimental methods including glycerol administration was commented on and regarded as establishing not the importance of uraemia in the pathogenesis of these vascular changes but simply that on a frequency basis the evidence in glycerol experiments in favour of uraemia was as poor as that in other experiments. Attention was drawn to the fact that ethionine feeding to rats produces the same pancreatic changes as follow glycerol, and the further point made that etnionine like glycerol, results in renal tubular necrosis, hepatic lesions and adrenal haemorrhages. A final comparison was made between the haemorrhagic liver necrosis following glycerol and that seen after certain dietary procedures in the rat, the examples chosen being cystine intoxication and choline- and vitamin E-deficient diets, all of which are known to cause renal tubular damage. None of these other experimental lesions appeared to offer any explanation of the glycerol lesions but the frequent occurrence of renal damage in such feeding experiments did suggest the question: 'Are the dietary procedures in such dietary experiments always necessary or would not renal damage induced by any agent such as glycerol prove just as successful?'

No attempt was made to relate the experimental findings to human pathology.

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