EXPERIMENTAL NON-DIETARY CIRRHOSIS IN RATS*

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A description was given of a Laennec-type cirrhosis produced in rats by the following method: On the first day of the experiment 2 ml. per 100 g. body-weight of egg yolk diluted 1 : 1½ in isotonic saline was injected intravenously and the left and right renal pedicle tied 4 - 6 hours later. Intravenous egg-yolk injections were then continued every second to fourth day until the rats were killed. During this time they were allowed water and rat cubes *ad lib.*

Although the injections were large they were well-tolerated. They did, however, cause oedema of the paws, redness and some swelling of the ears, and nose scratching. These signs are customarily regarded as evidence of histamine liberation in the rat. Cirrhosis occurred in 15 consecutive experiments when the method outlined was carefully followed, and developed in the surprisingly short time of 21 - 48 days. At autopsy the liver was finely granular and generally slightly enlarged. Microscopical examination confirmed the cirrhosis but showed no evidence of massive, zonal or focal necrosis. Necrotic liver cells were observed, but these occurred as single isolated cells or as small groups of cells at the periphery of the lobule and were most easily found in the earlier stages of the process when fibrous-tissue bands were just beginning to proceed from the portal tracts. A moderate infiltration of haemosiderin-laden histiocytes, plasma cells and eosinophils accompanied the fibrous-tissue response, but fatty change was absent in all cases.

Cirrhosis also developed in 2 of 3 rats in whom unilateral nephrectomy was substituted for unilateral renal-pedicle ligation and in a further 2 rats when 1% salt was put into the drinking water and no renal operation performed. Cirrhosis was absent in 5 animals subjected to unilateral renal pedicle ligation alone, but did develop in 2 of 6 rats given intravenous egg yolk alone. The limited success with egg yolk suggested that increased physiological strain on the kidney acts as an adjuvant in the pathogenesis of this type of cirrhosis, and attention was drawn to the renal lesions that occur in choline deficiency and after carbon tetrachloride poisoning.

Discussion was largely confined to the pathogenesis of the experimental lesion and little attempt made to relate the findings to human pathology, though they might seem applicable to the cirrhosis of porphyria. It was almost certain that some functional overload of the liver occurred after such large intravenous injections of egg yolk, but this did not seem to operate either by producing a relative deficiency of lipotropes or by any known hepatoxic action. The experiments appeared to have a precedent both in Eppinger's early work relating the action of histamine to experimental cirrhosis and also in recent reports from Japan of Laennec cirrhosis following partial ligation of the inferior vena cava and injections of histamine or egg albumin. However, some features of the present experiments as well as preliminary failure to produce cirrhosis with the histamine liberator 48/80 suggested that histamine liberation alone was probably not the most important factor in the production of cirrhosis in the egg-yolk experiments.

Bacterial infection was thought to be a most unlikely explanation of the cirrhosis following egg-yolk injections, but this possibility was only completely excluded in the later experiments.

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