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Changes in the Vascular and Lipoid Pattern of the Adrenal Cortex of the Rat following Hypophysectomy

As a preliminary to an investigation of the effect of adrenocorticotrophic hormone upon the circulation through the adrenal of the rat, it was necessary to study the normal adrenal vascular pattern and, in addition, that of the hypophysectomized rat, at weekly intervals after operation (1-16 weeks). The rats were injected intravitally with a mixture of equal parts of indian ink and distilled water pumped direct into the left ventricle at a constant injection pressure of 160 mm. mercury. The adrenals were fixed in 10 per cent formol saline after ligation of the vascular pedicle, and sections were cut at 50 μ after gelatine or celloidin embedding. Satisfactory preparations were obtained for a study of both the vascular pattern and the lipid distribution.

In normal rats the capillary pattern in the adrenal cortex as demonstrated by intravital indian ink injections shows three concentric zones. (1) An outer injected zone comprising the capillaries of the zona glomerulosa; (2) an intermediate 'zona lucida'¹ of poorly filled capillaries corresponding to the lipid-free cells of the 'zona intermedia'² ('transitional zone'³, 'sudanophobic zone'⁴, 'zone of compression'⁵), plus a small but variable depth of the outer part of the zona fasciculata; (3) an inner heavily injected zone of capillaries in the rest of the zona fasciculata and the whole of the zona reticularis. Careful measurements show that the outer edge of the zona lucida corresponds to the inner edge of the zona glomerulosa.

In hypophysectomized rats, owing to cellular shrinkage, which is most marked in the zona fasciculata and reticularis, there is a reduction in the inter-capillary distance with a resulting increase in the number of capillaries per unit area. These capillaries are also narrower than in the normal rat. For the first three weeks after operation a normal type of vascular zoning persists; thus with an increase in the depth of the zona intermedia there is a corresponding increase in the depth of the zona lucida (in ink preparations), and the sudanophobe zone (in lipid preparations). An increase in depth of the zona glomerulosa is a recognized sequel after hypophysectomy⁶, but it was found that this increase was maximal at about the fifth week, after which a decrease was observed¹. Between the fifth and eighth week there is a general reduction in the number and size of the capillaries throughout the cortex, which becomes much less vascular. By this time the zona fasciculata and reticularis are very narrow, and

there is a tendency towards homogeneity of cell-size throughout the cortex.

The lipid changes in the adrenal cortex of the rat during the first three weeks following hypophysectomy are well known. The striking change is the gradual widening of the fat-free zona intermedia or sudanophobe zone. We have noticed three additional points. (1) The outer half of the zona glomerulosa sometimes becomes free from lipid while the inner half is still heavily laden. To date we have not been able to correlate this change with any specific treatment such as castration or injection of adrenocorticotrophic hormone. We have observed differences in the capillary pattern of the inner and outer layers of the zona glomerulosa. It is possible that the zona glomerulosa might consist of two layers with different functions. (2) In rats hypophysectomized 16 weeks previously, the lipid-containing zona fasciculata and reticularis are very narrow or completely absent. Either these zones have disappeared or their cells have become completely depleted of lipid. The cortex of these rats is even more poorly vascularized than at 8 weeks. (3) From 5 weeks onwards after hypophysectomy, a few cords or lipid-containing cells from the zona glomerulosa are sometimes found invading the sudanophobe zone.

Conclusion. The poor filling of the capillaries in the zona intermedia of normal adrenals and in adrenals from recently hypophysectomized rats is a surprising finding. Large cells distended with lipid would be expected to press upon capillaries, but the capillary constriction is present at the site of small cells without lipid content. The cells of the zona intermedia still appear smaller than the cells of the adjacent zones in sections of freeze-dried vacuum-embedded adrenals. It is therefore unlikely that the cells of this zone have been artificially reduced in relative size by the ordinary methods of fixation. The Gomori method for alkaline phosphatase on these freeze-dried adrenals gives an excellent picture of the vessel walls and confirms the vascular pattern shown by intravital injection of indian ink.

The true function of the cells of the zona intermedia remains unsolved. There is no evidence for the widely held view that this is the zone of active mitosis in the adrenal cortex^{6,7}. If there is a vascular stop-cock mechanism present in this zone, it would not appear to depend upon the mechanical properties of the cells. There remains the possibility of local capillary constriction. Lever has recently described nerve endings in the zona glomerulosa⁸.

A more detailed report on the vascular and morphological findings has been prepared by one of us¹. We are grateful to the Nuffield Foundation for generous support of this work.

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Jan. 26.

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