

Experimental Chronic Hypertension in the Rat: Structural Changes in Blood Vessels, Heart and Kidneys.*

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Despite the frequent use of the rat in the study of experimental hypertension, microscopic studies of the organs of hypertensive rats are few.^{1,2,3,4} Moreover, since in most of these earlier studies, animals manifesting acutely fatal symptoms,² dead of pyogenic infections,³ or with suppuration⁴ were examined, the observations are not applicable to uncomplicated chronic hypertension.

Experimental. Varying degrees of chronic hypertension were produced in 16 piebald rats (Evans-McCollum strain) by application of a figure-of-eight ligature to one or both kidneys.⁵ The ligature was applied first to the right kidney of each rat when the animals were about 9 months old. Nine of the rats which failed to develop a rise in blood pressure to at least 150 mm of mercury within 3 or 4 months were then subjected to a similar operation on the left kidney. All of the animals were killed after the blood pressure had been maintained at levels between 150 and 240 mm of mercury for periods varying from 1 to 8 months. The blood pressures were determined by the plethysmographic method.⁶ During this period of observation a gradual rise in blood pressure occurred. However, the final pres-

sure as determined by daily readings had existed for at least 2 to 4 weeks, before the animals were sacrificed.

The heart, kidneys, spleen, liver, lungs, and occasionally other organs (pancreas, testis, brain, lymph node) were fixed in 10% formalin, imbedded in paraffin, and stained with hematoxylin and eosin. Microscopic examination of these organs and particularly of the heart and kidney disclosed the following pertinent data: Changes in the arteries of all the organs examined were minimal or absent. In every animal there was an increase in the width of the myocardial fibers of the left ventricle which in some instances were 2 or 3 times as wide as the fibers of the right ventricle. The striations of the fibers remained fairly intact. The nuclei were vesicular and retained their usual oval or "cigar" shape. Varying degrees of fibrosis occasionally accompanied these changes. The hypertrophy was usually commensurate with the degree and duration of the observed elevation in blood pressure.

In the kidneys, varying degrees of changes were observed involving individual or groups of nephrons. In the glomeruli, the changes ranged from slight focal fusion of the capillaries with Bowman's capsule to complete disappearance of the capsular space, increase of the connective tissue with hyalin change, and obvious obliteration of the structural pattern. The corresponding convoluted and collecting tubules contained a homogeneous bright pink material and were lined by flat cells. Their coarse convolutions occupied spaces larger than those of normal tubules. The widths of the cortical and medullary zones were decreased in proportion to the damage to the renal parenchyma. In focal areas there was an increase in the connective

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¹ Wilson, C., and Byrom, F. B., *Lancet*, 1939, 1, 136.

² Friedman, B., Jarman, J., and Klemperer, P., *Am. J. Med. Sci.*, 1941, **202**, 20.

³ Cromartie, W. J., *Am. J. Med. Sci.*, 1943, **206**, 66.

⁴ Smith, C. C., Zeck, P. M., and McGuire, J., *Am. J. Path.*, 1944, **20**, 721.

⁵ Grollman, A., *PROC. SOC. EXP. BIOL. AND MED.*, 1944, **57**, 102.

⁶ Williams, J. R., Harrison, T. R., and Grollman, A., *J. Clin. Invest.*, 1939, **18**, 373.

tissue stroma with some slight infiltration of lymphocytes, plasma cells and large mononuclear cells. The cotton thread with which the kidney had been constricted was demarcated by a zone of connective tissue with occasional giant cells of the foreign-body type about the constricting thread which was usually imbedded in the kidney substance. A fairly diffuse and almost uniform involvement was observed in all of the kidneys to which a ligature had been applied. Occasional single damaged nephrons were also observed in the kidneys not ligated. The structural changes in the two kidneys were always different. Without exception, the involvement was more marked and more extensive in the kidney to which a ligature had been applied than in the opposite kidney.

Discussion. The animals for these studies were selected from those manifesting a maximal degree of hypertension and were killed while still in good physical condition. In all instances, the hypertensive state was of sufficient duration to produce a marked cardiac hypertrophy particularly of the left ventricle. Renal lesions apparently responsible for the hypertension were observed in every kidney to which a ligature was applied. Focal lesions of a slighter degree apparently due to the hypertension were observed in the opposite intact kidney. Though there were marked alterations in both heart and kidneys, no pertinent changes of any degree were ob-

served in the large or small arteries of the heart, kidneys, spleen, liver, pancreas, lungs and brain. The inflammatory changes described by Cromartie³ and these noted by Smith, Zeek, and McGuire⁴ are explained by the fact that most of the animals used by Cromartie³ died of pyogenic infection and suppurative lesions were common in those used by Smith *et al.*⁴ The necrotic vascular lesions noted by Wilson and Byrom¹ were associated with an acutely developing severe hypertension and a rapidly fatal course. The findings of these authors are thus not applicable to chronic hypertension.

Summary. Varying degrees of chronic hypertension were produced in 16 rats by application of a figure-of-eight ligature to one or both kidneys. The animals were killed after the blood pressure had been maintained between levels of 150 to 240 mm of mercury for periods varying from 1 to 8 months. Microscopic examinations disclosed in each animal a marked cardiac hypertrophy particularly of the left ventricle. Renal lesions apparently responsible for the hypertension were observed in every kidney to which a ligature was applied and focal lesions of a slight degree apparently due to the hypertension were observed in the opposite intact kidney. No pertinent changes of any degree were seen in the large or small arteries of the organs examined.

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Effect of Quick Freezing at Very Low Temperatures of Donor Tissue in Corneal Transplants.*

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There are 2 concepts regarding the necessity of using living instead of dead tissue in corneal transplantation. Castroviejo¹ and

many others believe that living corneas must be used if successful, clear transplants are to be obtained. Others, Löhlein² and Salzer³

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¹ Castroviejo, R., *Am. J. Ophth.*, 1941, **24**, 1.

² Löhlein, W., *Klin. Mon. f. Augenheilk.*, 1938, **101**, 106.

³ Salzer, R., *Archiv. f. Ophth.*, 1921, **105**, 469.

⁴ Weiss, P., and Taylor, A. C., *Proc. Soc. Exp.*