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Parathyroid Enlargement in Rats Following Experimental Reduction of Kidney Substance.

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There is evidence from human pathology that renal disease is frequently associated with parathyroid enlargement. Renal lesions have been found to accompany hyperplasia or tumors of the parathyroids in over 50% of the reported cases of osteitis fibrosa,[1] and parathyroid enlargement has been demonstrated in various forms of chronic renal disease[2, 3, 4] and in renal dwarfism.[5, 6]

The nature of this relationship is not well understood and it seemed of interest to approach the problem experimentally. In this brief report, it will be shown that significant increase in the volume of the parathyroids may be brought about in rats by experimentally reducing the amount of functional renal tissue.

Healthy white rats, weighing from 150 to 250 gm., and maintained on a mixed diet were used for the experiments. One kidney was removed through a lumbar incision, and a considerable portion of the opposite kidney was destroyed by thermo-cautery in 2 operations.

The chief symptoms noted were drowsiness, roughness of the hair and loss of appetite. Although 3 of the rats showed a transient gain of weight after the second cauterization, the weight later remained stationary or declined progressively.

At autopsy, the parathyroids with attached thyroid tissue were fixed in Zenker's fluid, and serially sectioned at 10μ. Their volume was determined by multiplying the combined areas of the section, as obtained with the planimeter from drawings projected at known magnification, by the thickness of the section. The volume was calculated for 100 gm. of rat. Since all of the operated rats lost weight before death, the calculations were based upon the "normal" weight at time of death as estimated from Donaldson's tables, and not upon the actual weight.

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[5] Smyth, F. S., and Goldman, L., *Am. J. Dis. Child.*, 1934, **48**, 596.

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The operated rats fall into 2 groups according to the time of survival. Those allowed to live for a period of 113 to 124 days following the second cauterization showed much more intense lesions of the remaining kidney tissue than did those in the group killed or dying before 46 days.

The data are summarized in Table I.

TABLE I.

Average Combined Volume of Parathyroids per 100 gm. of Rat.

	Volume cu. mm.	PE_m	Standard Deviation
Group A—Controls (9)	0.1441	0.0130	0.0551
Group B*—Early nephritics (5)	0.1679	0.0066	0.0197
Group C*—Late nephritics (5)	0.4117	0.0553	0.1659

*Calculations of B and C are based on estimated normal weights at time of death.

In spite of the small numbers of animals, the difference in the mean volume of the parathyroids between the control group and the later group showing the more severe renal damage, is statistically valid.† In the case of the earlier group, the difference is suggestive, but not conclusive, although in each rat, the parathyroid volume exceeded the mean volume of the controls.

One may reasonably conclude that the reduction of functional renal substance has led to a decided increase in the size of the parathyroids. The question arises as to whether this increased volume is due to enlargement of the cells or to their multiplication. Measurements of the nuclei in 2 diameters indicated that the nuclei in the glands of operated rats were larger than those of the controls. Thus, the mean diameters of 250 nuclei in the 5 "nephritic" glands were 8.0x6.2μ, as against 6.8x4.4μ in 200 "normal" nuclei. It could also be demonstrated that this alteration in nuclear size was attended by an increase in cytoplasmic volume. Mitotic figures were only occasionally found. It would seem that the increase in bulk in the "nephritic" parathyroids may be accounted for, in part at least, by the increased volume of both nucleus and cytoplasm.

† The following formulae were used in the calculations:

$$\sigma = \sqrt{\frac{\Sigma x^2}{n-1}}$$

$$PE_m = \tfrac{2}{3} \times \frac{\sigma}{\sqrt{n-1}}$$

$$PE_{m_1 - m_2} = \sqrt{(PE_{m_1})^2 + (PE_{m_2})^2}$$

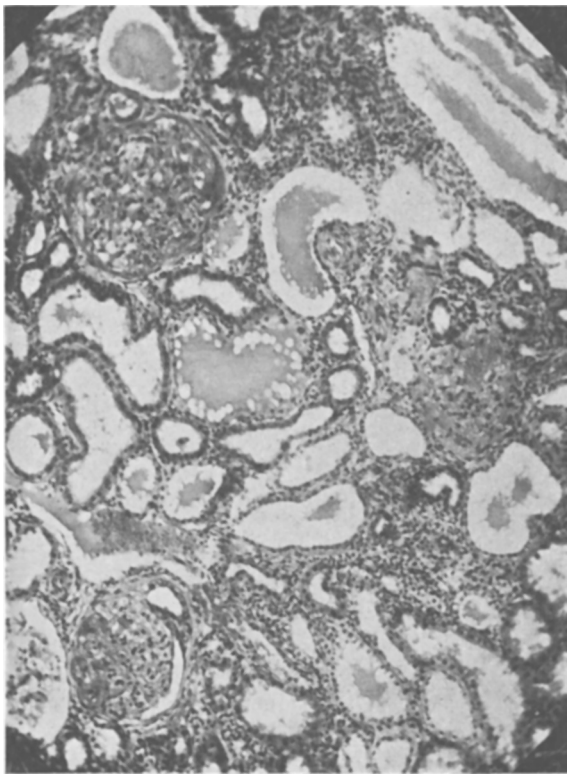

FIG. 1.

Rat AA2: Three glomeruli in section showing adhesions and partial hyalinization; dilatation of tubules with casts, interstitial fibrosis and lymphoid infiltration. × 100.

The pathologic alterations of the remaining kidney substance, in the later group, C, are diffuse and severe, simulating an advanced stage of glomerulo-nephritis (Fig. 1). At least 90% of the glomeruli are greatly enlarged, bloodless, the capillary loops distended with hyaline or granular material, the capsular space obliterated by adhesions. Often there is crescentic proliferation of epithelial cells. In many tufts, these changes have progressed to almost complete hyalinization.

The majority of the tubules are widely distended with dense hyaline coagulum. The epithelial cells are flattened, so that in some areas the tissue resembles thyroid. There is irregular interstitial fibrosis, with moderate lymphoid cell infiltration of the stroma. In a few of the larger arteries and in some of the arterioles, there is fibrinoid or hyaline material in the subendothelial tissue.

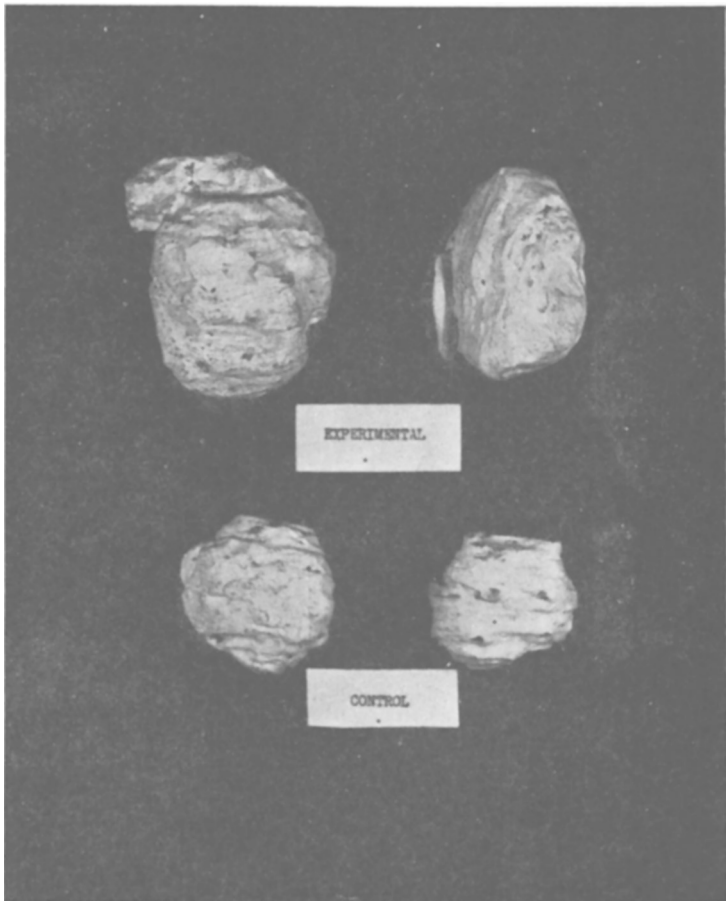

FIG. 2.
Wax reconstructions of parathyroids from Rat AA6 (experimental) and Rat 3B (control). Drawings at linear magnification of about 40.

With minor variations in intensity, this same picture is found in each of the 5 animals of the later group. Although the pathogenesis of the lesions is not clear, it is of interest that the cauterization leads to the gradual development of a severe diffuse nephritis, with glomerular lesions comparable to those of advanced human glomerulonephritis.

Such diffuse changes were not seen in the kidneys of group B, killed within 46 days of the last cauterization. The lesions in these rats were limited to the actual necrosis caused by the procedure, and did not involve to any extent the intact parenchyma. There was, however, a striking hypertrophy of both glomeruli and tubules,

as described in dogs by Allen, Bollman and Mason[7] after unilateral nephrectomy and partial resection of remaining kidney.

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Cardiovascular Studies in Patients with Single Functioning Lungs.*

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On the service of Dr. Harold Neuhof at The Mount Sinai Hospital, New York, we have had the unique opportunity of making cardiovascular studies of patients with one functioning lung. Multiple thoracoplasties were performed by Dr. Neuhof for unilateral chronic empyema, pulmonary tuberculosis or lung abscess. The lung on the non-affected side was normal. Table I.

Dyspnoea on exertion, not at rest, was universally present. There were no orthopnea and cyanosis. The hearts were normal, although perhaps displaced and slightly rotated. This was judged by physical examination, teleoroentgenogram, fluoroscopy and electrocardiogram. In 2 cases there was a tendency to right ventricular preponderance on the electrocardiogram, probably the result of the long standing previous pulmonary disease with slight rotation of the heart. In one case there was a definite left ventricular preponderance.

The pulse rate was always rapid. The blood pressure was normal. The respirations were usually 20 per minute, occasionally 28 per minute, but the slightest exertion increased the respirations. The vital capacity was markedly diminished, ranging between 1200-2700, the normal being 3500-4500. The venous pressure by the direct method[1] was definitely elevated on the involved side in one case. The velocity of the blood, measured from the arm to the tongue[2] or the arm to the lung,[3] was definitely increased, that is, the

7 Allen, R. B., Bollman, J. L., and Mann, F. C., *Arch. Path.*, 1935, **19**, 174.

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