OBSERVATIONS REGARDING THE PROGNOSIS AND DIAGNOSIS OF HYPERPARATHYROIDISM*

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THE material consists of 31 cases observed during the period 1930 to 1952. Of these, 28 were operated upon; one was subjected to roentgen therapy only, and two received no treatment. Eighty-five per cent of the patients were women. Renal calcifications or concrements without visible bone changes occurred in 45 per cent. With or without concomitant skeletal changes renal calcifications appeared in 74 per cent. A single ureter stone can be the first symptom in hyperparathyroidism. Of great importance is the fact that hyperparathyroidism may be present, although there are other factors to explain the development of calculi. Thus among 31 patients, three were treated many years for chronic staphylococcuria with stone formation and underwent several operations before the hyperparathyroidism was diagnosed.

Less often appreciated than renal calcification, but probably of greater significance from the prognostic viewpoint, are the renal changes, which, though not detectable radiologically, appear in all cases of hyperparathyroidism and lead to a more or less severe reduction in renal function. The kidney damage chiefly manifests itself in a reduced concentrating power, while in the beginning the nonprotein nitrogen may be normal, the clearance good, and the urine albumin-free. Table 1 shows the mean values for nonprotein nitrogen, the clearance and the water test in the cases I observed.

Table 1

MEAN VALUES FOR NONPROTEIN NITROGEN, CLEARANCE AND THE WATER TEST

N. P. N.	Clearance	Specific Gravity in Water Test
38 mg. per cent	82 ml./min.	1.006 to 1.012

In assessing the prognosis, the renal changes play a much greater part than the altered bone structure. Even a severe generalized osteitis fibrosa cystica can disappear functionally after a parathyroidectomy. Although the hyperparathyroidism disappears, kidney damage often persists and the patient dies from uremia.

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Another interesting, and very important complication in hyperparathyroidism is a steadily rising blood pressure. Hypertension regularly occurs in most cases of hyperparathyroidism. This blood pressure elevation, though initially slight and often transitory, becomes more extreme and persistent with time. Eventually hypertension or one of its complications results in the patient's death. Considering the obscure pathogenesis of hypertension, it is not surprising that the blood pressure rise accompanying hyperparathyroidism should be hard to explain. It scarcely seems likely that the tubular pathologic condition produces hypertension. They are more probably conditions which run parallel to each other. As the disease progresses, the kidneys begin to play a progressively greater role in the aggravation of hypertension due to nephrosclerotic and pyelonephrotic changes. It is clear that patients who have had overactive parathyroids removed require constant observation; their hypertension will need appropriate treatment, perhaps eventually including surgery.

Table 2

LATE RESULTS AFTER REMOVAL OF SOLITARY ADENOMA

Case No.	Blood calcium	Renal damage	Hypertension	Cap. for work; gen. condition	Observance time	Remarks
1	Normal	Increased	+	Excellent 13 years	20 years	Amput. both legs
3	Normal	Increased	+	Excellent 10 years	13 years	Died cerebral hemorrhage
4	Normal	Increased	+	Improved	7 years	Died nephrosclerosis
8	Normal	Increased	+	Improved	8 years	Died uremia
9	Normal	Increased	+	Improved	8 years	Died nephrosclerosis
10	Normal	Improved	+	Excellent	6 years	B. P. 200/100
11	Normal	Increased	+	Improved	7 years	Symptoms of hypertension
12	Normal	Improved	−	Excellent	6 years	Nephrolithiasis
13	Normal	Improved	−	Excellent	4 years	Nephrolithiasis
14	Normal	Improved	−	Excellent	2 years	Nephrolithiasis

Table 3

LATE RESULTS AFTER PARATHYROIDECTOMY IN CASES WITH DIFFUSE HYPERPLASIA

Case No.	Blood calcium	Renal damage	Hyper-tension	Cap. for work; gen. condition	Observ-ance time	Remarks
2	Elevated	Increased	+	Improved sev-eral years	12 years	Died of uremia
5		Increased	+	Improved sev-eral years	10 years	Hypertension; invalid
6		No increase	+	Improved	11 years	Working as nurse
7		Increased	+	Improved	10 years	Severe hyper-tension

The prognosis in hyperparathyroidism, even after parathyroidectomy, has been somewhat ignored because of incomplete follow-up investigations. In cases of hyperparathyroidism due to an adenomatous change of only one of the parathyroid glands, removal of this adenoma regularly results in an immediate and usually permanent disappearance of the hyperparathyroidism. But kidney damage and hypertension often persist and progress. Also, after years of relatively good health many patients become permanent invalids and finally succumb to renal insufficiency or cerebral hemorrhage. This is clearly illustrated in table 2 which shows the late results after removal of an adenoma. It is to be expected that the late results should be less satisfactory in cases with so-called diffuse hyperplasia of all the parathyroid tissue. Surprisingly, some of these patients may live for a long time in a relatively good condition despite an incomplete operation and persistent hyperparathyroidism (table 3).

The prognosis of a patient with hyperparathyroidism is often definite at the time when the diagnosis is established. An early diagnosis is therefore most important.

In most cases a distinctly elevated calcium level is highly indicative of hyperparathyroidism. And yet hyperparathyroidism may be accompanied by normal blood calcium levels, as occur in patients with far advanced renal damage with retention of phosphates in the blood.

Of greater interest is a normal blood calcium level in early cases of hyperthyroidism. It can well be asked whether a determination of the different plasma calcium fractions would not be desirable, if a deranged calcium metabolism is to be unmasked.

In table 4 three of the cases are tabulated in which no change in the total serum calcium could be found; but the diffusible fractions' concentration exceeded the upper limit of what is considered normal. Remarkable, too, is the return of the diffusible fractions to normal following operation.

Table 4

PRE- AND POSTOPERATIVE
FRACTIONAL BLOOD CALCIUM DETERMINATIONS

Case No.	Preoperative		Postoperative	
	Total serum calcium	Free serum calcium	Total serum calcium	Free serum calcium
25	10.1	6.3	8.9	5.2
26	10.0	6.8	10.0	5.1
27	9.9	6.8	9.5	5.4

Conclusions

The best known and most striking findings typical of hyperparathyroidism are, on the one hand, the decalcification of the skeleton, usually in the form of generalized osteitis fibrosa cystica; and on the other, renal concrement or calculus formation. However, more important than these findings from the prognostic viewpoint are: (1) renal damage most probably involving the tubules particularly, and reflected chiefly in the decreasing concentrating power, and (2) a rise in blood pressure, usually progressive in nature. No direct connection between renal damage and hypertension has been found in the earlier stages of the illness when the blood pressure elevations vary greatly. With the arrival of the secondary nephrosclerotic and pyelonephritic renal changes, hypertension occurs which is more permanent and more definitely determined by the state of the kidneys.

The prognosis following hyperparathyroidectomy is essentially dependent on two factors: whatever renal damage may have already occurred; and, on the severity of the blood pressure rise occasioned by the hyperparathyroidism. Early diagnosis and surgery are therefore of vital importance. A full realization of the fact that the serum calcium may lie within normal limits in hyperparathyroidism should lead to the performance of repeated blood calcium determinations in cases where this condition is suspected.

Further investigations will show if a relative rise in the free, diffusible calcium fraction is sufficiently pathognomonic of hyperparathyroidism.