requiring frequent determinations and corroboration by other tests.

3. In contrast to the previously emphasized hypophosphatemia, the serum phosphate levels have been normal in most of our recent cases of surgically proved hyperparathyroidism.

4. The tubular reabsorption of phosphate measured by a simplified technic was uniformly subnormal. This test was of diagnostic value in those patients with minimal hypercalcemia and normal phosphate levels.

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REFERENCES

1. Albright, F. and E. C. Reifenstein, Jr.: The Parathyroid Glands and Metabolic Bone Disease. Baltimore, Williams and Wilkins Co., 1948.
2. Chambers, E. L., Jr., G. S. Gordan, L. Goldman and E. C. Reifenstein, Jr.: Tests for Hyperparathyroidism: Tubular Reabsorption of Phosphate, Phosphate Deprivation, and Calcium Infusion. J. Clin. Endocrinol. and Metab., 16: 1507, 1956.
3. Clark, G. W.: The Microdetermination of Calcium in Whole Blood, Plasma and Serum by Direct Precipitation. J. Biol. Chem., 49: 487, 1921.
4. Eisenberg, E., R. Fraser and H. K. Ibbertson: The Use of Stable Strontium as a Tracer for Calcium Metabolism in Man. Presented to the Medical Research Society of England, at the Royal College of Surgeons, London, November 9, 1956.
5. Hellström, J.: Primary Hyperparathyroidism: Observations in a Series of 50 Cases. Acta Endocrinol., 16: 30, 1954.
6. Howard, J. E., T. R. Hopkins and T. B. Connor: On Certain Physiologic Responses to Intravenous Injection of Calcium Salts into Normal, Hyperparathyroid, and Hypoparathyroid Persons. J. Clin. Endocrinol. and Metab., 13: 1, 1953.
7. Kramer, B. and F. F. Tisdall: A Simple Technique for the Determination of Calcium and Magnesium in Small Amounts of Serum. J. Biol. Chem., 47: 475, 1921.
8. Munson, P. L.: Studies on the Role of the Parathyroids in Calcium and Phosphorus Metabolism. Ann. New York Acad. Sc., 60: 776, 1955.
9. Richter, C. P. and S. Helfrick: Decreased Phosphate Appetite of Parathyroidectomized Rats. Endocrinology, 33: 349, 1943.
10. Schaaf, M. and L. H. Kyle: Measurement of Per Cent Renal Phosphorus Reabsorption in the Diagnosis of Hyperparathyroidism. Am. J. M. Sc., 228: 262, 1954.
11. Sirota, J. H.: Renal Tubule Reabsorption of Phosphate in Hyperparathyroidism Before and After Removal of Parathyroid Adenoma. Fed. Proc., 12: 133, 1953.
12. Thompson, D. P. and H. H. Hiatt: Renal Reabsorption of Phosphate in Normal Human Subjects and in Patients with Parathyroid Disease. J. Clin. Invest., 36: 550, 1957.

DISCUSSION

DR. ROYSTER: I enjoyed this paper very much, since we certainly need more methods to diagnose this condition when there are borderline states. I have one question I would like to ask of Dr. Goldman. In these cases of borderline disease, where this test proved to be confirmatory, what did the pathology of the glands show?

I am reminded of a statement by Dr. Cope, in which he was writing of the thyroid gland as well as of the parathyroid, that when the endocrine gland is out of balance and produces disease, it is usually possible in most every case to find the cellular change indicating that there is actual disease. Also, I would like to point out another thing, that there are many causes of changes in the phosphorus excretion and in the test of tubular reabsorption. There have been studies to show that there is an increased excretion of calcium under various conditions, with or without the presence of hyperparathyroidism, and that when the patient is excreting calcium in excess, the calcium takes phosphorus with it. Therefore hyper-

calcemia and hyperphosphaturia, to my mind, will be a suggestive test, but not diagnostic. In borderline states the calcium excretion may be extremely helpful.

DR. COPE: Dr. Goldman is so right. If we could have some further and more accurate tests to reveal the disease of hyperparathyroidism, we would be just so much further ahead. I hope this proves to be one such, but I am a little in doubt.

First of all, it depends upon abnormalities in chemical levels, and the formula, of course, involves the phosphate level. There are so many things that disturb in the phosphate level, as compared with the calcium level, that one can question whether anything that deals with phosphorus is ever going to be quite as reliable a diagnostic test as the calcium.

That doesn't mean that the phosphorus metabolism is not disturbed, just as Dr. Goldman has said. After all, the value of a test depends upon how characteristic it is for a disease, and how seldom, therefore, it is found in any other circumstance.

The other trouble with all the tests that depend upon blood levels is that the less the disease, the less the disturbance, and the greater the disease, the greater the disturbance; and we are going to run into the same trouble here, inevitably, because the least amount of hyperparathyroidism will give us the least positive effect, and it may fall into the level of normal or into the range of normal.

Those were three very excellent slides that Dr. Goldman showed. First of all, he showed that in the calcium blood levels of his patients there was almost no overlap between the blood calcium level of the parathyroid patient and the normal, whereas, in the phosphates, as he emphasized, there was a big overlap.

The next slide showed the overlap of the normals in this new phosphorus test, and that is really the crux of the matter, so I wish he would comment a little bit more, if he will, on the observations in the normal and how the range appears in the normal. I hope it is very narrow, so that the test will be the more positive in the patients with disease. [Applause]

DR. ANLYAN: I appreciate the privilege of the floor for discussing this excellent presentation by Dr. Goldman. We have had a similar experience at the Duke University Hospital.

(Slide) This is no longer a rare disease in our institution, thanks to the efforts of Dr. Frank Engel and his staff on the metabolic service. In the past 2½ years we have had 26 parathyroid-adenomas removed surgically. The TRP was carried out in the last 16 cases and was low in 15 of the 16; it was low-normal in the 16th case. This 16th case had normal calcium and phosphorus levels.

We feel that all suspects of hyperparathyroidism should have periodic follow up examinations for these chemistries every 6 months, just as patients with suspected tuberculosis have chest x-rays periodically.

(Slide) We have been particularly interested in some of the unusual manifestations of hyperparathyroidism.

Twelve of our patients have had major gastrointestinal symptoms, with nausea, vomiting, cramping abdominal pain, and constipation. One patient had a duodenal ulcer which was aggravated by the ingestion of milk. One patient had a severe postoperative pancreatitis, proven by laparotomy following the removal of a large parathyroid adenoma.

Two patients had the presenting symptoms of arterial occlusive disease with diffuse arterial calcinosis. One patient had a picture of jugular and subclavian vein thrombosis with pulmonary embolism.

We had one patient with a rare instance of parathyroid psychosis, an elderly lady who was violent on the psychiatric ward, and who on a routine ECG examination was thought to have evidence of hypercalcemia. Following removal of the adenoma, she became a nice, pleasant old lady. For about a month the biochemistry department was flooded with calcium-phosphorus determinations from the psychiatric service.

There was one patient who came in moribund with an admission diagnosis of lupus erythematosis. At autopsy he proved to have nephrocalcinosis and a parathyroid adenoma. We feel that all patients suspected of having hyperparathyroidsm should be checked every 6 months with this battery of tests. Thank you very much. [Applause]

DR. GOLDMAN: We are all well aware that usually there is no single laboratory test that will always prove to be pathognomonic of a given disease. The trite expression that the laboratory test must fit the clinical picture is usually true.

In hyperparathyroidism, however, we depend more on the laboratory for diagnosis than we do for other diseases. This is the result of a lack of clinical manifestations of conditions that are usually complications of hyperparathyroidism. These include renal stones, nephrosclerosis, dimineralization, and symptoms such as Dr. Anlyan has just described.

We have several patients, still on our doubtful list, whose serum calcium or phosphorus determination is not compatible with the diagnosis of hyperparathyroidism, and whose T.R.P. determination is low. It may be that the only way the issue will be decided will be by exploring the neck. To date, however, we have not resorted to "exploration" in any of the patients who were included in this series. A positive preoperative diagnosis is important as a stimulus to the surgeon to find the tumor.

Concerning the pathologic findings in the gland that Dr. Royster asked about, all but 3 of these patients had adenomas, some of which were multiple. These three patients had primary hyperplasia of all parathyroid glands.

We are aware that there are other conditions which may produce a lowered tubular reabsorption of phosphate, such as osteoporosis, multiple myelomas, renal stones without hyperathyroidism, osteomalacia, and the Fanconi syndrome. However, the diagnosis of these conditions usually can be made on other grounds.

The normal range of tubular reabsorption in our cases varied from 78 to 94 per cent. Two patients had a T. R. P. of 74 per cent, which approximates the normal range. One patient, as I mentioned previously, had a T. R. P. of 90. She was being studied while on a phosphorus-restricted diet at the time, however, which may well have accounted for this finding.

We feel that every diagnostic aid available should be used in these borderline cases. Time is an important factor in the treatment of hyperparathyroidism; many patients develop uremia and severe hypertension even after the tumor is removed.

I wish to thank Dr. Royster, Dr. Cope and Dr. Anlyan for their discussion.