in March 1958, four enlarged parathyroid glands were found and subtotally resected. The glands showed primary chief cell hyperplasia. After this the serum calcium fell to a low normal value. It is still too soon to know what will be the stable postoperative calcium level. Gastric analyses before the first and the second stomach operations did not show a hypersecretion or undue acidity. This patient had a history of long standing mental worries.

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Discussion

Dr. H. A. Frank: We are grateful, as ever, to Dr. Cope and his associates for instruction and guidance in this field.

We encountered a patient recently with whom we could have used Dr. Cope's guidance, I think. This was a 58-year-old man who came to our hospital in November. In 1923, he had had a kidney stone; in 1933, a peptic ulcer. He entered the hospital, having passed another urinary stone, and was found to have the chemical findings of hyperparathyroidism.

In exploration of his neck, these are what we found: (Slide) We thought the right upper parathyroid was a little large, but were not sure it was outside normal limits and did not disturb it. The

left upper, we could not find. This is the excised right lower parathyroid, and this is the left lower. Conferring with the pathologist in the operating room, we were not quite sure whether we were dealing with general hyperplasia or multiple adenomas. We took out the larger of these lower glands, and, on frozen section, we were told it was an adenoma. We then thought perhaps we were dealing with bilateral adenoma, but if these two were hyperfunctioning, we were surprised to find a large normal gland in a third position. We ended by removing the two large glands at the lower poles, leaving the right upper gland, and not even finding a gland at the left upper position.

Histologic examination of these specimens disclosed chief cell hyperplasia identical with that presented by Dr. Cope. Dr. Freiman, our pathologist, compared these slides with Dr. Castleman's and it is the same entity.

Postoperatively, the patient returned to chemical normality. Perhaps we were wrong in leaving that single gland, and the patient may have trouble with this later, I suppose. It would seem that if the 1923 kidney stone was related to this, it is perhaps a slowly progressive process.

DR. LEON GOLDMAN: I enjoyed this paper very much and was particularly interested in it because it poses a problem that we have also been faced with during the past several years. We are well acquainted with the water clear cell type of hyperplasia that Dr. Cope and his associates recognized many years ago. When we saw four patients who had enlarged parathyroid glands that showed a chief cell pattern, however, we wondered for a time whether we were dealing with multiple adenomas or true hyperplasia.

We have found that our results after surgical treatment of either type of hyperplasia associated with hyperparathyroidism have not been as good as they have been in cases of single parathyroid adenomas.

In two of the four cases of chief-cell hyperplasia we saw, postmortem examination was made. One patient died 15 years after operation, and the other died three weeks postoperatively. During autopsy on the first patient, we found parathyroid tissue remaining in the mediastinum, as well as pancreatic islet cell adenomas and a chromophobe adenoma of the pituitary.

The second patient had uremia and severe toxic hyperparathyroidism. Because of her poor physical condition, a complete exploration was not done. A single, large, chief cell hyperplastic gland was removed. During the immediate postoperative period, this patient had a massive hemorrhage that originated from a gastric ulcer. At autopsy parathyroid tissue was found in the mediastinum; pancreatic islet cell adenomas and a chromophobe pituitary adenoma were also noted.

The other two patients are still living, one of whom still has evidence of hyperparathyroidism although he has been subjected to two explorations of the neck and one of the anterior mediastinum.

I would like to ask the authors if they believe that as such patients are studied more thoroughly, perhaps ultimately at autopsy, many who have chief cell hyperplasia will prove to have this syndrome of multiglandular adenomatosis. Since the chemical manifestations of hyperparathyroidism may be the only abnormality presently detectable by clinical means, the presence of pituitary and pancreatic adenomas may only be determined at autopsy. I enjoyed the paper very much.

DR. OLIVER COPE (closing): Dr. Keynes and I are very grateful for the additional observations. It is very hard to tell at this stage whether Dr. Frank's case is really a case of hyperplasia, because, obviously, it is possible that to have three adenomas—and I am not aware, really, of such a case. We have wondered about our own, but when we have been able to identify all four glands, we, as surgeons, have assumed that it must be a hyperplastic process since we cannot identify any normal tissue.

Now, Dr. Frank, that fourth gland is still missing, and we really don't know the full nature of the right upper, so it is still possible that he has adequately handled his patient. He has removed two adenomas, and we can only wait and see. He is exactly in the dilemma that we have been in, and in two of the patients we had to wait over a year, well, one of them, over a year, before there was a recrudescence of hyperparathyroidism which indicated that we had not done an adequate job.

Dr. Goldman has added a patient of enormous interest, because he goes right along with our experience, and his first patient with a fifth gland is most heartening. We had one such. We didn't allude to it because it added to the complications.

We dealt with four of the glands, doing a subtotal of one, and removing three, and the patient wasn't relieved, and we had to go into the mediastinum and find a fifth, and this is wonderful to find—an added experience—something again that we have got to be more aware of.

The last patient, the patient of Dr. Goldman, with the intestinal hemorrhage, is, of course, in line with the growing knowledge of the significance of endocrine tumors, pancreas, and parathyroid, possibly others in gastric ulcers and hemorrhage.

Now, Dr. Goldman asked, is it the disease type, the pathologic type, that we are likely to encounter in multiple endocrine disease? Well, since five of ours, certainly four and possibly five, fall into this type, it is natural that we should think so, and he lends strong support. So we have been delighted to hear of these additional cases, delighted to hear that you are having a little trouble, too. Thank you very much.