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THERAPEUTIC EFFECT OF TOTAL ABLATION OF NORMAL
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ROID FUNCTION. CLINICAL OBSERVATIONS
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STUDIES

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The occurrence of tetany as an infrequent postoperative complication following subtotal removal of the abnormal thyroid gland is well recognized (1) (2). McCullagh in 1932 (2), reported an incidence of tetany of 1.3 per cent in a series of 11,500 cases in which thyroidectomy was performed at the Cleveland Clinic.

The anatomical proximity of the parathyroid glands to the thyroid, the similarity of the signs and symptoms of postoperative tetany to those of idiopathic hypoparathyroidism, and the specific effect of calcium therapy, offer strong evidence that tetany following thyroid surgery is due to removal of, or injury to, the parathyroid glands during operation. Means and Richardson (1) observed that the frequency of postoperative parathyroid tetany depends roughly upon the amount of thyroid tissue removed. Thus, tetany rarely occurs after unilateral thyroidectomy; and is less common after the subtotal removal of adenomatous goitre than after that of exophthalmic goitre (1).

Blumgart and his associates (3) (4) (5) (6) have shown that in patients without thyroid disease, complete removal of the normal thyroid must be performed to assure a persistently subnormal basal metabolic rate. To accomplish complete ablation of the thyroid gland, the region of the parathyroid bodies must be deliberately invaded. It was feared, therefore, that intractable tetany might frequently follow this operation.

The present communication is a report of our clinical observations, and studies of serum calcium and serum phosphorus in relation to parathyroid function following the total removal of the normal thyroid gland for the relief of intractable heart disease and other conditions.² Studies of the

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² The operations in this series were performed by Dr. David D. Berlin and Dr. Charles G. Mixter.

blood chemistry have been made, not only in those patients who developed signs or symptoms of tetany, but also in other patients who showed no clinical manifestations of impaired parathyroid function at any time after operation.

CLINICAL AND CHEMICAL METHODS

Following operation, attempts to elicit Chvostek's and Trousseau's signs of tetany were made two to three times a day for the first postoperative week in each patient. If none of the signs or symptoms of tetany developed during the first postoperative week, these examinations were made only once a day during the following week. At the time of examination the patient was always questioned for symptoms of hypoparathyroidism.

Trousseau's and Chvostek's signs have been employed to indicate increased mechanical excitability of the motor nerves. To elicit Trousseau's sign, a tourniquet was applied above the elbow with a pressure above systolic for three to five minutes, unless the sign became evident sooner. To elicit Chvostek's sign, the region over the facial nerves was tapped with the fingertip. Chvostek's sign has been differentiated in accord with Chvostek's original description of three grades of activity (7) (2). "Mild," or "+" Chvostek's sign designates Type III of Chvostek's classification, when the angle of the mouth alone responds; "moderate" or "++" designates Type II of Chvostek, when the angle of the mouth and the nose are involved; "active" or "+++ " designates Type I of Chvostek, when the angle of the mouth, the nose, forehead, cheek and upper and lower lips are involved. The degree of activity of Trousseau's sign has been differentiated as "mild" or "+" when the cramping of the hand occurs only after application of the tourniquet for several minutes; "moderate" or "++" when cramping of the hand appears shortly after pressure is applied; and "severe" or "+++ " when severe spasticity of the hand occurs immediately on pressure.

The chemical methods employed were: serum calcium, Fiske and Logan (8); serum phosphorus, Fiske and Subbarow (9); serum protein, Dyer (10). Blood for analysis was drawn after a fast of twelve to fourteen hours, with the exception of a few of the specimens taken on the second to the fifth postoperative days at the onset of clinical manifestations of tetany.

RESULTS

Incidence of tetany following total thyroidectomy

Tetany sufficiently severe to give rise to convulsions or spontaneous spasms of the extremities did not occur in any of seventy-three consecutive patients on whom total ablation of the normal thyroid gland was performed. Twelve patients, or 17 per cent, however, showed clinical signs or symptoms of mild parathyroid insufficiency; in the last thirty-seven of the seventy-three patients only three, or 8 per cent, showed any clinical evidence of this disorder.

One or more parathyroid glands were identified at operation and left in situ in seventy-two of the seventy-three patients; in the remaining patient no parathyroid gland was identified at operation. Parathyroid glands

were identified and preserved at operation in all of the twelve patients who developed mild postoperative tetany; in one of these patients (Case 5) two parathyroid glands were identified and left in situ, and a third parathyroid was removed at operation. In one other patient an unrecognized parathyroid gland was removed; this patient did not develop any clinical signs or symptoms of tetany.

The frequency with which tetany occurred was not related to the age or to the sex of the patient (Table I). Ten of the thirty-eight patients

TABLE I
*Maximum signs and symptoms observed in patients showing tetany **

Case number	Paresthesia§	Chvostek's Sign	Trousseau's Sign	Serum calcium at time of maximum signs and symptoms	Serum phosphorus at time of maximum signs and symptoms
				<i>mgm. per 100 cc.</i>	<i>mgm. per 100 cc.</i>
1. B. Z.	++	++	++	9.2†	5.0
2. W. D.		++		8.6†	
3. L. B.	+	+		10.7†	
4. E. P.	+++	++	++	7.2	
5. J. T.	++			7.5‡	
6. B. R.	+++	+++	+++	8.3	3.6
7. S. B.	++	+++	+++	7.2	5.3
8. F. D.	+	+		8.3	3.3
9. L. M.	++	++		6.2	3.5
10. M. H.	+++	++		6.5	
11. G. O.	++	++	++	9.2	2.7
12. A. S.	++	++	+	6.6	3.9

* None of these patients had convulsions or spontaneous spasms of the extremities.

† These determinations were made by the Clarke permanganate method which, in our experience, gives values approximately 1 mgm. higher than the Fiske method.

‡ Determined on the second postoperative day. Maximum signs and symptoms on the fifth postoperative day.

§ Paresthesia— + = Numbness and tingling of fingers; in Case 3, also numbness and tingling in vicinity of operative wound.

++ = Numbness and tingling of hands and feet.

+++ = Numbness and tingling of hands, feet, face and other parts of the body.

operated upon for the relief of congestive heart failure developed tetany; signs and symptoms were manifest in only two of the nineteen patients operated upon for angina pectoris. Postoperative tetany tended to occur more frequently in patients in whom the serum calcium concentration before operation was slightly subnormal (Table II).

Clinical manifestations of tetany following total thyroidectomy

Signs or symptoms of tetany appeared between the first and third day after total thyroidectomy in eight of the patients; in the other four patients signs or symptoms were first manifest on the fifth postoperative day.

The most severe signs and symptoms were encountered in Case 6 (Case reports) and consisted of tingling numbness of the feet and hands and paresthesias of the face and legs, which were accompanied by a feeling of stiffness of the jaw and ankles. This patient also complained of a "smothering" sensation, nausea and extreme apprehension. Chvostek's and Trousseau's signs were active. Within an hour after intravenous injection of 20 cc. of 10 per cent solution of calcium chloride, all of her signs and symptoms disappeared. There was no recurrence except for transient paresthesias of the face and tips of the fingers which occurred on the thirteenth postoperative day, three days after the omission of oral medication with calcium chloride. Case 2 (Case reports) who suffered from none of the symptoms of tetany has been included in this series because a mildly positive Chvostek's sign, which had previously been negative, was elicited on the second postoperative day and persisted for approximately a week. Case 5 (Case reports) experienced only transient paresthesias of the hands and face lasting two days and disappearing without medication; Chvostek's and Trousseau's signs were absent at all times. The severity of tetany in the remaining nine patients varied between that encountered in Case 6 and the mild signs and symptoms observed in Cases 2 and 5 (Case reports).

Trousseau's sign was elicited in six and Chvostek's sign in eleven of the twelve patients with postoperative tetany (Table I). The most active Chvostek's and Trousseau's signs were elicited in those patients who experienced the most severe paresthesias.

The manifestations of tetany were usually temporary, disappearing within the first two postoperative weeks in ten of the twelve patients. The remaining two patients, one of whom was operated upon nine months ago (Case 7), the other two and a half months ago (Case 12) still have some of the symptoms of tetany whenever the amount of calcium administered is reduced.

Treatment of patients with signs and symptoms of postoperative tetany

Three patients with extremely mild clinical symptoms of tetany received no medication and recovered spontaneously two to six days after onset (Cases 5, 8 and 9). Oral administration of calcium chloride solution (35 per cent) in amounts from 4 to 16 cc. four times a day (2 to 8 grams of calcium daily) was usually adequate to control the symptoms of tetany; in three cases an initial dose of 10 to 20 cc. of 10 per cent calcium chloride solution was given intravenously. Occasionally, when symptoms persisted, a fifth oral dose of calcium chloride solution was given during the night. Because of its acidifying properties, calcium chloride has usually been em-

ployed; calcium lactate or gluconate has been substituted when the chloride was not tolerated. Besides the calcium medication, these patients have been given a quart of milk daily as a palatable means of supplying additional calcium. In the first patient of our series to develop tetany (Case 1), 1 cc. of parathormone was administered intramuscularly immediately on recognition of symptoms; viosterol (250 D) 0.5 cc. every six hours was given to the first three cases in the series (Cases 1, 2 and 3) on recognition of signs and symptoms of hypoparathyroidism, and viosterol in varying doses has been administered to Cases 7 and 12, as an adjunct to calcium therapy in these persistent cases.

In the first few patients who developed postoperative tetany, calcium administration was continued for several months after the disappearance of all signs and symptoms. In the later cases, medication was discontinued whenever possible within a few weeks after operation and before the patient left the hospital. In the two patients who, at times, still suffer from symptoms, oral medication with calcium chloride and viosterol are continued.

Studies of serum calcium and phosphorus in patients who developed tetany following total thyroidectomy

The concentration of calcium in the serum at the onset of signs and symptoms of parathyroid insufficiency was variable (Table I). The calcium concentration was less than 7 mgm. per 100 cc. of serum during the period when clinical signs and symptoms were present in only four of the twelve patients, while in six patients the calcium values were above 8.0 mgm. per 100 cc. (Table II). In Case 11 (Table I), for example, the serum calcium was 9.2 mgm. per 100 cc. at a time when the patient was experiencing paresthesias of the hands, feet and face, a sense of pressure over the chest, was apprehensive, and showed moderate Chvostek's and Trousseau's signs. Likewise, in Case 3, the clinical diagnosis of tetany was definite, although the serum calcium was normal. In Case 1, the serum calcium was 9.2 mgm. per 100 cc. (Clarke's method) one hour after the administration of parathormone, at which time the patient still experienced symptoms of tetany.

The concentration of inorganic phosphorus in the serum during early postoperative tetany was 5.0 mgm. per cent or more in only two cases (Cases 1 and 7), the highest value for phosphorus obtained being 5.6 mgm. per 100 cc. (Case 7; Table II). In Case 8 the serum phosphorus increased from a preoperative value of 3.7 mgm. per 100 cc. to 4.9 mgm. per 100 cc. on the eighth postoperative day. In all other instances the concentrations of serum phosphorus were normal, and not significantly different from the preoperative values throughout the tetany period.

Measurements made at intervals during the first year after operation, in those patients who showed tetany lasting only two weeks or less, re-

vealed a persistent slight decrease in serum calcium as compared with the preoperative level. Thus, in six cases in which measurements were made before and six months after operation, the average serum calcium value at the sixth postoperative month was 8.4 mgm. per 100 cc. as compared with the average preoperative value of 9.3 mgm. per 100 cc. (Table II).

The serum protein concentration was normal in two cases in which the serum calcium was very low on the second to fifth postoperative days. These, and other measurements of serum protein made during the early postoperative period (Table II) demonstrate that the decrease of serum calcium observed during this period was not dependent upon decreased protein concentration. Similarly, the slightly diminished concentration of serum calcium found in certain cases six months after operation was not dependent upon a decreased serum protein.

Studies of serum calcium and phosphorus in patients who did not develop tetany following total thyroidectomy

An appreciably decreased calcium concentration in the serum was evident in nine of thirteen cases, none of which developed clinical signs or symptoms of tetany following total thyroidectomy (Table II). The greatest decrease in serum calcium usually occurred during the second to fifth days after operation; the maximum decrease observed was 2.7 mgm. per 100 cc. (Case 24, Table II), the average decrease 1.2 mgm. per 100 cc. In several instances the calcium concentration decreased to values between 7.1 and 7.7 mgm. per 100 cc. The values for serum phosphorus following total thyroidectomy did not differ from those obtained before operation (Table II). No appreciable decreases in serum protein were observed during this early postoperative period (Table II).

Measurements in this group during the interval from one month to one year following total thyroidectomy revealed a persistent but slight decrease in serum calcium concentration in most instances (Table II). Thus, the average value for calcium six months after operation in the nine cases studied was 8.8 mgm. per 100 cc. compared to the preoperative average of 9.6 mgm. per 100 cc. The extent of these changes was similar to that observed at the same postoperative period in the cases which showed transient clinical signs of tetany early in the postoperative course.

The concentration of inorganic phosphorus in the serum was not significantly different from the preoperative value at any time after operation. The concentrations of serum protein six months after operation showed definite increases over the preoperative values in many instances and no appreciable changes in the other cases (Table II). The slightly lowered concentrations of serum calcium observed six months after operation were, therefore, not dependent upon decreased concentration of serum protein.

TABLE II

Studies of the calcium, inorganic phosphorus and protein of the serum following total thyroidectomy

Case number	Diagnosis	Preoperative			Postoperative																								Remarks	
		Calcium	Phosphorus	Protein	2 to 5 days			1 to 2 weeks			1 month			2 months			3 to 4 months			5 to 6 months			9 months			12 months				
					mgm. per 100 cc.	mgm. per 100 cc.	grams per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	grams per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	grams per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	grams per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	grams per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	grams per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	grams per 100 cc.	mgm. per 100 cc.	mgm. per 100 cc.	grams per 100 cc.		
Patients Who Developed Clinical Signs or Symptoms of Parathyroid Insufficiency Following Operation																														
1. B. Z.	Cong. Ht. Fail.	8.8	4.1	8.0	9.2*	5.0		9.4	3.6	†	8.1			8.8	3.6		8.1			8.0	3.6	8.1	8.2	3.6	9.2	7.5	3.8	8.1	Calcium medication discontinued 5 months after operation	
2. W. D.	Cong. Ht. Fail.	9.7	4.8	7.4	11.4*			8.7*		†	8.0			8.4						8.4	4.0	8.0	8.3	3.8	8.0	9.0	4.0	7.6	Calcium medication discontinued 2 months after operation	
3. L. B.	Cong. Ht. Fail.	9.1	3.4	6.8	8.6*	3.1	†													9.5	3.8	8.7	9.0	3.5	8.0	9.5	4.0	6.9	Calcium medication discontinued second week after operation	
4. E. P.	Ang. Pect.	10.5	3.7	6.6	10.7*			7.5	3.7	†	8.0	3.7		8.5	4.2		8.3	3.7		8.1	3.5	8.2				8.3	4.2	7.5	Calcium medication discontinued 3 weeks after operation	
5. J. T.	Cong. Ht. Fail.	8.5			7.2		†	7.5			7.9	3.2		8.7	2.8		8.7	2.8											No medication	
6. B. R.	Cong. Ht. Fail.	8.8			7.8		†	9.6	4.4	†	8.5	3.5		8.9	3.4					8.5	2.6	7.6							Calcium medication omitted second week after operation	
7. S. B.	Cong. Ht. Fail.	8.9	3.8	7.4	8.3	3.6		6.9	3.4		5.9	5.6					8.2	4.3		6.3	3.0		6.1	5.2	8.6	4.7		Calcium medication still continued 9 months after operation. Viosterol added		
8. F. D.	Cong. Ht. Fail.	8.7	3.7	6.8	8.3	3.3		7.7	4.9	†										7.7	4.5	7.1							No medication	
9. L. M.	Cong. Ht. Fail.		3.2	7.9	6.2	3.5	7.1	6.2	3.8	†																			No medication	
10. M. H.	Ang. Pect.				6.7			6.5		†	8.4	2.3		8.6	3.2					8.4	3.5	7.1							Calcium medication omitted second week after operation	
11. G. Or.	Cong. Ht. Fail.				9.2	2.7	†	9.1	2.8		9.7	3.4	7.3	9.8	3.8														Calcium medication discontinued 1 month after operation	
12. A. S.	Cong. Ht. Fail.				6.8	3.2		6.6	3.9		6.9	4.4(3 wk.)	6.2	4.0(6 wk.)	8.3	4.7													Calcium medication still continued 2 months after operation. Viosterol added	
	‡ Average basal metabolic rate (per cent deviation from normal)		-2								-14			-21						-24										
Patients Who Developed No Clinical Signs or Symptoms of Parathyroid Insufficiency Following Operation																														
13. E. W.	Cong. Ht. Fail.	10.0	4.5	8.1							8.4	4.3	8.0							8.6	3.8	8.1								
14. W. B.	Cong. Ht. Fail.	10.1	3.8	6.4							8.6	3.5	6.3							8.4	3.4	6.3				8.1	3.4	6.8		
15. C. C.	Cong. Ht. Fail.	9.4	3.3	6.5				8.3	3.1	5.9	8.7	3.4	6.5							8.1	3.0	6.4								
16. A. B.	Ang. Pect.	9.3	3.2	6.5				9.2	3.4	6.8										9.0	3.0	7.2								
17. F. C.	Cong. Ht. Fail.	9.7	3.7	7.5																8.1	3.8	6.5	8.4	3.8	8.3	9.4	3.8	7.1		
18. L. M.	Cong. Ht. Fail.	9.0	3.4	6.0	8.8															8.6	3.6	7.2				9.1	3.6	6.9		
19. M. V.	Cong. Ht. Fail.	9.2	3.3	7.0	9.2						8.4	3.6								8.6	2.7	8.5								
20. M. F.	Ang. Pect.	9.9	3.1	7.6				9.3	3.4					9.8	3.3					9.6	3.2	8.9								
21. F. F.	Non-cardiac	9.5	4.2	7.9	7.7			8.8	4.1					7.3	3.2															
22. W. Mc.	Non-cardiac	9.1	3.6	6.7	9.3						8.5	3.4					8.4	3.2												
23. A. R.	Non-cardiac	8.7	3.5	6.8	8.4			7.4	3.5		8.5	3.6																		
24. W. Bu.	Cong. Ht. Fail.	9.8	2.8	6.3	7.1			9.1	3.0		7.8	2.7																		
25. M. W.	Ang. Pect.	9.6	3.0	6.5	8.6			9.3	3.2		9.0	3.2														9.0	2.9	7.0		
26. M. C.	Ang. Pect.	8.7	3.2	7.0	7.7	3.2		9.2	3.1		9.0	3.2					8.3	3.1		10.1	3.1	7.7								
27. B. C.	Cong. Ht. Fail.	9.3			8.9	3.5		8.5	2.8								8.8													
28. H. G.	Cong. Ht. Fail.	8.8		7.0	9.4	3.5	7.6	8.8	3.6																					
29. G. O.	Ang. Pect.	8.5			8.9	3.0		9.1	3.2		8.3	2.9																		
30. H. B.	Cong. Ht. Fail.	9.0	3.4		7.7			8.7	3.8		9.0	3.5																		
31. F. Z.	Cong. Ht. Fail.	8.2	4.2	5.5	8.4	2.7	6.2	8.9	3.8					8.6	3.7															
	‡ Average basal metabolic rate (per cent deviation from normal)		-2								-14			-25						-25										

* Calcium measured by Clarke permanganate method.

† Permanent cessation of signs and symptoms of parathyroid insufficiency.

‡ Beginning with the second month after operation some of these patients were receiving small doses of thyroid (Armour's, 1/8 to 1/2 grains daily) to obviate distressing myxedema symptoms.

DISCUSSION

The incidence of transient tetany following total thyroidectomy in this group of seventy-three cases is greater than that observed following subtotal thyroidectomy. It is probable that the number of cases of mild postoperative tetany that are recognized depends to some extent upon the diligence with which attempts are made to elicit signs and symptoms; the frequent clinical examinations routinely made in our studies may, therefore, be responsible in part for the high incidence of mild tetany observed. The observations of others (1) (2) that tetany occurs more frequently after the removal of both lobes of the abnormal thyroid gland than after the removal of one lobe led us to anticipate that postoperative tetany would occur more frequently after total thyroidectomy than after the usual thyroid operations.

The interval of one to five days between removal of the thyroid gland and the development of tetany in the above cases is similar to the interval between parathyroidectomy and the onset of experimental tetany in dogs (11). This relationship as to time strengthens the hypothesis that the tetany which occasionally follows thyroidectomy results from decreased parathyroid function. Berlin (4) has outlined the method of avoiding removal of the parathyroid glands or destruction of their blood supply during total thyroidectomy. Since careful pathological examination of the extirpated thyroid tissue revealed that a parathyroid gland had been removed from only one of the twelve patients who developed signs and symptoms of tetany, we believe that most of our cases of tetany must have been due to trauma to the parathyroid glands or interference with their blood supply, nerve supply, or lymphatic drainage, rather than to removal of these glandules. The short duration of the disease in most of these patients is added evidence in favor of this point of view. These studies and the survey recently made by one of us (Berlin (12)), show that the specific measures employed to identify hidden parathyroid glands during operation in order to preserve them, do not necessarily protect the patient against tetany. It has been pointed out (12) that the problem of recognition of parathyroid bodies during removal of the thyroid gland is important in the sense that precaution should be taken not to remove or injure the parathyroid glands which are adherent to the tissue to be extirpated; parathyroid glandules which are sometimes found enclosed within the split layers of the true capsule of the thyroid gland should be excised and reimplanted in the sterno-mastoid muscle.

It is believed that the symptoms of tetany in many of these patients would have disappeared even if no calcium medication had been given. This occurred in three patients (Cases 5, 8 and 9) with mild symptoms, who did not receive medication while under careful observation for the development of further symptoms. There is no evidence available from our own studies or those of others that medication with calcium does anything more than alleviate the existing symptoms of tetany and prevent the

development of more serious complications; the actual duration of the parathyroid deficiency is probably not affected.

Albright and his associates (13), and Ellsworth (14) have pointed out that low serum calcium and high serum phosphorus values are cardinal features of parathyroid tetany. The patients studied by Albright (13) and Ellsworth (14) were cases of long standing hypoparathyroidism of idiopathic or postoperative etiology. Case 7 of our series showed changes in serum calcium and phosphorus one month after operation similar to those observed in chronic tetany (15) (16), the serum calcium concentration being 5.9 mgm. and the serum phosphorus 5.6 mgm. per 100 cc. However, our results show that at the time of onset of clinical signs and symptoms of parathyroid tetany in man, blood chemical findings characteristic of chronic hypoparathyroidism may not be present. In contrast to our findings in man, studies of others on parathyroidectomized dogs show that the serum calcium is, almost without exception, strikingly decreased and the serum phosphorus increased at the time of onset of symptoms of tetany (15) (16) (17).

The finding of a normal concentration of inorganic phosphorus in the serum at the time of onset of postoperative tetany in most of our cases was unexpected, in the light of the above considerations. There are, however, a few observations early in the course of postoperative tetany in man which accord with this finding (18) (19). Bauer, Marble and Clafin (18) observed carpopedal spasm three days after a second stage removal of the thyroid in a patient in whom the concentration of serum inorganic phosphorus was only 4.6 mgm. and the concentration of serum calcium 6.8 mgm. per 100 cc. Two weeks after operation the serum inorganic phosphorus in this patient was 6.7 mgm. and the serum calcium 5.2 mgm. per 100 cc. Bauer and his associates (18) pointed out that the concentration of calcium was abnormally low in this patient at the time when carpopedal spasms were first manifest, but that only subsequently did the concentration of serum inorganic phosphorus rise to an abnormally high level. Likewise, Taubenhaus (19) observed a patient who developed symptoms of severe tetany five days after subtotal thyroidectomy, at which time the inorganic phosphorus of the serum was 5.0 mgm. and the calcium 5.4 mgm. per 100 cc. Our findings and those of Bauer (18) and Taubenhaus (19) make it clear that the change in serum calcium in acute hypoparathyroidism may precede the change in serum phosphorus. This is in contrast with the primary change in serum phosphorus in acute hyperparathyroidism (13) (14) (23).

Our observations show that while studies of serum calcium and phosphorus are of great value in the diagnosis and management of postoperative tetany, the clinical signs and symptoms are of the utmost importance. McCullagh (2) observed that the clinical diagnosis of postoperative tetany is sometimes not corroborated by the serum calcium findings. He sug-

gested that the clinical diagnosis of tetany in such cases may have been incorrect, and noted that some normal individuals may have a mildly positive Chvostek's sign. In view of our observations, however, we believe that the early diagnosis of postoperative tetany can be made definitely without the confirmatory evidence of abnormal chemical findings. Although Chvostek's sign was mild in several of our patients, it appeared to be significant because of its clearly defined onset and disappearance. Experience in other clinics has shown that if postoperative parathyroid tetany is not diagnosed and treated early, convulsions may ensue, and death may follow (1).

It has been established, beyond reasonable doubt, that a sudden marked decrease in the physiologically active fraction of the serum calcium leads to the symptom complex of tetany in man, whereas some patients with chronic hypoparathyroidism may have no symptoms for years, in spite of markedly diminished concentrations of calcium in the serum (11) (20) (21). The cause of tetany is not clear in those of our patients who showed clinical signs and symptoms without a significant reduction in the total concentration of calcium in the serum. It may be that the amount of the sudden diminution of the active fraction of the serum calcium which is sufficient to precipitate mild tetany is, in certain cases, too small to be detected by the usual measurement of total serum calcium. With the persistence of the physiological derangement a sustained significant decrease in the active fraction of the serum calcium may, however, become apparent through a decrease in the concentration of total calcium. Studies of the concentration of magnesium in the serum during early postoperative tetany following total thyroidectomy are being made by Miss Dorothy Tibbetts at the Huntington Memorial Hospital, Boston. Kruse, Orent and McCollum (22) have recently demonstrated that tetany occurs in dogs with low concentrations of serum magnesium, but that the syndrome of this deficiency is different from that observed in parathyroidectomized animals (22).

Rabinowitch (24) found decreases in the concentration of serum calcium of 1.3 mgm. to 3.5 mgm. per 100 cc. during the first week following subtotal thyroidectomy in ten of thirteen thyrotoxic patients, none of whom developed tetany after operation. In most of these cases the serum calcium returned to the preoperative level by the end of the second week after operation (24). These observations of Rabinowitch following subtotal thyroidectomy (24) are similar to ours of a decreased concentration of serum calcium during the period immediately following total thyroidectomy in nine of thirteen cases, none of whom developed clinical signs or symptoms of reduced parathyroid function. The concentration of inorganic phosphorus in the serum remained normal in these patients throughout the postoperative period; the decrease of serum calcium was not attributable to a lowering of the concentration of serum protein (Ta-

ble II). From our findings after total thyroidectomy, and those of Rabinowitch after subtotal thyroidectomy, it appears that mild transient parathyroid insufficiency occurs in approximately 80 per cent of patients following these procedures. In patients who show such changes in serum calcium without symptoms of tetany the decreased calcium is of no clinical importance.

The persistence of slightly subnormal values for serum calcium for months following total thyroidectomy, both in patients who showed transient clinical signs of hypoparathyroidism and in those who showed no signs, is probably not dependent upon the hypothyroid state induced (as evidenced by low basal metabolic rates (Table II)), since the serum calcium in cases of myxedema of idiopathic origin has been found to be normal (25). Our results suggest that some thyroidectomized patients may have a slight reduction in parathyroid function for several months after operation although no clinical manifestations are evidenced.

It is probable that one of our patients, in whom symptoms of tetany have been manifest at various times during the nine months since operation (Case 7), will continue to show clinical evidence of parathyroid deficiency whenever medication is discontinued. Indeed, even when this patient is receiving large amounts of calcium salts, she occasionally experiences mild paresthesias. The efficacy of large doses of viosterol as an adjunct to calcium therapy (18) in this case is being studied; parathyroid extract has not been employed, since its effectiveness has been shown to be only temporary (26). In the other patient of this series who still shows clinical signs of reduced parathyroid function two and a half months after operation (Case 12), the symptoms are satisfactorily controlled by oral administration of calcium chloride, supplemented by viosterol.

SUMMARY

1. Tetanic convulsions or spontaneous spasm of the extremities did not occur in any of seventy-three consecutive patients on whom total thyroidectomy was performed. Clinical signs or symptoms of mild parathyroid deficiency were manifest after operation in twelve patients, or 17 per cent, of this entire series. Of the last thirty-seven patients of this group of seventy-three, only three, or 8 per cent, showed signs or symptoms.
2. In ten of the twelve patients clinical signs and symptoms of hypoparathyroidism were transient, disappearing within two weeks. One patient who was operated upon two and a half months ago, and another nine months ago, still show signs and symptoms when specific medication is discontinued.
3. The symptoms of hypoparathyroidism are attributed to injury, rather than to removal of parathyroid glands during operation.
4. Oral administration of calcium chloride solution and a diet rich in milk controlled the symptoms of tetany in most patients in whom the

disease was transient. An initial intravenous injection of calcium chloride solution was given to three patients; calcium lactate or gluconate was substituted when oral administration of calcium chloride solution was not tolerated. Viosterol, together with a large intake of calcium, is being employed successfully in the two cases with persistent hypoparathyroidism.

5. The serum calcium was reduced to 7.5 mgm. per 100 cc. or less in six of the twelve cases at the time of onset of tetany; in three cases the serum calcium was between 8.3 and 8.6 mgm. per 100 cc.; in the remaining three cases the serum calcium was within the accepted normal limits. The values for serum inorganic phosphorus in these patients with early postoperative tetany were usually normal, being 5.0 mgm. per cent or above in only two cases.

6. Appreciable decreases in concentration of serum calcium and no changes in concentration of serum inorganic phosphorus were observed during the first two weeks after total thyroidectomy in a group of patients who showed no clinical signs of insufficient parathyroid function.

7. The concentration of serum calcium was usually slightly below the preoperative level during the first year after thyroidectomy, both in those individuals who showed transient signs and symptoms of hypoparathyroidism soon after operation and in patients who showed no clinical signs of this disorder at any time.

8. It is pointed out that the chemical changes in the blood present during the early stages of postoperative tetany may be quite different from the characteristic markedly low serum calcium and high phosphorus values found in chronic hypoparathyroidism of either idiopathic or postoperative origin.

9. The transient tetany which sometimes occurs immediately following total thyroidectomy can be controlled by calcium therapy; persistent parathyroid insufficiency occurs so rarely that it does not constitute a contraindication to total thyroidectomy.

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CASE REPORTS

Case 1. Rheumatic heart disease; mitral stenosis; congestive failure; mild, transient tetany following total thyroidectomy. B. Z., a housewife, aged 42, was operated upon April 8, 1933. The early postoperative course was uneventful. On the third postoperative day the patient complained of tingling numbness in the face and hands, most marked in the tips of the fingers, and showed moderate Chvostek's and Trousseau's signs. The patient stated that numbness of the face and hands had gradually increased during the preceding two days, but that the symptom was so vague that she did not complain even on questioning. Chvostek's and Trousseau's signs were not elicited during these two days. Immediately on recognition of symptoms of tetany, the nurse in charge administered 1 cc. of parathyroid extract (Collip) intramuscularly in accordance with standing orders. The serum calcium one hour after injection was 9.2 mgm. (Clarke's method) and the serum phosphorus 5.0 mgm. per 100 cc. Following the injection of parathyroid extract, 4 cc. of 35 per cent calcium chloride solution each hour and 0.5 cc. of viosterol, 250 D, were administered orally. Within a few hours after medication was instituted, the clinical signs and symptoms disappeared. For the next two days the patient received 4 cc. of 35 per cent calcium chloride solution every two hours during waking hours, every three hours during the night, and 0.5 cc. of viosterol every six hours, with no recurrence of signs or symptoms. Blood drawn on these two mornings, three hours after calcium chloride medication, showed calcium values of 14.0 and 13.8 mgm. per 100 cc. of serum respectively (Clarke's method). On the following morning, after 72 hours of therapy, the serum calcium had increased to 16.6 mgm. per 100 cc. (Clarke's method) and the serum phosphorus decreased from a pre-operative level of 4.1 to 2.7 mgm. per 100 cc. Medication was therefore omitted. On the tenth postoperative day, four days after the cessation of therapy, the patient again complained of numbness and tingling of the hands and face. Moderately active Chvostek's and Trousseau's signs were elicited. The serum calcium was 9.4 and the serum phosphorus 3.6 mgm. per 100 cc. Calcium chloride, 4 cc. of 35 per cent solution every two hours, and viosterol 0.5 cc. every six hours, were again administered. All signs and symptoms of tetany disappeared late that day.

During the next few weeks the viosterol was gradually omitted and the calcium medication was reduced to 8 cc. of 35 per cent solution calcium chloride twice daily together with a quart of milk daily. The fasting serum calcium concentration remained around 8.2 mgm. per 100 cc. The lack of clinical significance of this slightly subnormal serum calcium was not appreciated at this time and therefore medication was continued until the sixth postoperative month. To the time of writing, approximately one year after operation and six months after cessation of calcium therapy, the patient has experienced no recurrence of signs and symptoms of tetany.

Case 2. Rheumatic heart disease; mitral stenosis; congestive failure; mild, transient tetany following total thyroidectomy. W. D., a man, aged 23, was operated upon April 15, 1933. The early postoperative course was uneventful.

On the second postoperative day a mild Chvostek's sign was elicited; no symptoms of tetany were manifest, however. Four cc. of 35 per cent calcium chloride solution every three hours was administered and on the fourth day after operation, because of the persistence of a moderate Chvostek's sign, 0.5 cc. of viosterol every six hours was added to the calcium therapy. The serum calcium on the third postoperative day was 8.6 mgm. per 100 cc. (Clarke's method). On the fifth postoperative day, the dose of calcium chloride was decreased to 4 cc. four times a day and once during the night. Viosterol was decreased to 0.5 cc. twice daily. No further signs or symptoms of tetany were manifest except on one occasion, the eleventh postoperative day, when a mild Chvostek's sign was again elicited. One month after operation, viosterol was discontinued and the calcium chloride medication gradually decreased until finally omitted approximately two months after operation. The serum calcium nine months after operation was 8.3 mgm. per 100 cc. It is now one year since operation and no signs or symptoms of tetany have been manifest since the disappearance of the Chvostek sign on the eleventh postoperative day.

Case 3. Rheumatic heart disease; mitral stenosis; congestive failure; mild, transient tetany following total thyroidectomy. L. B., a housewife, aged 45, had a total thyroidectomy April 17, 1933. The early postoperative course was uneventful. On the fifth day after operation the patient experienced tingling numbness of the fingers and in the vicinity of the operative wound. A mild Chvostek's sign was elicited but Trousseau's sign was negative. The serum calcium at this time was 10.7 mgm. (Clarke's method). She received eight cc. of 35 per cent calcium chloride solution orally every two hours during waking hours and every four hours at night and 0.5 cc. of viosterol every six hours. On the following day the signs and symptoms of tetany had disappeared and medication was discontinued. There was no recurrence of symptoms until about ten days later when the patient complained of a vague, numb sensation in the fingers; Chvostek's and Trousseau's signs were negative at this time. Although we did not believe this symptom was due to parathyroid tetany, one dose of 8 cc. of 35 per cent calcium chloride solution was given orally, and subjective numbness disappeared. Up to the time of the present writing, approximately one year after operation, the patient has had no recurrence of signs or symptoms of tetany.

Case 4. Arteriosclerotic heart disease; coronary sclerosis; angina pectoris; mild, transient tetany following total thyroidectomy. E. P., a woman, aged 58, was operated upon July 1, 1933. The early postoperative course was uneventful. No signs or symptoms of tetany were evident until the fifth postoperative day, when she experienced tingling numbness of the fingers, involuntary twitching of the mouth, and stiffness of the body. At this time a moderate Chvostek's and a moderate Trousseau's sign were elicited. The serum calcium was reduced to 7.2 mgm. per 100 cc.

Eight cc. of 35 per cent calcium chloride solution were administered every three hours, and a quart of milk was taken daily. She was unable to retain the calcium chloride solution, and the signs and symptoms of tetany, though somewhat diminished, persisted during this and the following day. On the next day she received four ounces of 4 per cent calcium gluconate solution every three hours, the quart of milk daily being continued. That day the signs and symptoms of tetany disappeared, and did not recur until five days later, when the patient again complained of transient numbness of the fingers. At this time Chvostek's and Trousseau's signs were negative; the fasting serum calcium was still reduced to 7.2 mgm. per 100 cc. During the next two weeks the serum calcium rose to 8.0 mgm. per 100 cc. and medication was omitted. At the time

of writing, nine months after thyroidectomy, the patient still remains free of clinical signs and symptoms of parathyroid insufficiency.

Case 5. Generalized arteriosclerosis; arteriosclerotic heart disease; congestive failure; mild, transient tetany following total thyroidectomy. J. T., a man, aged 59, was operated upon July 25, 1933. The early postoperative course was uneventful. On the fifth day after operation he complained of occasional tingling of the right hand and of the nose. On the following day he noted mild transient stiffness of the jaw and numbness of the face. These symptoms disappeared on the same day without medication. Chvostek's and Trousseau's signs were negative at all times. The serum calcium two days after operation had decreased to 7.5 mgm. per 100 cc.; calcium measurements were not made on the fifth or sixth postoperative days when the symptoms were present. One month postoperatively the serum calcium had returned to the preoperative level of 8.7 mgm. per 100 cc. Since the sixth postoperative day, no symptoms of tetany have been experienced up to the time of writing, approximately eight months after operation.

Case 6. Hypertension; hypertensive heart disease; congestive failure; transient tetany following total thyroidectomy. B. R., a housewife, aged 48, was operated upon July 28, 1933. The temperature was elevated to approximately 101° F. during the first five postoperative days. During the evening of the third postoperative day the patient noted a numb sensation of the feet. The serum calcium on the morning of this day was 7.8 mgm. per 100 cc. On awakening the following morning she noted tingling numbness of both feet, this sensation gradually increasing to the level of the knees and later to the abdomen. The patient called the nurse and complained of these symptoms for the first time. Numbness and tingling of the face, hands and arms, sensations of "smothering," heaviness over the chest, stiffness of the ankles and jaws, apprehension and nausea rapidly developed. Chvostek's and Trousseau's signs were active. Twenty cc. of 10 per cent calcium chloride solution were administered intravenously. One hour after this injection the symptoms of tetany and the Chvostek's and Trousseau's signs had entirely disappeared. The fasting serum calcium just prior to the calcium chloride injection was 8.3 mgm. per 100 cc. During the remainder of this day and during the following two days 8 cc. of 35 per cent calcium chloride solution were given orally every three hours, 0.5 cc. of viosterol every twelve hours, and a quart of milk daily. The patient experienced no paresthesias, and the medication was reduced on the fourth day after the onset of symptoms to 8 cc. of calcium chloride solution every six hours, and a quart of milk daily. On the tenth day after the onset of symptoms the serum calcium had increased to 9.6 mgm. per 100 cc. and calcium medication was accordingly omitted. On the thirteenth postoperative day the patient noted transient tingling numbness of the tips of the fingers and of the face. Chvostek's and Trousseau's signs were, however, negative. Since this time there has been no recurrence of the signs or symptoms of tetany up to the time of writing, eight months after operation.

Case 7. Rheumatic heart disease; mitral stenosis; congestive failure; chronic tetany following total thyroidectomy. S. B., a housewife, aged 52, was operated upon August 9, 1933. Early on the morning of the second postoperative day a Chvostek's sign was elicited. Two hours later she noted tingling numbness of the right leg and foot and of the skin about the mouth. Active Chvostek's and Trousseau's signs were elicited at this time. The serum calcium was 7.2 mgm. per 100 cc. and the serum phosphorus 5.3 mgm. Ten cc. of 10 per cent calcium chloride solution was administered intravenously, with the disappearance of all signs and symptoms within the next two hours. For the re-

mainder of this day she was given 8 cc. of 35 per cent calcium chloride solution orally every three hours, and for the following three days 8 cc. of 35 per cent calcium chloride solution every eight hours, and a quart of milk daily. Signs and symptoms of tetany did not recur, and medication was omitted on the sixth postoperative day. On the following day the patient experienced numbness of the face; a mild Chvostek's sign was elicited, Trousseau's sign was negative, the serum calcium was 6.3 mgm. per 100 cc. Eight cc. of 35 per cent solution of calcium chloride was again administered every eight hours. On discharge from the hospital, approximately two weeks after operation, she was advised to continue to take this calcium medication and a quart of milk daily.

She was seen three weeks after her discharge, at which time she complained that she had experienced transient numbness and tingling of the extremities and a shaking feeling and stiffness of the limbs on several occasions since her discharge from the hospital, although she stated that she had adhered to the calcium medication as ordered. The fasting serum calcium at this time was 5.9 mgm. per 100 cc., the serum phosphorus 5.6 mgm. per 100 cc., and Chvostek's and Trousseau's signs were active. Calcium medication was increased by the addition of 150 grains of calcium lactate daily.

During the next month the patient intermittently failed to take the calcium chloride solution for a period of a day or two, at which time paresthesias reappeared. From the second to the ninth months after operation, the patient continued to experience mild paresthesias at times, in spite of a high calcium intake. With large doses of viosterol (5 to 15 cc. daily of 250 D) as an adjunct to calcium therapy, she has been relieved of symptoms and the serum calcium has been increased to 8.6 mgm. per 100 cc.

Case 8. Rheumatic heart disease; mitral stenosis; congestive failure; mild tetany following total thyroidectomy. F. D., a man, aged 18, was operated upon August 25, 1933. The temperature rose to 103° F. on the first postoperative day, returning to normal the following day. On the second postoperative day the patient complained of tingling of the fingers. A moderate Chvostek's sign was elicited at this time; Trousseau's sign was negative. On the third postoperative day the patient experienced transient tingling of the right hand; a mild Chvostek's sign was elicited; the serum calcium was 8.3 and serum phosphorus 3.3 mgm. per 100 cc. Transient tingling of the right hand was experienced until the sixth postoperative day, and Chvostek's sign was occasionally elicited until the eighth postoperative day, at which time the serum calcium was 7.7 mgm. per 100 cc. and the serum phosphorus 4.9 mgm. per 100 cc. Up to the present writing, approximately seven months after operation, there has been no recurrence of the signs or symptoms of parathyroid insufficiency.

Case 9. Rheumatic heart disease; mitral stenosis; congestive failure; mild, transient tetany following total thyroidectomy. L. M., a man, aged 28, was operated upon August 23, 1933. The temperature rose to 102° F. on the first postoperative day and gradually subsided to normal by the eighth postoperative day. On the fifth day after operation the patient experienced tingling numbness of the hands and fingers; a moderate Chvostek's sign was elicited, Trousseau's sign was negative, and the fasting serum calcium was reduced to 6.2 mgm. per 100 cc. and the serum phosphorus level was 3.5 mgm. per 100 cc. During the following six days the signs and symptoms gradually disappeared without medication. The serum calcium on the tenth postoperative day, the day before disappearance of signs and symptoms, was still 6.2 mgm. per 100 cc. and the serum phosphorus was 3.8 mgm. This patient showed no recurrence of signs and symptoms of tetany up to the time of his death, due to bronchopneumonia and congestive heart failure, six weeks after operation.

Case 10. Arteriosclerotic heart disease; coronary sclerosis; angina pectoris; mild transient tetany following total thyroidectomy. M. H., a man, aged 54, had a right hemithyroidectomy October 14, 1933, and on January 2, 1934, the remaining thyroid tissue was removed. The temperature rose to 102° F. on the first day after the total ablation of the thyroid and returned to normal on the sixth postoperative day. On the second postoperative day the patient experienced numbness of the fingers; Chvostek's and Trousseau's signs could not be elicited at this time. On the third postoperative day the patient complained of numbness and tingling of the hands, feet and legs. On the fourth day after operation the serum calcium was 6.7 mgm. per 100 cc. The signs increased until the seventh postoperative day, at which time a moderate Chvostek's sign was elicited but Trousseau's sign was still negative. On the eighth postoperative day the serum calcium was still reduced to 6.5 mgm. per 100 cc. and the signs and symptoms did not decrease. Calcium medication was instituted. The signs diminished, but were still evident on the eleventh postoperative day, when the dose of calcium chloride was increased to 12 cc. every three hours, with disappearance of signs and symptoms on the following day. On the thirteenth postoperative day the patient was nauseated by the calcium chloride solution, and medication was omitted. The serum calcium five days after cessation of therapy was 8.4 mgm. per 100 cc. There has been no recurrence of signs or symptoms of tetany to the time of writing, three and a half months after operation.

Case 11. Congenital heart disease; patent ductus arteriosus; congestive failure; mild, transient tetany following total thyroidectomy. G. O., a woman social worker, aged 31, was operated upon January 17, 1934. Late on the first postoperative day the patient experienced numbness of the fingers, hands and feet; Chvostek's and Trousseau's signs were negative. On the second postoperative day she complained of tingling numbness of the hands, feet and face, a sensation of pressure over the chest, coldness of the feet, hot waves over the face, and apprehension. Moderate Chvostek's and Trousseau's signs were elicited. Ten cc. of 10 per cent calcium chloride solution were given intravenously. The serum calcium, before the calcium administration, was 9.2 mgm. and the serum phosphorus 2.7 mgm. per 100 cc. During the first hour after the calcium injection, the symptoms of tetany disappeared, Trousseau's sign became negative, but a mild Chvostek's sign could still be elicited. Eight cc. of 35 per cent calcium chloride solution were given orally four times daily. On the next day all signs and symptoms of tetany had disappeared except for occasional numb sensations of the face. Medication was gradually reduced and finally discontinued in the course of the next six weeks. Following the acute episode on the second postoperative day the patient, up to the time of writing, three months after operation, has had no recurrence of signs and symptoms of tetany, with the exception of occasional transient numbness of the face, which we believe may be due to the other causes. The serum calcium has remained above 9 mgm. per 100 cc. and the serum inorganic phosphorus has been consistently normal.

Case 12. Rheumatic heart disease; mitral stenosis; congestive failure; mild tetany following total thyroidectomy. A. S., a housewife, aged 34, had a total thyroidectomy February 9, 1934. The early postoperative course was uneventful. On the afternoon of the second postoperative day, the patient noted tingling of the feet and hands and numbness of the lips; Chvostek's sign was moderate and Trousseau's sign was mild. Eight cc. of 35 per cent calcium chloride solution orally, and a glass of milk were given every three hours for the rest of this day and evening. Signs and symptoms of tetany persisted until the next morning, at which time the serum calcium was 6.6 mgm. per 100 cc. and the serum phosphorus 3.9 mgm. per 100 cc. The calcium chloride medication was in-

creased to 16 cc. five times a day for the following three days. Attempts to reduce the calcium chloride medication to less than 8 cc. of 35 per cent solution four times a day during the next three weeks resulted in recurrence of mild signs and symptoms. The fasting serum calciums (taken twelve hours after medication) persisted at 6.6 to 6.9 mgm. per 100 cc. during this period. The highest serum phosphorus obtained was only 4.4 mgm. per 100 cc. On discharge from the hospital, approximately one month after operation, this patient was advised to take a quart of milk daily and 8 cc. of 35 per cent calcium chloride solution four times a day. During the following two weeks she experienced mild symptoms on two occasions when she tried to reduce the calcium medication. At the present writing, two and a half months after operation, the patient is free from symptoms on a regimen of 8 cc. of 35 per cent calcium chloride solution three times a day, a quart of milk each day, and 0.5 cc. of viosterol three times a day. The fasting blood calcium concentration at this time is 8.3 mgm. per 100 cc.