

10 NOVEMBER 1966

## HYPOPARATHYROIDISM

Case 1, [REDACTED] - Permanent hypoparathyroidism following thyroidectomy

This 57 year old [REDACTED] female was admitted to [REDACTED] for the first time from the county jail where she experienced a generalized seizure. Several days prior to entry the patient had been found in a confused state wandering the streets. She was taken to the County jail where she was being "investigated for lunacy". Shortly after arriving in the emergency room, the patient experienced another seizure characterized by tonic and clonic jerking movements of the upper extremities and head with biting of her tongue. There was no urinary or fecal incontinence, and an absence of post ictal state.

No past medical history was available. The pertinent findings on physical examination included the following. BP 158/78 P74 regular R 16 T98 Bilateral proptosis and aphakia were present. The fundi showed multiple small old exudates along the inferior temporal vessels. Bilateral firm non tender masses were present in the submandibular area. The PMI was 2 cms. outside the midclavicular line. A grade iii/vi holosystolic murmur was present at the apex. Motor and sensory function was grossly intact. No abnormal reflexes were present.

The laboratory tests revealed a serum Na 129 mEq/L, Cl 87 mEq/L, CO<sub>2</sub> 28 mEq/L, and K 2.8 mEq/L. The cerebrospinal fluid contained 12 lymphocytes with normal protein and glucose concentrations. The heart was enlarged by Xray and the ECG showed evidence of left ventricular hypertrophy with a QT interval of 0.60 secs.

The patient was initially treated with diphenylhydantoin, phenobarbital, and intravenous saline containing vitamins and thiamine. Further saline solutions contained 40 mEq KCl and 20 ml calcium gluconate (180 mgs. Ca<sup>++</sup>). The following day the laboratory reported a serum calcium value of 4.5 mgs/100 mls. The serum phosphorous was 4.9 mgs/100 mls.

On the third hospital day the patient's husband, alarmed by the failure of his wife to return to her home in Louisiana from a trip, provided additional medical history. Fifteen years ago the patient had undergone a thyroidectomy followed by three seizures. Since that time she had been taking "calcium pills", however, she had been known to stop her medications on other occasions. Lethargy and constipation usually followed but no other seizures had occurred.

Case 2, [REDACTED] - Transient hypoparathyroidism following thyroidectomy

This 26 year old [REDACTED] female gravida IV Para IV was found to have a 1 cm. palpable nodule in the left lower lobe of the thyroid. She was free of all symptoms of hyperthyroidism. The PBI was 5.7  $\mu$ gms%. The <sup>131</sup>I uptake was 14.5% and scan of the gland revealed a "cold" area in the region of the palpable nodule. The patient's neck was explored at surgery and during the operation a frozen section of the tissue was reported showing papillary adenocarcinoma. A total thyroidectomy was performed; the pathology report listed mixed papillary and follicular cystadenocarcinoma, Grade I, and two normal parathyroid glands. Approximately 18 hours following the operation the patient complained of drawing sensation in her hands and found to have positive Chvostek and Trousseau signs. She was given Vitamin D 100,000 units and calcium gluconate 8 grams daily. Over the next week the symptoms of hypocalcemia abated and the patient was discharged. Three months later, no longer taking Vitamin D or exogenous calcium, the patient maintains a normal serum calcium value and free of tetany.

DATE			O P E R A T I O N							
SERUM CALCIUM (mgs/100 mls.)	9.7			7.0	6.6	8.5	9.2	9.8	9.6	9.5
SERUM PHOSPHOROUS (mgs/100 mls.)	4.2			4.5		4.5	4.9	7.5	4.3	4.2

Case 3, [REDACTED] - Hypoparathyroidism following parathyroidectomy

This 19 year old WF was referred to [REDACTED] because of vaginal bleeding occurring during the sixth month of pregnancy. She had been found to have a palpable mass in the area of the right upper pole of the thyroid in association with a serum calcium of 15 mgs per 100 mls. and a serum phosphorous of 3.1 mgs per 100 mls. Repeat calcium and phosphorous determinations strongly suggested hyperparathyroidism. A 15 gram parathyroid adenoma was removed at surgery. Within 12 hours of the completion of the operation the patient developed regular uterine contractions and spontaneously delivered a dead male fetus. By the tenth postoperative day the serum calcium had fallen to 6.4 mgs per 100 mls; the CO<sub>2</sub> combining power was 13.0 mEq/L. A positive Chvostek sign was elicited and the patient placed on calcium lactate 2.4 gms four times daily. Vitamin D, 100,000 units daily was added to the regimen and the patient was discharged.

The patient was readmitted to the hospital four days following discharge, because of weakness. She had failed to continue her calcium and Vitamin D supplements. Once again she was found to be hypocalcemic, and was treated with calcium lactate and Vitamin D. As far as is known the patient still requires medication to prevent hypocalcemic symptoms.

DATE			O P E R A T I O N							
SERUM CALCIUM (mgs/100 mls.)	18.7	17.2		14.4	10.0	10.1	9.0	8.9	6.8	6.4
SERUM PHOSPHOROUS (mgs/100 mls.)	3.2	2.6		2.1		2.9	2.8		3.3	
ALK. PHOSPHATASE				9.2	14.2	16.3				26.0

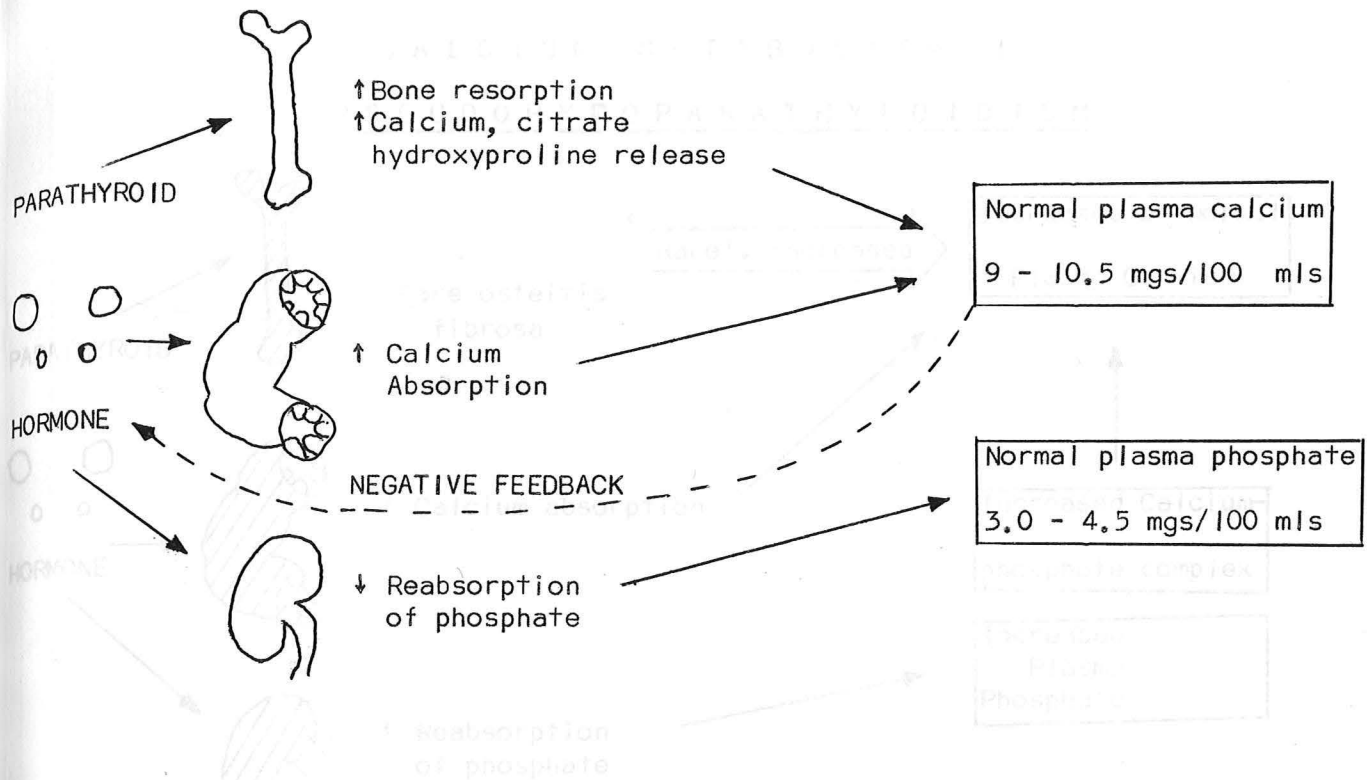
DATE				D I S C H A R G E					
SERUM CALCIUM	7.7	7.2	7.4		5.5	6.4		7.8	8.4
SERUM PHOSPHOROUS	3.2					3.3			
CALCIUM LACTATE (gms/day)	9.6	14.4	14.4			14.4			
VITAMIN D		100,000	100,000			150,000			

Case 4, [REDACTED] - Idiopathic Hypoparathyroidism

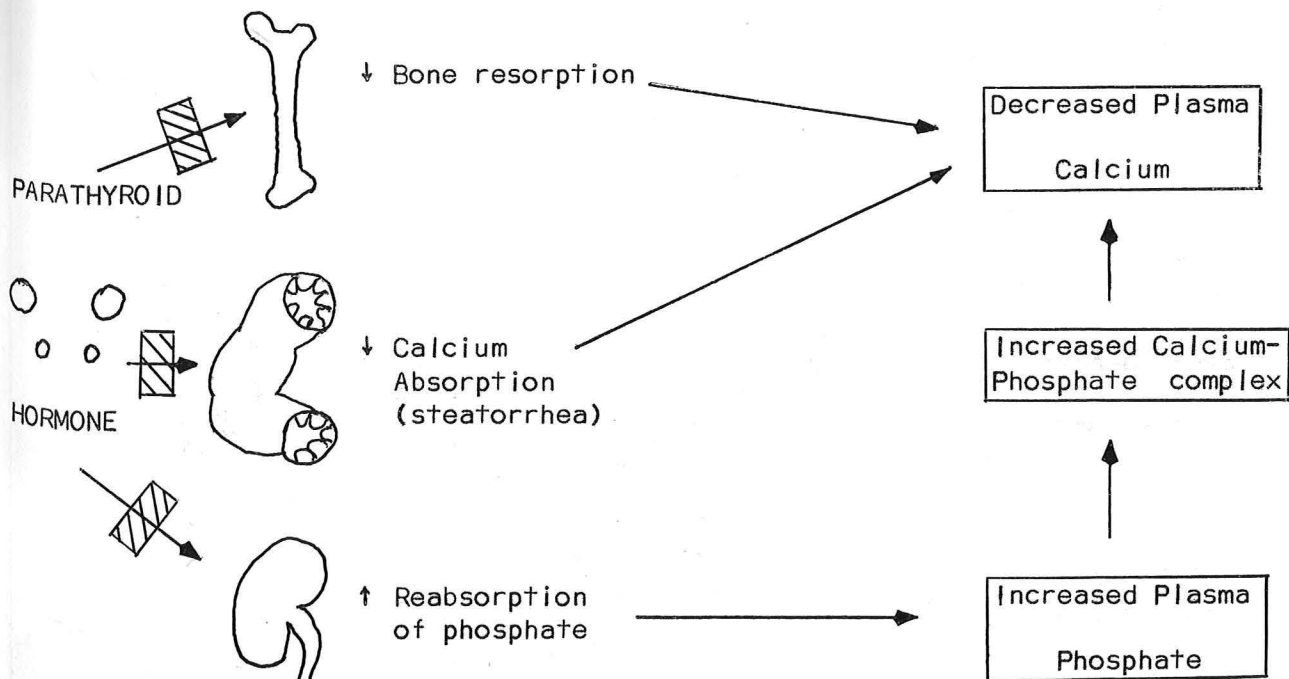
This 34 year old WM entered the [REDACTED] for the first time for evaluation of a convulsive disorder first documented three years prior to this admission. During this interval the patient had been hospitalized on eight occasions because of anxiety and convulsions. On the third hospitalization a diagnosis of idiopathic hypoparathyroidism was made on the basis of the physical findings, repeated generalized convulsions with basal ganglia calcifications, hypocalcemia and hyperphosphatemia. The patient was of short stature with small hands but a normal facial configuration. He demonstrated hypoplasia of the enamel of the teeth with several blunted dental roots. Positive Chvostek and Trousseau signs were present. An Ellsworth-Howard test was performed and interpreted as negative; however, since a positive control was not done, one can not be certain of the potency of that particular preparation of parathyroid extract. In the ensuing hospitalizations there was diagnostic confusion as to whether the patient had idiopathic or pseudo hypoparathyroidism. For the past two years the patient has been treated with calcium lactate and Vitamin D which corrects his hypocalcemia.



## ACTIONS OF PARATHYROID HORMONE

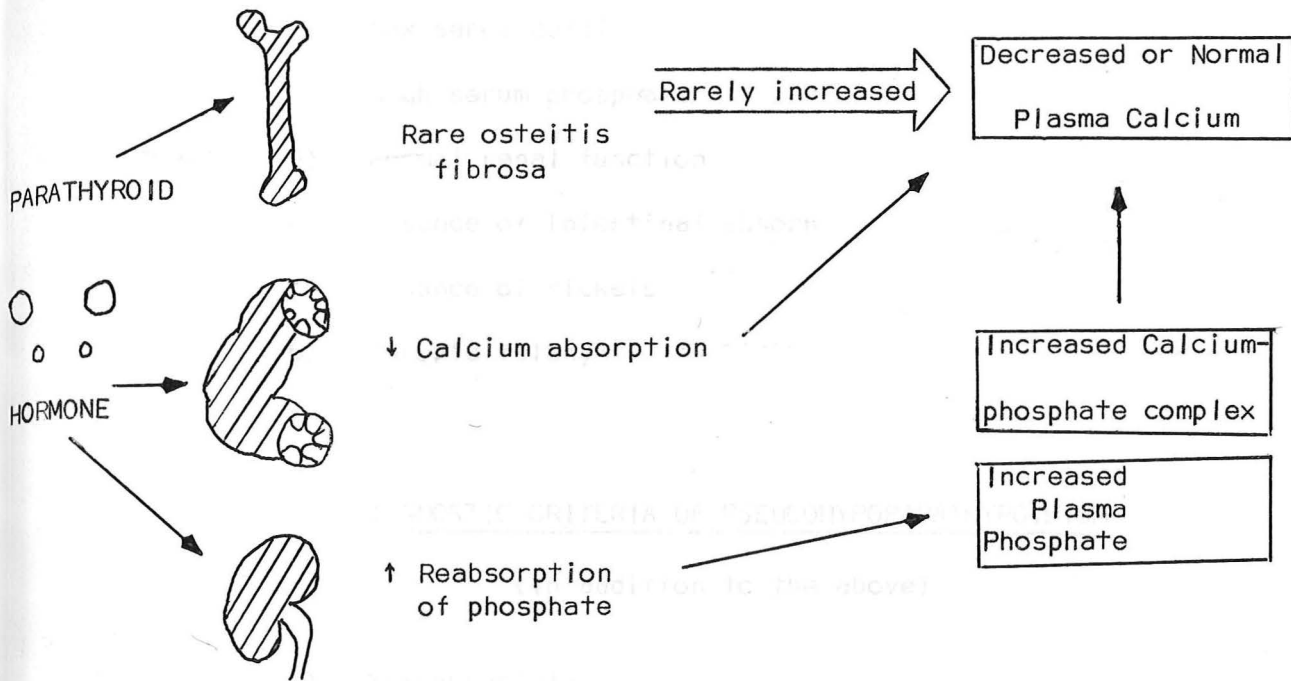


## CALCIUM METABOLISM IN THE ABSENCE OF PARATHYROID HORMONE





# CALCIUM METABOLISM IN PSEUDOHYPOPARATHYROIDISM



DIAGNOSTIC CRITERIA OF HYPOPARATHYROIDISM

- 1) Low serum calcium
- 2) High serum phosphate
- 3) Normal renal function
- 4) Absence of intestinal absorptive defects
- 5) Absence of rickets
- 6) Chronic tetany

DIAGNOSTIC CRITERIA OF PSEUDOHYPOPARATHYROIDISM

(In addition to the above)

- 7) Brachydactyly
- 8) Round face and thickset figure
- 9) Resistance to the action of potent parathyroid hormone
- 10) Demonstrable presence of parathyroid gland tissue

ETIOLOGY OF BILATERAL BASAL GANGLIA CALCIFICATION

(Analysis of 88 Cases)

Idiopathic Hypoparathyroidism	56	64%
Pseudo Hypoparathyroidism		
Post Thyroidectomy Hypoparathyroidism	2	3%
Toxoplasmosis	5	6%
Familial idiopathic basal ganglia Calcification	6	7%
Miscellaneous diseases with normal Calcium-phosphorous metabolism	10	11%
No definite diagnosis	8	9%

ETIOLOGY OF PAPILLEDEMA IN HYPOPARATHYROIDISM

(Analysis of 22 cases)

Idiopathic Hypoparathyroidism	11	50%
Postoperative Hypoparathyroidism	11	50%
Toxic Goiter	5	
Non-toxic Goiter	6	

CALCIUM AGENTS USED IN THE TREATMENT OF HYPOPARATHYROIDISM

Agent	Amount required to provide 1.0 gm. of calcium
Calcium citrate	4.7 gms
Calcium Lactate	7.7 gms
Calcium Gluconate	11.0 gms
Calcium Chloride	2.8 gms

EDTA TEST OF PARATHYROID INSUFFICIENCY

1. Patient placed on a 160 mgs calcium diet one day prior to the test.
2. On the day of the test between 10:00 a.m. and noon, Na EDTA (70 mgs/Kg) is infused in 500 ml of 5% dextrose in water containing 20 ml of 2% procaine hydrochloride.
3. Blood samples are taken without stasis at the start of the infusion and 2, 4, 8, 12, and 24 hours after its completion.
4. Serum calcium determinations should be done promptly.

INTERPRETATION

Normal: Serum calcium returns to pretest level within 24 hours.

Abnormal: Serum calcium fails to return to greater than 8.5 mgs% within 24 hours.

PHYSICAL SIGNS IN SPONTANEOUS HYPOPARATHYROIDISM

SIGN	IDIOPATHIC HYPOPARATHYROIDISM (50 Cases)	PSEUDO HYPOPARATHYROIDISM (40 Cases)
Body Habitus		
Round Face	5 (10%)	30 (75%)
Thickset, Stocky	5 (10%)	20 (50%)
Extremities		
Irregular length of metacarpals	1 (2%)	13 (33%)
Soft Tissue Calcification		
Subcutaneous	1 (2%)	23 (58%)
Basal ganglia	14 (28%)	19 (48%)
Ocular Signs		
Papilledema	9 (18%)	1 (2.5%)
Cataracts	24 (48%)	14 (35%)
Dental Signs		
Hypoplasia	3 (6%)	5 (12%)
Enamel defects	9 (18%)	4 (10%)
Unerrupted teeth	9 (18%)	13 (33%)
Root defects	2 (4%)	7 (17%)
Ectodermal Changes		
Hair, Nails, Skin	26 (52%)	7 (17%)
Moniliasis	8 (16%)	0



HYPOPARATHYROIDISM	ONSET	PERCENT	RESPONSE TO EDTA TEST	SERUM CALCIUM	RESPONSE TO PARATHYROID HORMONE
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post operative

Permanent	Widely	5.8%	Positive	Decreased	Positive
Partial	Variable (0-27 yrs)	24-28%	Positive	Normal	Positive
Post <sup>131</sup> I Therapy	Unknown	10%	Positive	Normal	Positive
Partial					
Idiopathic	Average (17 yrs.)		-	Decreased	Positive
Pseudo	None after 20 years		-	Decreased	Negative
Pseudo-pseudo	-		-	Normal	Negative

CATARACT FORMATION

5. Firschein, H. E., Lenticular effects of parathyroid hormone. *Endocrinology*, 58:626, 1953. Firschein, H. E., Komar, A., The relationship between parathyroid hormone and lens metabolism in The Parathyroid Glands, Univ. Chicago Press, 1953, Chicago, Illinois.  
These papers suggest that cataract formation occurring after the loss of parathyroid function results from lowered serum and aqueous humor calcium levels. A low level of the aqueous humor calcium results in an increased permeability of the lens. This change may be accompanied by the movement of small ions and water into the lens, resulting in vacuole formation.
6. Swan, K. C., Solit, P. W., Lens opacities associated with experimental calcium deficiency. Preliminary report. *Am. J. Ophthalmol.*, 26:611, 1941.  
Cataract formation was induced in rabbits by placing them on a low calcium diet, thereby reducing the serum calcium to 4.2 mg% as compared with 10.8 mg% in control animals fed a normal diet.
7. Haft, H. S., Idiopathic hypoparathyroidism and cataract. Report of four cases. *Arch. Ophthalmol.*, 50:455, 1953.

## REFERENCES

### HYPOPARATHYROID FUNCTION

#### TETANY

1. Bloomfield, A. L. A bibliography of Internal Medicine: Tetany, Stanford Medical Bull. 17:1, 1959.  
An historical review of the major advances in the recognition, pathogenesis and therapy of tetany. Clark and Kellie were the first to recognize tetany in infants. Steinheim is generally credited with having first described in 1830 adult tetany. In 1852 Lucien Corvisart appears to have been the first to use the term tetany. In 1862 Trousseau graphically describes the sign which has come to bear his name. "Chance made me discover this influence of compression" noted while he was bleeding a patient subject to tetany. By 1874 Erb reported "I have been the first to demonstrate precisely the increased galvanic excitability of the motor nerves, a not unessential contribution to the pathology of this disease". Chvostek noted muscle contraction following tapping of the nerve in 1876. To Sandström belongs the credit of first clearly recognizing the parathyroids as distinct from the thyroid. By 1891 Gley demonstrated that the removal of the parathyroids in dogs led to the development of tetany and death. It was finally MacCallum and Voegtlin who discovered the curative effect of soluble calcium salts upon the tetany of parathyroidectomy.
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A review of the signs and symptoms of latent and manifest tetany. A classification of tetany is listed and the pathophysiology discussed.
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The mechanism of Chvostek's sign is shown to be a mechanical stimulation of motor fibers of the facial nerve.

### CATARACT FORMATION

5. Firschein, H. E. Lenticular effects of parathyroid hormone. Biochem. Biophys. Acta. 58:626, 1962. Firschein, H. E., Kemrer, A. The relationship between parathyroid hormone and rat lens metabolism in The Parathyroid Glands. Univ. Chicago Press, 1965. Chicago, Illinois.  
These papers suggest that cataract formation occurring after the loss of parathyroid function results from lowered serum and aqueous humor calcium levels. A decrease in the aqueous humor calcium results in an increased permeability of the lens. This change may be accompanied by the movement of small ions and water into the lens, resulting in vacuole formation.
6. Swan, K. C., Salit, P. W. Lens opacities associated with experimental calcium deficiency: Preliminary report. Amer. J. Ophthal. 24:611, 1941.  
Cataract formation was induced in rabbits by placing them on a low calcium diet, thereby reducing the serum calcium to 4.2 mgs% as compared with 10.8 mgs% in the control animals fed a normal diet.
7. Haft, H. S. Idiopathic hypoparathyroidism and cataract: Report of four cases. Arch. Ophthal. 50:455, 1953.

## DENTAL ABNORMALITIES

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Hypoplasia of the enamel occurs if the hypoparathyroid state develops early in life. If the disease develops about the end of the first decade, the teeth tend to be entirely normal except for blunting of the root ends.

## BASAL GANGLIA CALCIFICATION

9. Frame, B. Parkinsonism in postoperative hypoparathyroidism. Arch. Int. Med. 116:424, 1965.  
Three cases of postoperative hypoparathyroidism with basal ganglia calcification and parkinsonism are described. In one patient correction of the hypocalcemia led to a disappearance of the tremor and rigidity.
10. Camp, J. D. Symmetrical calcification of the cerebral basal ganglia. Radiology 49:568, 1947.  
This paper provides histologic evidence suggesting that colloid deposition occurs about the fine cerebral blood vessels with subsequent calcification.
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These authors point out that patients with bilateral basal ganglia calcification, convulsions and mental symptoms may be well controlled with calcium and Vitamin D. However, the cerebral calcifications persist, suggesting that they are not the cause of the nervous system disorders.
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Describes a patient who was found to have basal ganglia calcification 24 years following thyroidectomy.
13. Palubinskas, A. J., Davies, H. Calcification of the basal ganglia of the brain. Amer. J. Roentgen. 82:806, 1959.  
A review of the differential diagnosis and findings in basal ganglia calcification with illustrative cases.
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An excellent survey of basal ganglia calcification in 88 patients. Two thirds of these patients had either idiopathic or pseudohypoparathyroidism. Of the latter 56 cases, convulsions and mental retardation was present in 61% and 64% respectively while cataracts were present in 45%.

22. Frame, B. Parkinsonism in postoperative hypoparathyroidism, clinical picture and convulsive seizures. Neurology 2:297, 1952.  
Seizures were present in 64% of 25 patients surveyed. They were all generalized, but focal seizures are also described.

## PAPILLEDEMA

15. Grant, D. K. Papilloedema and fits in hypoparathyroidism. *Quart. J. Med.* 22:243, 1953.  
An excellent review emphasizing the need to make an early correct diagnosis. The author stresses that the frequent accompaniment of increased cerebrospinal fluid pressure with papilledema and convulsions, although highly suggestive of a brain tumor, is equally suggestive of hypocalcemic hypoparathyroidism. Restoration of the serum calcium to normal controls the epilepsy, eradicates the papilledema, and returns the EEG to normal. Anticonvulsant drugs fail to correct the clinical picture in the face of hypocalcemia.
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A compendious review of neurological and psychiatric syndromes seen in hypoparathyroidism. The author adds four cases, three post surgical and one idiopathic.
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22. Frame, B., Carter, S. Pseudohypoparathyroidism, clinical picture and relation to convulsive seizures. *Neurology* 5:297, 1955.  
Seizures were present in 64% of 25 patients surveyed. The attacks were mainly generalized, but focal seizures are also described.

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#### SELECTED FEATURES

26. Krane, S.M. Selected features of the clinical course of hypoparathyroidism. JAMA. 178:132, 1961.  
A concise survey of diagnostic and therapeutic features seen in hypoparathyroidism.
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#### NEONATAL TETANY

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## ACQUIRED HYPOPARATHYROIDISM

### POSTOPERATIVE HYPOPARATHYROIDISM

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A comprehensive survey of post operative and idiopathic hypoparathyroidism. All patients who underwent thyroid surgery exhibited a decrease in serum calcium. In 239 thyroidectomies the incidence of hypoparathyroidism was 5.8%, the ratio of permanent to transient being 3:1 when these patients were examined three years after operation.
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Parathyroid insufficiency after thyroidectomy, review of 46 patients with a study of the effects of hypocalcaemia on the electro-encephalogram. Brit. J. Surg. 50:608, 1963.  
An interesting paper which investigates the prevalence of partial hypoparathyroidism using the EDTA test and calcium deprivation studies. The results suggest that parathyroid insufficiency cannot be excluded by a single serum calcium determination and



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An excellent discussion of the types of hypoparathyroidism following surgery. Critically reviews the world's literature. The incidence of hypoparathyroidism in the author's series of 112 subtotal thyroidectomies was 4.5%, the ratio of permanent to transient being 2:3.

#### POST <sup>131</sup>I THERAPY FOR THYROTOXICOSIS

41. Adams, P. H., Chalmers, T. M. Parathyroid function after <sup>131</sup>I therapy for hyperthyroidism. *Clin. Sci.*, 29:391, 1965.  
Of 60 patients who had received a therapeutic dose of <sup>131</sup>I for hyperthyroidism, all had fasting serum calcium values within the normal range. Twelve patients, whose serum calcium was less than 10 mgs/100 ml, were tested with the EDTA test; seven showed evidence of partial parathyroid insufficiency by this criterion.
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#### POST PARATHYROIDECTOMY HYPOPARATHYROIDISM

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## SPONTANEOUS HYPOPARATHYROIDISM

### IDIOPATHIC, PSEUDO, AND PSEUDO-PSEUDOHYPOPARATHYROIDISM

47. Bartter, F. C. Pseudohypoparathyroidism and pseudo-pseudohypoparathyroidism in The Metabolic Basis of Inherited Disease, Stanbury, J. B., Wyngaarden, J. B., Fredrickson, D. S. eds., McGraw-Hill, 1966, p.1024.  
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An analytical review of the world literature. The authors point out that the average age of onset of idiopathic hypoparathyroidism (17 years) is considerably later than pseudohypoparathyroidism which almost always begins before the age of 20.
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Using the relationship of the shortness of the fourth metacarpal to the third and especially to the fifth, the authors examined 2,594 outpatients. Their results showed this finding to be of frequent occurrence in patients with gonadal dysgenesis, having either male or female sex chromatin. In males (Klinefelter's syndrome excluded) this metacarpal sign occurs much more frequently in the presence of some gonadal anomaly. All males showing the sign had male sex chromatin. In five males with female sex chromatin the metacarpal sign was absent.
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