TETANY PARATHYREOPRIVA:*

A CASE REPORT, WITH A BRIEF DISCUSSION OF THE DISEASE AND OF THE PARATHYROID GLANDS.

BY EUGENE H. POOL, M.D.,

OF NEW YORK,

Attending Surgeon to the French Hospital, New York; Instructor in Surgery in Columbia University.

THE acquisition in recent years of an anatomical knowledge of hitherto unsuspected organs, the parathyroid glands, has engendered much investigation as to the physiological rôle and pathological import of these bodies. Dependent upon such studies, interest has coincidently centered on the subtle question as to the explanation of certain nervous manifestations which attend the removal of these structures in animals. The condition thus artificially produced appears to be of the same nature as a group of symptoms which occasionally occurs in man. These symptoms were first described by Steinheim[1] in 1830, and the name tetany was subsequently given to them by Corvisart.[2] Since then the same clinical picture has been repeatedly noted in association with various conditions of widely different character. For example, it has been seen to occur with severe gastro-intestinal affections, especially dilatation of the stomach, with pregnancy and the puerperal state, with some acute fevers, with various nervous diseases, and after removal of the thyroid gland.

The cause of its occurrence in most of these conditions is not understood. As a sequel, however, to thyroid operations it has been definitely, ascribed to the removal of the parathyroid bodies, and in consequence has been designated by Erdheim[3] tetania parathyreopriva.

Observation of a case which recently came under my care

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gave rise to an effort to collocate the clinical features and therapeutic possibilities in this variety of tetany. To do this clearly it seems necessary to supplement such considerations with a review of the history of the subject and of the anatomy, development, and theories as to the physiological rôle of the parathyroid glandules.

Case Report.—The patient, a seamstress by occupation, is a Swiss, thirty-three years of age. She was referred to my service at the French Hospital by Dr. Fellowes Davis, in April, 1906. The significant features of her history are as follows:

In 1903, she had considerable pain in the lower part of the neck and marked dyspnœa and dysphagia. For some time previous to that there had been a large tumor in the region of the left lobe of the thyroid gland. An operation was performed in Bern, Switzerland, and a tumor on the left side of the neck was removed. This was undoubtedly the left lobe of the thyroid. For one year after the operation she was relieved of her symptoms, but during the second year the dyspnœa, dysphagia and swelling returned and increased to such an extent that operation became imperative.

Besides the features mentioned above there was nothing of importance in her history. Though in childhood a number of operations had been performed upon her eyes, the last of which was eighteen years ago, she had always enjoyed good health and had never suffered from any nervous troubles.

Physical Examination.—The woman was thin and pale, her expression anxious, breathing labored, the sternomastoids prominent. There was a slight rounded projection, about one and a half inches in diameter, just above the sternum, and a faint scar of the incision of the former operation could be seen. The mass, which reached beneath the sternum, was firm and nodular and moved with the larynx on swallowing. The examination was otherwise negative.

On March 3, 1906, I operated under ether anæsthesia and exposed the thyroid by a curved incision. In the region of the isthmus there was a round, smooth mass, about two and one-half inches in diameter, which was to a great extent bound down by cicatricial tissue; it extended downward behind the sternum and

compressed the trachea. The left lobe of the thyroid was absent. Before any tissue was removed the right lobe was thoroughly exposed and found to be of normal size, appearance, and consistency. Accordingly, the thyroid gland was clamped at the junction of the isthmus and the right lobe, and cut across as close to the tumor as possible. Before doing this it was found necessary to ligate the inferior thyroid artery which ran close to the tumor. The whole of the right lobe, except a small part which lay close to the isthmus, was left. The wound was closed with drainage.

Postoperative Course.—The healing of the wound was uneventful. On the fourth day after operation, tetanic contractures occurred in both hands, which assumed an attitude similar to that produced by stimulation of the ulnar nerve, an attitude sometimes called the accoucheur's hand, since it is the same as the position taken for making a vaginal examination. Throughout the disease this was the usual contraction of the hands. The spasm was accompanied by cramp-like pains in the hands, and occasional twitching of the facial muscles, with some neuralgic pains in the right side of the face. This condition was present whenever the patient was seen during the next twenty-four hours, when cramps in the feet and calves occured together with forcible plantar flexion of both feet which lasted for about five minutes.

After that for about thirteen months the patient presented the typical clinical features of tetany. Of the symptoms, the most conspicuous were bilateral and symmetrical contractions of the flexor muscles of the hands, wrists, and feet (Figs. I, II and III), as previously described, preceded and accompanied by cramp-like pains in the affected muscles. To these spasms were added at times attacks of more general contractures, occasionally with cyanosis which necessitated the administration of chloroform, attacks of asthmatic breathing, of tetanic spasms of the muscles of the face, jaw, neck and back, slowness and thickness of speech, difficulty in swallowing, but apparently no dullness of mind. The skin and hair seemed unchanged beyond a slight growth of hair on the chin and upper lip. There was for several weeks marked edema of the left wrist and hand, and redness over the knuckles of this hand. Chvostek's and Trousseau's signs were present and typical almost all of the time. Thus, the facial muscles, as

a rule, contracted rapidly to mechanical irritation by tapping over the facial nerve; and by steady pressure on the nerves and vessels of the arm the usual contracture of the hand was brought on in about one-half to three minutes, sometimes with distinct fibrillary twitching over the thenar eminence. In this test, cramp-like pains regularly preceded the spasm which developed gradually and not suddenly. Contractures also resulted from making the sciatic nerve tense by holding the patient in a sitting position, so that the trunk and thighs were flexed beyond a right angle, with the legs extended; or by putting the nerves of the brachial plexus on the stretch by elevating the arm above the head with the forearm extended (extreme abduction). Figs. IV and V.) The contracted muscles were always board-like to the touch. Unfortunately, tests with the galvanic current were not made; but Dr. J. A. Booth reported on February 8, that with the faradic "even mild currents brought on tetanic contractions in both upper and lower extremities, showing a decided increased electrical excitability."

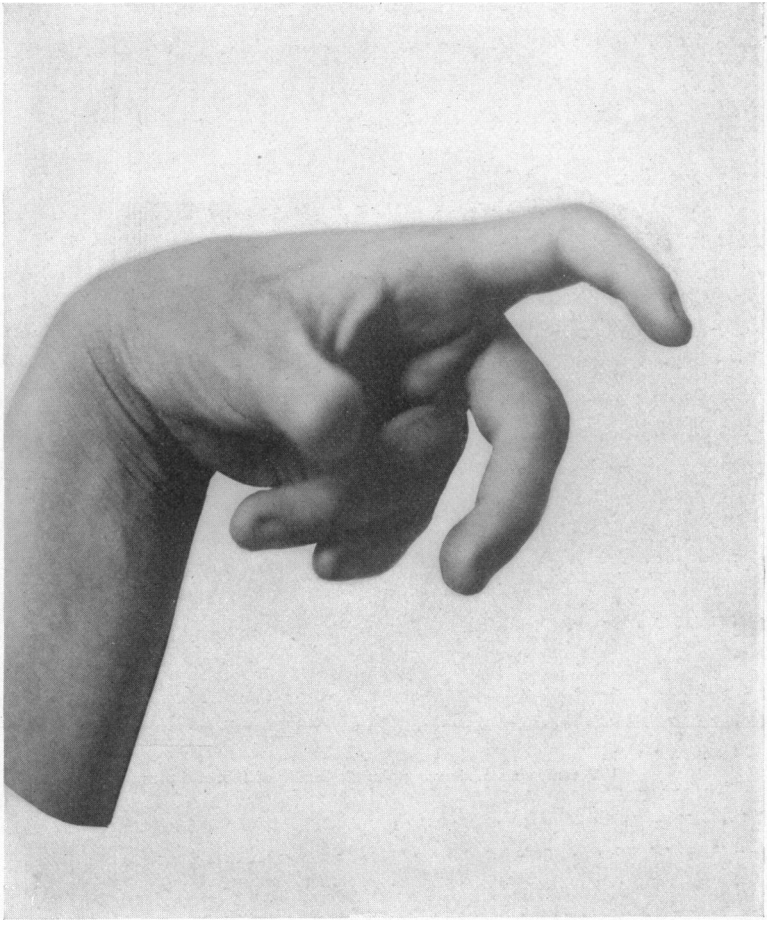
The above symptoms occurred in attacks at variable intervals. During the first six weeks and the last three months of the disease, there were from one to five attacks almost every day. The duration was from several minutes to several hours. During the intervening seven months, when the patient was not in the hospital, they were much less frequent, but prevented her from working.

About five weeks ago the attacks of typical tetanic spasms gradually ceased; the other tetanic symptoms also gradually disappeared, and Chvostek's, Trousseau's, and the other two tests mentioned above, became less marked, and now elicit no response. Moreover, the electrical tests made by Dr. Booth on April 23, showed only slightly increased galvanic irritability in nerves and muscles, the most marked being in the ulnar nerve ("Ca Cc>An Cc, 3 Ma").

Hysterical symptoms of various kinds have, however, become marked and are now striking. This is not surprising considering the prolonged sickness and the frequent use of hypnotics and other drugs. This condition, however, is improving under the care of Dr. Booth.

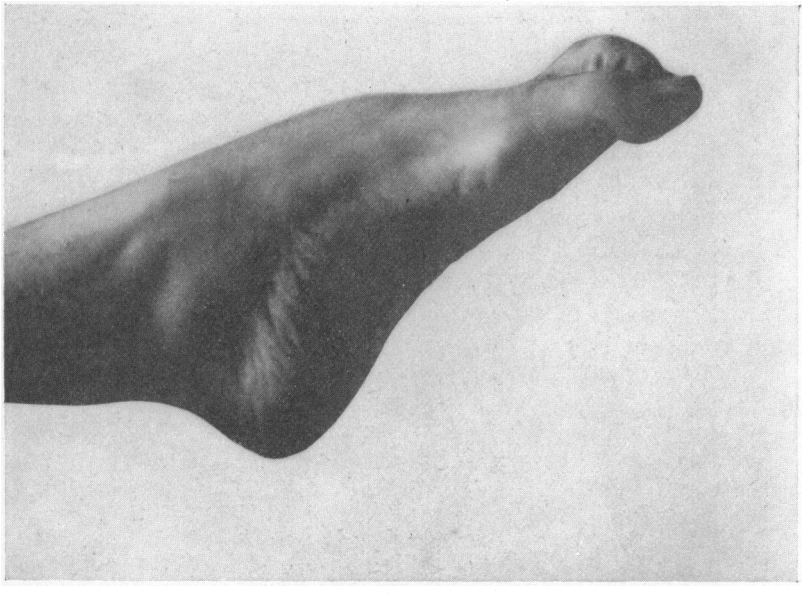
As regards treatment, the following were tried: various thyroid and parathyroid preparations by mouth and hypoderm-

FIG. I.



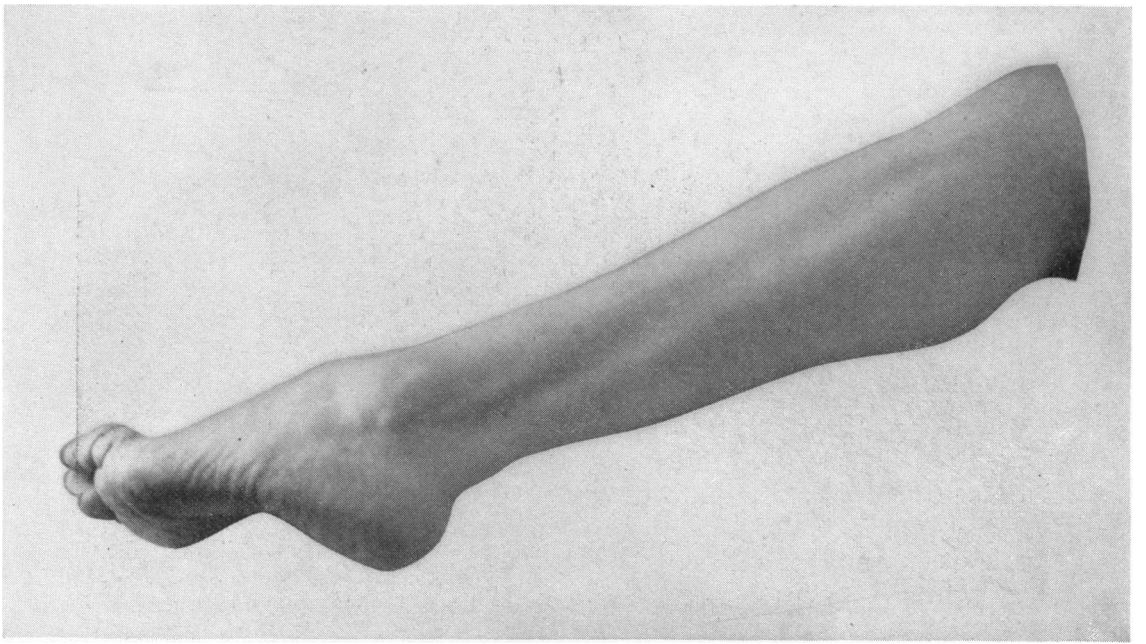
Tetanic spasm, showing flexion of wrist.

FIG- II.



Tetanic spasm, showing plantar flexion of foot and toes.

FIG. III.



Tetanic spasm showing contraction of muscles of calf.

FIG. IV A.

Method of producing a tetanic spasm in feet by stretching the sciatic nerve by means of forcible flexion of trunk on thighs. Taken immediately on sitting up, before occurrence of spasm.

FIG. IV B.

Method of producing a tetanic spasm in feet by stretching the sciatic nerve by means of forcible flexion of trunk on thighs. Taken 1½ minutes later, showing onset of spasm.

FIG. V.

Method of producing tetanic spasm of hand by stretching the brachial plexus by means of forcible abduction of arm, showing accoucheur's hand.

ically. The parathyroid material was supplied by Prof. Vassale, of Modena, by Dr. Beebe, of New York, and by Armour and Co. One saline infusion of twenty-four ounces was given, and five parathyroids were implanted subcutaneously. These were removed aseptically immediately after death from three accident cases, put at once into ascitic fluid, and implanted as soon as possible. Under general anæsthesia the implantations were made into the abdominal wall and the lobe of the ear. In the latter case a deep incision was made along the lower free margin of the lobe so as to divide it into two lips. Cocaine was not used on account of the disadvantage which might result from the infiltration of the tissues. The parathyroids, while in the ascitic fluid, were cut so as to expose two or more raw surfaces; the technique differed in this respect according to the size of the gland. The lobe of the ear seemed to present a particularly favorable site for the implantation because a perfect and permanent opposition of the implanted parathyroid and the two surfaces of the wound was readily obtained by gentle pressure produced by an appropriate dressing. All the wounds healed by primary union. The first two implantations were made on March 1; in this case the operation was finished ninety minutes after the death of the patient from whom the tissues were taken. The other three implantations were made on April 17.

The improvement which occurred about one month ago,* that is, the gradual disappearance of the true symptoms of tetany, was coincident with the repeated administration of Beebe's nucleo-proteid in large doses by hypodermic, and occurred from four to six weeks after the first implantation. No effect could be attributed to other therapeutic measures.

Historical.†—Operations for goiter were uncommon until about 1877; but since then, due largely to the impulse of Billroth and Kocher, they have progressively increased in frequency. The occurrence of tetany after such operations was first recognized by Weiss [6] in 1880. About three years later, Kocher [7] and Reverdin [8] called attention to the condition since known as

* This paper was read May 2, 1907.

† Since exhaustive histories have been published several times, only a résumé is given here, and the reader is referred to such articles as those by Erdheim,[3] Jeandelize,[4] and Welsh,[5] for a more detailed account.

cachexia strumipriva, and this was shown by Kocher to be a frequent sequel to complete thyroidectomy. The two diseases, tetany and cachexia strumipriva, were regarded for a considerable time simply as different phases of one condition which was supposed to be dependent upon insufficiency of the obscure funtion of the thyroid gland.

The above clinical contributions awakened a new interest in the study of the thyroid by animal experimentation, which had been carried on intermittently ever since the early thirties [9] of the last century, but with indefinite and contradictory results.

As a result, Schiff,[10] in 1884, clearly showed that certain animals, notably cats and dogs, regularly succumb to complete removal of the thyroid gland except in isolated cases which were explained on the supposition that the thyroid function was then carried on by aberrant or accessory thyroids.

In consequence of the dire effects which were thus noticed experimentally as well as clinically after complete thyroidectomy, it became a surgical mandate that part of the organ should be spared in goiter operations. This precept, which was fathered by Kocher,[11] has prevailed up to the present time and its practice accounts for the relative infrequency of postoperative tetany and cachexia strumipriva.

In the results of animal experimentation a perplexing inconsistency prevailed. Whereas total thyroidectomy in dogs, cats, and carnivora in general, was regularly followed by fatal tetany, in contrast to these animals, rabbits and other herbivora regularly survived the operation with no evidence of tetany, but with the development of the slower cachexia strumipriva.

The peculiar difference in the reactions of these two classes of animals to the removal of the thyroid gland was the crux which for a long time defied explanation and prevented further progress. Its ultimate solution, however, furnished the clew which resulted in rapid advances leading up to our present knowledge of the subject. The credit for this all-important step is due to Gley [12] who in 1891 called attention to the existence in the rabbit of two bodies entirely separated from the thyroid, the external parathyroids. He demonstrated that in this animal the removal of these together with the thyroid produced the same effects as complete thyroidectomy in other animals. His conclusions may be summarized as follows:

1. The removal of the thyroid alone (in the rabbit or dog), leaving the two external parathyroids, causes no tetany.

2. The removal of the two external parathyroids in the same species of animals, also causes no tetany.

3. The removal of the thyroid and the two parathyroids, at the same time or in two stages, results in tetany.

He explained incorrectly the negative effect of removing the thyroid alone (1, supra) by the assumption that the parathryoids which were left acted vicariously for the thryoid. Moreover, since he did not recognize the existence of the internal parathyroids, the negative results following removal of the two external ones suggested to him nothing significant.

Attention should be called to the fact that Sandstroem[13] in 1880, eleven years before Gley's contribution, had recognized the parathyroids in man, and had described their gross anatomy and histology minutely and accurately. Apparently little notice was taken of his report, and certainly it failed to stimulate scientific research. However, the name "glandulæ parathyroideæ" which he applied to the organs, has been generally adopted.

While a new theory was suggested by Moussu,[14] to the effect that the simultaneous ablation of the thyroid and parathyroids might possibly suppress two functions instead of one, the first practical step towards ascribing to the parathyroids an independent potency resulted from the work of Vassale and Generali[15] which was published in 1896. They demonstrated that the removal of the four parathyroids, the thyroid being preserved, led to fatal tetany; while no tetany resulted from the removal of the thyroid if the parathyroids were left. These conclusions were based upon the following striking experiments:

Ten cats; total parathyroidectomy; nine dead before 11th day. In all there were characteristic symptoms of tetany.

Nine dogs; total parathyroidectomy; all dead before the 9th day. In these animals the symptoms were analogous to those of complete thyro-parathyroidectomy. Every effort was made to exclude complications, such as injuries to nerves or to the thyroid as possible causes of the fatal results.

It has been urged by numerous experimenters, among whom are Biedl,[16] Walbaum,[17] Vassale and Generali, that the intensity of tetany parathyreopriva stands roughly in inverse ratio to the number of healthy parathyroids retained by the animal. Thus,

in a cat the removal of three parathyroids has been said to result generally in fatal tetany; of two, in lighter tetany; of one, in no tetany. But this rule is certainly far from absolute, for sometimes the presence of one parathyroid is sufficient to prevent the symptoms of tetany, while in other cases, two of the organs are necessary (Erdheim). The difficulty of formulating any exact deductions in regard to this phase of the subject is further increased by the fact that besides frequent variations in animals of the same species, there is a constant and marked difference in the reaction of different species to partial or complete parathyroidectomy, in respect to the rapidity of the onset and the intensity of the symptoms.

In 1903, Jeandelize, in an exhaustive treatise, reviewed and amplified the whole subject. The following summary from his work is a fair indication of the general attitude at that date.

1. The thyroid and parathyroids are different organs.

2. The results of ablation of the two are not the same.

3. Physiologically, the two organs are dependent upon one another, yet neither can assume the functions of both.

In elaborating the effects of ablation of these organs he calls attention to the fact that thyroidectomy alone does not cause the grave troubles of parathyroidectomy, but instead, especially in young animals, gives rise to troubles of nutrition. The animals remain undersized, their behavior is altered and sluggish, the skin becomes thick and edematous, and the hair becomes coarse. The onset of the change is less than a month after the operation.

On the other hand, he states, parathyroidectomy produces a more rapid onset of symptoms, which are briefly, fibrillary twitchings, tremors, local or general contractions (tonic or clonic), convulsions, dyspnœa, tachycardia, ptyalism, thirst, vomiting, diarrhœa, general weakness and prostration.

He therefore concludes that as a result of insufficiency of the thyroid there occur nutritional disturbances, whereas insufficiency of the parathyroid produces acute convulsive troubles. This, he says, is proved in several species of animals and is probably true for all vertebrates.

In consequence, it was assumed that operative myxedema, which is a nutritional disturbance, is due to removal of the thyroid, and tetany, which is a convulsive trouble, to removal of the parathyroids. Under such an assumption these two con-

ditions necessarily came to be regarded as radically different, a transition from one to the other being out of the question.

Erdheim has recently by clinical and experimental observations further elaborated the evidence of the potentiality of the parathyroids. After partial or total destruction of the parathyroids in rats, with the minimum of injury to the thyroid, he studied the symptom complex of the resulting tetany which occurred in all the cases of total parathyroidectomy. In the animals presenting tetany, by systematic serial microscopic sections of all the organs of the neck, he demonstrated the presence of the thyroid and absence of parathyroid, and thus established the fact that the lesion in every case was purely parathyreopriva.

Although individual differences were marked in his animals, tetany began, as a rule, several hours after operation, and reached its height usually in the first twenty-four hours in the form of epileptiform convulsions. The condition then passed into a chronic state. In the study of the symptom complex due to parathyroidectomy exclusively, besides demonstrating the regular occurrence of a typical tetany, Erdheim also verified the occurrence of regular nutritive changes, notably very excessive growth of the lower incisors. But the association with tetany of some trophic disturbances resembling those observed in cachexia strumipriva was not regarded as a justification for the conclusion that the two conditions are of identical origin.

Erdheim's studies of three cases of human tetany are remarkably significant. In each a partial thyroidectomy was performed for goiter. Unquestionably tetany developed shortly after the operation and death followed on the 131st, 5th, and 17th days. Very complete serial microscopic sections of the neck organs showed in each case the presence of considerable well preserved thyroid tissue, whereas in the first case none of the four usual parathyroids were found, and only two very small accessory parathyroids which lay in the thymus; in the second case only one parathyroid was recognizable, and that was practically entirely necrotic; in the third case not one of the regular four, nor even an accessory organ was found.

A review of all cases of tetany which have been reported as occurring after strumectomy would prove unfruitful. Only a small number are of practical interest in this connection, namely, partial thyroidectomies which permit definite conclusions as to

the involvement of the parathyroids in the extirpation. Pineles [18] compiled thirteen cases of this kind. Of these, there were six cases of extirpation of both lateral lobes, four cases of preservation of the upper portion of one lateral lobe, three cases of extirpation of a lateral lobe with the isthmus. As a result he pointed out that tetany follows partial thyroidectomy most frequently in those cases where extirpation of, or injury to, the parathyroids is most likely to occur; and consequently that tetany is most likely to follow those cases in which only the isthmus or upper part of a lateral lobe is left.

It seems then to have been proven by a long series of careful experiments, strengthened recently by the significant findings of Erdheim and Pineles in man, that tetany following goiter operations is due to the removal of the parathyroid glandules. Nevertheless, this attributes such marked potency to these little organs that, not unnaturally, there are still some observers who are skeptical as to the truth of the assumption, and among them are competent men who have weighed carefully all sides of the question. The explanation of this divergence of opinion lies in the fact that besides such apparently conclusive results as those described above, there have been numerous other investigations, the outcomes of which have not been uniform or positive. For example, even recently, Vincent and Jolly [19] have found that "removal of all four parathyroids was not necessarily fatal," and they "were unable to confirm some other statements which are very commonly accepted" on this subject. Further, Vincent wrote that "the question of the extreme importance of the parathyroids can not yet be considered as settled." Moreover, Caro,[20] although familiar with the extensive work of Pineles, has quite recently expressed the opinion that there is no reason for abandoning the former interpretation that tetany is an acute manifestation of the loss of thyroid (not parathyroid) substance. Animal experimentation has failed to convince him of the importance of the parathyroids. He states, moreover, that in goiter cases, the parathyroids are sometimes found to consist simply of atrophic and barely distinguishable lamellæ closely applied to the capsule, and he arrives at the conclusion that in Erdheim's three cases the dependence of the tetany upon the suppression of the parathyroids is by no means proven. However, it is fair to state that almost all observers at the present time regard tetany

following goiter operations as the direct result of the absence of the parathyroid function.

CASES OF TETANY PARATHYREOPRIVA, FOLLOWING PARTIAL THYROIDECTOMY, COLLECTED BY PINELES,[18] WITH LATER ADDITIONS.

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Reichel, (2 cases) Münch. med. Woch., 1905, p. 2012.
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Erdheim, (3 cases) Mitteil. a. d. Grenzgeb. d. Med. u. Chir., Bd. xvi, 1906.
Monnier, E., Beit. z. klin. Chir., Bd. liv, 1907, p. 63.

ANATOMY OF THE PARATHYROID BODIES IN THE HUMAN SUBJECT.*

In man parathyroid bodies are constantly present; the number varies. Exact enumeration in an individual case is difficult for two reasons; first, their small size and variable position render it an easy matter to overlook one or more of the bodies; second, various tissues may be mistaken for a parathyroid, especially lymph nodes, hæmolymph nodes, accessory thyroids, thymus rests, and fat. Microscopic examination alone can exclude these tissues.

Berkeley,[21] as a result of about one hundred and twenty-five autopsies, concluded "that while the number four seems

* For technique of dissection cf. Berkeley[21] or Petersen.[23]

to satisfy the demands of anatomical symmetry, this number is often diminished by one or more" and occasionally increased. He apparently found on an average about two and a half parathyroids per person. Most observers have reported smaller averages, but Verebely [22] found four parathyroids 108 times in 138 autopsies. In our own dissections,† the last sixteen resulted in an average of 2.9 per person. In all of these one-half of every suspected tissue was removed and examined microscopically. The other half was left in situ for further reference; a lettered drawing of each specimen facilitated identification of the sections.

The occurrence of the glands in pairs may properly be considered the typical arrangement, a superior and an inferior body being present on each side. Judging from our own dissections and the descriptions of Verebely, Thompson [24] and earlier writers, the following seem to be the most frequent situations, and correspond closely to the drawing (Fig. VI).

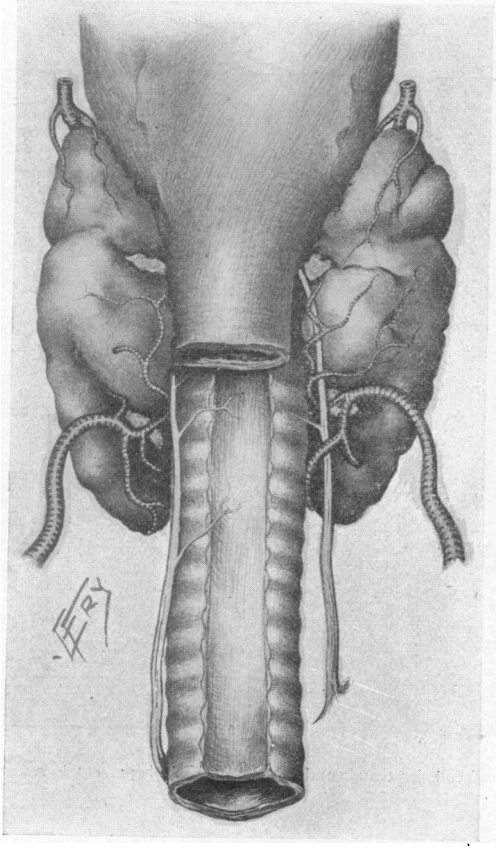
The superior, the more constant in position, lies close to the thyroid in the middle third of its posterior border, approximately on the level of the lower border of the cricoid cartilage (Welsh [5]). It lies in a plane posterior and external to the terminal branches of the inferior thyroid artery and recurrent laryngeal nerve. On the left side the gland is frequently further posterior than on the right.

The inferior, often intimately associated with the thymus (Verebely), lies at or below the inferior pole of the thyroid or on the posterior aspect of the lower third, in which case it is frequently found anterior to the recurrent laryngeal nerve and inferior thyroid artery, close to the thyroid gland at the entrance of the lower twigs of the artery.

Variations from these anatomical positions are frequent. The most striking which we have found was the presence of a large parathyroid on the anterior surface of the isthmus. As common variations in position may be mentioned the tip of the lateral lobe of the thyroid or even above this; anywhere on or

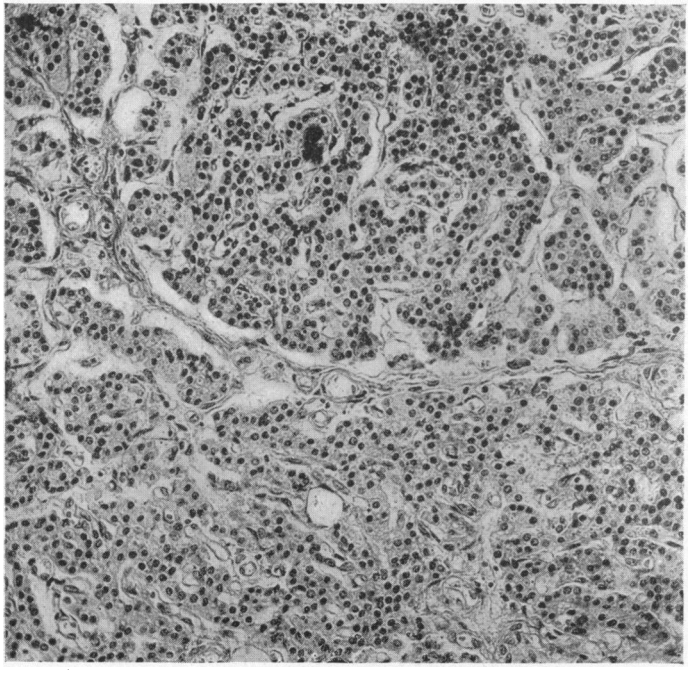
† These were done with the aid of G. C. Whitney, of the Third Year Class of the College of Physicians and Surgeons.

FIG. VI.



The parathyroid bodies, showing situations in which they are sometimes found.

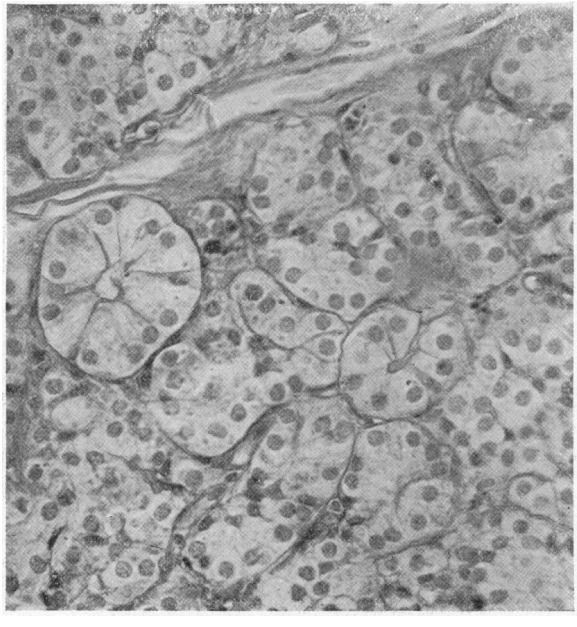
FIG. VIII.



A

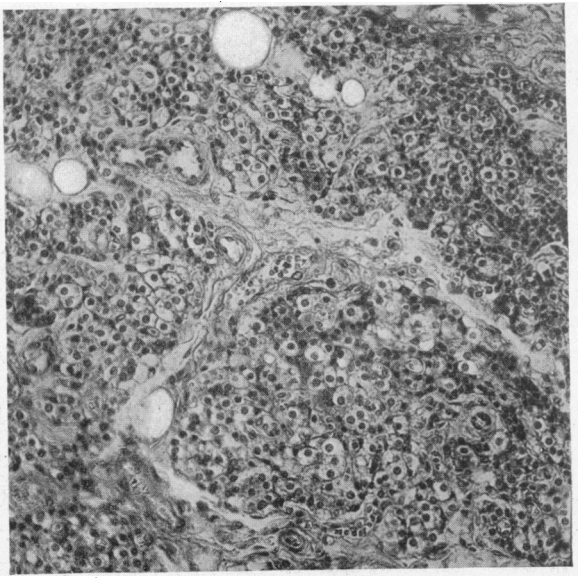
Distribution of cells in strands and groups. Colloid is present in several places. A.

FIG. IX.



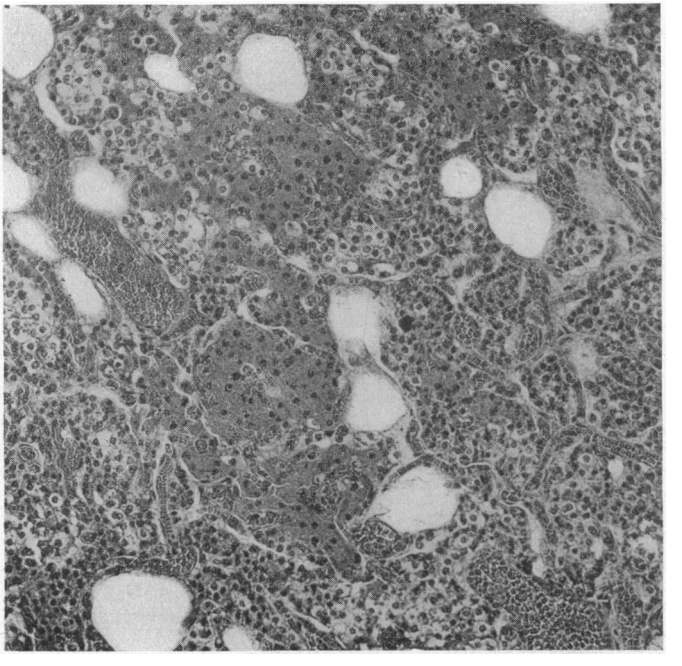
Showing an acinus with lumen.

FIG. X.



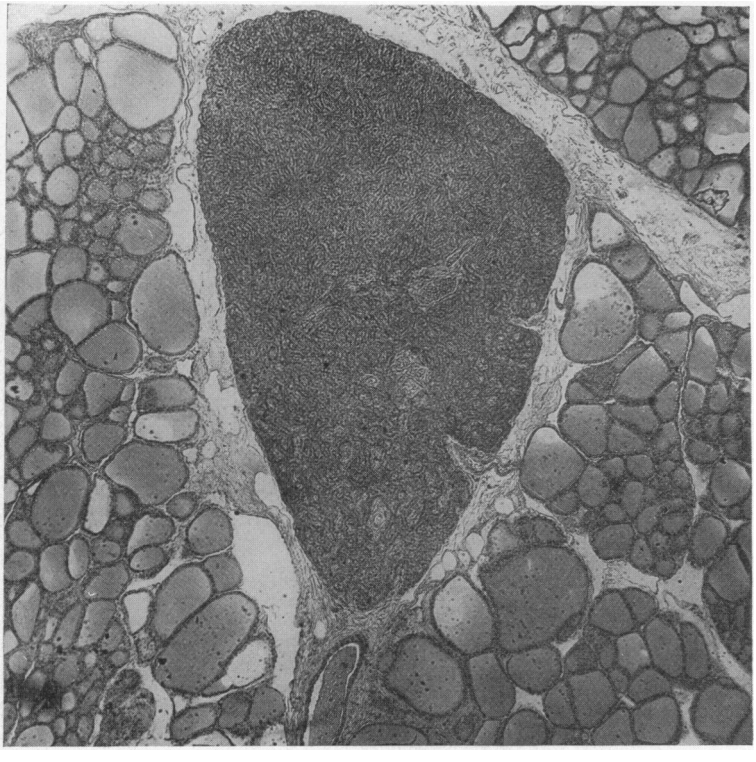
Principal cells.

FIG. XI.



Masses of oxyphile cells.

FIG. XII.



Parathyroid of a dog.

near the posterior border. These sites, however, do not limit the possibilities.

Accessory organs, that is, small accumulations of characteristic parathyroid cells, have been found not infrequently below the thyroid, especially within the thymus.*

While in most cases the glands lie embedded in fat outside of the thyroid, the position of one or more may be beneath its capsule, but only very rarely embedded in its substance (Verebely). Each parathyroid is completely invested with a thin fibrous capsule under which a fine anastomosis can be seen. The size of the organ varies from about 3 mm. to 15 mm., the average being about 6 x 4 x 2 mm. (Berkeley). The bodies are usually somewhat flattened, and may be of various shapes, but especially round, oval, or reniform. Occasionally a parathyroid is subdivided into two distinct parts. The color is a brown red or a reddish yellow. Often a glandule of regular outline presents a relatively large segment of fat. This is said to occur most often in advanced age.

The blood supply of the gland is derived from branches of the superior and inferior thyroid arteries, particularly the former.

Histologically (Figs. VIII–XII) the organ consists of a mass of cells invested with a thin fibrous capsule from which occasional irregular processes reach inward. The gland has a reticular stroma, and is as a rule strikingly vascular, presenting numerous large capillaries. Frequently fat is present, both as an infiltration of the stroma and as a cellular metamorphosis.[26] The amount is subject to very wide differences and to this is largely due the variable color of the gland. Especially in advanced life a considerable part of the gland may be replaced by fat. The distribution of the cells varies greatly. They may form an extensive cell mass with only occasional interruptions by vessels and fibrous strands, or they may be broken up by vessels and connective tissue so as to form clusters of lobules or net-like trabeculæ. Occasionally there is an alveolar group-

* They have also recently been described as occurring within the thyroid (Getzowa[25]).

ing of cuboidal or somewhat cylindrical cells with basal nuclei. These at times surround a lumen filled with colloid, which is said by Richardson [27] to be retrograde or degenerative material, and not a higher stage of glandular development. Intracellular and intercellular accumulations of colloid also occasionally occur, while glycogen has been demonstrated as a cell inclusion (Petersen).

The cell grouping rarely comprises one alone of the above structural types; as a rule there is a combination of the varieties, the divergencies presented by individual glands in this respect being very wide. The cells themselves are mostly polygonal, sometimes round or cuboidal. They are classified by Welsh [5] as of two distinct types:

Type I. "Principal cells." These are by far the more numerous. The cell body is relatively small and is either feebly stained with basic aniline dyes, or is clear and colorless. The cells then seemingly consist only of nucleus and membrane which takes a deep eosin stain. We have noted that some of the cells which belong to this group sometimes present an irregular stained peripheral zone and a clear cytoplasm immediately around the nucleus. The variations in the relative width of the clear and the stained zones suggest that under certain conditions the cytoplasm of the clear cells takes on a stain which acts first near the periphery and then progressively toward the nucleus until the whole cell body may be stained.* The nucleus with open chromatin network is large, pale, often ovoid, and frequently, eccentrically situated. The distribution of these cells conforms to the general description already given.

Type II. "Oxyphile cells." These have a relatively large, finely granular body, the granules of which stain deeply with eosin. The nucleus with closely arranged chromatin is small, and round, and takes a deep stain. Compact masses of these cells frequently occur, especially immediately beneath the capsule. They are also distributed as anastomosing columns and as single cells or small groups scattered among the principal cells; lastly, in rare cases, acini with colloid are met with.

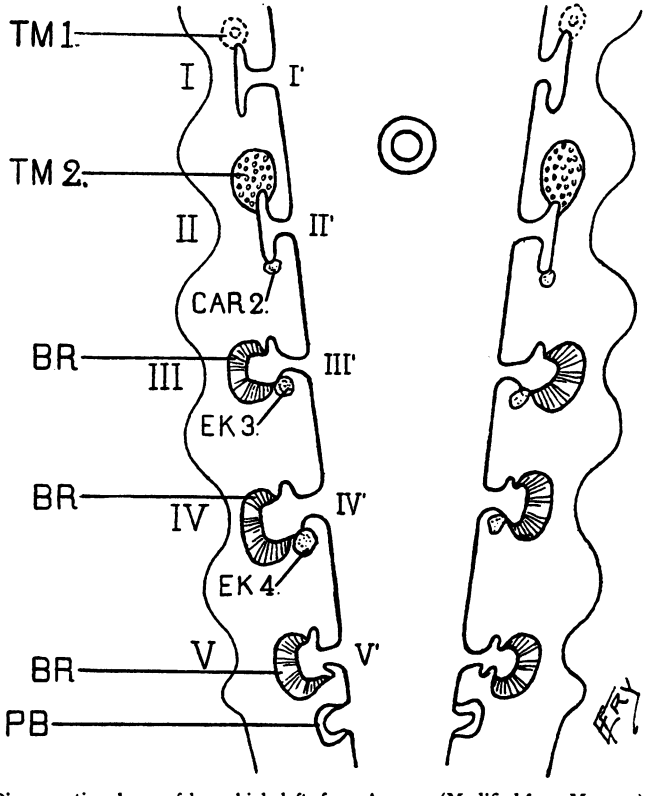
Petersen [23] adds a third type. His Types I and III are respectively the same as Types I and II of Welsh. He describes Type II as not characteristic. The cells are smaller than in I; there is no sharp boundary to the cells, of which the granular protoplasmic body stains deeply with eosin; in places

* Since the above was written, Getzowa has reported similar findings and has gone so far as to subdivide the group into "wasserhelle" or clear, and "rosarote" or pink cells.

the cells are so small that nothing is seen but a complex of deeply stained nuclei. He states that all possible intervening forms occur between Types I and II, and suggests that the organ is a glandular one, and that Type I represents the functionating condition.

In studying parathyroids microscopically, the three varieties of cells can easily be recognized. Further, careful exam-

FIG. XIII.



Diagramatic scheme of branchial clefts from Anura. (Modified from Maurer.)

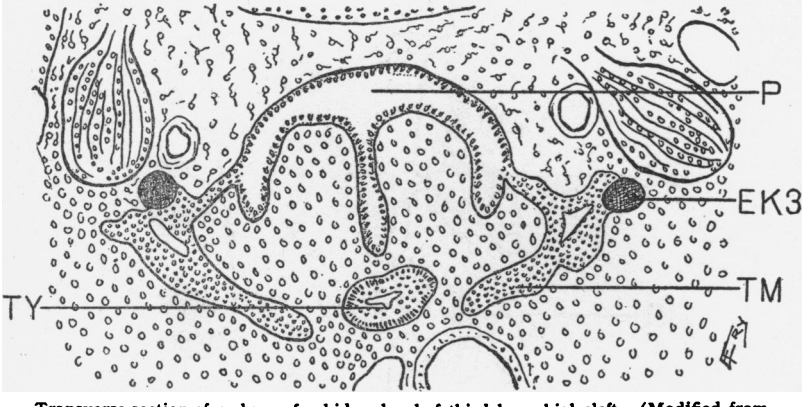
ination enables the observer to trace the cells in some glands from the clear ones of Type I through the above described granular condition to the small granular cells of Type II of Petersen. With more difficulty, gradations also may be traced

from the latter to the large granular cells (Type II, Welsh; Type III, Petersen), where these occur singly or in small groups; but the line of demarcation at the edge of the large groups is sharply drawn. Following the analogy of the salivary and other glands the question naturally suggests itself as to whether the granular cells are not the functionating and the clear cells the resting condition of the cells.†

EMBRYOLOGY.

It is necessary to touch briefly on the embryology of the parathyroids in order to establish their developmental independence of the thyroid.

FIG. XIV.



Transverse section of embryo of echidna, level of third branchial cleft. (Modified from Maurer.)

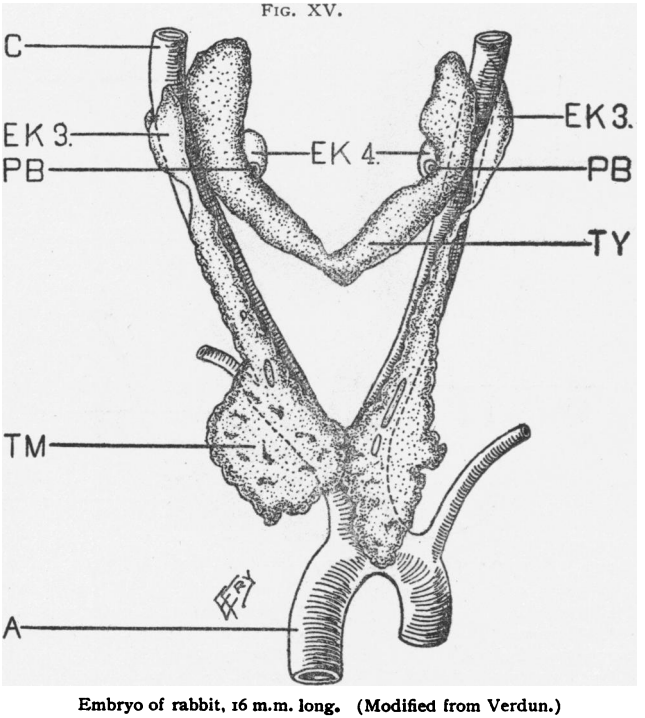
The parathyroids or "epithelial bodies" (Kohn[28]) are branchial cleft derivatives. In man and most mammals they develop from the third and fourth branchial clefts of each side as masses of compact epithelial cells which are in no way connected with the thyroid (Fig. XIV). Two on each side is the usual arrangement, though anomalies are not infrequent.

The third pharyngeal pouch with its derivatives, the thymus and the parathyroid body, becomes separated from the

† Getzowa[29] has recently expressed a similar view.

pharynx. This parathyroid body later comes into relation with the thyroid from the side and forms the inferior parathyroid or outer "epithelial body" (Kohn) (Figs. XV and XVI, EK 3). When the fourth pouch becomes separated, its derivatives, the parathyroid, thymus, and post-branchial body, are primarily connected. The post-branchial body and the superior parathyroid or "inner" epithelial body (Fig. XV and

FIG. XV.



Embryo of rabbit, 16 m.m. long. (Modified from Verdun.)

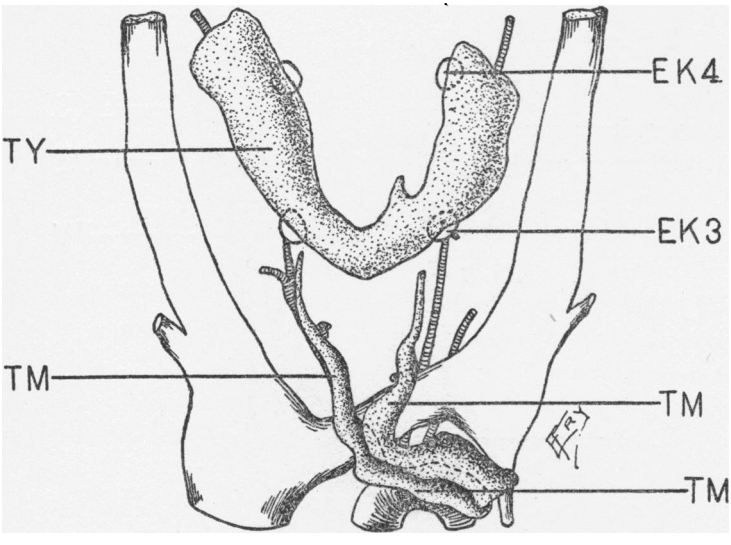
XVI, Ek 4) become annexed to the thyroid only secondarily in the course of development. There is no proof of the assumption that the parathyroids are embryonal thyroid tissue and that they may under certain conditions develop into the mature tissue of that gland. The relation of these bodies to the thyroid must, on the basis of our present knowledge, be regarded as purely topographical.*

* Sophia Getzowa in a very elaborate article has recently advanced

PHYSIOLOGICAL AND PATHOLOGICAL CONSIDERATIONS.

If we accept the view that the parathyroids have a function in part or altogether independent of the thyroid, there are certain hypotheses and experimental results which from a physiological standpoint are suggestive and offer a basis for further investigation.

FIG. XVI.



Human embryo 29 m.m. long. (Modified from Verdun.)

TY. Thyroid.	I-V Branchial clefts, outer aspect.
TM. Thymus.	I'-V' Branchial clefts, inner aspects.
Car 2 Carotid gland.	P. Pharnyx.
EK 3 Parathyroid of third cleft.	A. Aorta.
EK 4 Parathyroid of fourth cleft.	C. Carotid.
PB. Post branchial body.	BR. Branchial rests.

The hypothesis has been advanced by MacCallum,[29] Frommer,[30] Lundborg,[31] and others, that the parathyroids have an antitoxic action, the suppression of which results in the tetany reaction. By this hypothesis tetany parathyreopriva would be

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the hypothesis that there may be an independent third parathyroid developed from the fifth branchial cleft. In this way she would explain the occasional occurrence of parathyroid tissue within the thyroid gland in cases in which the extrathyroidal superior parathyroids are also present.

explained as an auto-intoxication. In support of this view is the fact brought out by MacCallum, that the disease in animals is temporarily relieved by bleeding and injection of salt solution into the veins; this, he thought, demonstrated the presence of a circulating toxin. The transmission of tetany to a healthy animal by transfusion of blood from one affected with the disease, although claimed by some as possible, can not be accepted as proved.

If the above hypothesis is accepted, and it seems the most plausible one yet advanced, it may fairly be assumed that whereas the thyroid secretes a substance which is necessary for metabolism, the chief function of the parathyroid is to prevent the action of certain toxic substances regularly present in the circulation.

Attempts to ascribe the etiology of all forms of tetany and even of certain allied diseases, as paralysis agitans, to an imperfect functional activity of the parathyroid glands, have not yet been successful. Nevertheless, Pineles [32] assumes the existence of a common etiology for all forms of tetany. He inclines to the belief that further research will trace the unopposed action of the tetanic toxin in all forms of tetany to a depressed functional state of the parathyroids. Chvostek [33] also expresses the view that all varieties of tetany are dependent upon the parathyroid bodies. His observations of tetany, apart from that following goiter operations, led him to believe that the essential feature in the etiology is a functional disturbance of the parathyroid glands so that they are unable to adapt themselves to various changes. It is due to this susceptible condition, he thinks, that menstruation, pregnancy, infectious diseases, etc., are prone to produce the tetany reaction.

The variety of food and the state of fullness or emptiness of the intestinal tract are said to have but little influence on the course of tetany (MacCallum).[34] Whether the iodin contained in the organ plays an important role is not known.

In regard to the nervous phenomena of tetany no conclusive explanation has as yet been offered.

Symptoms.—According to v. Frankl Hochwart,[35] with

whose descriptions of the disease the following account conforms, tetany parathyreopriva is characterized by certain very striking symptoms which render it practically unmistakable. The most conspicuous of these are intermittent tonic spasms of the voluntary muscles, those of the extremities being most affected. A salient feature is the exclusive involvement of the flexor groups of muscles. Intercurrent contractures of the facial muscles are relatively rare, and the muscles of the chest, back and abdomen participate in exceptional cases only. The tetanic spasms are usually preceded by certain prodromata which persist for a variable period before the onset of the attack. These include headache, sensations of weakness or prostration, more or less rigidity of the limbs, radiating pains and clonic twitchings. The contractions usually begin in the hands, and subsequently involve the feet; less often the feet are affected coincidently or independently. The spasms are almost always symmetrical and bilateral. As a rule, two or more of the fingers are flexed and the thumbs are forcibly adducted, sometimes tightly clasped by the contracting digits. In fifty per cent. of the cases, the wrist also becomes flexed, while flexion of the forearm with adduction of the arm to the trunk occurs infrequently. Exceptionally, the fingers are held wide apart, the terminal phalanges alone being flexed. The feet, when involved, take the position of pes equinus or equinovarus, as a result of contraction of the muscles of the calf. In the contractions of tetany, the affected muscles become very hard to the touch and oppose a powerful resistance to attempts at passive relaxation. Should this prove successful the tetanic attitude is at once resumed when the traction diminishes. Fibrillary twitchings are sometimes visible in the contracted muscles. The duration of an attack may not exceed a few minutes; or the attack may last for a number of hours; but it rarely persists as long as forty-eight hours. The termination of a tetanic spasm is frequently preceded by symptoms resembling those observed at the onset.

While there may be a free interval of days or weeks between the attacks, unfortunately this is far from being the rule.

There are generally several attacks in the course of the day, whereas the patient's rest at night is unbroken. In the severest cases one attack follows another with alarming rapidity.

Trousseau assumes three distinct degrees of tetany based upon the distribution of the spasms: first, a mild form, affecting the peripheral muscles only; some of these attacks may even be limited to the hands: second, a moderate form, with involvement of the facial, abdominal and trunk muscles: third, a severe form, extending to the involuntary muscles.

Besides the attacks of spasms there are other manifestations of the disease. Certain disturbances of sensation are regularly present, especially pain, which is a constant concomitant of the spasms. Hyperesthesia, paresthesia, or anæsthesia may also be noted. Temporary redness and edema are not infrequently observed over the joints. Trophic and secretory anomalies, such as sweating, loss of hair, and changes in the nails, are not very uncommon.

Of particular significance as bearing on the diagnosis are the tests of Chvostek, Trousseau, and Erb. In two-thirds of all cases of tetany it is possible to demonstrate Trousseau's phenomenon. The symptom consists in the occurrence of a tetanic spasm in a limb as the result of compression of its main vessels and nerve trunks. By the animal experiments of Frankl Hochwart and Kashida, this phenomenon has been shown to depend upon stimulation of the nerves.

Chvostek pointed out the facial phenomenon which can be elicited in tetanic patients by gently tapping over the area of distribution of the facial nerve. The resulting short twitchings are known as Chvostek's symptom, which is especially valuable by reason of the simple technique required for its demonstration.

Erb called attention to the fact that electric hyperexcitability of the motor nerves is regularly present in these cases. There is a marked increase of galvanic irritability, especially in the ulnar nerves; whereas an increased reaction to the faradic current is far less constant. The value of the two tests, dependent upon stretching the nerves of the

brachial plexus and the sciatic nerve, which were so striking in our case, can not be estimated properly until repeated trials have been made in further cases.

The tendon reflexes are normal or increased. A certain number of cases, too numerous to be interpreted as an accidental coincidence, present a combination of tetany with typical epileptic seizures. These symptoms have sometimes been observed after thyroidectomy in individuals previously free from nervous symptoms; and a possible connection between epilepsy and tetany has accordingly been suggested. Certain authors also include among the symptoms of tetany the hysterical attacks which are ocasionally present (cf. Frankl Hochwart).

The course of tetany following thyroidectomy has been divided by Frankl Hochwart into three classes: first, cases characterized by onset soon after operation, severe course, and fatal outcome; second, cases in which the symptoms appear soon after the operation but subside after a variable time and are followed by recovery; third, cases in which the patients live and symptoms of myxedema become associated in variable degree with those of tetany.

Diagnosis.—In regard to the diagnosis of tetany, Frankl Hochwart states that it is a simple matter and that there is only one condition, namely, hysteria, which may give rise to symptoms that are strikingly suggestive of those of tetany. But, he says, it will not do on that account to designate tetany or certain of its varieties as a manifestation of hysteria, for there are many features of tetany which can scarcely have anything in common with hysteria. Although he believes imitation of tetany to be uncommon, one can not overlook the possibility of imitation of the symptoms particularly after the tetany has run its course. Such was Minor's [36] explanation of a case observed by him.

Tetany, according to Frankl Hochwart, is at once suggested in the case of individuals who have recently undergone an extirpation of the thyroid gland. He emphasizes particularly the importance of Trousseau's sign as a differentiating test. It is unquestionable that responses can be obtained by

pressure in hysteria and other conditions, which may be readily mistaken for Trousseau's sign (Curschmann[37]). But in a given case, Frankl Hochwart says, the differential diagnosis should be based upon the sudden appearance of spasms as the result of pressure in hysteria, whereas in tetany tonic rigidity is very gradually induced by pressure. He goes so far as to say that in a considerable number of hysterical patients he never succeeded in producing anything akin to Trousseau's phenomenon.

The marked galvanic hyperexcitability of the motor nerves and especially of the ulnar nerves is an important feature for diagnosis. But whether its absence should be regarded as conclusive in ruling out the disease is questionable. Weiss[38] reported one case among thirteen cases of tetany examined by him, in which there was no hyperexcitability. Frankl Hochwart says that he observed a similar case but did not regard it as conclusive because it happened that the ulnar nerve was not tested in this particular patient. Recently, he says, a woman came under his observation who he knew had suffered for years from tetany strumipriva, and had generally presented a very marked galvanic hyperexcitability of the nerves. This time it was not distinctly increased and at best could be designated as rather "high."

Treatment.—Much experimental work has been done on this important phase of the subject. There is, however, considerable confliction in the results reported. This is not surprising since the course of the disease in animals is so irregular as to render it extremely difficult to estimate the effect of treatment. Even without treatment, some animals which present profound manifestations of tetany a few hours after operation, pass, after one or more such attacks, into a chronic condition and live for days, in contrast to others in which the first attack proves fatal.

Attention was naturally first directed to the administration by mouth of thyroid and parathyroid glands and their products. Hoffmann,[39] Levy-Dorn[40] and Westphal[41] and many others have reported improvement of the symptoms of

tetany in man after feeding thyroid gland or its derivatives. Most observers, however, disclaim any favorable results with exclusive thyroid therapy, and Loewenthal and Wiebrecht [42] ascribed the apparent effects of thyroid feeding to the admixture of parathyroids. Yet it does not appear to have been proven that either mixed thyroid and parathyroid or even pure parathyroid feeding can control the disease in animals. According to Biedl [16] (p. 321) "the sequellæ of parathyroidectomy cannot be prevented by parathyroid feeding." MacCallum [34] reported benefit as the result of intravenous injections in parathyroidectomized dogs of very large amounts of prepared parathyroids of dogs. Administered to animals in subcutaneous injections, thyroid gland derivatives have proved inefficient, whereas parathyroid products are said to have met with some success at the hands of Beebe,[43] and others. With the nucleo-proteid Beebe claims that amelioration or disappearance of the symptoms is almost constant.

Uncertainty prevails as to the effect of transplantation. Transplanted parathyroid tissue survived in the animal experiments of Cristiana,[44] and became atrophied after a variable time in the experience of Camus,[45] whereas Lusena [46] refers to cases in which the subcutaneous transplantation of parathyroid seemed to have a decidedly favorable effect.

Of the applicability of the above methods in man little has been demonstrated. Here the effects of treatment are difficult to estimate because of the impressionable character of the patients and the frequent modification of the disease by hysterical manifestations. Some successes with thyroid feeding have been reported, as stated above, and MacCallum,[47] Marinesco,[48] Lowenthal and Wiebrecht [42] and others have reported improvement following the administration of parathyroid material by mouth. Yet the results in animals apparently have demonstrated that in the treatment of tetany by parathyroid therapy, subcutaneous administration is the means which offers the best prospect of controlling the disease. Beebe's nucleo-proteid at present appears to be the most efficient product for this purpose.

There is no record before the present of attempts to establish a permanent cure in man by parathyroid transplantation.

Transplantation.—The important part which tissue transplantation now occupies in the experimental work which is being done in tetany, and its peculiar significance as a possible therapeutic agent in this disease warrants a brief review of the main principles of the subject.

Parenchymatous organs, in part or in entirety, seem to have been successfully transplanted in a number of cases between animals of the same species, and even between human beings. But the transplantation of such tissue from an animal to man or experimentally between animals of different species, has almost * uniformly failed, presumably by reason of some cytolytic property of the fluids of an animal towards tissues of another species. The implanted tissues certainly do not abide permanently, and temporary functional effects may fairly be assumed to result from absorption of the implanted tissue and its juices.

The behavior of individual glandular organs when transplanted is extremely variable. According to Payr,[50] those organs which have an internal secretion seem to be far better adapted to transplantation than those with an external secretion.

Of parenchymatous transplantation, that of the thyroid gland is by far the most important. The original experimental transplantations of this organ in animals were done by Schiff,[51] and the first attempt in man was made by Kocher in a case of cachexia strumipriva (1883). The functional results in both instances were transient only. It was tried by Bircher[52] and others for myxedema, but with similar results.

The first attempts which seem to have been successful in respect to the life and function of the transplanted thyroid tissue were those of v. Eiselsberg[53] and Cristiani.[54] But whether this functional activity is only temporary, as urged by Ender-

* Christiani[48] reported some success in the transplantation of thyroid tissue from one animal to another of a different kind.

len,[55] is still problematic. However, Payr [50] has recently reported striking and suggestive results in animals and in the human subject. He transplanted thyroid tissue from the mother into the spleen of a six year old child who was suffering from congenital myxedema. Marked improvement is said to have resulted, and to have persisted up to the time of publication eight and a half months after the operation.

Among other tissues of which successful transplantations in animals have been reported are the ovary, mammary gland, adrenal body, and kidney; in the human subject, besides the thyroid, the ovary may be mentioned.

Among Carrell's remarkable successes in transplantations of the kidney are some in which he demonstrated that the viability of the organ was preserved during an interval of two hours between its excision and its implantation. When an interval thus elapses it has been shown by Cristiani that the viability is best retained by preserving the tissue in serum from the same species of animal or in inactivated serum of an animal of another species; the ordinary salt solution proves toxic. Flexner found that this also applies in the case of pathological tissue.

As to the most favorable site for implantation, opinions differ. The main places to be considered are the subcutaneous tissue, extraperitoneal tissue, peritoneal cavity, omentum, and spleen. In determining the situation for election in a given case attention must be given to the freedom from serious danger which it offers and to its qualifications for supporting the life of the implanted tissue.

Looking now towards the possibility of parathyroid implantations, from general experience grafting between animals of different species would not appear promising; but for obvious reasons the question should be definitely settled on account of therapeutic possibilities. Between animals of the same species, on the other hand, some prospect of success seems offered. Payr mentions several cases in his experiments in which living parathyroid as well as thyroid tissue was found embedded in the spleen at a considerable interval after the

transplantation. Moreover, since his thyroid implantations were said to be functionally successful, by analogy one might reasonably look for similar results with the parathyroid. Finally, Lusena and Cristiani seem to have obtained some functional effects in pure parathyroid transplantations.

With the view of solving the therapeutic possibilities of parathyroid transplantation in man, experiments were undertaken to establish the following essential questions:

1. Can the parathyroid live if transplanted, first, between animals of different species, second, between animals of the same species?

2. If it lives, does it functionate; and, if so, is the function permanent?

In the first series, the rabbit was adopted as the donor, because of the accessibility and definiteness of the external parathyroids which were regularly employed. The dog was adopted as the recipient in both series because it seemed likely that the subsequent removal of the normal parathyroids would be relatively simple and certain. Experience showed that this choice was a mistake and that some other animal probably would have proved better.

The spleen was taken as the site for implantation because of Payr's successes and his claims in favor of it. He suggests that the spleen offers the most suitable combination of the two main factors necessary in tissue receiving an implantation, namely, high vascularity and richness in lymphatics.

The points of interest in my experiments were as follows: In one rabbit one external parathyroid was removed; the other was exposed and its size recorded; no tetany resulted. Eighteen days later the second external parathyroid had increased considerably in size. Similar enlargement has been noticed by others, and it has been suggested that it is in the nature of a compensation for the organ lost. In seven rabbits both external parathyroids were removed; there followed no tetany except in one animal which presented twitching of the head for about two days. In three rabbits complete thyro-parathyroidectomy was performed; in two, tetany developed with death in

thirty and forty hours; the third died on the ninth day, but no positive signs of tetany were noticed. In four dogs complete thyro-parathyroidectomy was performed. In all, tetany of variable intensity developed with death in two to sixteen days. In four dogs complete parathyroidectomy was done, leaving the thyroid. In three fatal tetany developed; in one, questionable tetany without death.

These results simply bear out the experience of many others in regard to the effect of removing the parathyroids. The tetany developed in the dogs in spite of the fact that in all except three of the cases implantations had been made.

Parathyroids were implanted into the spleen of twelve dogs, that is, the eight mentioned above and four others. In eight of these, sixteen rabbit parathyroid were used; in four, ten dog parathyroids. The technique of Payr was followed with some modifications. The implantations were made from eight to twenty-eight days prior to one of the above operations for removing the normal parathyroids, except in one case where the implantation and parathyroidectomy were done simultaneously.

CONCLUSIONS.

From the preceding considerations it is evident that the removal of all and possibly even of a part of the parathyroid bodies results in tetany, that the symptoms of this disease are striking, that the diagnosis is usually simple, and, finally, that efforts directed towards its cure have not as yet been proved to be successful.

In the case reported at the beginning of this paper, the diagnosis of tetany was based, in the absence of thorough electrical tests, first, upon the fact that the patient had never presented any hysterical or other nervous manifestations previous to the onset of the typical clinical features of tetany four days after an operation for goiter which thus supplied a direct anatomical basis for the disease: second, on the analysis of the symptoms, the most suggestive features being the frequent attacks of symmetrical and bilateral tonic contractures of hands and feet, the involvement of the flexor muscles exclusively, the

presence of Chvostek's and Trousseau's signs, the latter characterized by slow contractions accompanied and preceded by cramp-like pains, the additional demonstration of the mechanical excitability of the motor nerves by the stretching of the sciatic nerve and nerves of the brachial plexus; and, finally, the fact that coincidently with the typical spasms all of the above tests disappeared.

Assuming then that this was a case of true tetany, the explanation must be that at her former operation in Bern two parathyroids were removed with the left lobe of the thyroid. Since no symptoms occurred until after my operation this was undoubtedly the cause, presumably through the sacrifice of sufficient parathyroid tissue to upset the functional equilibrium, which must have been at that time very unstable as the result of the previous operation. It is not possible that both the remaining parathyroids were sacrificed, for in that case a fatal tetany would undoubtedly have resulted. Since no parathyroid could be found in the tissue removed, it is probable either that the lower and inferior one of the right side was crushed in the clamp which was placed across tissue in which this body sometimes lies, or that the blood supply of one or both of the parathyroids on this side was interfered with by the ligation of the inferior thyroid artery. The latter explanation was suggested to me recently by Dr. W. G. MacCallum.

In this case, although improvement and apparent cure resulted during the administration of Beebe's nucleo-proteid and after the subcutaneous implantation of human parathyroids, the fact can not be lost sight of that the improvement may have been due to a compensatory hypertrophy of the upper right parathyroid body which is supposed to have been left. Although it seems probable, on the basis of this case and the investigations of others, that by appropriate organotherapy the symptoms of tetany can be controlled at least temporarily during the administration, the question has not been definitely settled. Moreover, the effect of transplantation is still problematic. From animal to man it offers no prospect of success; and we are forced to admit that it is uncertain whether para-

thyroids transplanted between animals of the same species, even under the most favorable conditions, can functionate, even if they do survive. It is consequently equally questionable whether they can grow and functionate when transplanted from man to man. Although subcutaneous implantations seem warranted on account of their freedom from danger and the possibility that they were effective in the case under discussion, the obvious technical difficulties and dangers of implantation into such a place as the spleen, are so great as to forbid the attempt until success in animals has been thoroughly demonstrated.

Considering then the uncertain status of all proposed methods of treatment, the importance of prophylaxis is self-evident. In this connection it is significant that the frequency of the disease has markedly diminished since the adoption as routine practice of leaving part of the thyroid in goiter operations.

The practical side of this subject has been furthered by recent researches only in so far as it has been demonstrated that not merely sufficient thyroid must be left in order to prevent the occurrence of myxedema, but also that a definite part of the thyroid must be retained in order to ensure sufficient parathyroid tissue and thus guard against tetany. The truth of this statement is demonstrated by the case presented in this paper and by the cases of tetany following partial parathyroidectomy collected by Pineles and quoted above with later additions.

The operator must attempt to leave at least two of these bodies in situ, with blood supply unimpaired. When we consider how difficult it is to locate the parathyroids at autopsy on account of their small size and variable situation, it is evident that under the conditions which prevail in an operation, their recognition could not be depended upon and would prove a matter of chance. Therefore, in order to preserve the parathyroids, it is necessary to leave the posterior part of at least one lobe of the thyroid, in connection with which two of these bodies usually lie. Whether this is done by leaving one lobe

completely or in part, is a matter for individual choice in a given case; but in pursuing either course the thyroid vessels, especially the inferior, on this side should not be ligated. The practice of leaving the isthmus only is obviously a very dangerous procedure. In addition, to ensure still further immunity from tetany, even when one entire lobe or the posterior part of a lobe is left, certain precautions should be taken if the whole of the other lobe is removed. In the removal of this lobe the dissection of the thyroid gland should be carried as close as possible to the true capsule of the organ, and independent, small bits of tissue should be sought for in this situation, stripped from the thyroid, and left uninjured. Moreover, in ligating the inferior thyroid artery on this side care should be taken to avoid including in a ligature or clamp the inferior parathyroid which frequently lies in close relation to this vessel.

From the preceding review and discussion it is evident that numerous questions relating to the parathyroid bodies and tetany are still unsolved. Two important points, however, may be accepted as proved by the overwhelming evidence of experimental and clinical observations: first, that tetany following goiter operations is due to operative interference with the parathyroid bodies; and, second, the corollary of this, that in operative procedures parathyroids and their blood supply must be maintained inviolate.

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