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**TETANY FOLLOWING EXTIRPATION OF THE
THYROID.***

WITH REPORT OF A CASE.

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BEFORE the function of the parathyroid glands was known, Reverdin and Kocher noticed that symptoms of tetany followed the complete removal of the thyroid gland, but that if a part of the gland was left the patient as a rule escaped tetany and also cachexia strumapriiva. Before these observations were published, Billroth had 10 cases of tetany out of 38 thyroidectomies, Reverdin 3 cases out of 17, and Mikulicz reported 3 cases of tetany out of 7 thyroidectomies. It was thought that tetany was due to thyroid removal, and the importance and function of the parathyroids was not established until considerably later and after much experimental work had been done on animals.

The parathyroids were discovered by Sandström, of Upsala, in 1880, and Gley in 1891-1897 proved for the first time by experiments on animals that post-operative tetany was due to the removal of the parathyroids and not to the thyroid. Soon after (in 1896) Vassale also connected tetany with removal of the parathyroids. Benjamins in 1892 first examined the

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thyroids removed in operations for goitre in the human subject. He examined 20 thyroids surgically removed. In nine cases where there were complete clinical histories the parathyroids were found removed with the thyroid in five, in four cases no parathyroids were removed. Of the five cases four developed tetany, of the four not one.

Erdheim did much experimental work on rats, but also examined histologically the neck tissues of three patients dying of tetany. In all three cases, though some thyroid gland was discovered, he failed to find any trace of parathyroids. From post-operative tetany and its supposed cause in the destruction of parathyroids, Jeandelize suggested that other forms of tetany, such as infantile, gastric, etc., were due to disease or insufficiency of the parathyroids, and this theory was accepted by Chvostek. Although most observers reported that complete excision of the parathyroids in dogs, rabbits, and rats proved fatal with few exceptions, Vincent and Jolly, Halpenny and Forsyth held the contrary and reported observations where the thyroids and parathyroids had been completely removed and yet the animals lived, and when killed after many days no trace of parathyroids were found post mortem. Vincent and Jolly said that rats and guinea pigs do not seem to suffer at all as the result of extirpation (*Jour. of Physiol.*, 1904-1906).

However, notwithstanding the observations of the above mentioned, the weight of opinion tends to prove that post-operative tetany is dependent on the removal, or destruction, or injury of the parathyroids. I do not intend to go into the proofs of this contention, for in many papers by MacCallum, Erdheim, Vassale, Generali, Pineles, and others, and in the excellent treatise by Ochsner and Thomson on the "Surgery and Pathology of the Thyroid and Parathyroids," a full account of the experiments may be obtained.

Now there are two theories of the functions of the parathyroids: (1) That an antitoxin is developed by the parathyroids which neutralizes certain waste products of tissue metabolism (Berkeley), so that when the parathyroids are destroyed a toxic material is formed in the blood which causes

tetany. (2) That the calcium metabolism of the cells of the body is controlled by the parathyroids, and that their removal causes a rapid disappearance of the soluble salts of calcium from the blood. This theory was advanced by W. G. MacCallum, who found that calcium lactate injected into the veins of parathyroidectomized dogs immediately resulted in the improvement of the symptoms of tetany and that the dog remained well for twelve hours, when tetany again came on. The effect of the injections becomes less as time goes on and each subsequent injection is less effective and finally the dog dies. The same effect is produced by salts of strontium and magnesium; sodium chloride acts very slowly.

In 1911 Voegtlin and MacCallum (*Jour. of Phar. and Ex. Ther.*, May, 1911) somewhat modified this calcium theory and said: "It is quite evident from these experiments that the introduction of large quantities of salt solution of concentration greater than that of the blood does indeed, as pointed out by Joseph and Meltzer, stop the symptoms of tetany." But they go on to say "that it produces this effect by dulling the excitability of the motor nerves, rendering them insusceptible to the influence of any circulating poisonous substances which may appear as the result of parathyroidectomy, or possibly by affecting some structure of the neuromuscular apparatus peripheral to the point of attack of the poison." That there must be something in the calcium theory is rather favored by the facts stated by Morel (*Compt. Rend. Soc. Bioch.*, 67-780) that fractures in parathyroidectomized animals heal much slower than normal animals, also that parathyroid extract administered to young rabbits favors growth of bone quite independent of the calcium contents of food grains, and Erdheim (*Frankfurter z. Path.*, 175-250) states that after parathyroidectomy the skeleton as a whole takes on changes resembling rickets in young animals and more like osteomalacia when the animals are old. Erdheim (*ibid.*, 238-48) says that in rats after the removal of the parathyroids, the dentine calcifies late or not at all and the enamel is deficient in places, and fractures often result. If parathyroids are transplanted and they take, the dentine rapidly calcifies.

That there is truth in our first hypothesis of a toxic material in the blood produced when the parathyroids are removed or destroyed is evident, for if a dog in tetany be bled and an indifferent salt solution be transfused, the symptoms of tetany are at once relieved by thus reducing the amount of poison circulating in the blood. This does not greatly reduce the hyperexcitability of the motor nerves. Simple bleeding in tetany will also have a beneficial effect.

The idea advanced by the earlier observers that the parathyroids are really embryonic remnants or portions of fetal thyroid has been almost entirely given up, and most observers admit that the parathyroids are organs of vital importance to the economy. There are still some, such as Vincent and Jolly, Forsyth, Kishi, Halpenny, and others, who assert that the parathyroids take the place of the thyroid when that gland is extirpated and that there is thus an intimate relationship between the thyroid and parathyroids, for if the parathyroids be left after thyroidectomy the hypertrophied parathyroids to all intents and purposes become converted into thyroid tissue with vesicles containing colloid, so that it is likely there is some interdependence between the thyroid and parathyroids. The same changes occur in the pituitary body after both thyroidectomy or parathyroidectomy (Herring, Rogowitsch).

Now as to the recognition of parathyroids during operation on the thyroid in the human subject. This is by no means easy in my experience and I do not think any one can be certain of recognizing positively a parathyroid gland without a microscopical examination. I have removed inadvertently what I thought without doubt was a parathyroid, but it was found to be only a small lymph-gland.

Rulison (*Anatomical Record*, July, 1909) says that after an extensive investigation on the dead human subject only 41 per cent. of the probable parathyroids identified as such by gross inspection actually contained parathyroid tissue when examined microscopically. Rogers and Ferguson, out of 189 supposed parathyroids examined, found that only 61 were true parathyroids. The gross appearance is often misleading. Many of the supposed parathyroids were adenoid or thyroid

tissue. Forsyth, who examined some 59 human subjects, found that most unlikely portions of tissue contained parathyroids, and that much parathyroid tissue was mixed up with supernumerary thyroids or thymic tissue (*Trans. Path. Soc., London, 1907*). Halpenny has found the same difficulty in animals, not only in recognizing them but in finding them. As a rule, their yellowish-brown color distinguishes them from the deep red of the thyroid.

Treatment of Tetany.—Many measures have been employed. Transfusion of blood, bleeding alone or followed by transfusion of salt solution has prolonged the life of dogs but has not been curative. Improvement occurs for a time and then the dog dies. Parathyroid feeding and injection has been extensively tried in animals but the improvement has been only temporary, and although frequently repeated the animal eventually dies. Beebe (Berkeley and Beebe, *Jour. Med. Res., 1909*) has prepared a nucleoproteid principle of parathyroid from which he reports good results, and others who have used it speak highly of it. Halsted and Pool report each a case in which tetany has been averted for a considerable period by the frequent hypodermic injections of Beebe's nucleoproteid. The administration of the lactate of calcium has been successful in warding off attacks of tetany. Many cases are reported, but the treatment has to be kept up. In the case I report below calcium lactate was used most successfully in keeping the patient free from attacks.

Transplantation of parathyroids of animals has been tried in tetany following thyroidectomy on the human subject with only a temporary benefit. Autotransplantation appears to be usually successful, while isotransplantation invariably fails. Eiselsberg has reported a case of successful transplantation of parathyroid in a woman forty-two years old who for many years had suffered from tetany. She attended his clinic when a goitre operation was performed and finally a suitable case appeared and one of the parathyroids was transplanted. Kocher transplanted thyroid into the bone marrow of the tibia. In this way in dogs the animal was kept alive, but when the bone containing the transplanted thyroid was resected the

animal died of acute tetany, another proof of the interdependence of thyroid on parathyroid.

W. H. Brown, of Victoria, Australia, reports (*ANNALS OF SURGERY*, February, 1912) a successful case of autotransplantation of the thyroid in a case of tetany following thyroidectomy. This was a most severe case and was not controlled by implanting the parathyroids of animals, including monkeys, or the taking of fresh parathyroids by the mouth. He also injected parathyroid emulsion. Finally he managed to get some human parathyroids from a patient half an hour after death, and successfully transplanted them into the left rectus abdominis muscle. From that time the patient began to improve and a couple of months later had gained 15 pounds and was perfectly well. Mr. Brown had given lactate of calcium in this case without the least benefit, but when we learn the dose was only ten grains we do not wonder at his want of success.

Isaac Ott reports the temporary cure of tetany after complete parathyroidectomy by the administration of pituitary extract.

Now I have always thought there was little danger of removing all the parathyroids or injuring them in performing total thyroidectomy, for I had in quite a number of cases removed the whole thyroid and in others left only the isthmus or a part of one of the lateral lobes, and I never saw a case of tetany or cachexia strumapriiva. However, last January I operated on a case in which I was forced to remove nearly all the thyroid, and this operation was followed by severe tetany. In this case no trace of any parathyroids was found in a most careful examination of the removed gland by Dr. Rhea, the pathologist to the Montreal General Hospital, so we must conclude that the parathyroids were so injured at the operation that they were rendered useless. I thought I recognized the right lower one at the time of operation and studiously avoided injuring it, but it no doubt was something else. The following is an account of the case, which is reported by my house surgeon, Dr. H. H. Hepburn:

Mabel W., aged thirty-four, consulted me on January 2, 1912, for an enlarged neck. She has had a swelling of the neck since thirteen years of age, which has gradually enlarged and latterly somewhat altered her voice; she has frequent attacks of dyspnoea, and difficulty in swallowing is a constant symptom. When lying down she is unable to swallow fluids; has attacks of palpitation at times. Married and has two children, and it was noticed that the swelling in the neck always increased and remained larger during pregnancy. Has frequently reduced the size of the gland by taking thyroid extract. On examination a much enlarged thyroid was found, larger on the right than on the left side. On the right side also was a solid globular mass in front of the sternomastoid the size of a tangerine orange. The left lobe although much smaller than the right seemed to push out the left sternomastoid. The enlarged right lobe extended on the right side above the level of the angle of the jaw. The whole gland was smooth and soft but did not appear to be vascular. No signs of exophthalmic goitre, no tremors, tachycardia, or other signs. On examination of the larynx there was paresis of the right cord and some compression of the third to the fifth rings of the trachea.

The patient has always been a perfectly healthy woman and was normal in every way. She was advised operation and came into the hospital on January 14 and was operated on under general anaesthesia on the fifteenth. I intended to remove the right lobe and isthmus only, but after having freed the enlarged right lobe and left what I thought was a parathyroid at its lower end posteriorly, I found another large tumor below the first, and on examination this proved to be a portion of the left lobe which had pushed its way beneath the trachea and oesophagus and appeared on the right side of the neck. At the point where this portion of the thyroid crossed behind the trachea, the rings of the latter were much atrophied and the trachea was much compressed laterally, the portion above the narrowed trachea was dilated and thinned, and on touching it a noise like squeezing a ping-pong ball was made. This was a condition that at any moment might have resulted in kinking of the trachea and so producing fatal dyspnoea, as in the cases reported by Rose. I freed this part of the thyroid with some difficulty and pushed it to the left side. There I found the lower pole of the left lobe

was much larger than I had thought and went behind the sternum and into the thorax. Not liking to leave so large a piece of gland in such a position I decided to remove it, and tied off the upper horn of the left lobe, leaving a considerable portion of thyroid tissue, then tied the inferior thyroid artery, and pulled up the lower part projecting into the thorax. In doing so I looked carefully for parathyroids but failed to find any. I then cut off a piece the size of half a large egg which lodged under the sternomastoid and was still connected with its bed by connective tissue, and left it there, the whole of the rest of the gland coming away together in one piece.

The operation was rather prolonged, but the patient had stood it well and was in first-rate condition. A tube was introduced and the wound closed. Next day there seemed to be some distention of the neck, and a clot of blood filled the tube and on its removal a good deal of bloody serum escaped. On January 18 (third day), the patient complained of a feeling of formication over the whole body and of a great weight which pressed on her brain. She had slept well the night before and had a normal pulse and temperature. Toward evening she complained of severe pain at the base of both lungs and next day felt dizzy and had numbness of the legs and feet. On January 20 (fifth day), in the early morning she felt fairly well but complained of numbness and tingling in the legs and face and a feeling as if ants were crawling over her skin. A few hours later she had cramps in both hands and pains in the joints and considerable stiffness of the fingers and flexion of the toes. Then there were severe paroxysms in both arms and legs. The thumbs were contracted in the palm of the hand, the fingers flexed at the metacarpophalangeal joint, the wrist flexed, and elbows bent. The toes were flexed and adducted and the feet extended. She complained of great pain in the legs, which was at times spasmodically increased; her face twitched and there was numbness and stiffness about the jaws. Chvostek's sign was well marked, and pressure on a nerve trunk produced spasms (Trousseau's sign). Pulse was 80 to 100, and she had no temperature. Her voice was very husky and she seemed stupid; she complained most of the acute pain in the legs, which at times was very severe.

As soon as I saw her I put her on drachm doses of the lactate of calcium every three hours. This was about eleven in

the morning and at 5 P.M. the spasms and cramps had disappeared; the fingers were relaxed, the voice became natural, and she said she felt very well, only tired. After five doses the lactate of calcium was discontinued as she disliked it so, and some parathyroid extract was sent for, there being none in town. On the morning of January 22, the seventh day after operation, she began to feel the sensation of formication again, with a feeling of weight in front of head and great depression. She was again put on calcium lactate drachm doses with $2\frac{1}{2}$ grains of thyroid extract every four hours. She had slight cramps in her extremities that night with pain in the left side. Next day she was free from cramps but still had pressure symptoms in the head and a creepy sensation over the body. For the next two days she remained about the same and refused to take any more calcium lactate.

On the eleventh day (January 26) she was fairly well in the morning, but by noon was worse than ever, all previous symptoms being much exaggerated. The face was flushed, she was irritable, and much depressed. The parathyroid extract had now arrived and she was given $1/20$ grain every four hours with three grains of thyroid extract. As she was no better next day she was persuaded to commence taking the calcium lactate again in addition to the extracts, and in consequence the improvement was rapid, the cramps disappeared, and she felt very much better. But at this time she developed a dry pleurisy on the left side which gave her much pain. On the fourteenth day she had some slight cramps, but these soon disappeared. The pleurisy was relieved by strapping. The wound had healed completely some days before.

The patient left the hospital on February 5 and was directed to take 30 grains of calcium lactate and $1/20$ grain parathyroid extract every four hours. I gave the dried parathyroid, as I could not succeed in getting the fresh from the slaughter-houses. All the specimens sent me or brought by my house surgeons proved on microscopical examination to be isolated portions of thyroid tissue, so the dried preparation was continued. Twice the lactate of calcium was discontinued and the symptoms always returned, though parathyroid was still administered. She asked for the calcium lactate, for she said she always got relief within an hour after taking it. I saw her several times after she left the hospital and she told me she was never well without the

calcium lactate and whenever she omitted it the stiffness in her fingers, joints, and jaws came on, accompanied by mental depression and great irritability. I saw her on one occasion when she had not taken the calcium for 24 hours and Chvostek's sign was very marked and she complained of stiffness in her fingers and toes. She then resumed the calcium and two days later when I again saw her there was no feeling of stiffness and no Chvostek sign; she felt well and was bright and lively, going out driving for several hours each day. She always felt best when both the calcium and parathyroid were taken, and with calcium alone she was much better than with parathyroid alone. When I last saw her in March she still had some dry pleurisy on the left side.

I heard a couple of weeks ago from her home in Vermont and she was then well and able to attend to her household duties; she still continued to carry out the treatment she was pursuing while in Montreal, and she said she could not do without the calcium lactate.

This case agrees with the conclusions found by Voegtlin and MacCallum, that calcium can cure temporarily any case of tetany due to insufficiency or removal of the parathyroids. In this case, although no parathyroids were found in the removed thyroid, still there must have been some injury to these glands, due perhaps to the after-hemorrhage and distention of the cavity with blood-clot after the operation. The transplanted thyroid under the left sternomastoid muscle was tender for a few days, but afterward could be felt and was apparently functioning. What the ultimate result of this case may be I cannot tell; perhaps in time the damaged parathyroids may resume their function, for Eiselsberg and Kummer report cases of recovery after one year. If recovery does not take place after that time has expired, I should endeavor to get human parathyroids for transplantation.

June 6, 1912: I saw patient to-day. Is looking and feeling well, has gained about 20 pounds. The only symptom is oppression in head, which was corrected by lactate of calcium, of which she now takes only 20 grains twice a day.

