IV. THE EFFECT OF THYROPARATHYROIDECTOMY ON BODY ACTIVITIES.

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The Effect of Thyroparathyroidectomy on the Composition of the Blood

Blood was drawn from the vein on the leg under sterile conditions, alcohol being used for the sterilization. Very small amounts of sodium oxalate was placed in the syringe to prevent clotting of the drawn blood. Fifteen to twenty c. c. of blood wa-

drawn each time. Always before or at least eight hours after feeding the blood was drawn. The animals were trained to lie down during the bleeding, the holding of them was not necessary. The protein free blood filtrate was prepared by the method of Folin and Wu (1). From this the total non-protein nitrogen, uric acid, urea nitrogen and sugar was determined.

The total non-protein nitrogen was determined by the method of Folin and Wu (1). From the data for Dog. No. 1 the non-protein nitrogen remained fairly constant from October 23, 1923 to the day of death March 6, 1924. After thyroparathyroidectomy there was but a very slight increase in total nitrogen to the day of death. This agrees with the findings of Haden and Orr (2), and Togawa (3). If the increase is due to ammonia nitrogen, the findings agree with those of MacCallum and Voegtlin (4), Berkeley and Beebe (5), Coronedi and Luzzatto (6), Cool (7) and Underhill and Saiki (8). This increase in total non-protein nitrogen is so slight that it is well within normal.

Dog No. 3 shows a slight increase in total non-protein nitrogen after thyroparathyroidectomy on the lactose diet. On April 6, 1924 the diet was changed from the carbohydrate to a meat one. There was still no gain in non-protein nitrogen. When the animal was in tetany on March 6, 1924 the total non-protein nitrogen was actually less than it was two days previous when there were no symptoms of tetany whatever. Again on April 20, 1924 after having symptoms of tetany for three days the non-protein nitrogen was actually lower than it was on previous days when there was no tetanic symptons.

The non-protein nitrogen of Dog No. 4 which was on a standard meat diet during the entire experiment showed no appreciable increase in non-protein nitrogen after thyroparathyroidectomy. When the dog was in severe tetany on March 29, 1924 the non-protein nitrogen was lower than on previous days when there was no tetany.

The feeding of calcium lactate does not affect the composition of the blood, since there was no change in it before and after thyroparathyroidectomy where calcium lactate was a constant factor.

The result on the non-protein introgen of the blood of the dogs Nos. 3 and 4 do not agree with the findings of Haden and Orr (2) and Togawa (3). The urea nitrogen was determined by the urease method of Folin and Wu (1). The urea nitrogen remains practically constant. This does not agree with the work of

Haden and Orr (2) who found an increase in blood urea.

The uric acid was determined by Benedict s (9) method. There was no change in the uric acid content of the blood before or after thyroparathyroidectomy. In dog No. 4, which was fed a standard meat diet, the uric acid remained about two mg. per 100 c. c. of blood above that of dogs Nos. 1 and 3 which were fed the standard carbohydrate diet; but in all cases the uric acid remained markedly constant.

The blood sugar was determined by the method of Folin and Wu. No change was noted in the blood sugar after thyroparathyroidectomy from that of the normal. These results agree with the work of Stoland (10) and Haden and Orr (2).

The non-protein constitutents of the blood as far as the author has been able to determine remains the same after thyroparathyroidectomy as before. The cause of tetany is yet unknown. All true tetany probably has a common origin regardless of the conditions with which it is associated.

The carbondioxide capacity of blood plasma was determined by the direct method of Van Slyke and Cullen (11).

The carbondioxide capacity of blood plasma in dogs Nos. 1 and 4 showed a decrease after thyroparathyroidectomy, while dog No. 3 showed a slight increase. These results throw more doubt upon the facts that acidosis, as demonstrated by Watanabe (12), accompanies or is partly the cause of tetany; nor do they support the results of Wilson, Stearns, Janney and Thurow (13) (14) and McCann (15) that alkalosis is a factor. Relatively little variation was there in the carbondioxide capacity. This agrees with the findings of Haden and Orr (2). The slight change in the carbondioxide capacity was probably at all times well within the range of the normal. The author believes that alkalosis does not at all times accompany tetany and is therefore no criterion. This is in accord with the results of Hastings and Murry (80) (16) and Underhill and Nellams (17).

The Effect of Thyroparathyroidectomy on the Blood Pressure.

Since Major and Stephenson found a prolonged rise in blood-pressure from guanidin injection the author thought it advisable to take the blood-pressure of the thyroparathyroidectomized dogs in an attempt to prove that guanidin may be present.

An indirect method, by using the "Tycos" sphygomanometer, of the same principle as that for the measurement of the blood pressure of man wsa applied to the dog. The cuff, which was made specially for the dog, consisted of a suitable leather

covering placed around a rubber bag. The cuff was placed around the left hind leg of the dog above the knee joint. By palpating the femoral artery and some of its branches, using both hands, the cessation and reoccurance of the pulse can be readily detected. The blood pressure was taken always before feeding when taken in the mornings; but it was also taken before, after and during tetany. Real small dogs were not used because the cuff was not suitable to fit such animals.

By examining the data it is found that the blood pressure in every case is always subnormal with the onset of tetany, and that the blood pressure after thyroparathyroidectomy is on the average below normal. Occasionally, after the dog has been in tetany for twelve or more hours, the blood pressure may increase a little or even go above normal.

If guanidin or methylguanadin is present in the blood in sufficient amounts to produce tetany, there should also be a rise in blood pressure as shown by the experiments of Major and Stephenson (18). The author has shown that a rise in blood pressure does not accompany the onset of tetany; but that the pressure actually becomes less. In some cases at the onset of tetany the pulse was so weak and feeble that the pressure was not determined. From these results it is doubtfull that guanidin or methylguanidin is the cause of tetany. If it is the cause, it is not present in sufficient amounts to cause an increase in blood pressure above that of the normal or if it is present, some substance or mechanism coexist which lowers the blood pressure with the conset of tetany.

The Effect of Thyroparathyroidectomy on Basal Metabolism.

The Sanborn Benedict metabolimeter was used for the determination of oxygen consumption. The dogs were trained to lie down and to remain perfectly still. At all times the animals were allowed to remain still for from twenty minutes to an hour before the determination was made, depending upon the activity of the animals, to assure as nearly basal conditions as possible. The calculations were made for the special kymograph with the apparatus using the special scale card in all cases. The length of each determination extended over a period of at least ten minutes and the oxygen consumption per minute was calculated.

It was necessary to have the room at a temperature of about 25 degrees C. and in addition an electric pad was often required to keep the animals warm enough to prevent shivering. In every

way an attempt was made to make the conditions for the animals comfortable as possible during each determination.

The muzzel used consisted of a rubber tube that comfortably fitted the length of each animal's nose and was connected to a suitable metal piece which was in turn connected to the metabolimeter. The apparatus was tested for air tightness with almost every determination. Each animal's nose was shaved completely around and far enough back so as to include the corners of the mouth.

All thyroparathyroidectomies were performed under ether anesthesia and under strictly aseptic conditions.

The basal metabolic rate is increased when the feeding of calcium lactate is stopped and the symptoms of tetany appear. This is a never failing phenomenon appearing in all dogs with which the experiment has been tried. In dog No. 1 after the injection of calcium lactate and the symptoms of tetany disappeared the basal rate fell to as low as 50 c. c. per minute whereas the normal is about 70 and a short time before tetany the oxygen consumption was 83.05 c. c. per minute.

The calcium lactate probably only indirectly lowers the basal rate by the fact that it in some way prevents tetany. The data will show that calcium lactate generally brought the oxygen consumption to normal, rarely below.

The author concludes from these results that there is a general increase in metabolism associated with the onset of tetany. The parathyroids, as well as thyroids, probably play a part in the regulation of general metabolism. Regardless of what the cause of tetany may be an increase in general metabolism accompanies its onset. An increase in general metabolism occurs after thyroparathyroidectomy without the development of tetany; but the converse is not true.

The Effect of a Carbohydrate Diet, the Intestinal Flora and Calcium Lactate on the Prevention of Tetany

Each dog was placed on a carbohydrate diet for at least two weeks and three for as long as four months before thyroparathyroidectomy. Dogs No. 1, and 3, were fed 30 grams. of lactose, one quart of milk and 150 grams of white bread daily; while dogs No. 5 and 6 were fed daily 70 grams. of lactose, 100 grms. of white bread and 1 quart of milk. Dog No. 4 was fed 200 grms. of meat, 1 quart of milk and 100 grms. of white bread daily.

During the cold winter months the dogs were kept in cages

in a comfortably warm room. When the weather become warm the dogs were placed out of doors in large pens. They were allowed to drink water at will.

Every thyroparathyroidectomized dog which was fed the standard lactose diet and which had diarrhea and acid feces developed severe tetany. Calcium lactate was required in all cases to assist recovery and to prevent future attacks. The Ca lactate was not given until each and every dog developed tetany. This was done to prevent the action of the Ca lactate and determine whether the carbohydrate diet was an adequate preventative of tetany. These results do not support the theory of Dragstedt (19) and his co-workers.

In every case where lactose was first fed and when the animals lost their appetite and such body weight and were on the verge of death after thyroparathyroidectomy a change of diet from lactose to meat promptly caused a great improvement in them. The meat diet with the use of Calcium lactate was the only effective method for preventing tetany.

The author's findings agree with those of Luckhardt and Goldberg (20), MacCallum (21) and MacCallum and Voegtlin (22). Within thirty minutes after calcium lactate as given with the stomach tube to a dog in tetany a great improvement could be noticed. The dog's appetite improved, it became more active, gained in weight and in every way appeared normal.

After dogs No. 1, 2 and 3 had been on the lactose diet for at least two months and their feces were disinctly acid; bacillus acidophilus, bacillus acidophilus aerogenes and other lactobacilli were isolated from the feces.

Summarized Conclusions

1. The change of total nitrogen and urea nitrogen after thyroparathyroidectomy is well within the normal range. In some cases the total non-protein during tetany was actually lower than it was on previous days.

2. The uric acid and sugar content did not change after thyroparathyroidectomy.

3. The condition of alkalosis does not at all times accompany tetany and is therefore no criterion as to its cause.

4. Both the oxygen content and capacity decreases after thyroparathyroidectomy. The cause is unknown.

5. In every case with the onset of tetany the blood pressure is always subnormal. In general there is a fall blood pressure

after thyroparathyroidectomy; but after tetany has continued for several hours, the blood pressure may rise to normal or above.

6. If guanidin or methylguanidin is present in the blood in sufficient amounts to cause tetany, there will probably also be a rise in blood pressure; but as there is no rise in blood pressure guanidin or methylguanidin is probably not present in sufficient amounts to cause tetany.

7. If guanidin or methylguanidin is the cause of tetany, some substance or mechanism co-exist which lowers the blood pressure with the onset of tetany.

8. An increase in general metabolism occurs after thyroparathyroidectomy; but the converse is not true, the parathyroids, as well as the thyroids, probably play a part in the regultaion of general metabolism.

9. The calcium lactate probably only indrectly lowers the basal metabolic rate by the fact that it in some way prevents tetany. The calcium lactate generally brought the oxygen consumption to normal, rarely below.

10. The change of intestinal flora, brought about by a lactose diet, does not prevent tetany.

11. A meat diet and the giving of calcium lactate via the stomach is the best known method of prolonging the life of and preventing tetany in thyroparathyroidectonized dogs.

12. The lactose diet, due to the formation of acids caused by the biological activity of the lactobacilli, produce conditions unfavorable, because of these formed acids, to the growth of proteolytic bacteria and render the intestinal contents distinctly acid.

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