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The undersigned, acting as a Committee of the Graduate School, have read the accompanying thesis submitted by Chas. C. Palmer for the degree of M.S. They approve it as a thesis meeting the requirements of the Graduate School of the University of Minnesota, and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science

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THYROIDECTOMY IN THE PIG

A Thesis Submitted to the

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C. C. Palmer

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THYROIDECTOMY IN THE PIG.

Introduction.

The symptoms observed, following thyroidectomy, vary according to species, and to some extent in individuals of the same species. This statement is warranted after the vast amount of literature on this subject has been studied.

Vincent[1] reviews the literature upon thyroidectomy in considerable detail, and from this it is quite evident that the variations in the results reported by different early workers, were owing to the fact that the anatomy of the parathyroid glands was not clearly understood. It is now known that these small glands vary greatly in location and number in different species, and even in individuals of the same species; and if they are involved in the operation of removing the thyroid, the animal will exhibit symptoms which are not the true symptoms of thyroidectomy.

Thyroidectomy in young animals in which the parathyroids are not included induces symptoms of cretinism in a large percent of the animals operated. Perhaps our best example of this is seen in the case of the rabbit. Basinger[2] has recently reported his studies in the control of experimental cretinism and describes cretinism in this animal. He states that "about two weeks after the operation the hair becomes noticeably drier and does not lie smooth and flat on the skin as normally. It stands up and can be pulled out very easily. At the same time there is a gradual retardation of growth. This is noticeable as early as the third week after the operation. This retardation of growth is greatest from the eighth to the twelfth week. By the tenth week the average weight of the cretin rabbits is 750 gm., while the normal controls weigh approximately 1,400 gm. From this time the growth curve of the cretins deviate even more rapidly from that of the normal, but the growing period is longer in the case of the cretins". He further states

that "the posture of the cretin is typical. The limbs are short and the muscles are too weak for support. The bones show a pseudorickety condition (chondrodystrophia thyreaprivea of Hofmester). The hair becomes coarse and can be pulled out in bunches. The skin becomes dry, thick, and scaly, gradually turning into a typical eczema covered with crusty scales. This is always most marked about the head, ears, shoulders, and legs. The proportionate growth of the abdomen over that of the rest of the body gradually increases and the cretin acquires the descriptive "pot belly" type of abdomen. They are slow, awkward, and move about very reluctantly. If not disturbed, they may remain for hours in the same place".

There was no typical myxedema noticed in any of these cretins. Basinger kept sixteen cretins alive for over a year without any evidence of cachexia. There was a marked muscular weakness, especially noticeable in the limbs, but the animals always appeared to be in a fairly well nourished condition.

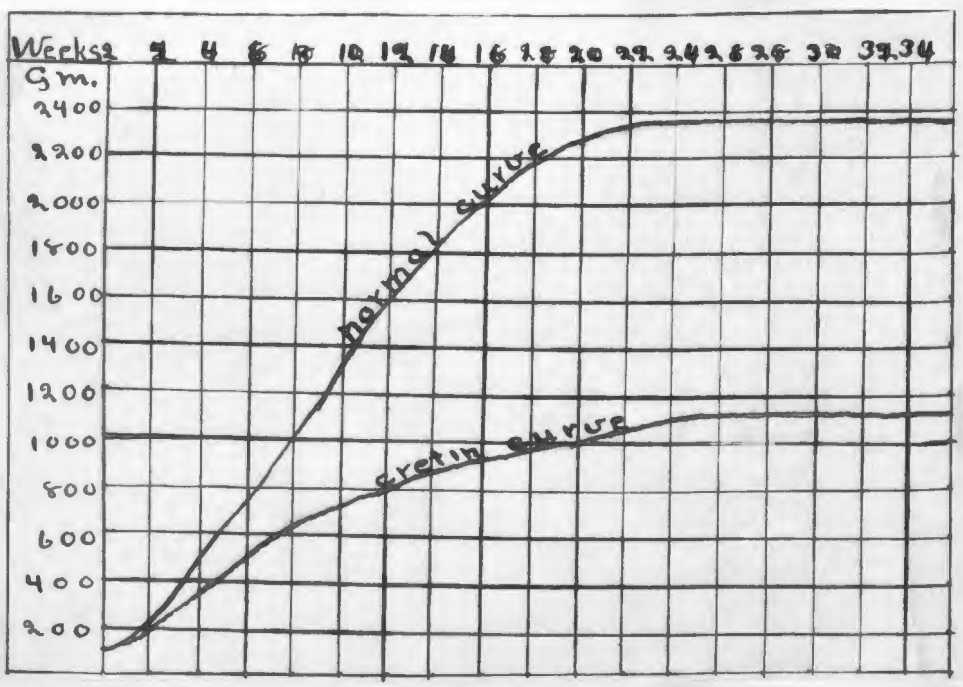

Fig. 1.- Growth curves from four normal and three cretin rabbits. (After Basinger[2])

From the anatomy of the thyroid and parathyroids in the pig one would think it possible to induce cretinism in this animal by the removal of

the thyroid gland, if cretinism results from the removal of this structure. There is very little literature regarding this subject, in the pig.

In 1886 Horsley[3] reported that removal of the thyroid in two pigs was followed by characteristic symptoms of tremors, leucocytosis and anaemia with subnormal temperature. He also states that the period of incubation in these animals was rather long. At this time Horsley believed that the size and histological arrangement of the gland played an important part in the symptoms produced, following extirpation; for he states "where the gland and acini are small functional activity is slight and the symptoms following thyroidectomy are less severe and the period of incubation is quite long." In this connection he cites the case of a donkey which lived for 205 days after the operation. Horsley evidently did not take into account the part played by the parathyroids.

In 1892 Horsley[4] reported that observations by himself and Munk yielded negative results, but that the animals were not observed for a sufficient length of time, the more especially as the glands in these animals are relatively small. He leaves the impression that the second group of pigs would have very likely developed the characteristic symptoms and died had they been observed longer. He also states in this article that the results are much more serious in young animals, and that compensatory hypertrophy can take place very readily in young animals. Later in this same article he classifies pigs as well as sheep, goats and donkeys in the group of animals which slowly develop cachexia, with death after a lengthened period.

Eiselsberg[5] removed the thyroid gland from a pig four weeks of age. He reports a marked arrestation in growth, unaccompanied, however, by apathetic iediocy, the animal being as lively as normal animals.

Moussu[6] operated upon one pig when the animal was 15 days of age. It remained normal until about one month later when it began to show symptoms of myxoedema. It became sickly in appearance, the skin became bald in places,

and in others was covered with remarkably long and thick bristles. There was swelling of the abdomen and formation of infiltrated cutuneous folds. There was also arrestation of growth. The animal died at the age of two months and four days. Postmortem symptoms were stated to be similar to those found in man.

The Animals.

From three pigs the thyroid was removed by the operation described below. Three other pigs were kept as controls. The six pigs were from the same litter of 7 pigs, The mother, a grade, white sow, belonged to the Hog Cholera Serum Plant. She was immune to cholera and was to be used for serum production, but owing to the fact that she was pregnant, she was not hyper-immunized, but was permitted to farrow. On April 11, 1915, she gave birth to seven healthy, strong pigs. In the litter were two females and five males.

At the age of one week the little pigs were doing very nicely. They weighed five pounds a piece, and all seemed to be perfect in health and vigor. The pigs, with their mother, were kept in a warm, clean box stall; and on bright, sunshiny days enjoyed the freedom of an outside pen.

In the bunch were two black and white spotted pigs, and although one was a male and the other a female, they were so nearly alike in size, conformation, and markings, that it was decided to use them for the first pair. Accordingly the male was operated upon when he was eight days of age and tagged (No. 6938). The female was designated as his check and tagged (No. 6942). There were remaining four very similar white pigs. One of these white pigs was a female, and it was decided to operate upon her, which was carried out when she was twelve days of age. She was tagged (No. 6945) and a white male of similar size and conformation designated as her check and

tagged (No. 6941). There still remained in the litter two white males and a red and black male. On April 26, 1915 when these pigs were 15 days of age, one of these white males was operated upon. The operated pig was tagged (No. 6937) and the remaining white male was designated his check and tagged (No. 6946).

When the little pigs were eight weeks of age, they were weaned, and then placed in pens along with the University herd. At first the operated pigs were placed in one pen and the checks in another, but they were soon afterwards placed all together in a large pen with an open yard adjoining. They were well cared for, and given all they would eat of a properly balanced ration.

When four months of age the pigs were given a protective dose of hog cholera serum. Hog cholera existed on the farm and the pigs were vaccinated as a matter of precaution, assuming they would pick up some infection and thereby acquire active immunity.

In November the animals were placed in one of the hog houses of the serum plant. They were placed in a large inside pen, and were well fed and taken care of. They were in a building which was used for quartering hog cholera virus pigs, and accordingly were carefully watched for any symptoms of cholera, but as none developed, they were thought to be immune from the disease.

Anatomy.

In the pig the thyroid consists of two lobes, closely attached to one another by means of connective tissue, so that an isthmus cannot be distinguished. The gland varies slightly in position in different individuals, but is always situated on the ventral surface of the trachea, and usually a couple of inches below the larynx, but may be in contact with it. Sisson[7] states that in the adult the lateral lobes are irregularly triangular in outline and in a large adult are two inches or more in length; and that the chief artery enters at the posterior extremity.

In the week old pig, the gland is similar in general arrangement to that of the adult. Each lobe is thin, rather ovoid in shape, and about the size of a bean. The two lobes are intimately connected except at the posterior end, where each lobe is pointed, and not connected with its fellow. The gland varies in size, but on an average weighs about one-half gram. On section the alveoli are about twice the size of those in an adult normal hog.

The parathyroids in this animal, according to Ellenberger[8], vary from those found in other animals in that the median pair are missing, that they are never formed or disappear early. He further states that the lateral parathyroids in ruminants and pigs do not extend to the thyroid, but remain permanently at the cranial end of the thymus; and that in mature animals as the thymus disappears, they are surrounded by a small amount of thymus tissue or fat. If the position of the lateral parathyroids can be in any way judged by the position of the thymus, they are quite apt to vary greatly in position. Sisson[7] states that the thymus in the pig may extend up the cervical region to a varying extent, that it may extend to the larynx or even to the mandibular space. The wrter has found the position of the thymus to vary greatly in the fetus, but more often it was found at or near the thoracic inlet. Owing to the location of the parathyroids in this animal, there is not much danger of removing them in a thyroidectomy; and the symptoms following such an operation should not be accompanied with the symptoms following a parathyroidectomy.

Accessory thyroids are known to be present along the trachea to a variable extent, but very little work has been done on these structures in this animal.

The Operation.

The little pigs were taken directly from the mother to the operating room. The seat of the operation was shaved and then painted with iodine. Ether was administered and an incision was made through the skin, ventral to the trachea, and just posterior to the larynx. The ventral muscles

of the neck were parted which exposed the small thyroid gland. The lobes were found to be but loosely attached to the trachea, but intimately connected with one another, and it was found possible to pull the gland away from the trachea and to the outside. The recurrent laryngeal nerves are not in contact with the thyroid, so there was no danger from this source in this animal. The gland was easily separated from the trachea without causing any haemorrhage except at each end; and, here it was found to be attached rather firmly by bands of connective tissue, which contained the blood vessels and nerves. These thyroid vessels were so small that they did not require ligation, and all that was necessary to control the haemorrhage was to crush the vessels with artery forceps. The connective tissue bands were then severed and the gland freed. The incision was closed with interrupted sutures, and a dressing of iodoform and colloidin applied. The little pig was then returned to its mother, where it immediately began to nurse, and in all cases the young animals did not miss a feed. The little fellows took the ether quite readily, only a few inhalations being required to produce anaesthesia. The wound healed by primary intention in all cases and the sutures were removed on the seventh day respectively.

Results.

During the first month or two no changes in physical condition could be determined. All of the pigs were of equal size and weight.

The first pig to show any change was the operated white sow No. 6945. She developed many circumscribed, inflamed, swollen areas about the size of a dime or nickel, along the ventral surface of the abdomen, which were very resistent to treatment. The only other pig to show any such lesions was the operated white boar No. 6937. No specific cause for this condition could be determined, and in pigs skin lesions of this kind are unknown to the writer. Scrapings from the diseased areas were negative when examined under the microscope. Owing to the slop feed which the mother received and the nature of the

animals, the cement floor of the pen in which these animals were kept was wet most of the time, but plenty of clean dry straw was provided, and in general the pen was much cleaner and dryer, than the average pig pen. This skin disease could hardly be attributed to the pen because only two of the pigs showed symptoms (both operated pigs) and such lesions are not common in pigs which are quartered in much poorer pens. An outbreak of necrobacillosis existed among the young pigs of the University herd, but in these the lesions were confined to the mouth and internal groups. These sores of operated animals did not become necrotic, nor could the necrosis bacillus be demonstrated. After several weeks the lesions disappeared. The affected animals were given plenty of sunshine and antiseptic, astringent baths.

The next indication of a lowered resistance was manifest by the operated black and white boar No. 6938. In June he was noticed to be lame and upon examination one of the digets of the left fore limb was found to be swollen and painful. No infection developed, The injury was probably a bruising of the tissues, which was very slow to heal. The animal remained lame for over six weeks. This condition is rarely seen in the pig and when bruising does occur, the lameness is of short duration unless infection develops.

During the late spring and early summer when about 3 months old, all of the pigs showed symptoms of parasitism, especially lung worms, with much counghing. No treatment was given but this invasion interfered with the growth and thrift of all the pigs. The symptoms were more marked in the operated pigs, and they made a much slower recovery than the normal. The operated white boar seemed to suffer the most. He did not gain very rapidly and soon became the smallest pig in the litter. His hair coat became rough, and the bristles came out. He became almost entirely bald over his body and the skin very read and congested. This pig looked and acted sick and was not expected to live.

In the fall when the cold weather set in, the pigs began to improve and gain in weight more rapidly, and none of them showed any signs of

parasitism. Even the white boar which was not expected to live showed a very marked improvement and although a little undersized, weighed nearly as much as the other operated pigs. The parasites did not interfere with the growth and development of the testicles in the male pigs, and it became necessary to castrate them. They were castracted on October 13, 1915, with the exception of the black and white boar, which was left entire, because it was intended to experiment with his fertility. No difference was noted in the size and appearance of the testicles of the operated and check pigs. The testicles represented 0.76% and 0.56% of the body weight in the check pigs and 0.77% of the body weight of the operated pig.

The body temperatures of all the pigs were taken at frequent intervals but they showed no variations other than normal.

The operated pigs grew well but did not gain in weight as rapidly as the check pigs. Each pig was lighter in weight than his check and the average weight curve is shown in the following chart:

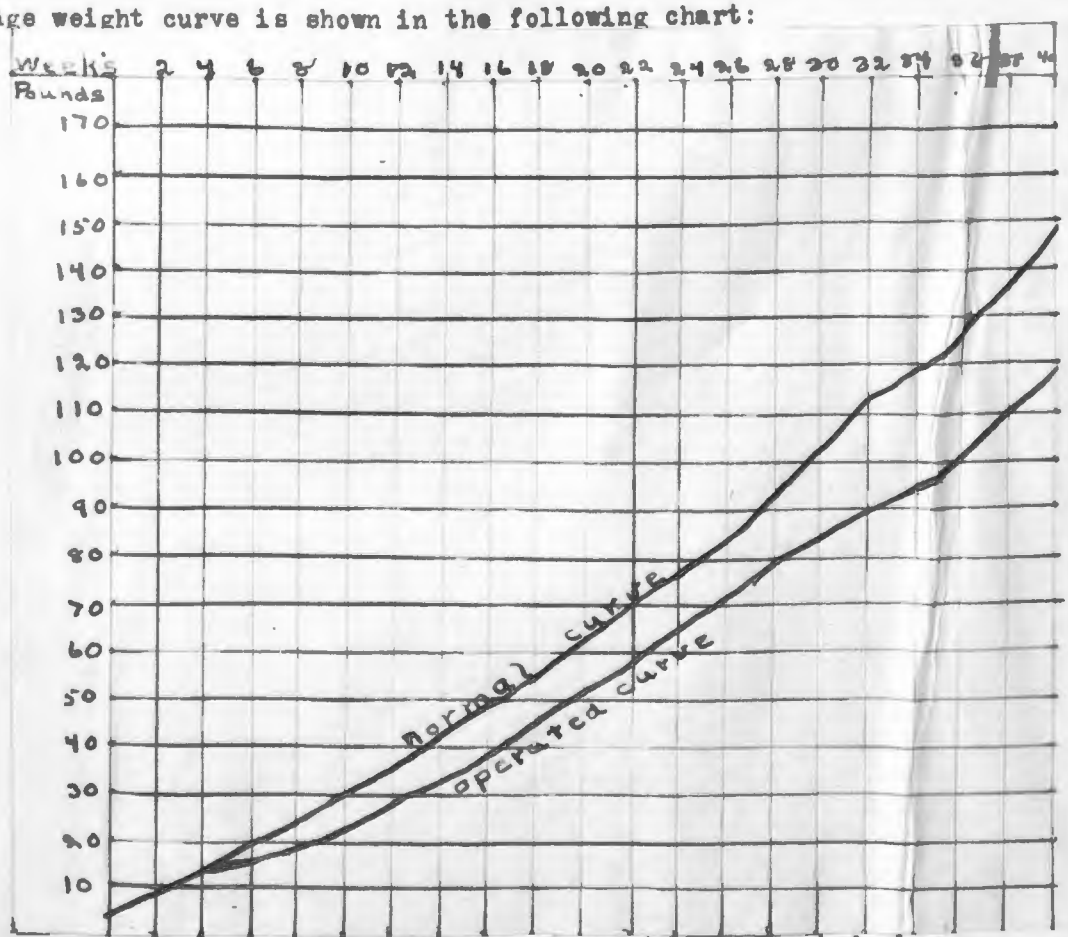

Fig. 2.- Growth curves from three normal and three operated pigs.

It will be noticed that during the first few weeks the weights of both groups were equal. From the 4th to the 9th week there was quite a marked difference in the rate of growth in the two groups, but after the 9th week the rate of growth in the operated pigs was equal to that of the checks. This equal rate continued until the 27th week, when the rate of growth increased in the checks, but remained about the same in the operated pigs. At 40 weeks, which is about the time of market maturity in this animal, there was an average difference of 30 pounds between the checks and operated pigs.

Sexually all of the males were very active, but owing to the fact that they were grade stock, there was no opportunity to try out the reproductive powers of the thyroidectomized boars on mature breeding sows. Early in November the two sows (operated and check) came in heat. They were bred to the operated boar and evidently conceived as dioestrum did not recur. These females did conceive, and on post mortem which was held shortly before the time of parturiation, the operated sow presented one mummified foetus in the uterus, and the check sow presented one fully formed foetus, which appeared normal and probably would have been born in a short time. This fact is interesting as normal sows bred to normal boars usually have 5 or 6 pigs at the first litter and older sows may have as many as 15 or 16. That the operated boar retained his sexual activity was demonstrated by the fact that whenever any of the sows in his buildings were in heat, he would make violent efforts to reach them and several times did get over the high partition of his pen.

Death and Post Mortems.#

On February 4, 1916 the operated white sow was reported sick by the feeder, and when seen was found to be in a dying condition. The feeder reported that for a couple of days she had not been eating very well. Post mortem revealed pneumonia and pleurisy involving both lungs and the parietal and visceral pleura of both sides. The digestive organs showed gastritis. Abdominal and thoracic lymph glands were congested. All other organs were

#Dr. Kernkamp of the serum laboratories co-operated in the post mortem examinations.

normal, except the uterus. Here there was considerable exudate and a mummified foetus was found. The head of the foetus was fairly well developed, the body small in diameter, but very long, and the legs were not developed to any appreciable extent. The region of the larynx and trachea of this operated animal was carefully examined and numerous gland-like structures varying in size from a small seed to a large bean were found and retained for microscopic study.

The pigs were carefully watched and none of the remaining animals showed any signs of sickness, but on February 14, 1916 two more were found dead. The pigs had last been seen by myself the day before and at that time they all appeared normal. The dead pigs were the operated white male No. 6937 and the check black and white sow No. 6943. The check sow was posted first, and the only lesions found were in the lungs. These organs showed lesions of pneumonia involving only the distal parts of the cardiac lobes. The uterus was normal and contained one normal fetus. The operated white male was next posted, and he showed very marked lesions in many organs. There was extensive pneumonia and pleurisy. Digestive tract showed a congested intestine. The spleen was haemorrhagic and the kidneys showed a few petechiae. Lymph glands of the entire body were swollen and congested. All gland-like structures in the cervical region were removed and sectioned.

Although the lung lesions in this last posted animal were the predominating post-mortem findings, and the primary cause of death was very likely a pneumonia, this case somewhat resembled hog cholera. Therefore when the remaining operated pig, the black and white boar, showed a slight temperature a few days later and was off feed, he was given 60 cc. of hog cholera serum. A blood inoculation would have been made from this animal to determine if he really had cholera but no known susceptible pigs could be obtained at that time. The boar's condition remained about the same for a few days. Then he grew worse, and died on February 20, 1916. Post mortem examination revealed pneumonia and pleurisy involving both lungs, and pleura, gastritis blood stained stomach contents, lymph glands of thorax congested and swollen.

The kidneys showed a few petechia, but all other organs were normal. All glands from the cervical region were removed and sectioned, as in the case of the other operated pigs.

The remaining check pigs did not become sick, the appetite remaining good, and they did not show any rise in body temperature.

Discussion of Death.

All of the operated pigs died, the female with the mummified fetus first and the boar last. They all showed extensive lesions with those of pneumonia and pleurisy predominating and constant. Only one check pig died and this was the pregnant sow. She showed only slight lesions of pneumonia.

Death in these animals was in the opinion of Dr. Kernkamp and myself caused primarily by pneumonia. Pneumonia is rather common in pigs during the winter months. During cold weather the pigs will pile up on one another. Those on the bottom become very warm and later when they come in contact with the cold air chill and if their resistance is low are quite apt to develop pneumonia.

While some of these pigs showed slight lesions of cholera, they were not typical. Further, these pigs had been given serum when young and very likely became actively immune. If they were not,they would certainly have shown symptoms in the fall shortly after being placed in the shed occupied by virus pigs. The boar which died last was given serum when he first showed signs of sickness. Serum is sometimes effective as a curative agent for cholera, especially when administered early and in large doses.

Microscopic Study of Tissues Removed.

At the time of the post mortem examination, all glands in the region of the larynx and trachea were removed and sectioned. These structures varied in size from a small seed up to that of a large bean or hickory nut. Most of the smaller glands proved to be lymph glands but in each operated pig several glads were found which proved to be accessory thyroids. The glands were for the most part located at or near the thoracic inlet along the trachea. The

largest accessory thyroid was found in the case of the black and white boar No. 6938. The gland measured 4 cm. long and 2.5 cm. wide and ½ cm. thick, located along the ventral surface of the trachea at the thoracic inlet. The alveoli in the accessory thyroids were about the size of those found in the thyroid of the week old pig.

Remarks

Definite conclusions can hardly be drawn from such a small number of animals, but owing to the fact that the variations from the normal in these three animals were so constant, I believe I am justified in drawing the following conclusions:

(1) Cretinism can not be induced in the pig by removing the thyroid owing to the fact that the accessory thyroids undergo compensatory hypertrophy which serves the function of the thyroid in its absence.

(2) That the thyroid gland does in some way play an important part in the normal body resistance and when removed, the accessory thyroid structures can not completely compensate this action. This fact is demonstrated by the lowered resistance which all of the operated pigs showed at some time during their lives, and finally the death from pneumonia, and the extensive tissue changes in the operated pigs as compared with the tissue changes which took place in the one check which died as a result of this disease.

(3) Slightly impaired thyroid function, though not sufficient to lead to marked changes in physical appearance of the animal, can apparently lower body resistance to quite a degree and impair the functions of reproduction, but this latter fact needs further investigation.

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