

THYMECTOMY IN THE RABBIT.

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PLATE 1.

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Despite extensive investigations, the effect of surgical removal of the thymus in animals is still somewhat uncertain. This uncertainty is due, in part, to the difficulty that has been experienced in distinguishing between effects of thymoprivia and effects that might be attributable to other causes, especially complications arising during or subsequent to operation, postoperative care of animals, and the use of methods that give varying degrees of success with respect to operative injury and complete removal of the gland.

In the course of studies that were being carried out in these laboratories, it became desirable to compare the behavior of thymectomized rabbits with that of normal rabbits and rabbits from which other glands had been partially or completely removed. This necessitated an investigation of the operation of thymectomy itself and the immediate or early results of removal of the thymus. It was necessary, first, to devise an operation that could be depended upon for complete removal of the thymus with a minimum loss of animals, and, second, to determine whether the thymus could be removed from rabbits of certain ages without producing any serious impairment of health, within specified periods of time, which would interfere with their use in other experiments. A preliminary report on one phase of this work has been published (1). The object of this paper is to report the early or immediate results of thymectomy, obtained by a method that was developed for use in connection with the experiments referred to above.

Methods.

As the success of any experimental study of thymoprivia hinges upon the operation, it will be described in detail.

Reviews of the various methods which have been recommended for removal of the thymus in animals may be found in the papers by Asher (2), Matti (3), and Park and McClure (4). The two principal types of operation are represented by the closed method of Friedleben (5), which was introduced in 1858, and the open or transthoracic operation suggested by Basch (6-9) in 1902. In the method of Friedleben, an incision is made at the base of the neck, exposing the upper poles of the thymus; these are seized with blunt forceps and the gland withdrawn from the chest without attempt at hemostasis. At best, complete ablation is not certain by this approach and mortality is high.

In the transthoracic operation of Basch, the mediastinum is exposed anteriorly by splitting the sternum and the gland is removed by dissection. Unfortunately, Basch left no detailed description of his technique. The method has been modified by MacLennan (10) for use in rabbits, by Ranzi and Tandler (11), who introduced the Sauerbruch chamber, and by Klose and Vogt (12-15) and Park and McClure (4) in using positive pressure anesthesia.

Method Used.—The method of operation employed by us is essentially that of Basch, adapted to the rabbit. All operations were done under ether anesthesia; at first, we used positive pressure apparatus for the prevention of pulmonary collapse but found that this measure might be omitted.

Regional Anatomy.—The thymus of the rabbit is a bilobed organ, flat and roughly triangular in shape. It lies almost entirely within the chest and occupies the anterior mediastinum, the lobes uniting along the midline. The base of the gland usually lies at the level of the fourth rib; the apex reaches through the upper thoracic strait and in the form of two separate strands follows the carotid arteries upwards a variable distance into the neck; the lateral margins of the lobes lie in contact with the pleuræ. Ventrally the thymus is confronted by the chest wall, from which it is separated only by an aponeurosis containing muscle fibres, the substernal extension of the pretracheal muscle layer. Behind the thymus at its lower third is situated the base of the heart covered by the pericardium, at its middle third the aortic arch, and behind its apex is located the great carotid trunk which bifurcates at this point to form the two common carotid arteries. The blood supply of each lobe is received at the lateral margin at the level of the first rib, the artery branching usually from the corresponding internal mammary, and the vein contributing to the subclavian vein (see Fig. 2). Occasionally the gland receives a branch underneath from the carotid artery. The intrathoracic portion of the thymus is encased in loose, cellular connective tissue, which can be made to separate easily, but in the neck the gland processes are held firmly attached to the adjacent vessels. Important nerve structures, as for instance the vagus and phrenic, lie well behind and lateral to the thymus and are not encountered in the operative field. There is one other structure to be noted. This is a vein of good size that runs transversely in a position just above the upper end of the sternum and superficial to the pretracheal muscle layer and connects the jugular veins.

Operation.—On the day of operation, the usual feeding should be omitted. The

fur over the neck and chest is clipped and the skin is shaved from the larynx to the ensiform, dried, and treated with alcohol.

Ether is given by the ordinary open cone method. The animal is draped with two towels wrung out of 1:10,000 bichloride solution, the margins meeting in the midline over the field of operation and widely overlapping elsewhere. The operator should work from the left side.

The incision is made in the midline from the level of the fifth rib to the thyroid cartilage, and the skin is excluded from the operative field by clamping its edges to the margins of the draping towels. The incision is then continued into the left pectoral muscle, following the margin of the sternum from the fifth rib upwards to the base of the neck, where the attachment of the left sternomastoid muscle to the sternum is also divided. This exposes the costal cartilages at their sternal extremities together with the adjacent intercostal muscles. The soft tissues of the neck are entered along the midline by incising between thumb forceps, exposing the trachea from the sternum to the larynx. During this procedure the transverse vein at the base of the neck is sought for, double clamped, and divided. The thorax is then opened as follows: The upper end of the sternum is elevated with thumb forceps and the tissues are separated from its under surface by blunt dissection for a distance of about 1 cm. This permits the blade of a pair of scissors to be inserted beneath the first left costal cartilage close to the sternum and this structure divided without injury to the underlying parts. Elevation of the sternum is maintained while the second, third, and fourth ribs and adjacent intercostal muscles are cut at the left sternal margin. Bleeding from the intercostal vessels is controlled with clamps. The extensive opening into the chest thus obtained is prevented from diastasis by the presence of the substernal aponeurosis, and this must be divided with scissors. The incision may then be widely opened and the anterior mediastinum brought to view (see Fig. 1).

Before proceeding further, preparations are made for the closure of the chest. For this purpose a heavy silk suture is passed about the tip of each cut rib and tied as illustrated in Fig. 1. Care should be taken to avoid piercing the internal mammary vessels. Sutures are also passed and tied around the sternum just above each rib stump. One end of each suture is left long after tying, to form a leash of four threads attached to the bony framework on each side of the thoracic incision. These serve temporarily as retractors.

Removal of the thymus is now begun, commencing at the apex. One of the tongue-like processes of the gland in the neck is grasped with thumb forceps and separated by blunt dissection from the corresponding carotid artery as far downwards as the aortic arch. The other apical tag is freed in the same way (see Fig. 2). This dissection is somewhat difficult because of firm attachments and must be done with care, and one should watch for the glandular vessels that occasionally spring from the carotids. Then the base of the thymus is located in the pericardial fat; its edge is picked up in the midline, and by drawing upwards upon it the gland is peeled away readily, and without dissection, from the pericardium. A tunnel is now burrowed beneath the thymus from top to bottom, and through this is

passed a thread to act as a retractor. Separation of each lobe margin from its pleural attachment is now undertaken. The lower edge of a lobe is grasped near to the pleura with fine mouse tooth thumb forceps and separated by gentle traction (see Fig. 2). The pleural leaf in the rabbit is exceedingly delicate and will rupture at the touch of an instrument. All dissection must be avoided and separation accomplished by traction alone, although it is of advantage at times to wipe the pleura gently away from the gland with a small wet gauze sponge. A steady pull upon the lobe margin serves to anchor the gland, and the respiratory undulations and cardiac pulsations furnish sufficient pull to disengage the gland from the pleura. 3 or 4 minutes time may be required for each side. Should the pleura be injured, the rent must be stopped immediately by a wet sponge to prevent complete collapse of the lung. Once both lateral margins are free from the pleuræ, there remains only the hilus of each lobe to be dealt with. By blunt dissection, the fatty tissue in the region of the first rib on either side is cleared away and the glandular vessels brought to view (see Fig. 2). With these secured the gland may be removed.

Closure of the incision is done in three tiers. The chest wall is brought together by tying corresponding ligature ends; the divided muscles are united by a running, heavy silk suture; and the skin margins are approximated with a fine silk suture. No dressing need be applied.

Material.

The operation described above was performed on 50 male rabbits; of these 36 were between 1 and 2 years of age, 8 were 3 years old or more, and 6 were between the ages of 4 and 6 months. 36 of the rabbits that survived operation were subsequently inoculated with tumor or *Treponema pallidum*; the others were held for control observations. The period of observation prior to inoculation was from 10 to 22 days, in most instances 2 to 3 weeks; 29 of the 36 rabbits survived the inoculation and permitted observation over a period of from 2 to 7 months. The majority of the uninoculated rabbits were observed for approximately 3 months.

RESULTS.

Operative Results.—Among the 50 rabbits on which thymectomy was performed there were 5 deaths related immediately or remotely to the operative procedure. 1 of these was due to air embolism, and the others to shock. In our last series of 29 operations there was only 1 death; this occurred in an old animal. Pneumothorax occurred

on the right side in 14 cases, on the left in 4 cases, and bilaterally not at all. There were no ill effects from the pneumothorax.

The chest wall incision united firmly in all of the animals that survived the operation with very little deformity of the thoracic framework and no interference with the function of the fore legs.

Postmortem examination showed that removal of the thymus was complete in all but one animal so far as could be determined, without resorting to microscopic examination. In one rabbit, a small nodule of thymic tissue was found high in the neck; this may have been overlooked at the time of operation. If any fragments were left, they showed no appreciable tendency to hyperplasia. The thymic bed was obliterated by firm fibrous adhesions between the pericardium and the chest wall and the lungs were expanded to their normal proportions.

Postoperative Complications.—Wound infection occurred in 8 animals. Usually an abscess developed within the mediastinum. These infections became encapsulated and pursued a chronic, indolent course which in most cases did not appear to affect the general health of the animals. There were no pulmonary complications, except in the preliminary operations in which intubation of the trachea was done for positive pressure anesthesia. Several of these animals developed pneumonia, atelectasis, or empyema.

Effects of Thymoprivia.—Our study of the effects of thymoprivia was limited to observations on the general physical condition and the reaction of operated rabbits to disease. The results of the latter investigation will be reported elsewhere.

Removal of the thymus produced no appreciable effect on the general health and state of nutrition of the animals. Recovery from the operation was prompt and the operated rabbits showed a gain in weight or a maintenance of weight comparable in all respects to intact normal rabbits. A number of these animals were observed over a period of from 2 to 7 months but during this time no difference in the appearance and physical condition of thymectomized and of normal rabbits was detected. The behavior of young, adult, and old animals which had been operated upon was essentially the same.

DISCUSSION AND CONCLUSIONS.

Thymectomy in the rabbit is a comparatively simple procedure. The open method described above offers many advantages over any of the closed methods and success depends largely upon the observance of a few precautions; chief among these is the avoidance of haste and the observance of aseptic technique.

The operative mortality in our series of rabbits was 10 per cent and there was an additional loss of useful animals, due to secondary complications, amounting to 16 per cent. Among the last 29 rabbits, however, there was only 1 operative death, in an old animal, and 2 cases of slight infection. It appears, therefore, that with some experience the operation can be carried out successfully in nearly all animals, especially so if comparatively young rabbits are used. Old rabbits present greater difficulties on account of the presence of dense fibrous tissue within the field of operation.

While the animals of this series showed no immediate symptoms or alteration in physical condition that could be referred to thymoprivia, it is not to be assumed that removal of the thymus is entirely without effect even on rabbits of mature age. Our observations on the reaction of thymoprivic rabbits to disease show that this is not the case and that in all probability decided effects can be demonstrated if the problem is approached on another basis. The object of the present investigation was, however, to determine whether the thymus could be completely removed from rabbits of certain ages without producing any serious disturbance of health which would interfere with their use in other experiments or complicate the interpretation of results. It was found that this could be done.

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EXPLANATION OF PLATE 1.

FIG. 1. Thymus exposed preparatory to removal.

FIG. 2. Technique employed in removal of the thymus.

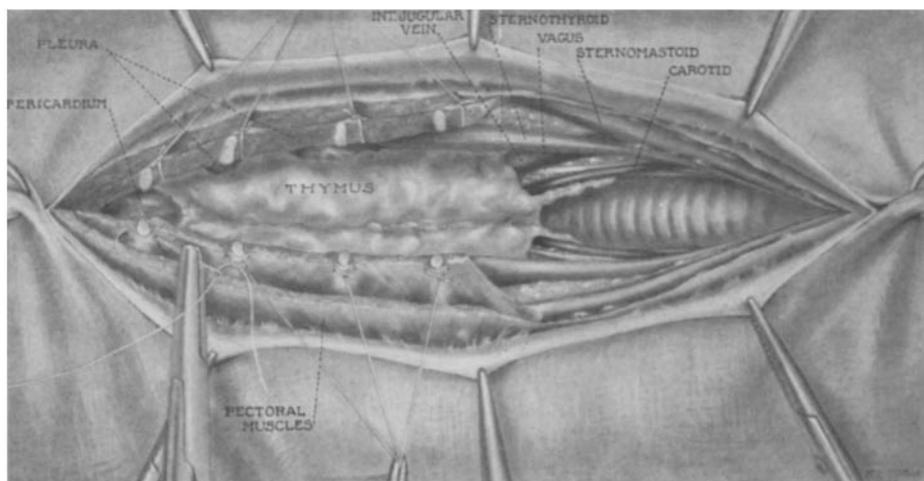


FIG. 1.

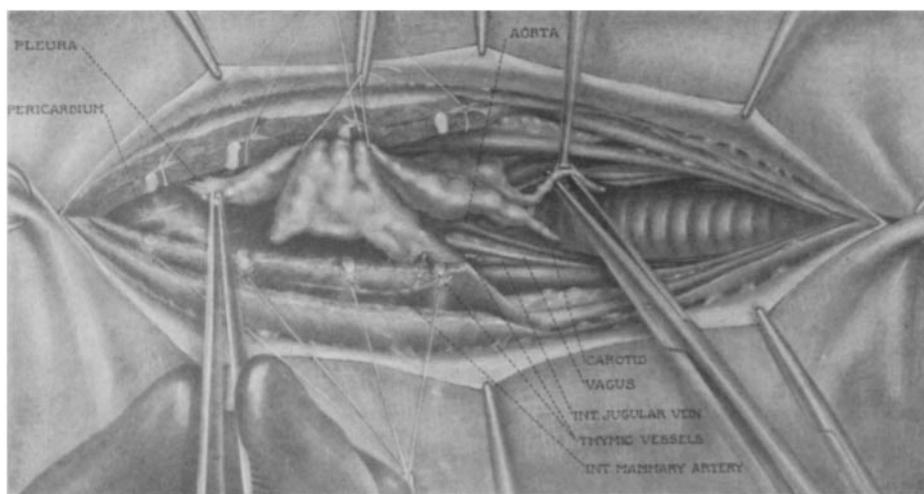


FIG. 2.

(Van Allen: Thymectomy in rabbit.)