

THE POST-NATAL CHANGES IN THE THYMUS OF
GUINEA-PIGS, AND THE EFFECT OF CASTRA-
TION ON THYMUS STRUCTURE. BY ALEXANDER
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It has recently been shown by Henderson⁽¹⁾ that castration in cattle, rabbits and guinea-pigs causes a persistent growth and a retarded atrophy of the thymus gland.

During the course of a research by Dr Noël Paton and myself⁽²⁾, a large amount of material has accumulated in the laboratory, giving me an opportunity of ascertaining whether Henderson's results as regards the size of the thymus have any relationship to histological structure. At the outset I was met with the difficulty that the thymus in normal animals shows great diversity in histological characters according to age. A necessary preliminary study, therefore, was the changes which normally occur in the thymus. As the series of specimens derived from guinea-pigs was practically complete, I have confined myself to observations on these animals.

Methods. The thymuses had either been removed under anæsthesia by Dr Noël Paton during life, or were removed immediately after death. The weight of the animal and the weight of the thymus were noted. The specimens were fixed in formal-alcohol, cut in paraffin, and stained with methylene-blue and eosin, iron hæmatoxylin, and hæmatein and eosin. In the case of the castrated animals the operations had been performed under full anæsthesia by Dr Noël Paton before the animals were a week old.

In the guinea-pig, the thymus at all stages has the following characters. It consists of two lobes situated entirely in the neck. Each lobe is subdivided by means of a small amount of fibrous tissue, more or less fatty, into lobules. In median longitudinal section about 30 such lobules are visible to the naked eye; in cross section at the

broadest part about 20. In stained sections each lobule shows a lightly stained central area and a more deeply stained cortex.

As Schedel⁽⁹⁾ has pointed out, germ centres as seen in lymph glands and spleen do not exist in the thymus. Schedel further holds that cell-division (indirect) occurs mainly in the cortex. I consider that each lobule is comparable to a typical germ centre. Mitotic figures are numerous, and the lymphatic vessels around the lobules contain a large number of lymphocytes, and from these facts, along with the observation of Dr Noël Paton and myself⁽⁹⁾, that removal of the thymus causes a slight leucopenia which persists while the thymus is active, may be taken as proof that the thymus is a source of lymphocytes of considerable importance.

In the centre of each lobule one or more Hassall's corpuscles may be found.

For further examination I have classified the material as follows.

A. *Normal Animals.*

Series	Limits of weight of animal	Number of animals observed	Average weight	Average weight of Thymus	Percentage weight of Thymus
1.	Under 100 grms. (Under a week old)	3	71	·12	·16
2.	100 to 150 grms. (Under 14 days old)	5	141	·156	·111
3.	150 to 200 grms. (Under a month old)	12	173	·253	·136
4.	200 to 300 grms. (About 2 months old)	12	251	·294	·109
5.	Over 300 grms. (Over 2 months old)	8	419	·394	·09

B. *Castrated Animals.*

<i>a. Males.</i>					
6.	Over 300 grms.	4	379	·582	·15
<i>b. Females.</i>					
7.	Over 300 grms.	5	432	·646	·15

SERIES 1 AND 2. GUINEA-PIGS WEIGHING UNDER 150 GRMS.

At this stage the lobules are never invaded by fat. The lymphocytes are not very densely packed, and the reticulum is fairly evident. The cortical and medullary portions of the lobules are distinct, but the cortical area is not very large.

Hassall's corpuscles are numerous and large. Typical "concentric corpuscles" are practically absent.

In the medullary portions of the lobules irregularly shaped islands of squamous epithelium may be seen. In many cases these are lying among the lymphocytes with no definite arrangement (Figs. 1 and 3 *e*). Occasionally long strands of epithelium may extend almost from end to end of the medullary portion.

A more common appearance is a large rounded mass of degenerated epithelial cells. In some cases, round these larger masses, the fibres of the reticulum of the lymphoid tissue may form an apparently homogeneous membrane; in some cases its cells may form a definite endothelium. Bunting⁽⁴⁾ has recently shown that the cells of the reticulum form an endothelium in lymphatic glands. The masses of epithelial cells in Hassall's corpuscle become invaded with polymorphonuclear leucocytes, and later by lymphocytes. These leucocytes cut off layers of epithelium, and both epithelium and leucocytes degenerate, and the latter soon lose their pseudo-eosinophil granulation.

In some cases the leucocytes cut off a central mass of cells which rapidly degenerate as their source of nutrition has been cut off, while the epithelium of the outer part of the epithelial perle (Gulland⁽⁵⁾) remaining in contact with the lymphoid tissue, remains for a longer time undegenerated. As the central degenerated mass stains with acid dyes, this appearance has given rise to the view that the Hassall's corpuscles are blood vessels whose endothelium has proliferated, containing fused and degenerated blood corpuscles (Afanassiew⁽⁶⁾). This view has been contested by Watney⁽⁷⁾. Vessels may be seen in relationship with the Hassall's corpuscles, and may degenerate with them, but the masses of epithelium are altogether outside them.

This appearance has also been interpreted as the presence or persistence of ducts in the thymus (Schambacher⁽⁸⁾). The interpretation occasionally gains in plausibility from the fact, that in a few cases the central necrosed mass may have altogether disappeared from the section. Both these views, however, absolutely fail to account for the presence of compound concentric bodies.

Instead of cutting off only one more or less central mass of epithelium, the polymorphonuclear leucocytes may cut off several such masses, which will later become concentric corpuscles, and thus we may find a large Hassall's corpuscle actually containing three or four smaller corpuscles within itself.

Wallisch⁽⁹⁾ has recently shown that the total volume of the Hassall's corpuscles in young children, up to the age of six months, is greater than the total volume of the whole thymus in a three months

embryo. He therefore objects to the view that the corpuscles are epithelial "rests" (Stieda⁽¹⁰⁾), and also holds that this view fails to explain the concentric form of the corpuscle. So long as the epithelial island is intact, there is no reason why it should not grow in proportion to the rest of the organ, and in the first stage of leucocyte invasion it may further gain in volume. The concentric character of the corpuscle, as seen on section, necessarily arises from the fact that large squamous cells are separated by leucocytes, and compressed by the surrounding adenoid tissue. A simple concentric corpuscle will eventually be formed, whether it has passed through a "compound" stage or not.

Source of the granular leucocytes. The appearance of numerous granular leucocytes in the neighbourhood of the Hassall's bodies has given rise to the view that these cells are formed in the thymus (Schaffer⁽¹¹⁾, Beard⁽¹²⁾).

The polymorphonuclear cells (pseudo-eosinophils) found in the Hassall's corpuscles are mostly degenerated. They are certainly not formed there and can quite readily be traced in from the vessels in the neighbourhood. Thus the post-natal thymus is not capable of itself

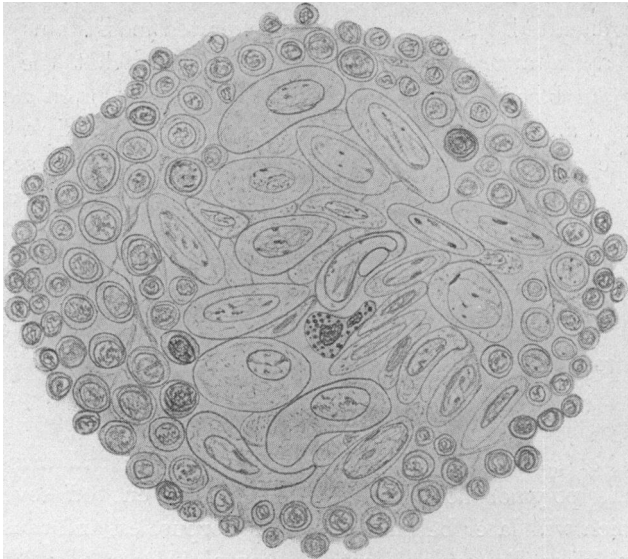


Fig. 1. Centre of a thymus lobule from a guinea-pig on day of birth, showing an epithelial island into which a polymorphonuclear leucocyte has wandered.

producing those cells which are requisite for the removal of the epithelial masses it contains. As the present research does not deal with the

embryo thymus I am unable to controvert the view that the thymus produces granular or polymorphonuclear leucocytes, but I think its indications are much more in favour of the views of Bryce⁽²⁸⁾ who has recently found that granular leucocytes are present in lepidosiren before the thymus contains lymphoid elements.

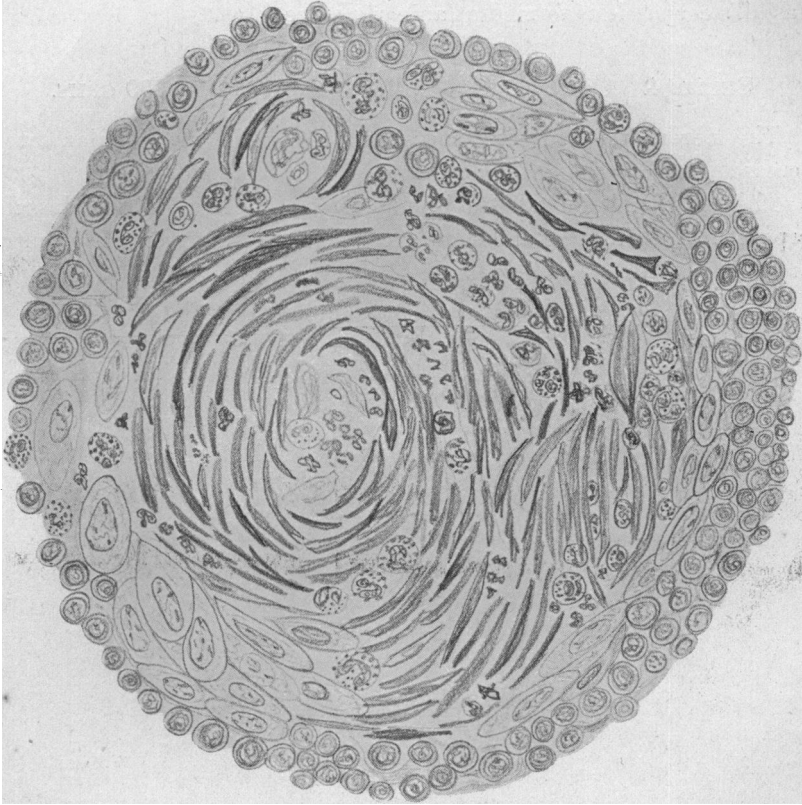


Fig. 2. Large Hassall's corpuscle from a guinea-pig on day of birth. Polymorphonuclear leucocytes have invaded and broken up the epithelium. The central cells have degenerated (they are stained deeply with eosine). On the left side a "concentric corpuscle" is being formed.

SERIES 3. GUINEA-PIGS WEIGHING FROM 150 TO 200 GRMS.

In this group the intralobular fat is increased but the lobules are not encroached on. The interlobular fibrous tissue is more vascular. The cortical area is relatively larger and the lymphocytes seem more densely packed.

A few specimens show unaltered epithelial islands but the majority of the Hassall's corpuscles show infiltration with polymorphic leucocytes. Along with these large Hassall's bodies small concentric corpuscles are seen in the medullary portion of many of the lobules. These may be simple or compound according to the nature of the leucocyte invasion, and if the original island of epithelial has been small a simple concentric Hassall's corpuscle is formed at an early stage.

SERIES 4. GUINEA-PIGS WEIGHING FROM 200 TO 300 GRMS.

The fibrous tissue is still more vascular. The interlobular fat is increased and may slightly encroach on the lymphoid tissue.

There are no uninvaded epithelial islands. Many of the Hassall's corpuscles are still large and show great leucocyte invasion. Concentric corpuscles are numerous.

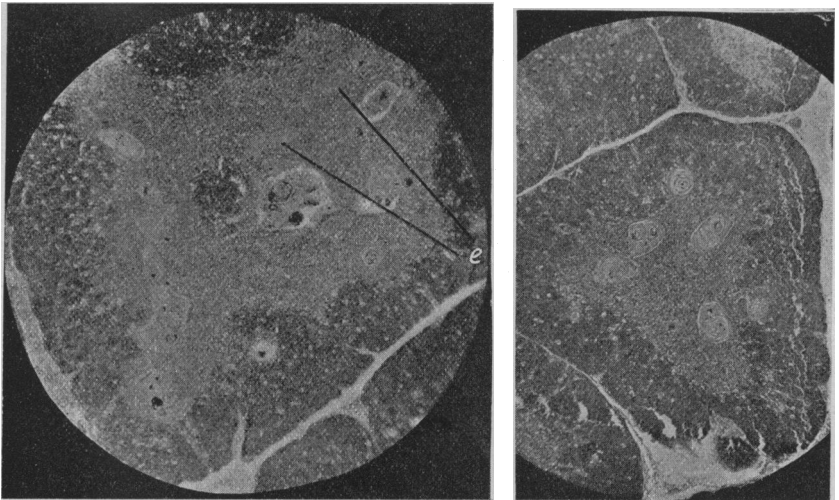


Fig. 3. From guinea-pig weighing 170 grms. *e.* Islands of squamous epithelium. Also shows infiltrated and degenerated epithelium and formation of simple and compound concentric corpuscles.

Fig. 4. From guinea-pig weighing 250 grms. Iron hæmatoxylin.

SERIES 5. GUINEA-PIGS WEIGHING OVER 300 GRMS.

In animals between 300 and 400 grms. the appearances are practically identical with those of the last group, but after the animal has attained

a weight of 400 grms. the thymus begins to undergo a marked change which is very well marked in animals over 500 grms.

Three of the animals over 500 grms. (average 533) had an average thymus weight of .15 and an average percentage weight of only .03. In the older animals there is great fatty encroachment so that the thymus lobules are widely separated and some of them show an arrangement of lymphocytes between the fat cells like the arrangement in bone marrow. In the latter no trace of Hassall's corpuscles can be found. Wherever masses of lymphoid tissue persist, uninvaded by fat, the arrangement into a cortical and medullary portion persists and in the medulla small concentric corpuscles can frequently be found.

SERIES 6 AND 7. CASTRATED ANIMALS WEIGHING OVER 300 GRMS.

No essential difference exists between the thymus of the males and that of the females. The whole organ shows increased vascularity both in the interlobular fibrous tissue and in the lymphoid tissue. The interlobular fibrous tissue is fatty, but there is no fatty invasion of the lymphoid tissue. The lobules are large. The cells seem tightly packed and there is a wide cortical zone. The Hassall's corpuscles are for the most part large and show polymorphonuclear leucocyte infiltration. There are some areas of unaltered epithelium and a few small concentric corpuscles—in a word the arrangement of Hassall's corpuscles is precisely that described in the case of guinea-pigs weighing between 150 and 200 grms. (Series 3).

It would therefore appear that castration causes a persistence and an actual increase of the activity of the growth of the lymphoid tissue in the thymus and at the same time produces a retardation of the process of disintegration of the epithelial islands, so that for the age of the animal, the Hassall's corpuscles appear unduly large and unduly numerous. How long this retardation persists may be the subject of further investigation.

SUMMARY.

1. In guinea-pigs the thymus at birth consists of lobules of adenoid tissue containing islands of squamous epithelium, many of which are invaded by polymorphonuclear leucocytes.
2. This invasion results in cutting off masses of epithelium from their source of nutrition, hence they rapidly degenerate and form a concentric Hassall's corpuscle.

3. If only one mass is thus cut off, a simple Hassall's corpuscle will result; if several such masses, a compound corpuscle which may for long remain surrounded by one or more of the peripheral layers of epithelium which have not been cut off from the lymphoid reticulum and hence do not degenerate.

4. As has been shown by others, with advances in age of the animal the Hassall's corpuscles become small and largely disappear, while the lymphoid tissue diminishes and becomes to a great extent replaced by fat.

5. The post-natal thymus is a source of lymphocytes, but does not produce pseudo-eosinophil or eosinophil leucocytes.

6. I can confirm Henderson's observation that castration produces a persistent growth and a retarded atrophy of the thymus in guinea-pigs.

7. This is due, histologically, to a persistent growth of the lymphoid tissue, a delay of the fatty invasion and a delay in the process of disintegration of the epithelium composing the Hassall's corpuscles.

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