

## THE SECRETION OF THE THYMUS GLAND

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A study of the thymus gland in children dying from various diseases showed that the contents of the involuted thymic corpuscles are emptied directly into lymphatic sinusoids in a parenchyma of the gland.

Most workers associate the secretory function of the thymus with its reticulo-endothelium and, in particular, with the formation of thymic corpuscles\* [1, 8]. The view has been expressed that the humoral factor produced by the reticulo-epithelium is transported outside the gland by the thymocytes [11-13, 16].

### EXPERIMENTAL METHOD

The dynamics of morphological changes in the thymus gland was studied in children with various pathological conditions [5, 6]. Besides a systematic study of the state of the thymus undertaken in the post-mortem department of the No. 1 City Children's Hospital during the last six years, a special investigation was made of the thymus from 133 children, of whom 54 died between the ages of 1 year 6 months and 15 years from leukemia, 24 between the ages of 1 and 8 years from malignant tumors, 39 between the ages of 1 day and 10 years from infectious diseases, and in 16 cases from stillborn infants and from newborn infants dying from intrauterine asphyxia and birth trauma during the first two days after birth.

The thymus was investigated microscopically in sections stained by the methods of Paccini, Foot, Goldman, Brachet, and McManus, and also with hematoxylin-eosin and Sudan black.

Because of the great variety of nosological forms and age groups in which the thymus was investigated, it was possible to make a dynamic study of the morphology of the reticuloendothelium and thymic corpuscles.

### EXPERIMENTAL RESULTS

The thymic corpuscles were found to have an extremely labile morphological structure directly dependent on the age of the child and the character and duration of the disease. Activation of the thymic reticulo-endothelium during the first three phases of accidental involution (to use the author's terminology [6]), led to the formation of thymic corpuscles not only in the cortex, but also in the medulla of the gland. In the initial phases the thymic corpuscles appeared as small cellular formations which, as they grew, lost their cellular structure and were gradually converted into cysts filled with heterogeneous contents. Histochemically nucleoproteins, lipids, and mucopolysaccharides were found in the contents of the cysts. The walls of the cysts consisted of one layer of thin, flattened reticulo-endothelium. In the other cysts, the contents showed signs of liquefaction, and small lamellar structures resembling individual small thymic corpuscles, floated in these liquid contents. These large cysts were named "mature" thymic corpuscles. Some of the thymic corpuscles contained eosinophilic and neutrophilic leukocytes, lymphocytes, and erythrocytes. A distinctive type of picture was frequently seen: usually in phase III, wide lacunae or sinusoids,

\*Thymic corpuscles is the name given to Hassall's corpuscles in the *Nomina Histologica* [15].

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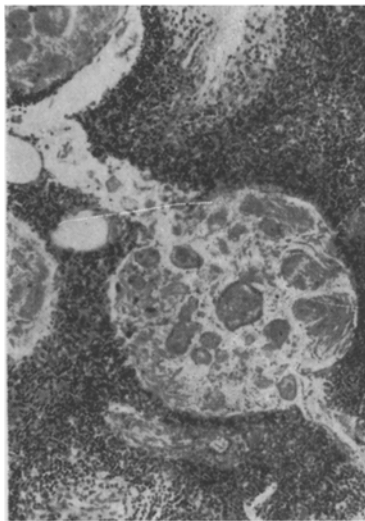


Fig. 1. "Mature" thymic corpuscle in stage III-IV of accidental involution of the thymus. The thymic corpuscle appears as a cyst with heterogeneous contents, discharging into a broad lacuna. Hematoxylin-eosin, 100  $\times$ .

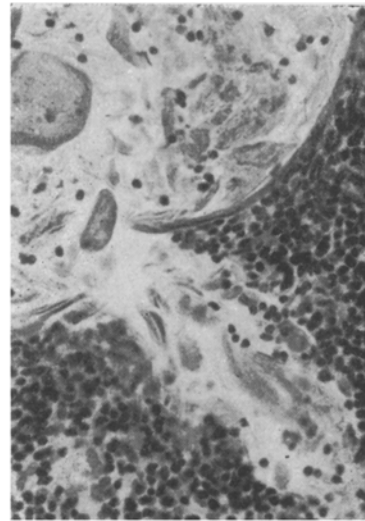


Fig. 2. "Mature" thymic corpuscle and evacuation of its contents. Rupture of reticulo-epithelial lining with discharge of contents of thymic corpuscle into lacuna. Contents of corpuscle include many formed elements of lymph. Hematoxylin-eosin, 200  $\times$ .

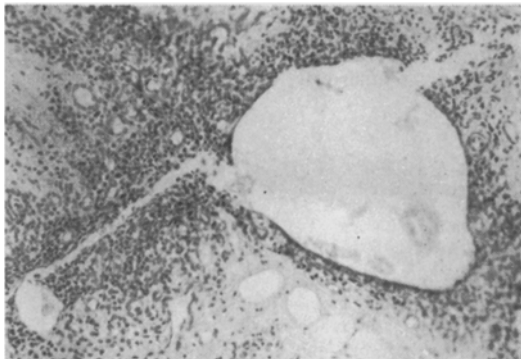


Fig. 3. Thymic corpuscle after emptying. Remnants of contents in corpuscle and collapsed lacunae are visible. Hematoxylin-eosin, 100  $\times$ .

without distinct walls and filled with protein contents in which lamellar structures resembling thymic corpuscles floated, were found in the tissue on the gland (Figs. 1 and 2). The formation of these wide spaces or lacunae, containing elements of thymic corpuscles, and also the presence of formed elements of the lymph in the thymic corpuscles, raise the question whether there is any direct connection between the thymic corpuscles and lymphatic system of the glands. Serial sections through the thymus were investigated (every 5th section, altogether 2000 sections) in three cases: from an infant aged 11 months with chicken pox complicated by septicemia, from a child aged 4 years with a reticulosarcoma of the small intestine, and from a child aged 9 years with acute lymphatic leukemia. In all three cases the thymus was in phase III or IV of accidental involution.

The investigation showed that these spaces in the thymus are dual in character. Some lie in the parenchyma of the gland and have indistinct outlines and walls; they are either wide lacunae or narrow, long clefts. When stained by Paccini's method, delicate connective-tissue fibrils were detected in their wall, and no endothelial lining was apparent. Others, lying in the septa of the lobes of the gland, have walls with a more definite structure, with a clearly defined endothelial lining. They can be described as lymphatic vessels.

The character of the connection between spaces in the parenchyma and the thymic corpuscles discovered in this investigation, which is directly connected with the problem of the ways by which the thymus discharges its secretion into the lymphatic system, is most interesting. Serial sections revealed the mechanism of emptying of the thymic corpuscles into the lymphatic spaces (Fig. 2). This emptying process was observed in "mature" thymic corpuscles. At a certain stage, focal destruction of the reticulo-endothelial lining took place, so that it ruptured and the contents of the "mature" corpuscle escaped into

the spaces in the parenchyma. The thymic corpuscles were emptied, the spaces collapsed (Fig. 3), but the ultimate fate of the thymic corpuscles has not yet been determined.

Some workers [3, 10] have considered that the parenchyma of the lobules of the thymus gland contains numerous lymphatic spaces or extremely fine capillaries, while others [9] stated that the medulla of the human thymus has no lymphatic capillaries. Ikonnikova [7] injected the lymphatic vessels of the thymus and showed that they are present both in the cortex and in the medulla. Vorob'eva [4] found that the lymphatic capillaries of the thymus form a deep, continuous three-dimensional network in the medulla and cortex of the gland. She showed that the lymphatic capillaries surround the thymic corpuscles, form a deep network in the parenchyma, and then empty into the lymphatic vessels of the interlobular connective tissue. She postulated that contact between the thymic corpuscles and lymphatic capillaries allowed removal of the secretion from the gland.

It was possible to shed further light on this problem only after the study of the pathological thymus. In the phase of functional rest, no lymphatics could be found in the parenchyma of the thymus. Not until phase III of accidental involution were lymphatics visible, a result attributable in part to the sharp decrease in number of the thymocytes with the formation of a reticulo-epithelium, and the more rapid rate of formation and maturation of the thymic corpuscles.

It is concluded from the results of these observations that secretion accumulating in the thymic corpuscles of the gland is discharged through rupture of the lining of these corpuscles into the deep lymphatic network of the parenchyma. This mechanism of discharge is analogous to the phenomenon of rupture of the Graafian follicle at the times of ovulation. Accumulation of secretion in the thymic corpuscles through degeneration and death of the reticulo-epithelial cells is similar to the holocrine type of secretion, the only difference being that secretion of the thymus is discharged not by ducts, but by lymphatic capillaries, i.e., it enters the internal medium of the organism directly in accordance with the principle of incretory secretion.

However, the morphological data alone are insufficient to prove conclusively that the secretion of the thymic corpuscles is the same humoral factor of the thymus which regulates lymphopoiesis and immunogenesis, and that the cells of the reticulo-epithelium outside the thymic corpuscles are functionally inactive. This investigation of the mechanism and pathways of secretion of the thymus cannot be regarded as complete, and further study of this problem is required.

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