
**CLINICAL AND MORPHOLOGICAL FEATURES OF THE
THYMUS STRUCTURE**

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Resolution. *Despite extensive knowledge about the morphofunctional state of the thymus in conditions of physiological norm, the literature presents isolated works devoted to the study of its accidental involution in general and the epithelial component in particular in various pathological processes. The article presents modern literature data on the structure and development of the thymus.*

Key words: *thymus, ontogenesis, thymocytes*

The thymus is the central, or primary, organ of the lymphoid (immune) system. As is known, its main functions are to ensure the maturation and differentiation of thymocytes, the integration of various populations of thymocytes and macrophages for the implementation of immune responses. The morphofunctional state of the central organ largely determines the activity of the secondary (peripheral) structures of immunogenesis and the severity of protective reactions of the whole organism [16, 17, 23, 29]. In all mammalian animals, the thymus is located in the mediastinum. In humans, it is located in the anterior part of the upper mediastinum. The body of the sternum, the sterno-hyoid and sterno-thyroid muscles, the parietal pleura are attached to its ventral surface, and the pericardium, trachea, aortic arch, internal jugular and brachiocephalic veins, recurrent laryngeal nerve are attached to the dorsal surface [5, 8, 11, 12]. In rats, the thymus is localized in the ventral mediastinum. It is well known that the thymus consists of lobes. Back in the 19th century, it was noted that the number of lobes in the human thymus varies from one (when the right and left lobes merge) to five, which was confirmed in the 20th century. Nevertheless, it is believed that the main

variant of the structure of the human thymus is its two-lobed organization [1, 5, 24].

In rats, the thymus consisting of two lobes is also most common. At the same time, in adult rats, a thymus consisting of three lobes was found in 4.3% of cases, and in newborn rats, such a variant of the organ structure was found in almost 21.8% of observations [12, 15]. Like all parenchymal organs, the thymus is covered with a connective tissue capsule. The septa extending from it reach the boundary between the cortical and cerebral matter and divide the parenchyma into lobules of various sizes. Vessels and nerves pass through these partitions. Traditionally, two parts are distinguished in the lobule of the thymus: the cortical substance (cortex) is dark, with a dense arrangement of lymphoid cells (thymocytes) and the medulla is lighter, in which there are significantly fewer thymocytes, but reticular epithelial cells are well defined; thymus corpuscles are also detected here. 90 % of the cellular composition of the thymus is represented by thymocytes [3, 5, 8, 31, 34]. There is no consensus in the literature on structurally functional zones in the lobules of the thymus. Some authors distinguish four zones within the lobule:

- 1 — the outer subcapsular zone,
- 2— the inner cortical zone,
- 3 — medulla,
- 4 — perivascular connective tissue [25], others describe three zones:
 - cortical,
 - cortical-cerebral and
 - brain [6, 26].

Individual authors define four zones in the thymus lobule:

- subcapsular,
- internal cortical,
- medullary (medulla) and
- intra-lobular perivascular spaces.

However, in later studies, five zones began to be distinguished in the thymus lobule: three in the cortical substance (subcapsular, central zone of the cortex and

border with the medulla) and two in the medulla (zone bordering the cortex and central) [7, 19]. The subcapsular zone of the cortex is formed by a network of epithelial reticulocytes. The cells of this network contain prethymocytes, lymphoblasts, and a small number of macrophages [7]. In this department, proliferation takes place under conditions of a specific microenvironment and the initial stages of maturation of the prethymocytes that immigrated here from the bone marrow take place [28, 33]. In the inner cortical zone, which is formed by a wide-leaved network of reticular epitheliocytes, antigen-independent differentiation of thymocytes ends, selection and elimination of autoaggressive thymocytes are carried out, and mature autotolerant cells migrate into the medulla or exit the thymus in the cortical-medullary zone [23]. Thymocytes of the inner cortical zone account for up to 80% of all thymus lymphocytes and are characterized by the presence of T10, CD2, CD5, CD7, CD1, CD3, CD4 and CD8 antigens [7, 22]. Antigen-dependent maturation of thymocytes is carried out in the thymus medulla. This zone is formed by a dense network of epithelial reticulocytes, and its cells are small in size. Thymic corpuscles are also defined here. Thymocytes of this zone have the morphology of medium and small lymphocytes, have a high degree of differentiation, the ability to react to blast transformation, they have antigenic signs of helpers, killers and suppressors. From here they enter the bloodstream and thymus-dependent zones of the secondary organs of the immune system [20, 27, 30]. Thymus corpuscles (TT) defined in the medulla are formed from overlapping reticular epithelial cells (RE) with hyaline grains in the cytoplasm and dystrophically altered nuclei. Further, necrosis and calcification of the center of the forming thymus corpuscle sequentially occur. TT can be determined even after complete replacement of the thymus lobule with adipose tissue [3, 7, 21]. It is believed that TT serve as irritants for RE and cause accelerated proliferation, an increase in the size of the thymus and its colonization by lymphocytes [21]. In addition to thymocytes of varying degrees of maturity and RE, the cellular composition of the thymus includes interdigitating cells with phagocytic activity and, probably, providing antigens to thymocytes and activating lymphocytes at rest.

In the thymus, mast cells, granulocytes, plasmocytes, cells of the APUD system can be identified, and basophils in the interlobular connective tissue [7, 9, 20, 32]. The formation of the thymus in ontogenesis occurs earlier than other organs of the lymphoid system and endocrine glands. In humans, the rudiment of an organ in the form of paired epithelial strands is revealed at the 4th week of intrauterine development [20, 21]. In the early stages of development, paired strands of multilayer epithelium surround mesenchymal cells, which are believed to migrate from the neural crest. These cells develop a capsule, interlobular septa, and reticular tissue of the thymus [10]. At the initial stage of development, the epithelial rudiment of the thymus in the cervical part has a lumen — the thymopharyngeal duct, which subsequently, as a rule, undergoes obliteration. In rats, the epithelial rudiments of the thymus, located on the sides of the pharynx, are detected on the 12th-13th day of intrauterine development, and this period is defined as the period of "dense rudiment" [4, 13]. Further, during the 14-16 days of prenatal ontogenesis, mesenchyme and blood vessels are introduced into the epithelial lining of the organ, RE differentiation occurs and the organ is populated with lymphocytes [4]. During the 17th-19th days of intrauterine development of the thymus, its capsule, interlobular septa, lobules, intraorgan vascular bed and subcapsular zone are formed. By the time of birth, the formation of thymus lobules continues, the differentiation of parenchyma into cortex and medulla. The first lymphoid cells in the epithelial rudiment of the rat thymus are detected on the 14th day of intrauterine development. Initially, the cellular composition of the thymus is characterized by a large number of RE and lymphoblasts, and the content of medium and small lymphocytes is low. By the time of birth, the number of small and medium lymphocytes increases, a well-formed subcapsular zone consisting of 5-6 rows of cells is determined, mast cells appear in the perivascular spaces and interlobular connective tissue [13]. During the first month of postnatal life, the process of formation of new lobules slows down in the thymus of rats. The subcapsular zone is preserved only at the top of the lobules, and for the rest it is populated by small lymphocytes and disappears. In the lobules of the organ, the growth of brain matter

continues, in which TT is formed, their small number is a specific feature of rats [2]. After birth, both in the cortical substance and in the medulla, the number of small lymphocytes increases, while the number of medium and lymphoblasts decreases [4, 13, 14].

Thus, the formation of the main structures of the thymus occurs in humans at the 17th week of intrauterine development, and in rats it continues in the postnatal period of ontogenesis.

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