Journal of Korean Medical Science
Vol. 8, No. 6, 431-436 December 1993

Reticular Network of the Human Thymus

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To investigate the development of the reticular network of the thymus with aging and under pathologic conditions, we performed reticulin stains on the following samples; 5 fetal thymi (22 to 33 weeks of gestational age) and 35 postnatal thymi (less than 1 month to 33 years of age). The latter included 1 hyperplastic thymus, 4 pathologically involuted thymi and 1 physiologically involuted thymus as well as 29 normal thymi. Reticulin fibers were invariably seen along the capsule and interlobular septae of all the thymi. In fetal thymi, reticulin fibers circumscribed only cortical blood vessels and Hassall's corpuscles. Postnatal thymi from the children aged less than 1 month showed discontinuous reticulin fibers along the blood vessels of the corticomedullary junction. With aging, the amount of reticulin fibers increased and formed a "fibroreticular network(FRN)" from the branching point of the interlobular septae along the corticomedullary junction. It completely circumscribed the outer medulla in fully developed thymi. In the hyperplastic thymus, the reticular network retained its original structure. Both pathologically and physiologically involuted thymi revealed irregularly collapsed reticulin fibers. These findings suggest that the reticular network of the thymus consists of FRNs as well as capsule and interlobular septae and matures with aging before involution.

Key Words: *Thymus, reticulin fibers, fibroreticular network*

INTRODUCTION

Thymic structure is relatively well known on the basis of its cellular composition (Bearman et al., 1978;Janosy et al.,1980; Wood, 1985; Haynes, 1990; Suster and Rosai,1990). However the reticular framework of the thymus is poorly understood (von Gaudecker, 1986; von Gaudecker, 1991). The thymus as a lymphoepithelial organ has several types of epithelial cells, some of which form the network of the thymus (Weiss,1988). Although this network was thought to be made of epithelial cells alone without reticulin fibers, Rosai and Levin (1976) described reticulin fibers separating the cortex and the medulla in a hyperplastic thymus of a myasthenia gravis patient. In this study, we investigated the distribution of reticulin fibers in the normal human thymus with special emphasis on aging as well as pathologic thymi.

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MATERIALS AND METHODS

Thymic tissues were freshly obtained either during open heart surgery or from aborti ranging from 22 to 33 weeks of gestational age. Age distribution and diagnoses are summarized in Table 1. Postnatal thymi were obtained from patients aged from 5 days to 33 years during open heart sugery. Stress involuted thymi were obtained from patients with congenital heart diseases; atrial septal defect, and ventricular septal defect. The tissues were fixed in 10% buffered formalin and paraffin embedded. Four to six μm sections were made for hematoxylin and eosin staining and Gomori reticulin staining.

RESULTS

Thymic samples used in this study included normal thymi, hyperplastic thymi, and thymi of stress and age involution. Normal thymi were grouped by age as in Table 1. In fetal thymi, the lobular structure was well developed. The cortex was larger than the medulla and the corticomedullary junction was distinct. Cortical vessels were easily seen. In the medulla, Hassall's corpuscles were occasionally seen. By reticulin staining, capsule and interlobular septae were clearly delineated. In addition, reticulin fibers circumscribed cortical blood vessels and Hassall's corpuscles (Fig.1). Postnatal thymi from children aged less than 1 year showed well developed blood vessels in the outer medulla along the corticomedullary junction. Reticulin fibers were closely associated with the blood vessels. Fragmented reticulin fibers were also seen in the inner medulla (Fig.2). With aging, the reticular network became more complete. Blood vessels were more prominent and were completely circumscribed with reticulin fibers. They were connected with interlobular septae. The inner medulla consisted of Hassall's corpuscles which were concentrically surrounded by reticulin fibers (Fig.3). In the thymi of 1 year old children, the amount of reticulin fibers gradually increased especially at the terminal portion of interlobular septae, forming a so called "fibroreticular network (FRN)"(Lee et al., 1993) (Fig.4a). They encircled groups of thymocytes, epithelial cells and small arteries (Fig.4b). Thirteen cases from the children aged over than 1 year showed the well developed FRN.

In stress involuted thymi, their cortex was diffusely thin due to depletion of thymocytes and the corticomedullary junction was indistinct. Cortical lymphocytes were depleted and subcapsular epithelial cells were distinctly clustered. Tingible body macrophages were diffusely scattered. Blood vessels were relatively increased in contrast with normal thymi of the same age. Reticulin fibers increased in parallel with blood vessels throughout the cortex and the medulla (Fig.5). Age involuted thymi showed marked fatty infiltration along the septae and depletion of the cortex. Only islands of thymic medulla were scattered. Neither capsule nor inter- or intralobular septae were identified. The reticulin network was irregularly collapsed (Fig.6). FRNs were not discerned in both stress- and age- involuted thymi. The thymus from 33 years old male showed pure thymic hyperplasia retaining fully developed normal reticular network.

DISCUSSION

In this study, we could detect variable amounts of reticulin fibers in parallel with blood vessels through the cortex and the medulla as well as intralobular reticulin fibers in every thymus examined. Weiss (1988) described a thymic cytoreticulum made of epithelial-reticular cells alone without reticulin fibers. In contrast, Kendall (1981) described extraparenchymal connective tissue compartments rich in reticulin fibers. Although the thymus is highly cellular organ as the lymph mode, it has reticular network similar to that of then spleen. Ontogenetically connective tissue septae extends deep into the cortex from 10 weeks of gestational age. By the 15th gestational week, lobulation becomes distinct (Haynes, 1984). In this study, we confirmed that lobulation was complete, but intralobular septae and the reticular network of the cortex were incompletely developed in 5 thymi of 22-33 weeks gestation. Reticulin fibers were increased gradually with aging until 1 year and became organized as a distinct structure at the

Table 1. Human thymic samples examined in this study

Group	Age	No. of cases	Diagnosis
Ⅰ	22-33 weeks of gestational age	5	unremarkanle
Ⅱ	< 1 moth of age	6	"
Ⅲ	1 month-1 year	10	"
Ⅳ	1 year-8 year	13	"
Ⅴ	5 days-20 months	4	stress involution
Ⅵ	26 years	1	age involution
Ⅶ	33 years	1	thymic hyperplasia
Total		40	

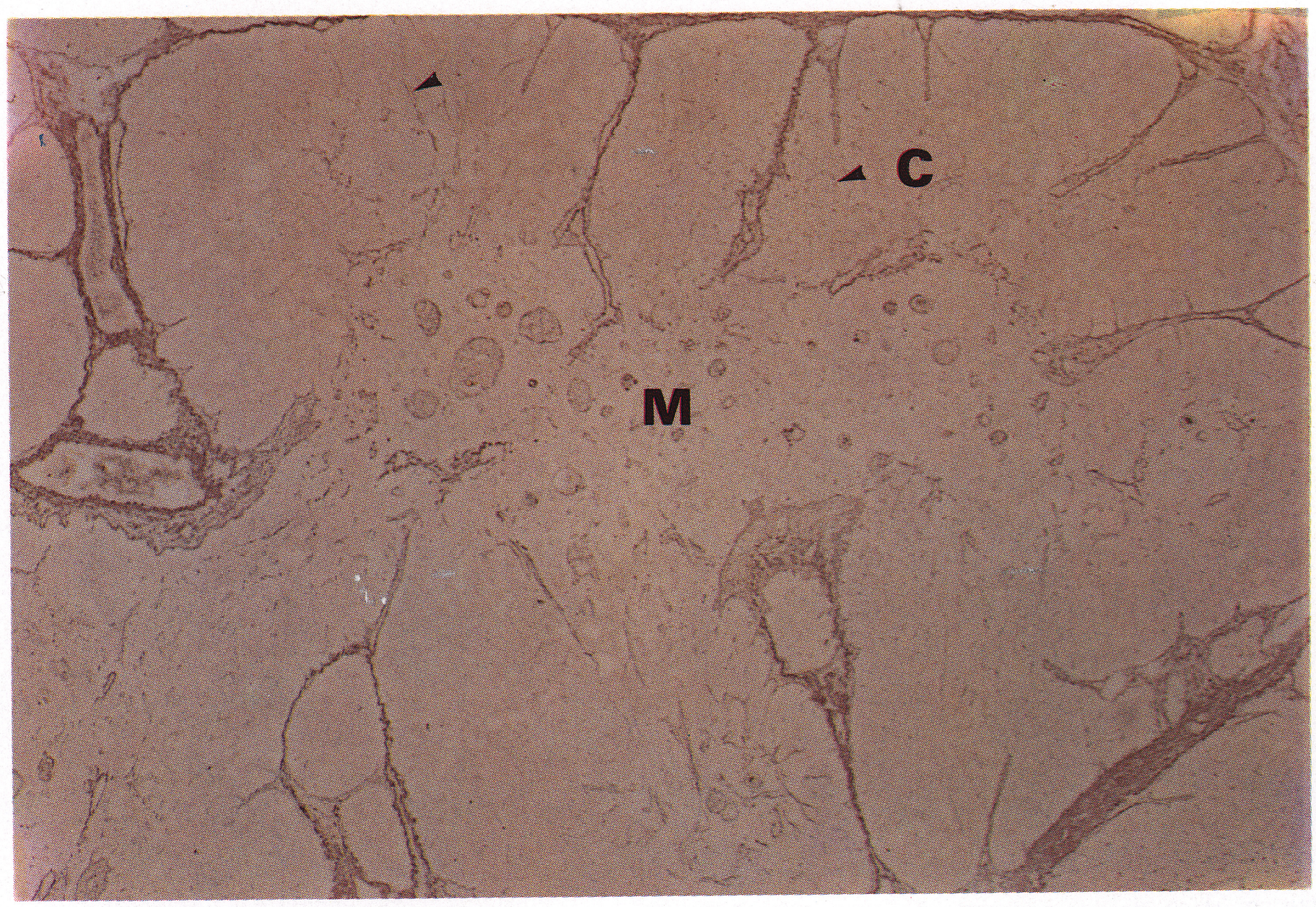

Fig. 1. Incompletely developed reticular network of a postnatal thymus (15 days); reticulin fibers are seen in capsule, inter- and intralobular septae. Note scanty perivascular and pericorpuscular reticulin fibers (arrow head) (Gomori stain, x 13.2). C:cortex, M:medulla.

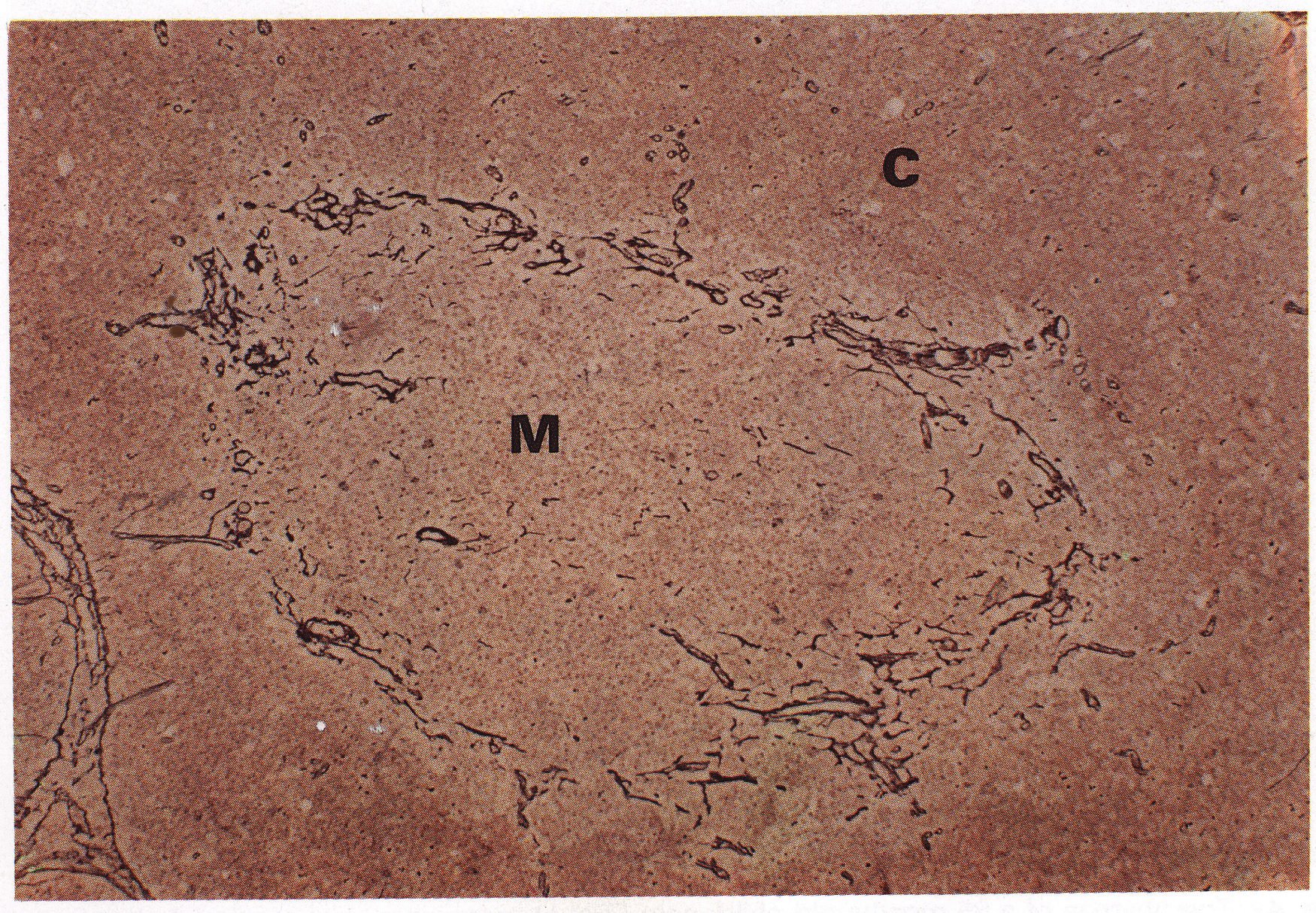

Fig. 2. The thymus of a two months old infant; reticulin fibers are regularly arranged along the corticomedullary junction (Gomori stain, x 25). C:cortex, M:medulla.

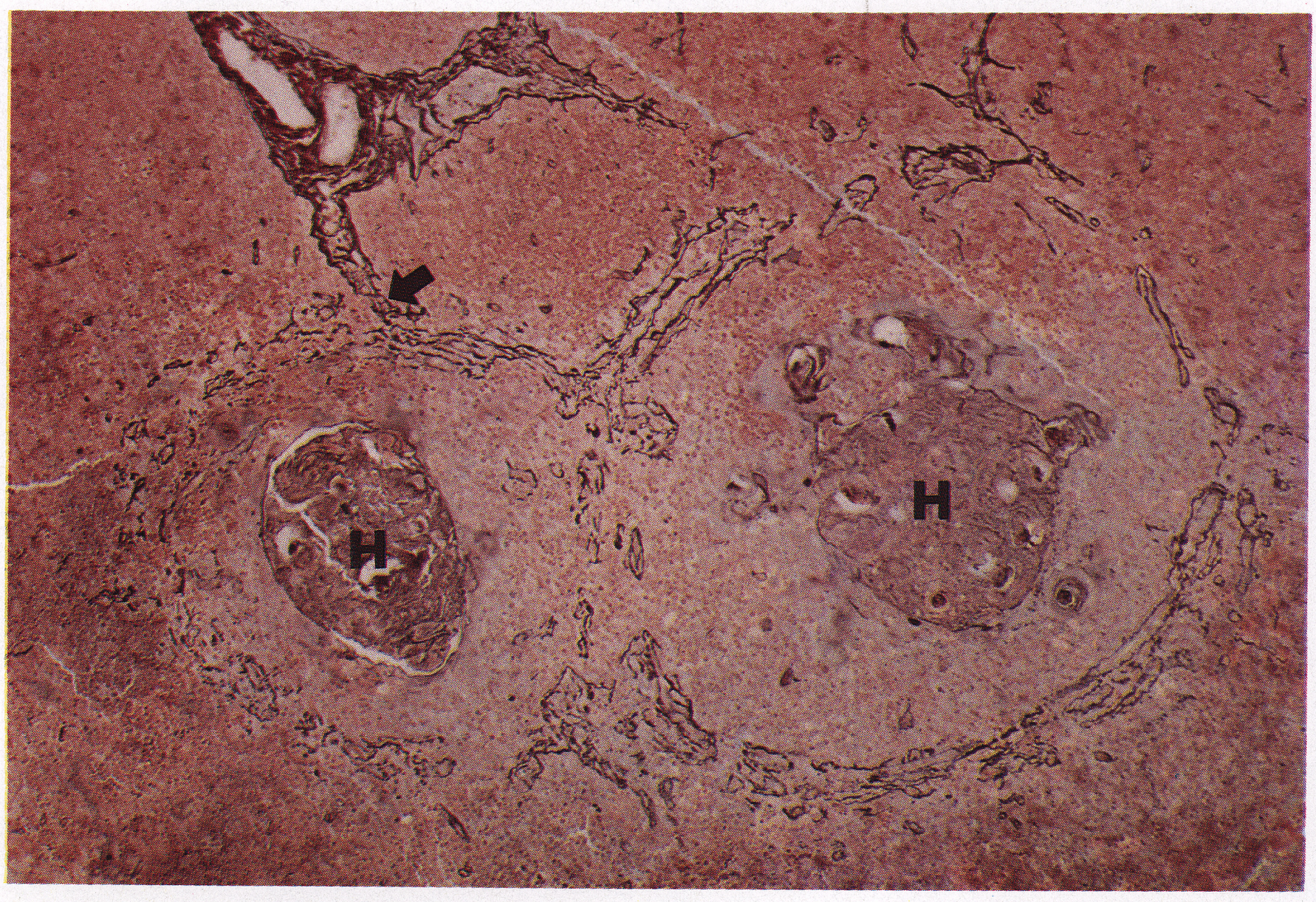

Fig. 3. Well developed reticular network of the thymus (4 months old infant) along the corticomedullary junction as well as the inner medulla (Gomori stain, x10). Reticular network of the outer medulla was connected with interlobular septae (arrow). H:Hassall's corpuscle.

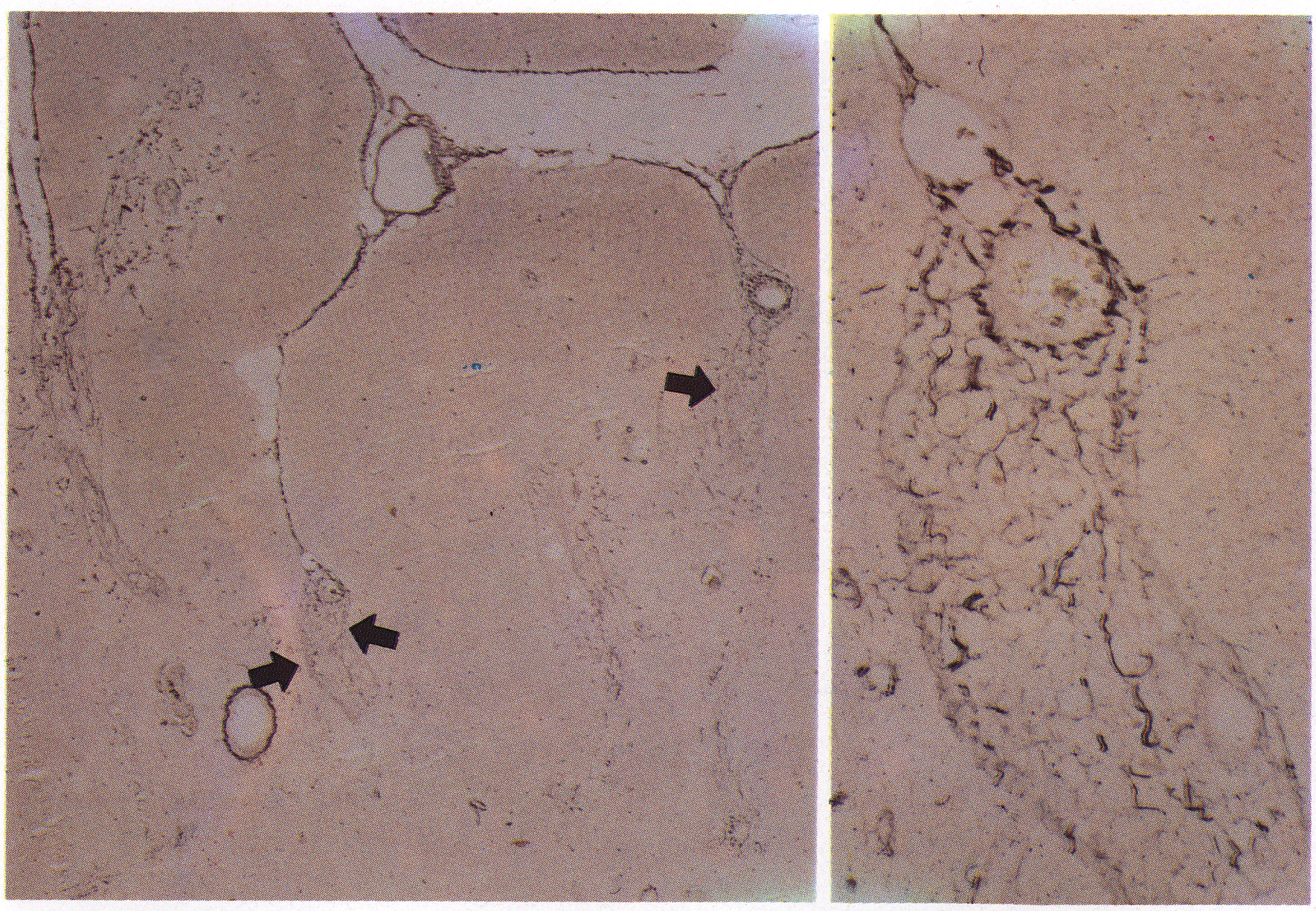

Fig. 4a. The thymus of a 35 months old child; note FRN at branching point of intralobular septae (arrow) (Gomori stain, x10). **4b**. Higher magnification of FRN; reticulin fibers encircle groups of thymocytes, epithelial cells and small blood vessels (Gomori stain, x 50).

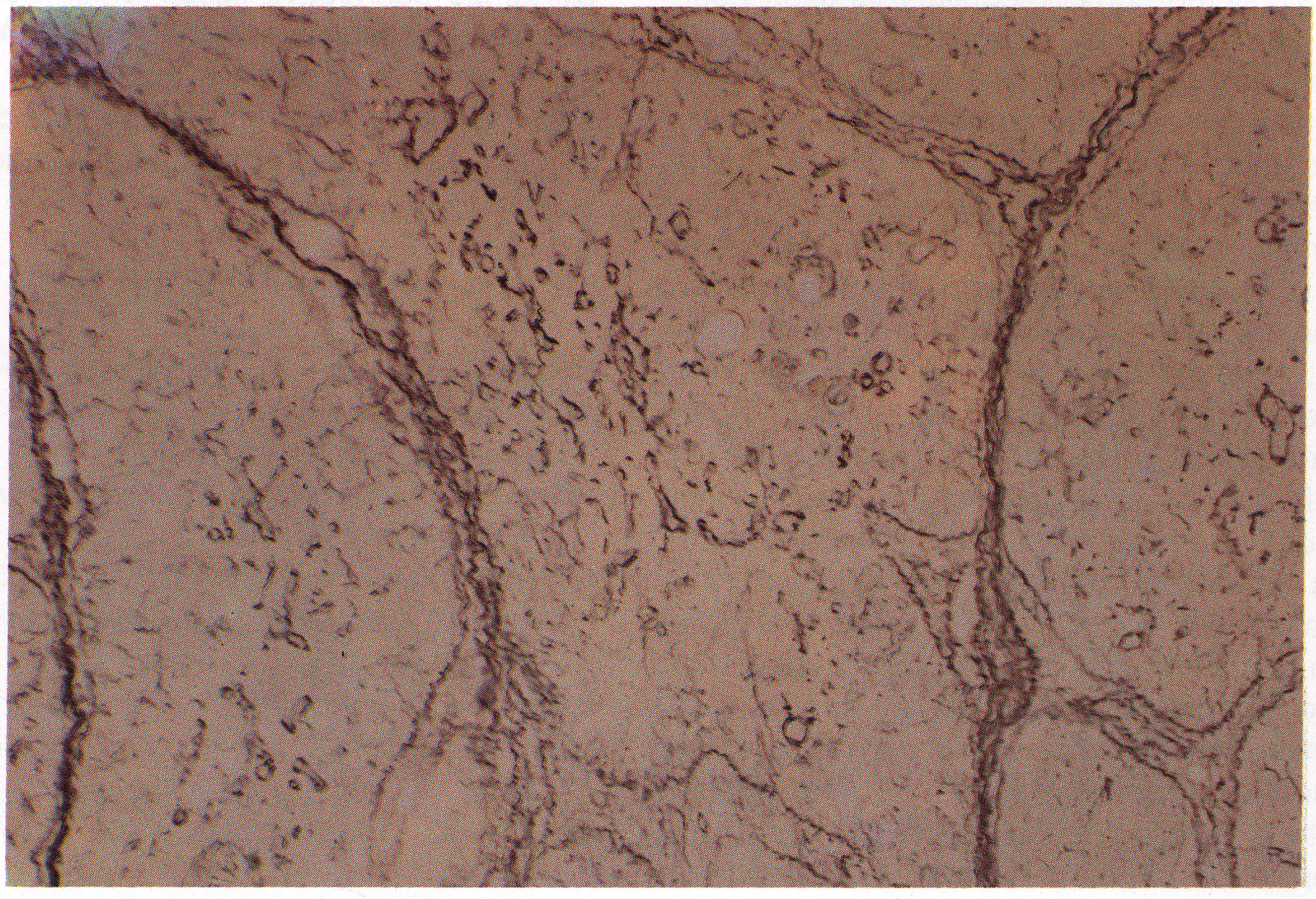

Fig. 5. Stress involuted thymus (15 days); cortical cells are markedly depleted and the corticomedullary junction is indistinct. Blood vessels are relatively increased and the reticular network is disorganized (Gomori stain, x 16).

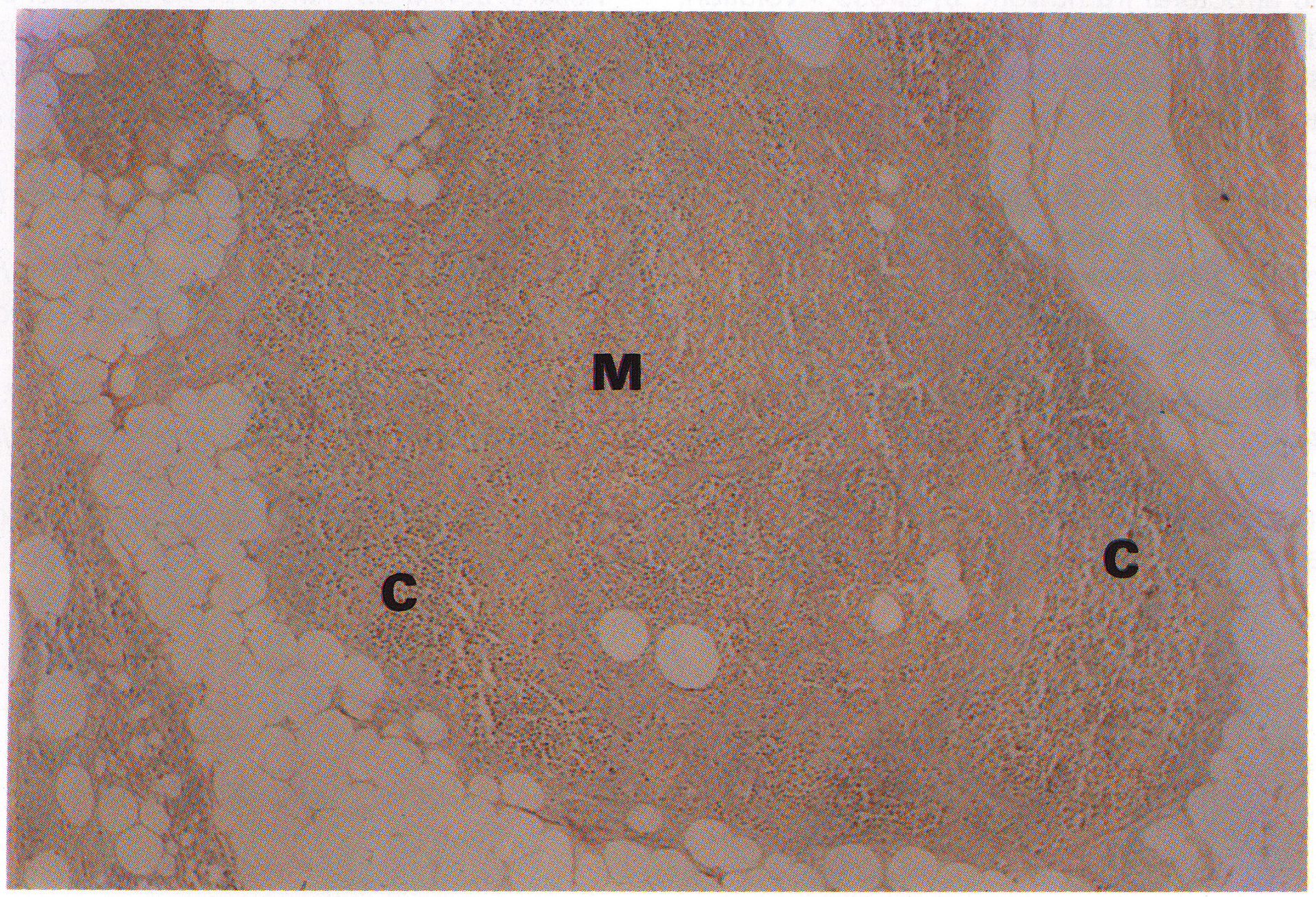

Fig. 6. Age involuted thymus shows fatty infiltration and irregular islands of thymic parenchyma; note collapsed reticulin network in the medulla (Gomori stain, x 25). C:cortex, M:medulla.

branching point of interlobular septae and outer medulla along the corticomedullary junction postnatally in 29 cases. In every postnatal thymus, reticulin fibers associated with blood vessels draining the thymus ramified from intralobular septae along the corticomedullary junction of the outer medulla (Lee et al., 1993). They showed a bulbous structure, forming a labyrinthine network in the outer medulla in some cases. It is known that intralobular septae are opened directly to the medulla in fetal thymi. Although it topologically corresponds to the blood-thymus barrier which is enclosed as an extraparenchymal compartment (Kendall, 1981), it is a partly opened structure merging directly with the medulla or cortex. Within the FRN, thin reticular fibers circumvent some epithelial cells and lymphocytes without intervening blood vessels. The FRN is a structural unit which couples intralobular septae to the inner medulla. The amount of reticulin fibers in association with blood vessels in the outer medulla gradually increased with aging, leading to a complete reticular network. Thus, development of the reticular network is an indicator of lobulation as well as corticomedullary separation.

In both stress- and age-involuted thymi, depletion of cortical thymocytes was closely related with a thymic structural framework. In stress involution, marked increase of reticulin fibers in the cortex suggests that epithelial cells may participate in a reticular network formation. Age-involuted thymi showed fatty infiltration as well as cortical depletion where the amount of reticulin fibers did not increase. In contrast, relative amounts of medullary reticulin fibers increased.

It has not been clarified whether epithelial cells produce reticulin fibers or if other cells producing reticulin fibers exist. In the thymus, inner cortical and medullary epithelial cells can perform some functions as reticular cells in other tissues topologically. In physiologic involution, epithelial cells acquire a spindle, mesenchymal-like appearance. Thin elongated epithelial strands are surrounded by dense connective tissue which contains reticulin fibers (Suster and Rosai, 1990). Another possibility is that distinct fibroblast-like connective cells may exist and can play the role of producing reticulin fibers and constituting a reticular meshwork in the thymus.

REFERENCES

Bearman RM, Levine GD, Bensch KG: *The ultrastructure of the normal human thymus.A study of 36 cases. Anat Rec. 190: 755-781, 1978.*

Hynes BF: *The human thymic microenvironment. Adv Immunol 36:87-142, 1984.*

Hynes BF: *Human thymic epithelium and T cell development: current issues and future directions. Thymus 16:143-156, 1990.*

Janossy G, Thomas JA, Bollum FJ: *The human thymic microenvironment. An immunohistologic study. J Immunol 125:2055-2059, 1980.*

Kendall MD: *The thymic gland. Academic Press, New York, p63, 1981.*

Lee IC, Yu ES, Cho JH, Gong GY, Song MK, Kim SH, Sohn KH, Ikehara S: *Eosinophilic precursors in fibroreticular network of human thymus. Submitted in Acta Pathol Jap 1993.*

Rosai J, Levine GD: *Tumors of the thymus 2nd series, Atlas of Tumor Pathology. Washington, DC: Armed Forces Institute of Pathology. pp26-30, 1976.*

Suster S, Rosai J: *Histology of the normal thymus. Am J Surg Pathol 14: 284-303, 1990.*

Von Gaudecker B: *Functional histology of the human thymus. Anat Embryol 183:1-15, 1991.*

Von Gaudecker B: *The development of the human thymus microenvironment. Curr Top Pathol 75:1-41, 1986.*

Weiss L: *Cell and tissue biology, 6th ed. Urban & Schwarzenberg. Baltimore. Munich. pp481-491, 1988.*

Wood GW: *Macrophages in the thymus. Surv Immunol Res 4:179-191, 1985.*