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General principles of structure and ultrastructural differences in the interstitial pathways of tissue fluid movement

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Motivation and Aim: Not being part of the lymphatic system, the interstitium is an important link in the continuous circulation of tissue fluid (carrying metabolic substrates, waste products and immune mediators) and it is the initial link in the lymphatic drainage of the internal environment of the body [1]. The structure and composition of the interstitium in different organs and tissues have common structural features and can also vary. The purpose of the study was to identify the features of the structural organization of the interstitium of various organs under normal and pathological conditions.
Methods and Algorithms: The study used archival materials carried out in different years to study the structure of the mucous membrane of the gum, adenocarcinoma of the colon, eye (cornea, ciliary body, choroid), human synovial membrane. Organ fragments were fixed in a 4 % solution of paraformaldehyde prepared in Hanks' medium, further fixed for 1 hour in a 1 % solution of osmium tetroxide (OsO4) in phosphate buffer pH 7.4, dehydrated in ethyl alcohol of increasing concentrations and embedded in Epon. Ultrathin sections with a thickness of 70–100 nm were obtained on a Leica EM UC7 ultratome (Leica Microsystems, Germany) and contrasted with a saturated aqueous solution of uranyl acetate and lead citrate. Digital photographs were taken using a JEM 1400 electron microscope (JEOL, Japan) at the Center for Microscopic Analysis of Biological Objects of the Siberian Branch of the Russian Academy of Sciences. Morphometric analysis was carried out using the Image J computer program (Wayne Rasband, USA). The mean (M) and standard deviation (SD) were calculated using Microsoft Excel software (Microsoft, USA). The significance of differences between the studied parameters was determined using Statistica 6.0 software (StatSoft, USA) and the Mann-Whitney U test at a confidence level of 95 % ($P < 0.05$).
Results: The interstitium makes up about 20 % of body weight. Interstitial spaces exist between the cells of any organ. The structure of the interstitium is usually represented by a framework of three-dimensional fibrous collagen network, in which collagen fibers form thick bundles [2]. The interstitium is considered a structure of the extracellular matrix in which the main substance is formed from proteoglycans, consisting of glycosaminoglycans and free hyaluronan. They form gel-like structures due to their ability to attract water due to their high polarity. Glycosoaminoglycans interact with the collagen structure of the extracellular matrix but can also be found in the interstitial fluid. Interstitial fluid is an ultrafiltrate of plasma and containing protein. The structure of non-vascular pathways for the movement of interstitial fluid may have similarities and vary

in different organs. There are interstitial fluid of tissue channels, fluid of hydrophobic channels, fluid of hydrophilic channels, perivascular fluid, cerebrospinal fluid and interstitial fluid of fascia [3]. When analyzing the interstitium of the studied organs, differences in its structural organization were noted (Fig. 1).

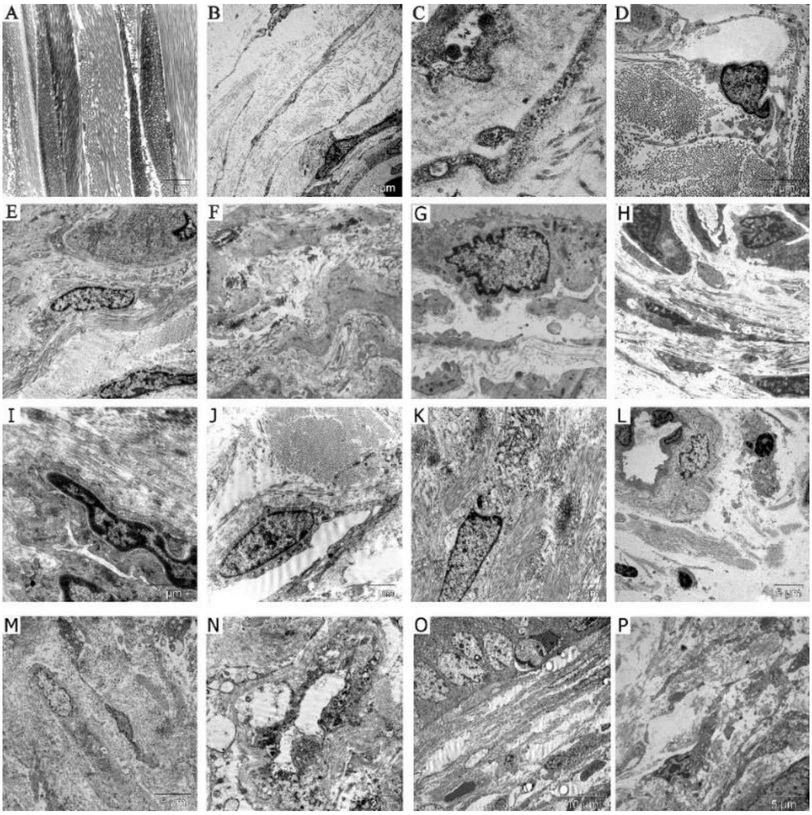

Fig. 1. Various states of interstitial pathways of tissue fluid movement in the structures of the eye, synovium, gums and colon. A – narrow spaces between parallel oriented collagen fibers in the cornea. B – wide interstitial spaces in the ciliary body formed by unidirectional collagen fibers and limited by fibroblasts and their processes. C, D – channels formed by fibroblast-like cells in the choroid (C) and in the ciliary body (D). E – interstitial spaces in the synovium formed by parallel oriented collagen fibers. F – multidirectional arrangement of collagen fibers in the interstitial space of the synovial membrane in stage I arthrosis. G, H – wide interstitial spaces limited by collagen fibers and fibroblast-like cells in synovial membrane in stage II arthrosis. I – narrow pericapillary and interstitial spaces in the gingival mucosa. J – expanded pericapillary and interstitial spaces in the gingival mucosa during inflammation. K – multidirectional arrangement of collagen fibers in the gum interstitium during inflammation. L – wide interstitial spaces limited by collagen fibers in the gingival mucosa during inflammation. M – moderate density and unidirectionality of collagen fibers in the interstitium of moderately differentiated colon adenocarcinoma. N – multidirectional arrangement of collagen fibers in the interstitium of well-differentiated colon adenocarcinoma. O – formation of narrow channels in the interstitium of moderately differentiated colon adenocarcinoma. P – gluing of collagen fibers and formation of wide channels in the extracellular matrix of poorly differentiated colon adeno-carcinoma

The common features of the studied organs interstitium structure under normal conditions were the presence between cells and vessels of narrow spaces formed by parallel collagen fibrils, which determine the direction of movement of tissue fluid. A feature of the choroid and synovium was the presence in the interstitium of channels formed by collagen fibers and fibroblast-like cells. Similar channels have been described in the structure of the interstitium of the extra-hepatic bile ducts [4]. Under pathological conditions, an increase in pericapillary spaces, disorientation of collagen fibers, and expansion of interstitial spaces were observed. Analysis of co-lon adenocarcinoma revealed abnormal remodeling of interstitial collagen, resulting in excessive collagen deposition, fibril adhesions, and the wide interstitial channels formation (Fig. 1).

Conclusion: When analyzing the interstitium of the studied organs, differences in its structural organization were noted. Under normal conditions, narrow pericapillary and interstitial spaces formed by parallels located unidirectional collagen fibrils were noted. Under pathological conditions, disorientation of collagen fibers and expansion of interstitial spaces were observed. In the choroid and synovium, the presence of interstitial channels bounded by collagen fibers and fibroblast-like cells was detected. Under conditions of malignant growth, there was excessive deposition of collagen, gluing of collagen fibers with the formation of channels for migration of tumor cells.

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