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MACRO- AND MICROSCOPIC MORPHOLOGICAL RESULTS OF THE APPLICATION OF XENOTRANSPLANTED SHEEP PERICARDIUM IN TYMPANOPLASTY IN RABBITS WITH CHRONIC OTITIS MEDIA

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ABOUT ARTICLE

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Abstract: When an autologous fascia is placed on the drum membrane, at first all kinds of reactive changes develop around it, and in a short period of time a border of demarcation from lympho-histiocytic and monocyto-macrophage cells appears, but these cells do not grow into the fascia, on the contrary, a fibrous membrane appears around it, its surface on the 21st day completely epithelized. When the pericardium of the sheep heart is transplanted into the tympanic membrane for the purpose of closing it, a strong and extensive reactive change develops in response. Necrosis and destruction develop in the xenograft, and a proliferative infiltrate appears around it. Then the xenograft intermingles with the proliferative infiltrate cells that appear around the tissue structures. Young lympho-histiocytic cells turn into fibrocytes and histiocytes, produce fibrous structures and the surface is covered with epithelium.

INTRODUCTION

Historical aspects of surgical interventions and various procedures to restore the integrity of the eardrum are interesting and have a long history [5].

The observation of hearing improvement in patients with chronic otitis media during separate periods of pus discharge time has been noted much earlier [4-7]. This situation led to the discovery of "artificial" eardrums, which are used to temporarily cover perforation of the tympanic membrane [1]. They have

been widely used since the 17th century. Various materials were used for their preparation [2]. For example, Banzer suggested using a piece of pig's bladder for this purpose, and Yarsley - moistened cotton, while Toynbee used a rubber disc attached to a silver rod for easy insertion into the external auditory canal [7-11]. It is known that mechanics and watchmakers in London were engaged in the production and sale of prostheses of the drum head in large quantities. Due to the inconvenience of their use and the high probability of additional infection of the middle ear, since the end of the 19th century, various prostheses of the tympanic membrane have been rarely used [13], and currently they are used only for differential diagnosis and determining indications for surgical interventions aimed at improving hearing [12].

Later, to eliminate the defects of the drum curtain, the method of burning the edges of the perforation described by some authors was used [8]. The essence of the method was that the frosted edges of the perforation were systematically burned with 3-chloroacetic acid, which led to its spontaneous closure. According to some authors, this method is sufficient for small defects of the tympanic membrane and does not require the patient to be hospitalized, however, the treatment can last for months and is not always successful. Currently, this method is not used in practice [14-16]. Thus, the modern surgical treatment of SO'O includes operations such as rehabilitation of the middle ear cavity, creation of neotympanal membrane and air tympanal cavity, and reconstruction of the sound conduction system.

An important stage of tympanoplasty is the rehabilitation of the middle ear cavity and the stage after ossiculoplasty. In small perforations of the tympanic membrane, the dried fascia of the temporalis muscle itself is used, while in subtotal and total perforations, thinned auricle and (or) mixed skin clots are used to hold the material in place [2,7] . Fascial grafts used in the plastic surgery of subtotal and total perforations have the following disadvantages: slowness of adhesion, sliding into the drum cavity and formation of adhesions with the medial wall of the drum cavity, formation of retraction pockets, lateralization of the anterior area of the plastic flap, and accumulation of the anterior meatotympanal angle in the anatomical and functional results of surgical procedures. has a significant negative effect [17].

Thus, taking into account the above, the development of tympanoplasty surgery has been in the focus of attention of surgeons in otomicrosurgery for many years.

Results and their discussion. The results of the morphological examination of the xenograft prepared from sheep pericardium in tympanoplasty showed discirculatory changes in the form of blood filling in the microcirculatory flow vessels in and around the tympanoplasty zone, diapedesis blood flow in the

perivascular zone, expansion of subcapillary venules and peripheral white blood cells . These changes around the pericardium were followed by hemorrhages, softening and fibrinoid necrosis in the soft tissues of the wall of the external auditory canal . Blood vessels are expanded, they are in a state of proliferation in the form of new vascular buds consisting of endothelial cells (r asm .1). Proliferation of endothelial and pericytic cells is observed in their wall . Between the vessels, especially in the postcapillary venules, it was determined that neutrophilic leukocytes and monocytes in the blood are located in the peripheral part, and some of them migrate to the wall of the venules and form a small cellular infiltration around the vessels. The fibrous structures of the connective tissue in the middle shells of the soft tissues of the middle ear are in a state of fragmentation and infiltration with inflammatory cells . The above-mentioned morphofunctional changes of the soft tissues of the middle ear indicate the development of acute discirculatory, edematous-destructive changes in relation to the operative injury and xenograft.

The softening and homogenization of the outer surface part of the transferred pericardium was determined . Fibrous parts are irregularly arranged, homogenized and form a layer of fibrinoid necrosis with more intense basophilic staining with hematoxylin (Fig . 2). Fibrous parts of the pericardial middle shell are swollen, softened and slightly swollen . In this case, the cellular elements of the middle layers of the pericardium were in the form of nuclear structures and cytoplasmic elements .

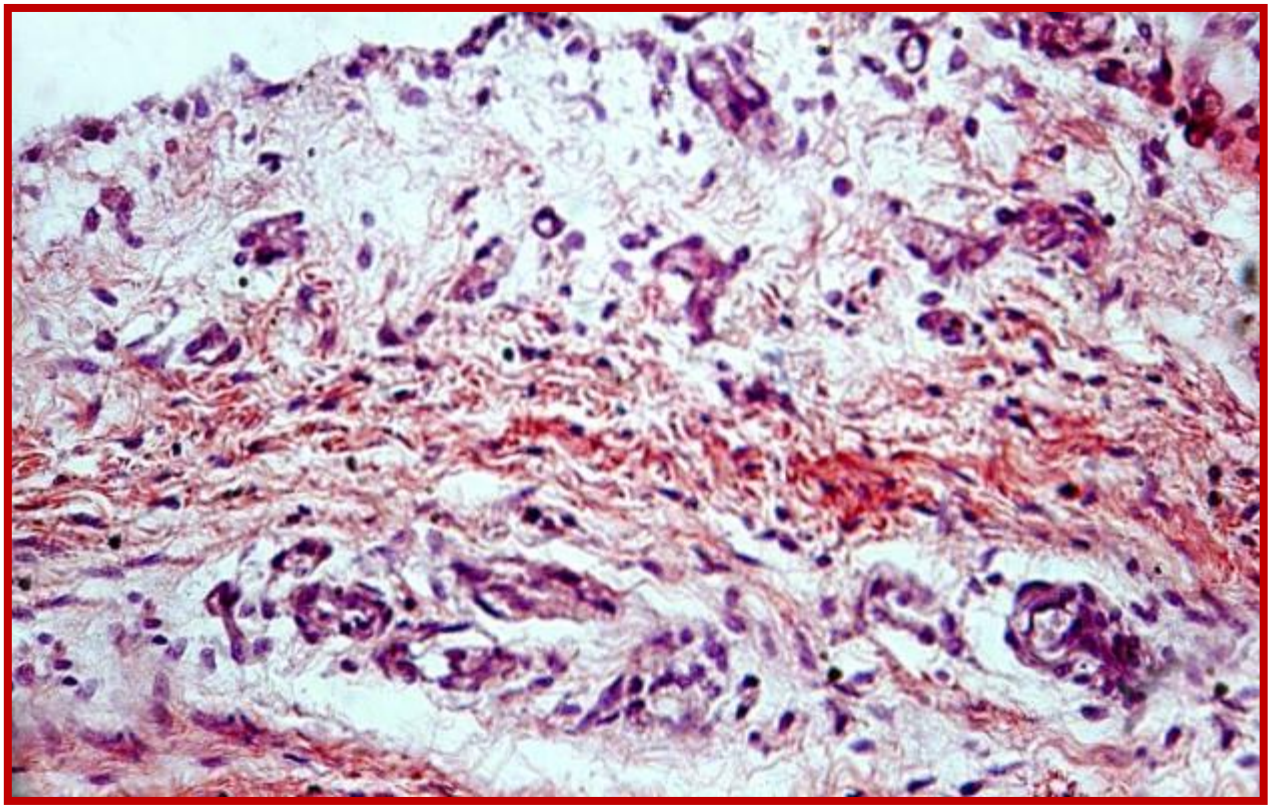


Fig. 1. Day 3 of tympanoplasty .

In the xenograft, proliferation of blood vessel elements, migration of leukocytes and monocytes in the surrounding tissues, formation of swelling around the formation of fibrous structures. Staining: with hematoxylin and eosin. Cat: ok. 10, ob 20.

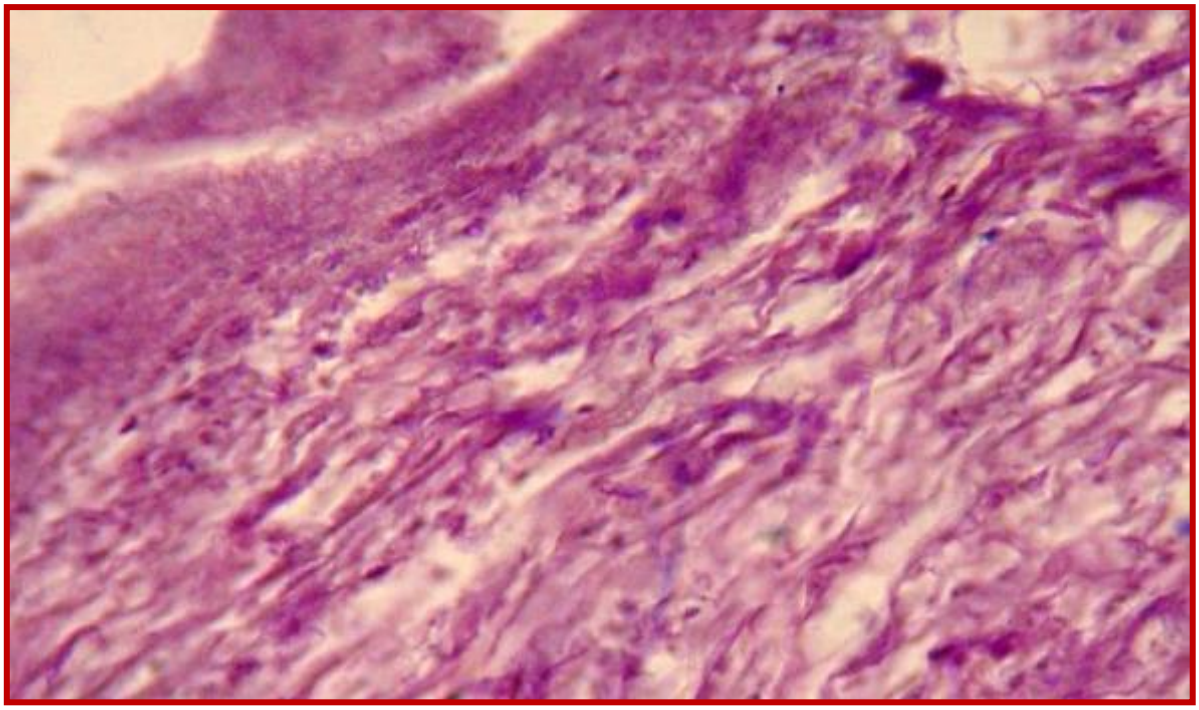


Fig. 2. Day 3 of tympanoplasty.

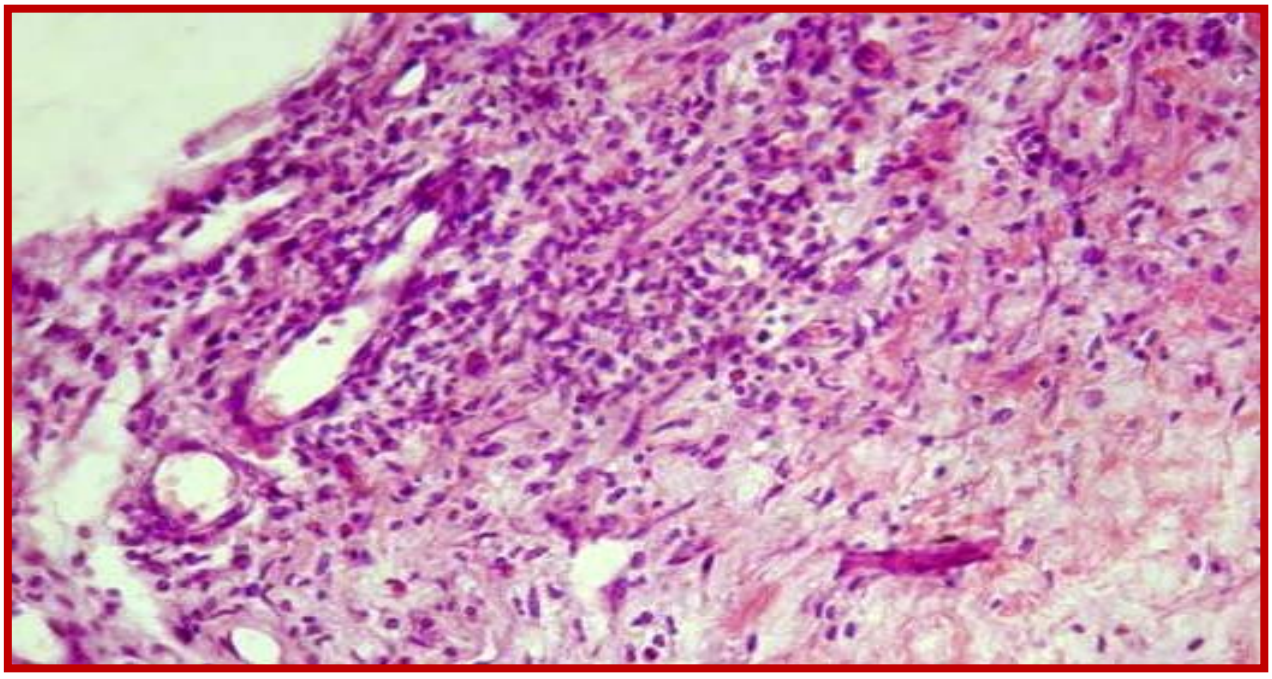
Occurrence of necrosis (Ne) in the outer layer of the pericardium, spreading of fibrous structures of the middle layer. Staining: with hematoxylin and eosin. Cat: ok. 10, ob 20.

7 days after myringloplasty, the discirculatory changes in the myringloplasty zone and its surroundings turn into inflammatory hyperemia of the microcirculatory flow vessels, thinning of their walls, migration of polynuclear and mononuclear leukocytes to the perivascular zone, the formation of an inflammatory infiltrate at the border of the pericardium and surrounding tissue . In this case, the postcapillary venules are widened, their walls are thinned, endothelial cells are suffocated, the space between these cells is widened, where interendothelial passing lymphocytes and monocytes are detected. An inflammatory infiltrate consisting of lymphoid and histiocytic cells was formed at the border of the transferred pericardium and soft tissue of the middle ear (Fig. 3). It is a proliferative infiltrate of graft regeneration. Softening and thickening of the corresponding connective tissue, homogenization of fibrous parts is observed in some places, and connective tissue cells between them

are in a state of proliferation and activation in the form of hypertrophy and hyperchromasia of nuclear structures.

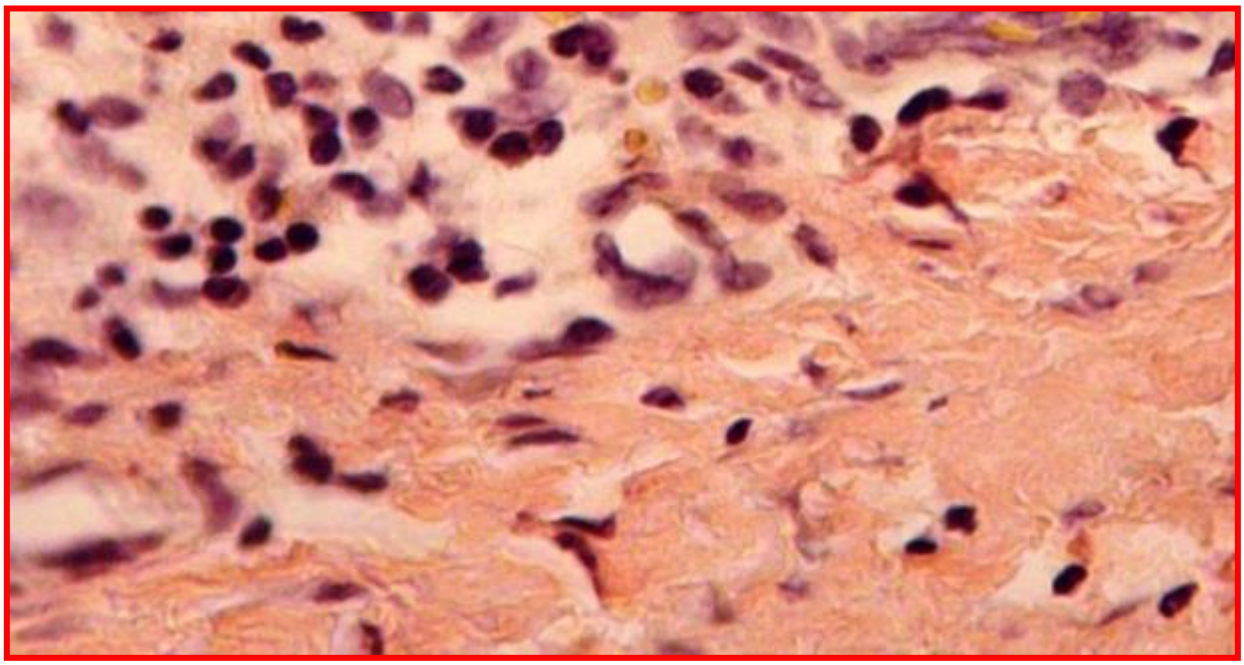
The xenograft preserves its outer shell and slightly deepens the process of softening, as well as its destruction in the form of fibrinoid necrosis, activated lymphoid and macrophage cells appear in its composition (Fig. 4). Lymphoid and macrophage cells absorb the fibrinoid bundle and reach the middle layers of the pericardium. Here, inflammatory cells merge with pericardial cellular elements in the form of perivascular swelling and proliferation of connective tissue cells. In the middle layer of the pericardium, on the basis of the softening and homogenization of fibrous parts, the appearance of active cells of pericardial and reactive origin was observed. In addition to these changes, with the appearance of interfibrous swelling foci in the middle layers of the pericardium, mucoid swelling and myxomatous foci of fibrous parts appear.

Thus, in this period after sheep pericardial xenotransplantation, graft healing in the form of the formation of an inflammatory infiltrate consisting of lympho-histiocytic cells at the border of the soft tissue of the middle ear wall is observed, which is a proliferative infiltrate of recovery. It was determined that private lympho-histiocytic cells penetrate into the middle layers of the transferred pericardium in the form of fusion and formation of cell infiltrates of mixed composition.



Ris. 3. 7th day of tympanoplasty.

Inflammatory infiltrate between xenograft and surrounding soft tissue due to lymphoid and histocytic cells. Staining: with hematoxylin and eosin. Cat: ok. 10, ob 20.



Ris. 4. 7th day of tympanoplasty.

A strong appearance of inflammatory infiltrate (I) at the border of the xenograft with the surrounding tissue, homogenization of fibrous structures (TT) in the middle layer and the appearance of active cells. Staining: with hematoxylin and eosin. Cat: ok. 10, ob 20.

Morphological examinations on the 14th day after tympanoplasty show that during this period pericardial tissue structures merge with the surrounding soft tissue and bony base on the peripheral parts of the xenograft. In this case, the tissue structures of the pericardium are completely destroyed and replaced with the surrounding soft and bony tissues. From the skin of the external auditory canal, a complete connection of the pericardium with the structural elements of the skin was observed. Only in the zones of the operative section, the appearance of a small proliferative infiltration consisting of granulation tissue and inflammatory cells was determined.

In this case, it was observed that the fibrous parts of the pericardium were displaced and densely adhered to the fibrous parts of the soft tissue of the middle ear wall. In the fibrous-cellular parts of the pericardium, more swelling was observed at the expense of the interstitium, and it was in the form of wavy structures. The cellular elements were few in number and elongated, and densely connected with the fibrous parts (Fig. 5). The fibrous-cellular parts of the local tissue are more rigid and hyperchromic

due to the intense staining of the fibrous parts and cellular elements. The vessels are relatively narrowed, the wall is thickened due to the proliferation of endothelial and pericytic cell elements.

The presence of inflammatory proliferative infiltration in the surrounding soft tissues is observed, which surrounds the graft from all sides and is observed with hardening and thickening of tissue structures. Dilation of blood vessels, infiltration of lympho-histiocytic cells in and around their wall was determined. Fibrous parts and cellular elements are thickened due to the new formation of homogeneous protein structures. Skin thickening is observed mainly due to the presence of inflammatory proliferative infiltration in the private plate of the skin dermis. The multi-layered epithelium with coating is thickened due to acanthosis and hyperkeratosis of epitheliocytes (Fig. 6).

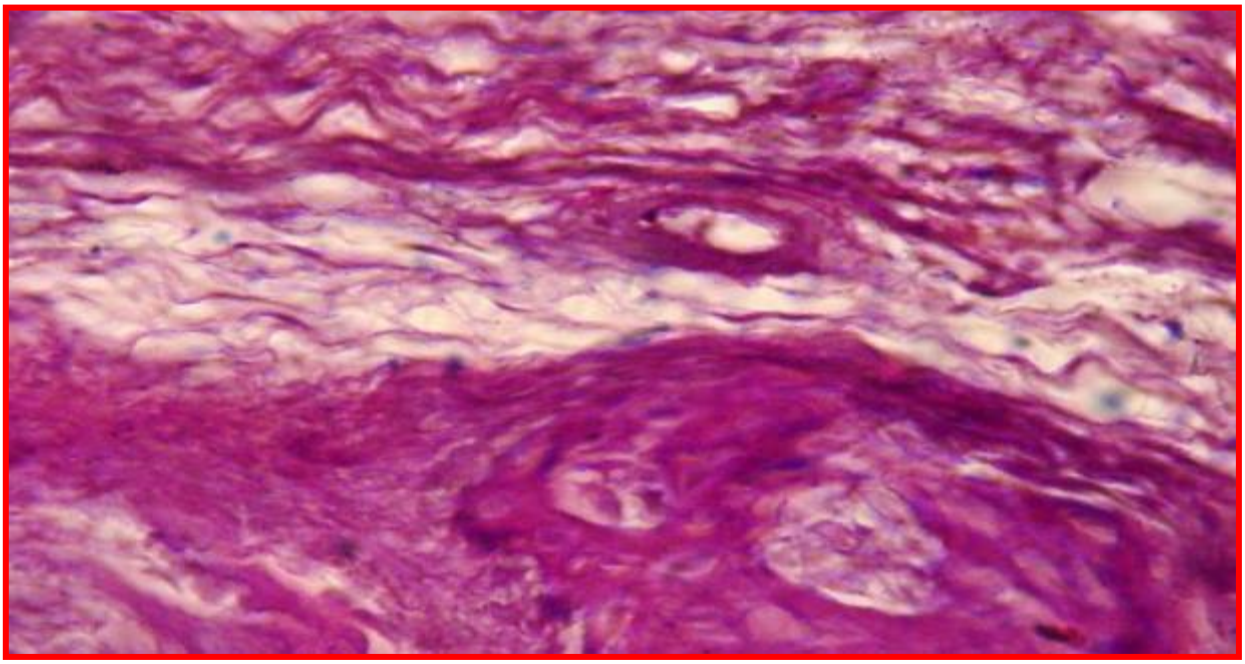


Fig. 5. 14th day of tympanoplasty.

Further spreading of pericardium fibrous cellular structure develops due to intercellular edema. The denser appearance of fibrous cellular structure (TT) in local tissue is associated with good staining of fibers and cellular elements. Staining: with hematoxylin and eosin. Cat: ok. 10, ob 40.

Fig. 6. 14th day of tympanoplasty .

The thickening of the skin on the outer surface of the xenograft develops due to inflammatory proliferative infiltration (IP), and the thickening of the multi-layered squamous epithelium (KYaE) occurs due to hyperkeratosis (Gkz). Staining: with hematoxylin and eosin. Cat: ok. 10, ob 40.

On the 21st day of tympanoplasty, the size of destructive changes in the xenograft structure was reduced. In the foci of pericardial inflammation, young histiocytic cells into mature histiocytes and fibrocytes and differentiation are observed, along with the formation of fibrous parts, which combine with the fibrous elements of the pericardium to form hard and thick fibrillar structures. The results of histochemical examination by the Van-Gieson method showed that fibrous parts consisting of thick tufts stained bright red with picrofuchsin were increased in the transferred xenograft (Fig. 7). On the surface, there are newly formed epithelial cells of the regenerative multi-layered epithelium, which are painted in yellow-brown color.

Formation of a thin layer of cellular-tissue connective tissue, similar to the bone top layer, was established by the bone tissue. It contains large and hyperchromic fibroblasts and newly formed fibrous parts, which are densely attached to the compact bone plate (Fig. 8). Activation of osteoblasts, thickening and calcification of fibrous parts are also observed in the composition of the bone plate. The formation of mature connective tissue from the inflammatory-granulation tissue and its joining with hypodermis and fibrous tissue of the dermis was determined by the skin of the external auditory canal.

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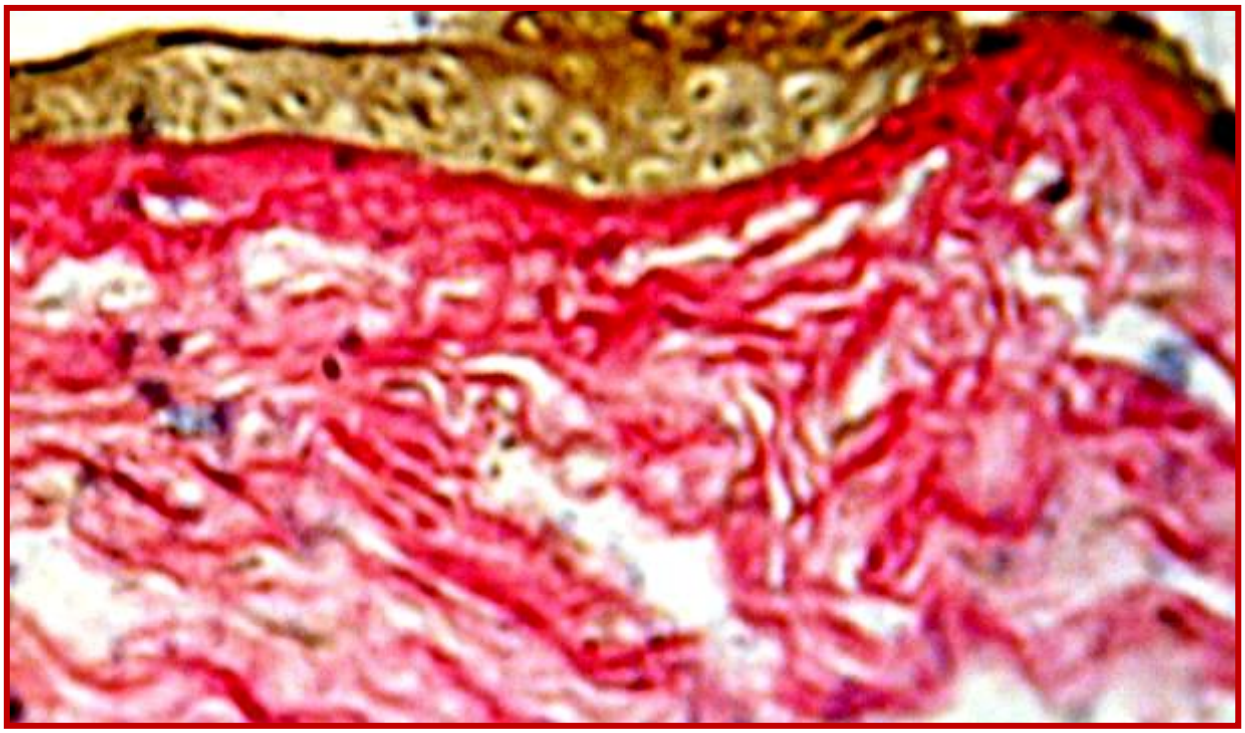


Fig. 7. Day 21 of tympanoplasty .

Increase in the number of fibrous structures (TT) in xenografts and the regeneration of the multilayered squamous epithelium covering the outer layer. Staining: with hematoxylin and eosin. Cat: ok. 10, ob 40.

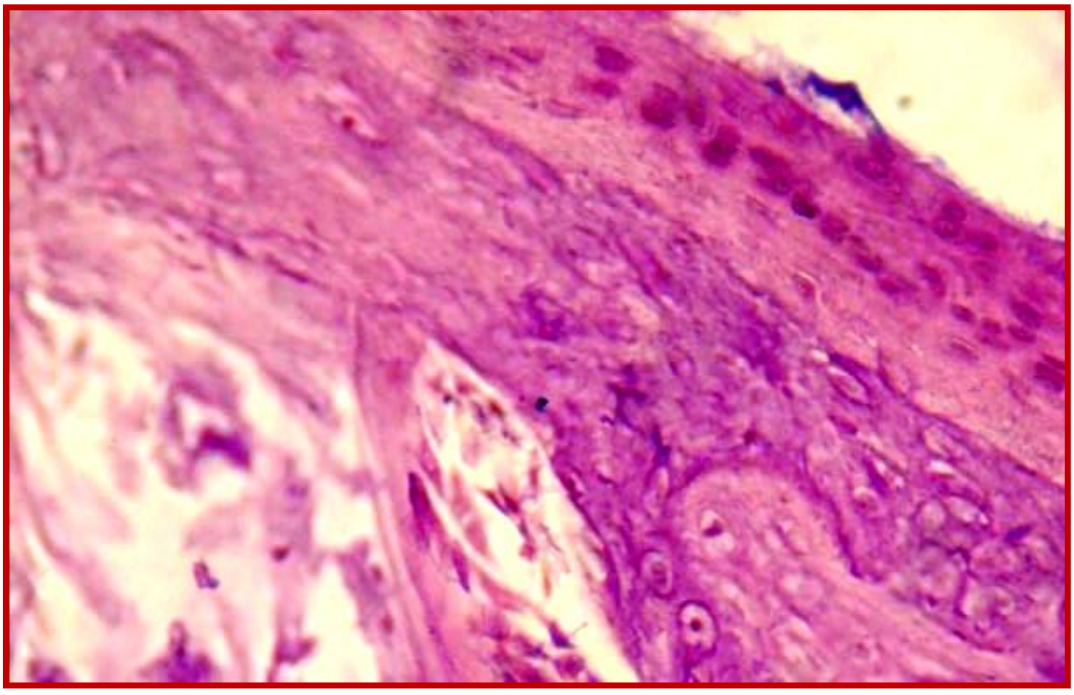


Fig. 8. Day 21 of tympanoplasty .

Acceleration of the formation of the outer auditory canal (SUP) and the densification of bone plates (SP). Staining: with hematoxylin and eosin. Cat: ok. 10, ob 40.

The results of morphological examinations for 1 month after xenotransplantation showed that during this period of the study, there was a development of regressive conditions in the form of the destruction of inflammatory cells in the composition of the xenograft and the surrounding tissues, the development and differentiation of cambial histiocytic cells into mature histiocytes and fibrocytes. Such regressive differentiation of connective cells was observed with a decrease in the volume of inflammatory proliferative infiltration, rapid conversion of young histiocytic cells to fibrocytes and histiocytes, and the formation of thick bundles of fibrous parts . Vessels have decreased, their space has narrowed, the wall has become thinner due to the differentiation of endothelial and pericytic cells. Also, the number of thin-walled vessels decreased, with hemodynamic and swelling conditions stabilized. The size of newly formed connective tissue and fibrous parts of the pericardium is reduced, turning into separate solid and differentiated fibrous bundles (Fig. 9), firmly connected with bone tissue on one side, and bone dermis on the other.

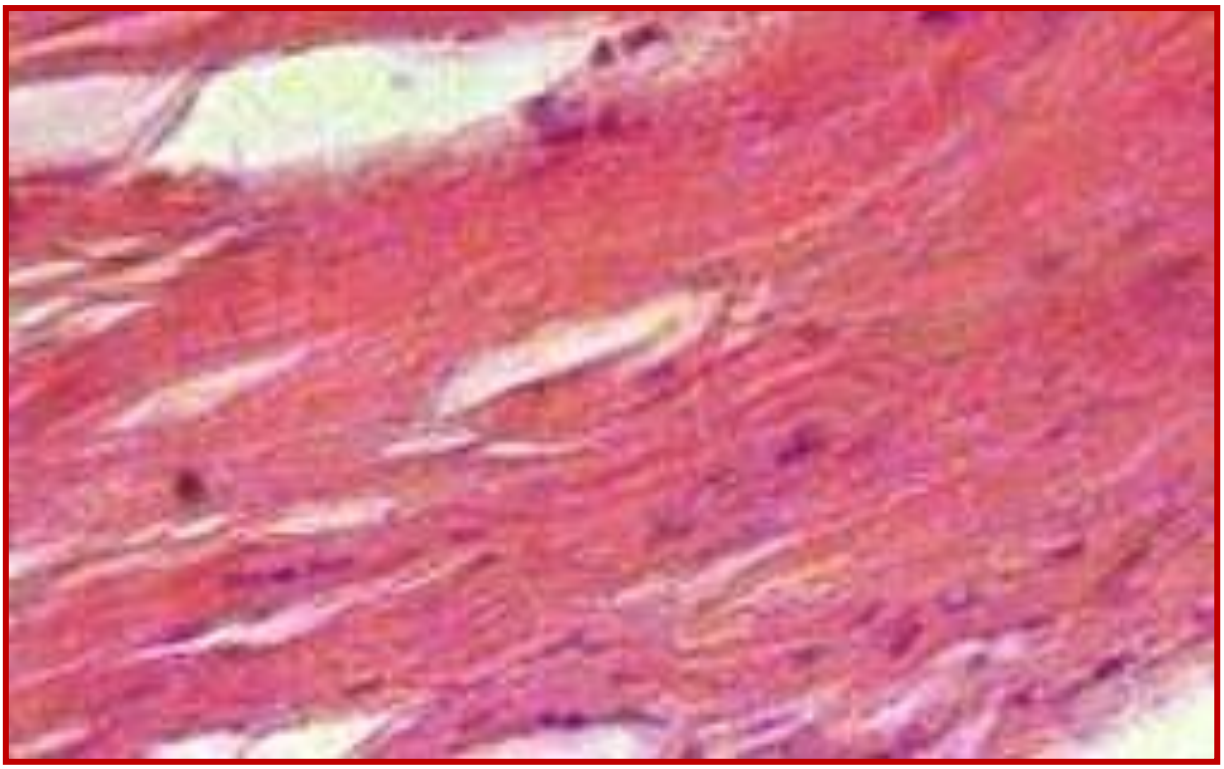
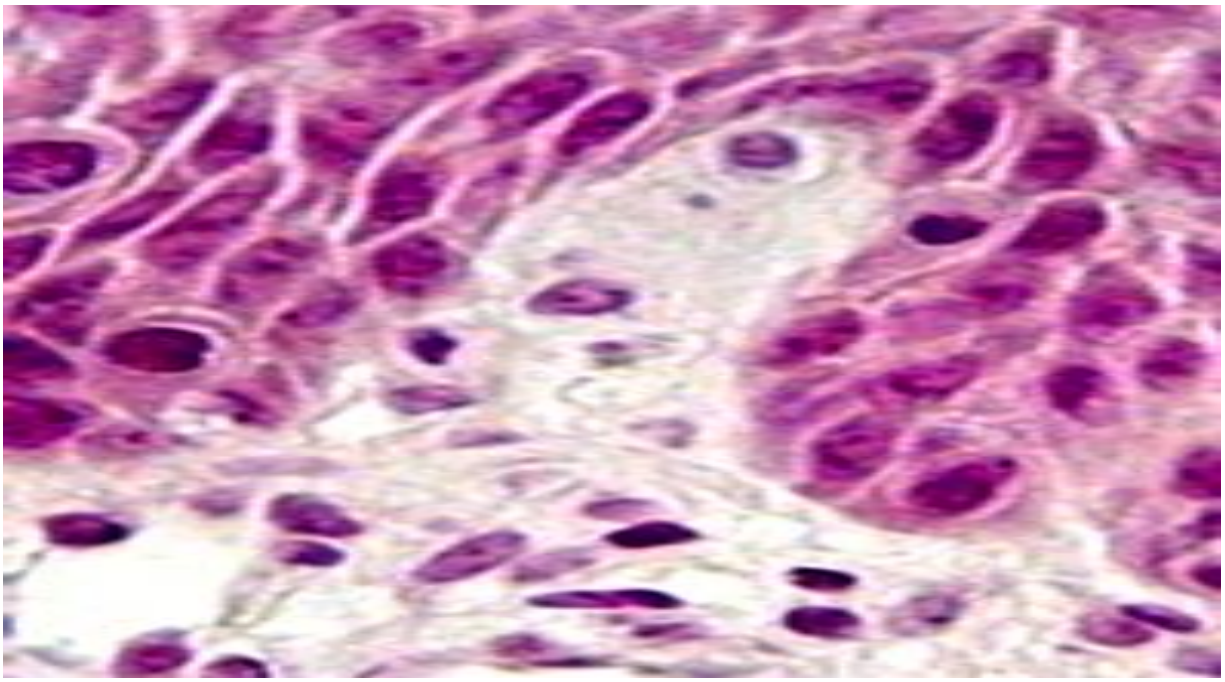


Fig. 9. 1 month after tympanoplasty

Differentiation and densification of fibrous structures in the xenograft. Decrease in the number of cellular elements in the transplant. Staining: with hematoxylin and eosin. Cat: ok. 10, ob 40.

3 months after pericardial tympanoplasty, complete disappearance of all pathological, inflammatory and regenerative changes was observed in the operative field. It was found that pericardial tissue was fully connected with the surrounding tissue, and microscopically it did not differ from the local connective tissue in terms of its composition and maturity. Only slightly differentiated fibrocytic cells and small areas with signs of angiomatosis were preserved.

In this case, it was found that there was an increase in fibrous parts consisting of bundles of collagen fibers in the xenotransplant. Fibrocytes and fibroblasts, as well as individual cellular elements in the form of single vessels of the arterial type, were detected between the fiber bundles. The formation of a multi-layered epithelium on the surface of the xenograft was determined, but the epitheliocytes were softened and irregularly arranged, forming a new multi-layered epithelium where it was impossible to distinguish the separate layers of the multi-layer. The surface layers of the epithelium are in a state of disintegration and desquamation (r asm . 1 0).



Ris. 1 0. 1 month after tympanoplasty

In this period, xenotranlantate is covered from the outside with a multi-layered flat epithelium, which does not differ from a separate epithelial layer. In some places between the fibers, arterial-type vessels and cell elements consisting of individual fibrocytes and fibroblasts are observed. Staining: with hematoxylin and eosin. Cat: ok. 10, ob 40.

CONCLUSION

Thus, morphological studies after xenotransplantation of sheep pericardium showed that in the early periods after the transfer, a proliferative inflammatory infiltrate of local tissue recovery develops, and the transplanted pericardium shows disintegration and necrosis of the surface layers, and infiltration of the middle layers with inflammatory cells. In the later periods of the study, displacement of transplant tissue elements with local tissue elements and reduction in the volume of inflammatory infiltration, development and differentiation of lymphohistiocytic cells in the pericardium to mature cellular structures in the form of fibrocytes and histiocytes, then the formation of thick fibrous parts and the regeneration of the lining multilayered epithelium will occur.

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