# Tissue Reaction to Implantation of Light Polypropylene Meshes

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 142, No. 12, pp. 687-692, December, 2006
Original article submitted July 10, 2006

Comparative histological and electron-microscopic studies of tissues at the site of implantation of Vypro and Ultrapro polypropylene mesh endoprostheses and the meshes coated by fibroblasts were carried out. Tissue reaction to implantation of meshes coated by fibroblasts was more pronounced, particularly during the early period, and the process of connective-tissue capsule formation and implant growth was more rapid. The meshes integrated with the adjacent tissues at the site of implantation, which recommends them for clinical use.

**Key Words:** *cell reaction; mesh endoprostheses; fibroblasts*

Herniotomy is the most frequent surgical intervention; it constitutes 10-15% of all interventions [5]. Methods involving no tissue stretching are now preferred in surgical treatment of external hernias of the anterior abdominal wall; these methods suggest the use of various synthetic endoprostheses [1]. In some countries more than 90% of all interventions for hernias are carried out with the use of mesh prostheses [9,12]. However, many-year experimental and clinical studies of synthetic mesh materials indicates that their implantation leads to the formation of seromas and infiltration, the implant wrinkles and migrates, adhesions and injuries to the adjacent organs with the formation of fistulas sometimes develop, and the implants are rejected [2,13]. Biomaterials should be infection-resistant, prevent the formation of adhesions to the viscera, be well fixed in human body, be strong and endure lasting tension, without deep cicatrization and encapsulation [6]. Special attention is now paid to studies of the relationship between the reparative function of the connective tissue in the implantation zone and the quality of polymeric material from which the endoprosthesis is made [3]. Endoprostheses with low content of polypropylene attract special attention among polypropylene-based meshes (so-called "light" meshes). Mesh implants with various types of coating, for example, by titanium [11], β-glucane [7], and collagen [8] are developed for the prevention of complications.

We compared the time course of tissue reaction after subcutaneous implantation of Vypro and Ultrapro light polypropylene meshes (Ethicon) and of these meshes coated by fibroblasts.

## MATERIALS AND METHODS

Experiments were carried out on 100 male Wistar rats. Mesh endoprostheses were implanted subcutaneously on the back. The animals were divided into control and four experimental groups, 20 per group (5 mice per term). In group 1 Vypro polypropylene meshes were implanted under sterile conditions and general anesthesia (0.5 ml sodium thiopental 1:10, intraperitoneally); group 2 animals received fibroblast-coated Vypro implants; group 3 were implanted Ultrapro; and group 4 received

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fibroblast-coated Ultrapro implants. The implants were not specially fixed; the skin was sutured by nodular sutures with Biosin 4/0 thread. Controls received no implantation. The animals were sacrificed on days 3, 7, 14, 28 after surgery. Material for morphologic analysis was collected (tissue from the implantation area together with endoprosthesis). All experiments were carried out in accordance with "Regulations for Manipulations on Experimental Animals".

Tissue fragments with the implant were fixed in 10% neutral formalin. Histological study was carried out on paraffin sections (5 μ) stained with hematoxylin and eosin. Quantitative evaluation of cell composition was carried out on a MEKOS-C TV image analyzer; the data were statistically processed by Statistica software. Specimens for electron microscopy were fixed in 2.5% glutaraldehyde and 1% osmium tetroxide. The material was dehydrated in ascending alcohols and embedded in Epon-araldite. Ultrathin sections were examined under a Philips CM-10 electron microscope.

## RESULTS

Long-term implantation of alloplastic materials caused the development of acute or subacute inflammation with moderate edema and infiltration with neutrophilic granulocytes and macrophages during 1-3 weeks. The maximum changes were observed after 14-21 days, later transforming into chronic inflammation surrounding the foreign body. This was paralleled by the formation of cicatricial tissue with numerous collagen fibers, which formed a three-dimensional structure around and inside the mesh implant [14].

Histological examination of soft tissues in control mice showed a picture characteristic of healing of uncomplicated operation wounds (pronounced edema and slight cellular infiltration by lymphocytes). The formation of mature connective tissue and typical foreign body granulomas including epithelioid and giant cells in the zone of implanted mesh endoprostheses is a natural reaction to introducion of a foreign body [4].

A sufficient number of acidophilic (eosinophilic) granulocytes, less numerous mast cells, and solitary fibroblasts were seen at the site of implantation of both mesh types. Cell reactions in the Vypro and Ultrapro implantation zones were different. On day 3 after implantation of Ultrapro endoprosthesis, lymphocytic/macrophage cell reaction with moderate content of neutrophilic granulocytes was observed (Fig. 1, *a*). Implantation of Vypro mesh (Fig. 1, *b*) was associated with severe edema in the prosthesis zone; and the cell infiltrate contained 2.8 times more neutrophils ($p<0.05$) than after implantation of Ultrapro mesh (Fig. 3). Collagen fibers were detected mainly at sites of contact with the implant and were more abundant after implantation of Ultrapro mesh. Electron microscopy showed numerous neutrophilic granulocytes and macrophages. These cells were functionally active, because the cytoplasm contained numerous va-

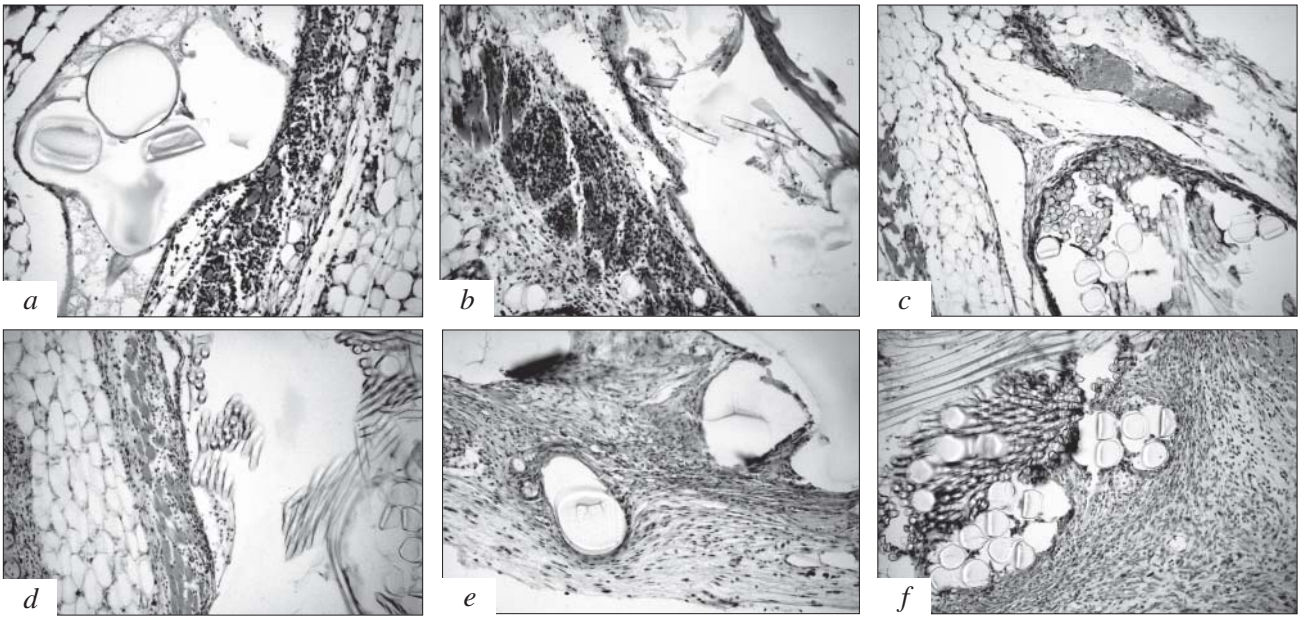


**Fig. 1.** Histological changes in tissues 3 (*a*, *b*, *d*), 7 (*e*), 14 (*f*), and 28 (*c*) days after implantation of Vypro (*b*, *c*, *d*, *f*) and Ultrapro endoprostheses (*a*, *e*) intact (*a*, *b*, *c*) and coated by fibroblasts (*d*, *e*, *f*). Hematoxylin and eosin staining, ×170.

cuoles with floccular contents, phagosomes with tissue detritus, and lipid granules. Endoplasmatic reticulum of macrophages was represented by narrow short membrane profiles, with eccentric nuclei and chromatin concentrated along the nucleolemma (Fig. 2, *a*). By day 7 of the postoperative period granulation tissue developed in the zone of intervention, the number of macrophages and neutrophils at the site of Ultrapro mesh implantation decreased almost by half, while the content of fibroblasts sharply increased (18-fold) in comparison with the previous term. Ultrastructural study showed poorly differentiated and proliferating fibroblasts, whose granular endoplasmatic reticulum was presented by parallel tubules, the lamellar complex was located near the nucleus and was surrounded by small and large bubbles. Numerous round mitochondria with clear matrix were seen. The nuclei were eccentric, chromatin was evenly distributed in the entire nucleus. A similar picture was observed after implantation of Vypro mesh. Collagen fibers formed bundles, which were most numerous in the zone of contact with the implant. Fine collagen fibers grew between endoprosthesis fibers. The number of eosinophilic granulocytes sharply decreased and remained minimum until later terms. Many new vessels were seen. By day 14, the bulk of cells in the implantation zone were fibroblasts; there were still many macrophages and lymphocytes and few neutrophils. Ultrastructural organization of fibroblasts indicated their high collagen-producing activity. They were elongated or spindle-shaped, with large nuclei and nucleoli, with a thin strip of chromatin concentrated along the nucleolemma. The endoplasmatic reticulum tubules were filled with fine granular contents. Secretory vacuoles were located mainly at the cell periphery along the cytoplasmic membrane. Fibroblasts were

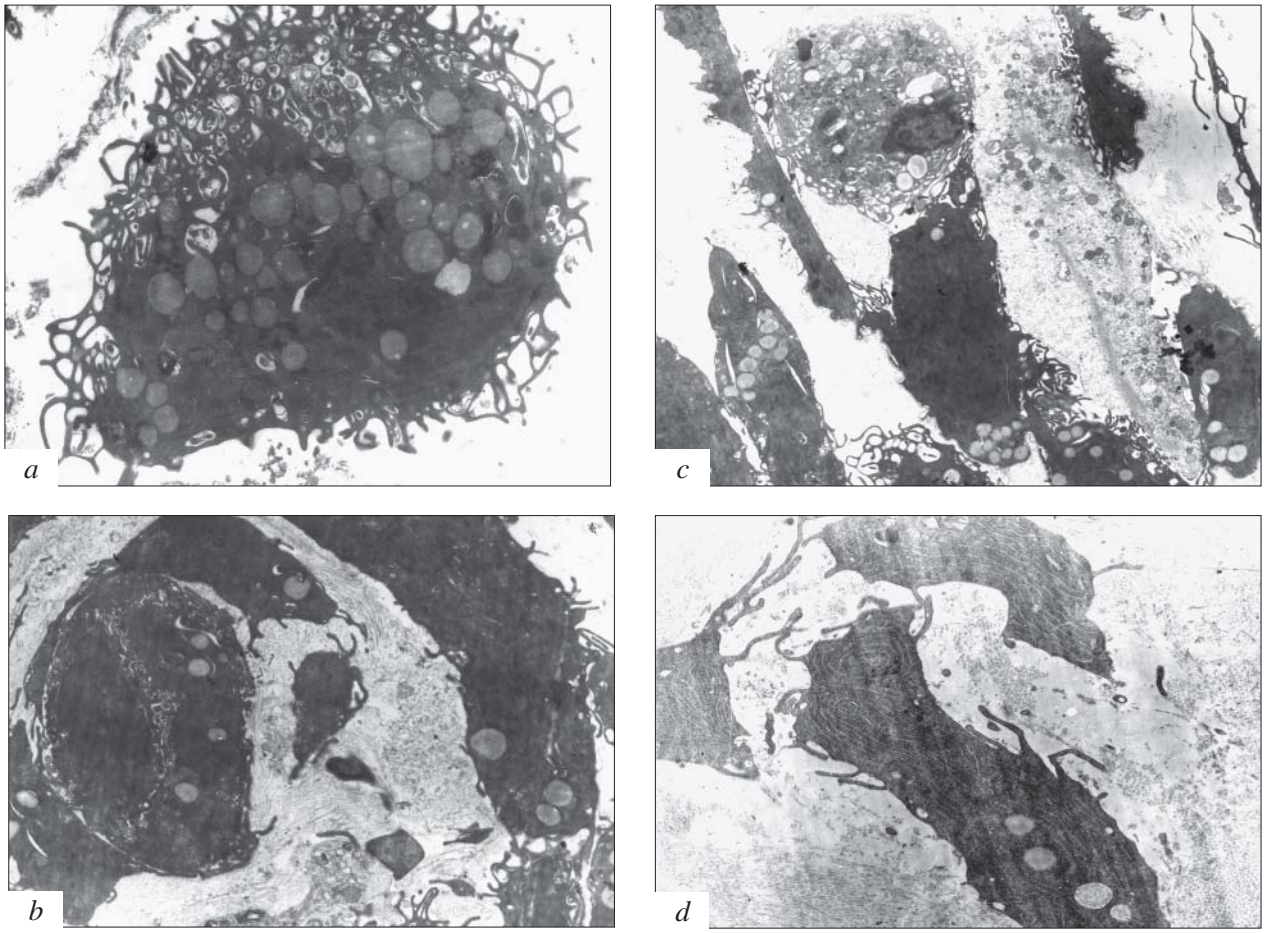


**Fig. 2.** Ultrastructural changes at the site of implantation: Vypro (*a*, *c*) and Ultrapro endoprostheses (*b*, *d*), intact (*a*) and fibroblast-coated (*b*, *c*, *d*). *a*) functionally active macrophage with numerous phagosomes, containing tissue detritus and myelin, in the cytoplasm (×10,000); *b*) granulation tissue fragment on day 3 after endoprosthesis implantation: cell-to-cell contacts between a functionally active macrophage and a fibroblast and between fibroblasts; *c*) new vessel (vascular bud) with slit-life lumen, contacts between large endotheliocytes and neighboring pericytes, functionally active fibroblasts near the vessel, collagen fibrils in cell-to-cell spaces; *d*) collagen-producing fibroblast: dilated cisterns of endoplasmatic reticulum and lipid granules, collagen fibrils around fibroblast. *b*, *c*, *d*: ×8000.

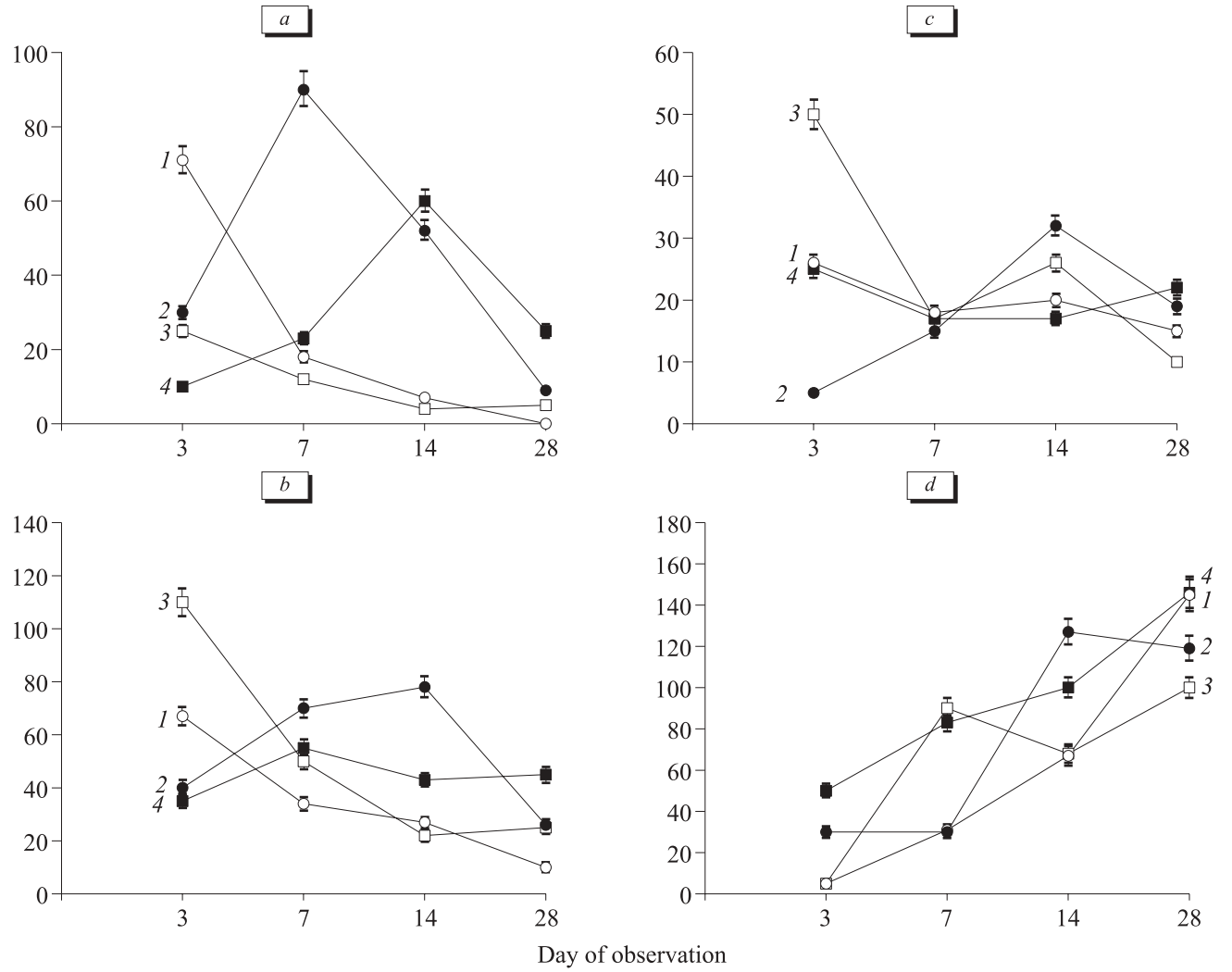


**Fig. 3.** Time course of cell composition at the site of implantation of Vypro (*1*, *2*) and Ultrapro (*3*, *4*) endoprostheses without coating (*1*, *3*) and coated by fibroblasts (*2*, *4*). *a*) neutrophilic granulocytes; *b*) macrophages; *c*) lymphocytes; *d*) fibroblasts. Ordinate: number of cells in 10 visual fields.

surrounded by forming collagen structures of different degree of maturity (from fine fibrils with blurred striatedness to large collagen bundles with characteristic periodicity). Collagen fibers were arranged in thick bundles mainly at the periphery of the implant, forming the connective-tissue capsule. By day 28 the reticular endoprosthesis cells were completely filled with collagen fibers and vascularization of the connective-tissue capsule, enveloping the implant (Fig. 1, *c*). Implantation of Vypro mesh led to the formation of cell infiltration, presented by macrophages and lymphocytes, around the endoprosthesis. Giant foreign body cells did not appear.

Implantation of polypropylene-polygalactin mesh (Vypro) to rats was associated with inflammatory reaction, at first serous fibrinous with moderate leukocyte-macrophage infiltration at the site of sutures and in the subcutaneous fat and later granulomatous, with macrophage transformation into epithelioid and giant cells, the maximum number of the latter cells being observed on day 21 [10]. The formation of foreign body giant cells near the implant was observed. None of these cells was detected in the studied histological preparations. These discrepancies can be due to animal species and the time course of formation of the foreign body type giant cells.

In general, our results indicate a common pattern of cell reaction to implantation of fibroblast-coated meshes (groups 2 and 4) and meshes without coating, but some quantitative differences are worthy of note. The number of neutrophilic granulocytes on day 3 was 2.5 times lower ($p<0.05$) and macrophage count was 3-fold lower ($p<0.05$) after implantation of fibroblast-coated Ultrapro mesh; ma-

crophage number was 1.6 times lower ($p<0.05$) after implantation of fibroblast-coated Vypro mesh (Fig. 1, *d*). The count of fibroblasts at this term is very high. During the same period we detected collagen fibers, sometimes growing between the endoprosthesis fibers. Ultrastructural study showed functionally active macrophages and fibroblasts. Morphological signs of phagocytosis activation presented as digital cytoplasmic processes in macrophages, these processes branching and anastomosing with each other. Numerous cell-cell contacts (between macrophages, fibroblasts, macrophages and fibroblasts) were seen; extracellular spaces were sometimes so narrow that the cell boundaries were hardly discernible (Fig. 2, *b*); numerous growing capillaries were detected. Their endothelial cells were large, the cytoplasmic reticulum was presented by short profiles, the mitochondria were numerous (small with dense matrix). Vascular buds with slit-like lumen and adjacent pericytes were seen (Fig. 2, *c*). By day 7 the number of neutrophils sharply increased, particularly after implantation of fibroblast-coated Vypro mesh: 3-fold in comparison with the previous term ($p<0.05$). Macrophage count somewhat increased after implantation of both mesh types. Lymphocyte count was about the same as after implantation of intact meshes, which was characteristic of not only this period of observation. The fibroblast reaction was similar to the reaction to uncoated endoprostheses, but broad connective-tissue capsule formed around the meshes, with replacement of more than half of the implant cells by the connective tissue (Fig. 1, *e*). Electron microscopy showed functionally active fibroblasts, which was seen from well-developed endoplasmic reticulum and lipid granules in the cell cytoplasm, as well as many collagen fibrils around the cells (Fig. 2, *d*).

On day 14 the number of neutrophils still increased after implantation of Ultrapro meshes and decreased after implantation of fibroblast-coated Vypro mesh. The count of macrophages decreased smoothly, this process was more pronounced after Ultrapro implantation. During this period the count of fibroblasts was significantly higher than after implantation of uncoated meshes: their number was 1.9 times higher after implantation of fibroblast-coated Vypro mesh ($p<0.05$) and 1.5 times higher after implantation of fibroblast-coated Ultrapro mesh ($p<0.05$). Collagen fibers formed numerous bundles, most pronounced at the sites of contact with the implant (Fig. 1, *f*). A connective-tissue capsule enveloped the endoprostheses, the implant cells being completely replaced by the connective tissue. By day 28, cellular reactions to implantation of all endoprostheses were similar both qualitatively and quantitatively.

Hence, Vypro and Ultrapro endoprostheses are biologically compatible and stimulate the growth of connective tissue in the implantation zone even during early period after implantation. Implantation of Vypro mesh was associated with attraction of numerous neutrophilic granulocytes and their longer elimination. These differences seem to be caused by different composition of absorbed fibers and by the fact that Vypro is a multifilament and Ultrapro a monofilament mesh.

Tissue reaction to implantation of analogous meshes coated with fibroblasts was more pronounced, particularly during the early period, while the process of connective-tissue capsule formation and implant growth was more rapid. These mesh endoprostheses can be used in non-stretching plastic repair of the abdominal wall for hernias. However, the results of animal experiments should be verified by clinical trials.

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