INTERACTION BETWEEN TISSUE SYSTEMS IN IMPLANTS

A. G. Ginovker and G. S. Solov'ev

UDC 612.6.02-08

The cartilage and prostate gland of albino rats were implanted into homologous intact recipients. True union of the connective tissue of donor and recipient into one system was found not to take place, mismatching is found between the glandular epithelium and the recipient's connective tissue, and optimal relationships are established between the cartilage and connective tissue.

The object of this investigation was to study interaction between tissue systems in the course of their differentiation.

EXPERIMENTAL METHOD

Two series of experiments were carried out on noninbred albino rats. Implants (implantation by Lazarenko's method beneath the skin of the anterior abdominal wall) of cartilage (series I) and prostate gland (series II) of donors aged 10 days were studied. The recipients were animals aged 4 months and weighing 200-220 g. The material was treated histochemically (tetrazonium coupling reaction, detection of SH- and NH_2-groups) and by autoradiography using methionine-S^{35}. Methionine was injected intraperitoneally in a dose of 0.5 μCi/g body weight 6 h before fixation. The autoradiographs were prepared with type R NIKFI emulsion. The numerical results were subjected to statistical analysis. Altogether 48 implants were studied over periods ranging from 1 to 12 days.

EXPERIMENTAL RESULTS

Regardless of the series of experiments the stages of the tissue interrelationships were uniform in type and were determined by the stage of growth of the implant: adaptation, activation and growth, differentiation and atypical function. In the period of adaptation (1st-3rd days) three zones of connective tissue could be distinguished in the implants and the surrounding bed: pericelloidin (first zone), intercelloidin (second zone), and peripheral – the connective tissue of the bed (third zone). This zonal pattern is the result of activation of components of the transplanted tissues and the bed.

In the first zone the highest intensity of accumulation of total protein, containing amino acids (histidine, tyrosine, tryptophan) and NH_2- and SH-groups, was found in cells of the fibroblastic series. Breakdown of collagen fibers of the transplanted connective tissue was negligible.

In the second zone the intensity of the histochemical reactions for protein was lowest, but the highest mitotic activity was found in cells of the fibroblastic series. This zone lies at the boundary between two interacting systems and, in the writers' opinion, it performs the role of intermediary between these tissues. Lymphocytic infiltration near to the fragments of cartilage was observed in this zone also. The lymphocytes gave a strong tetrazonium coupling reaction and were arranged around the border of the cartilage fragments (Fig. 1a). Only solitary lymphocytes could be found at this time beneath the epithelium, some of them dead. Components of disintegrating lymphocytes are evidently utilized as building material

Department of Histology and Embryology and Department of Normal Physiology, Tyumen Medical Institute. Laboratory of Experimental Histology, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Leningrad. (Presented by Academician of the Academy of Medical Sciences of the USSR A. M. Shabad.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 74, No. 8, pp. 89-92, August, 1972. Original article submitted December 21, 1971.

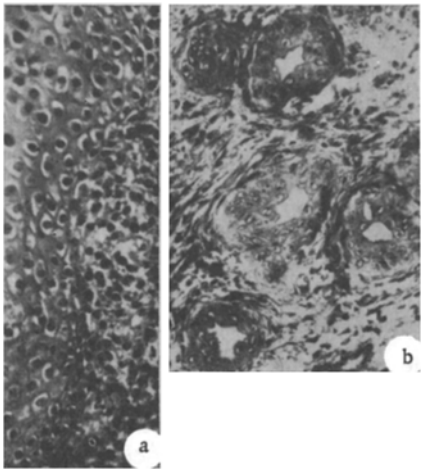

Fig. 1. Implants of cartilage and prostate gland tissue: a) cartilage implant. Donor: male rat aged 10 days, recipient: male rat aged 4 months. Stage of experiment 6 days. Lymphocidal elements surrounding implanted fragment of cartilage. Tetrazonium coupling reaction, fixation in Carnoy's fluid, 140×; b) prostate implants. Donor: rat aged 4 months, stage of experiment 12 days. Tetrazonium coupling reaction, 140×.

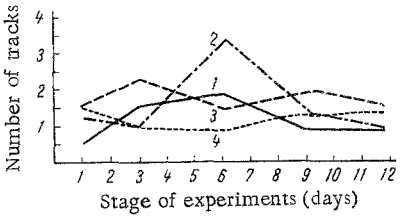

Fig. 2. Incorporation of methionine-S^{35} into connective tissue joined to implants. Implants of prostate: 1) subepithelial connective tissue; 2) intercelloidin connective tissue; 3) interfragmentary connective tissue; 4) intercelloidin connective tissue.

[4-7]. Some lymphocytes also disintegrated between the fragments of implanted cartilage. Their material was utilized by cells of the chondroid series. The main mass of the connective-tissue cells surrounding the cartilage was performing a different function. At this stage of the experiment the number of lymphocytes in the perichondrial zones of the implant showed a decrease. Some of them were evidently excluded from the immune response and differentiated in osteoid and chondroid directions. There is evidence in support of the validity of this hypothesis [1].

Disintegration of the donor's collagen fibers was predominant in the third zone, and the fragments were surrounded by dilated blood vessels. By the 6th-8th day the breakdown products (protein substrates) could be found near foci of epithelial proliferation in the form of droplets and masses of different sizes. They disappeared during differentiation of the epithelium. This fact suggests that they are utilized in the metabolism of the differentiating structures [3].

The secretion of protein substrates by fibroblasts varied in intensity in different zones in the course of the experiment. The intensity of secretion in the fibroblasts was highest in the stage of growth in the subepithelial connective tissue.

In these experiments the intensity of protein synthesis in the cells of the proliferating glandular tissue correlated with that in the underlying connective tissue. The boundary between the connective-tissue zones as defined above could be clearly traced in subsequent stages in the prostatic implants. This fact was morphological and histochemical evidence of mismatching between the prostatic connective tissue and the connective tissue of the skin of the abdominal wall, at the site of implantation. On the other hand, it also reveals the stability of the relations arising in the course of individual development between the epithelium and connective tissue. This is one of the causes of death of the glandular fragments transplanted into connective tissue uncharacteristic of the prostate gland. Fragments of regenerating epithelium, differentiating in the donor's connective tissue, were able to survive longer (Fig. 1b).

After the stage of 8 days and until the end of the experiment, osteogeneis took place in the cartilage tissue implants. A change in the maturity of the cartilaged tissue during growth of the implant thus modified its inductive powers and led to manifestation of the osteogenic properties of the connective tissue.

Analysis of the incorporation of methionine-S^{35} showed that during the first 3 days of the experiment protein metabolism in the connective tissue between the fragments differed in the implants of cartilage and prostate gland (Fig. 2). The intensity of incorporation was higher in the implants of the cartilage than of the prostate. Activation of protein synthesis in the cartilage implants corresponded to the histochemical data. The level of protein synthesis in the prostate implants, on the other hand, indicated prolonged adaptation of the gland cells. The level of incorporation of the isotope was about equal in the intercelloidin connective tissue. In confirmation of the morphological and histochemical findings, by the 6th day incorporation

of the isotope into the intercelloidin and interfragmentary connective-tissue zones of the prostate implants reached its maximum. In the cartilage implants, on the other hand, incorporation into the connective tissue was minimal at this stage. This was due to variations in the character of synthesis of polysaccharide substrates in the differentiating connective tissue. Incorporation of the isotope into prostate implants later decreased, and by the 12th day the intensity of incorporation was the same in both connective-tissue zones, indicating that the level of metabolism of the protein substrates was becoming equalized throughout the connective-tissue stroma of the implant, although it still remained morphologically heterogeneous. In the cartilage implants no significant difference could be observed in incorporation of the isotope, but the intensity of incorporation into connective tissue between the cartilage fragments was always higher than in the intercelloidin space. This is evidence of the continuous action of the implanted cartilage on the recipient's connective tissue.

Analysis of this factual material shows that interaction between the two tissue systems in the implants takes place in different ways: an exchange of metabolites and establishment of functional interaction take place between the connective tissue of the donor and recipient, but true union of these tissue into one system is not observed; optimal relations are established between the cartilage and connective tissue; connection between the epithelium and connective tissue arises through reutilization of building and energy-forming substrates.

Among the causes of death of transplanted glands are the specificity of the connective tissue of the organ and mismatching between the epithelium and the newly formed tissue of the recipient.

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