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TRANSPLANTATION OF HUMAN EMBRYONIC TISSUES INTO NUDE MICE

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Tumors have now been successfully transplanted directly from man into nude mice [1, 3]. However, normal human tissues have been successfully transplanted into them extremely rarely. As regards normal adult human tissues, only skin has been successfully transplanted into nude mice [6]. Human tumor cells from tissue culture proliferate well in nude mice [4, 5], but no such proliferation could be obtained when normal human embryonic fibroblasts were transplanted into them from culture [2].

In the investigation described below tissue from human embryonic and fetal skin and muscle, stomach, large intestine, and liver was transplanted into nude mice.

EXPERIMENTAL METHOD

Nude mice based on line BALB/c, aged 8-10 weeks and reared by ourselves, were used. The different tissues for transplantation were obtained from 6-8-week human embryos and 5-8-month human fetuses. The material was injected subcutaneously into the mice in the form of a suspension in a dose of 0.5 ml, which contained 150 mg of human tissue. Sections were cut from the transplants 20-40 days after injection, and stained with hematoxylin and eosin, and picrofuchsine.

EXPERIMENTAL RESULTS

Transplants of liver, stomach, large intestine, and skin and muscle tissue taken from 8-10-week human embryos grew rapidly. If the tissue was taken from 5-8-month human fetuses the transplants grew much more slowly.

The transplants of embryonic liver consisted of a system of cavities (honeycomb) lined with cylindrical, cubical, and thickened epithelium. The cavities were separated by connective-tissue septa of varied thickness. Accumulations of cells resembling hematopoietic tissue were present in the lumen of some cavities. The transplant thus preserved the structure of the embryonic liver (Fig. 1a). The transplant of the fetal liver had a honeycombed struc-

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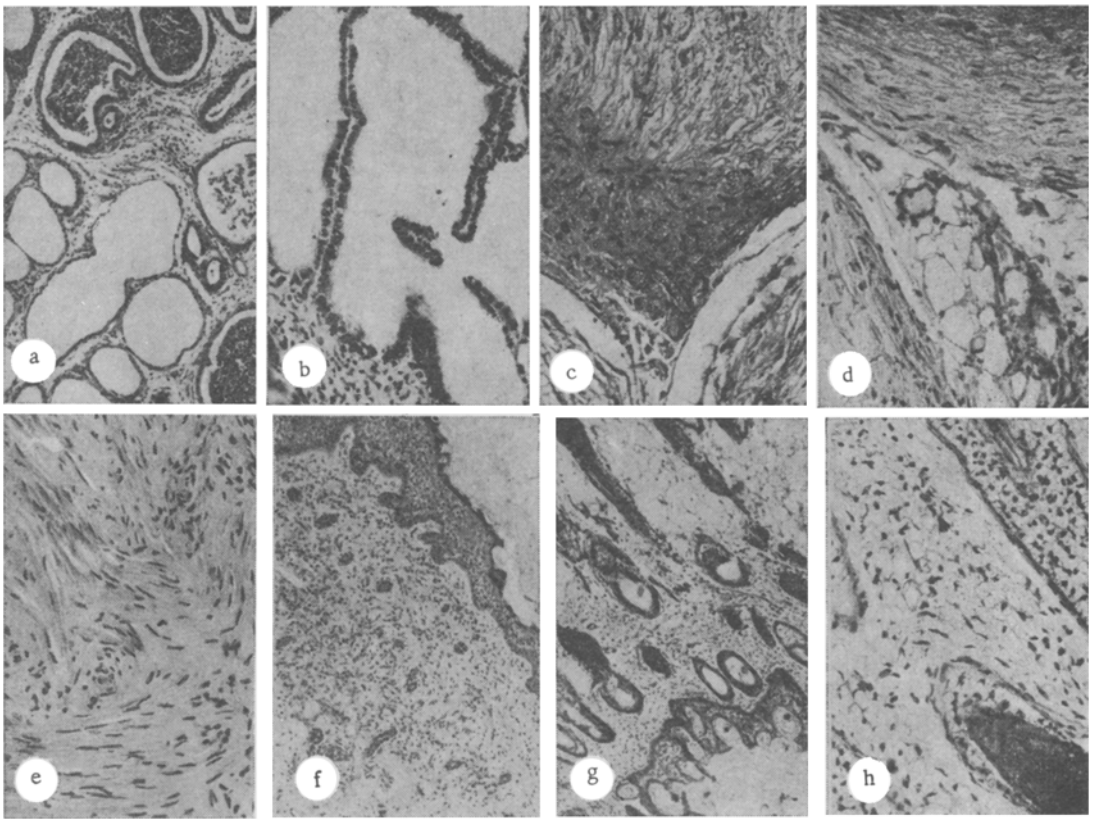

Fig. 1. Transplants: a) embryonic liver, b) fetal liver, c) embryonic large intestine, d) fetal large intestine, e) fetal stomach, f) fetal skin and muscle tissue, g, h) embryonic skin and muscle tissue. a, b, d-h) Stained with hematoxylin and eosin; c) stained with picrofuchsine. Magnification: a, g) 63×; b-f, h) 160×.

ture and consisted of cavities lined with simple epithelium. This formed small outgrowths and papillae, pointing inside the cavities. Foci of round "hepatocyte-like" cells, not forming trabeculae, and single foci of cartilage-like tissue in the bands of connective tissue between the epithelium were observed (Fig. 1b).

Cells of hepatocyte type appeared in the fetal liver transplants, but no evidence of embryonic hematopoiesis was present.

The transplant of embryonic large intestine consisted of connective-tissue complexes which differed in shape and size: fibroblasts with intensive collagen production (in the form of bundles of thin fuchsinophilic, PAS-positive fibers). Collagen predominated over the cell components with fatty areolar tissue. No epithelial cells were found (Fig. 1c).

The transplant of fetal large intestine also consisted of fibroblast tissue. Cells of fibroblasts and fibrocyte type formed collagen fibers: delicate in the center, coarser at the periphery of the modules. No epithelial cells were present (Fig. 1d). The transplant of fetal stomach consisted of smooth-muscle tissue, around which bundles of collagen (fibrous) tissue, of varied thickness, were arranged. An area of fatty areolar tissue was adjacent to the main mass of tissue, and no epithelial cells were present (Fig. 1e). The transplant of embryonic skin and muscle tissue consisted of haphazhardly arranged cystic formations, lined with flattened stratified epithelium, containing structures of keratin type and fragments of pigmented hair. The transplant was a teratoid formation consisting of malformed epidermoid cysts and hair follicles. Macroscopically the graft contained bundles of pigmented hairs about 1 cm long (Fig. 1f).

The graft of human fetal skin and muscle tissue was an organoid formation of epidermoid cyst or hair follicle type: the lumen was lined by stratified squamous epithelium and contained laminated masses of keratin type. The cavity was surrounded by loose connective tissue which contained poorly developed appendages of the skin: cavities and tubes of sweat gland type. Rudimentary structures of the skin and its appendages appear in the transplant (Fig. 1g).

The transplant of fetal skin and muscle tissue differed from embryonic by the presence of keratin masses.

Transplants of different human tissues in nude mice can be used in experimental oncology for the dynamic study of conversion of normal into tumor cells under the influence of oncogenes, viruses, chemical carcinogens, hormones, and irradiation.

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