A MORPHOLOGICAL STUDY OF TRANSPLANTATION IMMUNITY

(Transplantation by the Method of F. M. Lazarenko)

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Homograft may fail to take on account of transplantation immunity; the effect is produced by the reaction of the recipient to the foreign antigens of the donor. If there is sufficient incompatibility of the antigens the graft is rejected within 12-20 days [5].

Several methods are known which can be used to extend appreciably the time before rejection. Each is based on the destruction of some link in the transplantation immunity reaction. Thus, small nonvascularized grafts are not rejected because the recipient does not receive from him a sufficient quantity of antigen [6]. In transplantation into the brain or into a region from which the lymphatic nodes have been removed the grafts will take, because their antigens do not reach the lymphatic nodes, and produce no immunization [8].

In making grafts onto animals exposed to x-rays [7, 9] or treated with cortisone [10], or made artificially tolerant [3], the graft is not rejected and the lymphoid tissue does not respond to the introduction of foreign antigens. Finally, in the transplantation of tissue in diffusion chambers thegraft is not rejected because the walls of the vessel allow of no contact between the lymphocytes of the recipient and the donor tissue [2].

Evidently any occasions whereby the life of the transplant is prolonged and which is brought about by methods other than those already elaborated will be of great interest. If such effects are produced not by interrupting already known links in the transplantation immunity reaction they may help to explain the unknown aspects of this response. Here we must note the results obtained in grafts which remained in situ for 100 days; they consist of skin or thyroid grafts introduced subcutaneously as small portions mixed with finely divided celloidin [1].

Implantation by the method of F. M. Lazarenko has nothing in common with the methods already mentioned for overcoming transplantation immunity. In this case the graft is in the connective tissue, which is in a state of reactive inflammation. The question to be decided is whether this state really influences the fat of homograft.

We have attempted to determine whether the survival time of the graft transplanted by the Lazarenko method is prolonged in cases when the amount of transplanted tissue is sufficient to induce a transplantation immunity such as will lead under normal conditions to the resorption of such graft within 10-20 days.

EXPERIMENTAL METHOD

The experiments were carried out on adult rabbits of impure lines weighing 2-2½ kg. Fragments weighing 400-600 mg were washed in physiological saline with antibiotics, and were cut up into small pieces with scissors. The mixture introduced subcutaneously without any further addition by means of a U-section probe, or else it was mixed with three times its volume of finely divided celloidin. After a certain time the transplanted tissue was fixed in alcohol-formol and embedded in celloidin-paraffin. Serial sections were stained with hematoxylin-eosin. We used eighteen rabbits. In four, autografting was made with celloidin (grafts fixed after two months), in four they were made without celloidin (grafts fixed after one month), and in ten homografts were made with celloidin (grafts fixed after one month).

EXPERIMENTAL RESULTS

All four autografts showed a good epithelial growth and the formation of cysts lined with stratified squamous epithelium which was considerably cornified. In the surrounding connective tissue there was no lymphoid infiltration. In places the pieces of celloidin had induced the formation of giant foreign-body cells. On the whole the grafts showed complete differentiation of epithellium, and there were no signs of an immunological reaction by the recipient to the graft.

In experiments on homografting without celloidin, in no case was any epithelial tissue found at the site of the graft after one month. There remained only traces of cells surrounded by giant foreign-body cells. The epithelial portion of the graft had therefore been completely absorbed.

In the experiments with colloidin in no case was any living epithelial tissue found after one month. The connective tissue surrounding the portion of celloidin contained numerous foreign-body cells. Of the epithelial portion of the graft there remained only the roots of the hairs surrounded by cells; the whole of the transplanted epidermis had been absorbed.

The fact that an autograft of skin mixed with celloidin (F. M. Lazarenko's method) survived for at least two months shows firstly that when there is no immune response to the subcutaneous transplantation of finely divided adult skin the necessary conditions are created for the grafted cutaneous epithelium to take, to grow, and to differentiate; secondly, just as F. M. Lazarenko supposed, the reaction to celloidin neither hinders the growth of the graft nor influences the extent to which it takes.

However, under conditions where the antigens of the homografted tissue constitute a fairly strong immune stimulus F. M. Lazarenko's method, i.e., transplantation with celloidin, does not influence the time for which the homograft remains. The extent of the stimulation depends upon antigenic differences between donor and host, and on the size of the homograft. In this experiment we used half the size of the homografts for which Medawar established the mean survival time, which was 10.4 ± 1.1 days when tested on impure strains of rabbit.

The shortness of the times of survival of the homograft with celloidin in relation to those mentioned in F. M. Lazarenko's report may probably be attributed to the fact that Lazarenko used very small amounts of grafted tissue, i.e., he introduced a very small amount of antigen. A special review has been made of the influence of the amount of antigen on homograft survival time [4]. From what Medawar has said, it would follow that Lazarenko used approximately one-twentieth of the amount of tissue required to induce the development of an intense transplantation immunity.

Therefore, the reactive condition of the connective tissue due to the presence of a foreign body does not appreciably influence the development of transplantation immunity. However, it cannot be deduced from this result that no other changes in the surrounding connective tissue influence the fate of the graft. This important problem requires further investigation.

SUMMARY

A comparison was made of the periods of the survival time of skin homografts or autografts implanted subcutaneously into a site in which aseptic inflammation had been induced by celloidin. The autografts were not absorbed for at least two months or more. Homografts were absorbed in one month. The absorption period was unaffected by the presence of celloidin. Consequently if sufficient antigen was given, aceptic inflammation prevented neither the immunization nor the immune reaction.

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