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The reactive power of the white rat to tissue implantation. Second communication.

By **ISAAC LEVIN.**

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At the November meeting of the New York Pathological Society,[1] I reported briefly on a series of experiments I have undertaken on white rats, with the aim to investigate whether the great success attained lately in the transplantation of malignant growths from one rat into another is not due, in part at least, to the different behavior of the organism of the white rat to tissue implantation, as compared with other laboratory animals.

The majority of the workers who have experimented with the tumors of the white mouse or rat seem to be of the opinion that the success in the transplantations of these tumors is due to the great intrinsic power of limitless proliferation of the cells of these tumors, and they ignore the possible cellular reaction of the organism of the host to the implanted tissue. But the fact that pieces of the same tumor from the same rat or mouse grow readily on white mice of one race, and not at all on the white mice of another race; the fact, further, that while the original tumor, when implanted, grows in only about 10 per cent. of animals used, and, when re-implanted, it grows in 90 per cent., and some other similar instances, seem to indicate, *a priori*, that the white mouse or rat reacts differently to implantation of tumor, as well as of normal tissue, than the other laboratory animals.

My first set of experiments consisted in the implantation of normal tissue from one animal into another. Pieces of skin, liver, spleen, testicle, or mammary gland are implanted under the skin or in the peritoneal cavity of another animal. In the great majority of the experiments (about 60 to 75 per cent.) the pieces remained unabsorbed for as long as three weeks, even when, as in the peritoneum, they do not become attached anywhere, but float like a foreign body. Usually, the pieces are either surrounded by

[1] Levin: *Medical Record*, December 14, 1907.

a capsule consisting of an outer fibrous layer, and an inner one made up chiefly of round cells, or else the round cells invade the implanted tissue. One is impressed with the great amount of organization going on around the implanted pieces. On the other hand, the pieces themselves seem to retain the cell structure much longer than is usual in other animals.

It seemed interesting to investigate whether the white rat will also react differently from other animals to an introduction of an irritating foreign body.

An emulsion of aleuronat produces, in the ordinary laboratory animals, an abscess, when injected under the skin, and empyema, when injected into the serous cavity. In nine rats an *emulsion of aleuronat* was injected under the skin, and in each animal there developed in the place of injection a freely movable tumor the size of a small nut, which on examination proved to be a cyst filled with thick cheesy detritus. In only two animals did the skin become eroded; in the others the growth retained the same size during two to three weeks.

In six white rats I introduced into the peritoneal cavity one or two *triturate tablets of aleuronat.* The animals were killed in three days to two weeks after the operation. At the autopsy there was found in the place of each tablet a little growth of white grayish color, the consistency of a granulation, loosely adherent to the omentum, occasionally with some cheesy detritus in the center. Microscopically the growth consists of a conglomeration of round cells and leucocytes towards the center, and round cells and some beginning of fibrous connective tissue formation towards the periphery.

While even this last named formation is not a tumor in the true meaning of the word, but a connective tissue reaction to an irritation, it seems to be clear from all these experiments that the reactive cell proliferation and cellular organization is much more extensive in a white rat than in the other laboratory animals. On the other hand the absorption of the implanted tissue is a great deal slower, consequently there is a better chance for the implanted cell to proliferate and for the implanted tissue to grow. Whether there is still a qualitative difference between a tumor cell and a normal tissue cell, or conditions may be found under which normal cells will acquire the power of limitless proliferation, for the

study of this question the white rat is certainly the most appropriate animal.

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The hemolytic reactions of the blood in dogs with transplantable lymphosarcoma.

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Dogs with lympho-sarcoma in every stage of growth were made use of, including those in which growth was active and progressive, those in which the tumor was quiescent, those in which the growth was regressing, and those in which recovery with complete absorption of the tumor had taken place. Some of the dogs were in good general condition, others were cachectic. Controls were also made use of, including dogs in poor and in good condition. In all, the material comprised 34 dogs, 18 with a tumor history, and 16 without. These were all bled from the femoral artery or jugular vein. In all of these dogs, blood was obtained for serum, and for a 1 per cent. suspension of corpuscles. The serum of each animal was tested on the corpuscles of a number of other animals in order to determine its hæmolytic power. Up to the present time over 300 such tests have been made. The serum obtained from tumor dogs is almost without exception possessed of hemolytic power. This is least marked in the early and active stages of tumor growth, more so in the broken down and softened tumors. It persists even in the dogs which have recovered of their tumors. The corpuscles of the tumor dogs manifest a much greater resistance to this hemolytic activity of the serum than do the corpuscles of other dogs. The resistance is not absolute in the test tube, but in dilutions which are just sufficient to demonstrate the hemolytic activity of the serum from tumor animals on normal corpuscles, the corpuscles from tumor animals remain intact. The serum of animals without tumors has almost without exception failed to show any hemolytic power and the corpuscles have not been resistant to the serum derived from tumor dogs.