35 (81). **"On experimentally produced variations in the energy of tumor growth": LEO LOEB.** (Presented by **JAMES EWING.**)

Inoculations of different tumors (sarcomas of the thyroid, mixed tumor of the submaxillary gland) through several or many generations have shown that, under the influence of experimental conditions, the energy of tumor growth varies in a definite way. The rate of growth is relatively slow in the animal originally affected by the tumor; after the inoculation into the first generation there is a certain latent period, after which the tumor begins to grow. The growth in the first generation is more rapid than in the original animal. After the inoculation into the second generation the latent period is abbreviated, more or less, and the succeeding growth is likewise more rapid than the growth in the original animal, or in the first generation. A further shortening of the latent period, or an increase in the rapidity of tumor growth, does not take place in the succeeding generations. Duration of the latent period and rapidity of growth may remain stationary through many generations, or the energy of the tumor growth may even somewhat decline.

These facts permit the conclusion that transplantation of a tumor has a tendency at first to increase the energy of tumor growth, and that this increase may be cumulative. That this increase does not continue in succeeding generations may perhaps be explained by the existence of counteracting influences, the actual existence of which can be demonstrated, as will be shown later.

The energy of tumor growth can be increased directly, and not only indirectly, merely by removal of the tension of the surrounding capsule or by better conditions of nourishment. Such a direct stimulating effect of the wound upon the cell growth causes probably a phenomenon not infrequently observed by surgeons, namely, the increase of malignancy in recurrent tumors. It is also possible to diminish the energy of tumor growth. In the course of tumor inoculations it not rarely happens that certain tumors remain stationary or apparently even retrogress spontaneously. This is especially found in the course of later inoculations, and it probably indicates that after many inoculations one or several of

the factors determining a vigorous tumor growth become gradually weakened. In such cases one can observe that even a long time after the expansive growth of such a tumor piece has ceased, many mitoses are present in the cells of the stationary or retrogressive tumor.

It is possible to diminish the virulence of tumor cells directly by subjecting them to certain physical or chemical conditions. By heating tumor cells up to 43° C. or 44° C. for half an hour outside the body, or by leaving them before inoculation in glycerin for 12 to 24 hours, and washing them afterward in 0.85% sodium chlorid solution, or by keeping them one or two days in $n/700$ KCN solution, before transplantation, we are able to diminish considerably the energy of the succeeding tumor growth and to increase the period of latency. In the author's recent tumor inoculations of a salivary tumor, a similar action of glycerin in increasing the period of latency was found to occur. Frequently such tumors remain stationary after a short preceding period of growth. In the first experiments of this kind on rat tumors, it was found that a temperature of 45° C. during half an hour kills the tumor cells. Jensen found a similar sensitiveness of his mouse tumors. Sticker's lymphosarcoma could be heated to 45° C. without being killed. The power of resistance of different varieties of tumor cells varies somewhat, therefore, and the means to be adopted to obtain a diminished virulence in the growth of an inoculated tumor will vary accordingly. In this connection it might be mentioned that these facts may perhaps find a practical application, insofar as pieces of tumor previously subjected to such treatment might be used to procure active immunity against tumor growth. That such active immunity is possible, at least in the case of certain tumors, is especially indicated by the observations of Sticker.

If now we wish to analyze the cause of this decrease in the rate of growth of tumor cells we have to consider several possibilities. It might be that the physical or chemical means employed kill most of the cells, and leave only a few cells alive and able to give origin to the developing tumor. Two facts speak against such an interpretation. In the case of any tumor transplantation, the growth starts from a relatively small number of cells, inasmuch as the central part of the transplanted piece becomes necrotic. In

his first series of tumor transplantations the author obtained well growing tumors after injection of cystic tumor-fluid into rats. In such cases one or very few cells must have given rise to the tumor growth, and these tumors developed in a few cases quite rapidly. Such an explanation is, therefore, improbable. Further, we would have to consider the possibility that the means employed to decrease the virulence of tumor cells are favorable to the growth of bacteria, and that they inhibit in this way the development of tumors. It is certain that bacterial toxins frequently act unfavorably upon the growth of tumors. Against this explanation, however, the objections can be raised that tumors with experimentally diminished virulence did not show any sign of putrefaction, nor did they, after inoculation, cause a formation of abscesses, occurrences which are frequent after transplantation of infected material.

It is, therefore, most likely that the cause of this decrease in virulence is the result of the direct decrease of the vitality of the tumor cells as expressed in their energy of growth. It is, however, desirable to further analyze these facts in future experimental work on tumors, especially as the character of such work necessarily limits greatly the number of experiments a single observer can make. With this restriction it may be stated that the observations here recorded point to the conclusion that it is possible to cause an experimental increase or decrease in the energy of tumor growth, that these variations may be caused by a direct stimulating or depressing influence upon the tumor cells, and that such a stimulating effect may be cumulative.

36 (82). **"Demonstration: Photographs and plumage-charts of hybrid poultry,"** with remarks: **CHARLES B. DAVENPORT.**

Dr. Davenport exhibited photographs and plumage-charts of four hybrids between different races of poultry, and also of their parents, and remarked on the nature of the inheritance illustrated by each example.

37 (83). **"Experimental cirrhosis of the liver": RICHARD M. PEARCE.** (Presented by **EUGENE L. OPIE.**)

The experimental studies upon which this communication is based were suggested by an investigation of the necrosis produced