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The influence of an inoculation with tumor material of experimentally decreased virulence upon the result of a second inoculation with tumor material of experimentally decreased virulence.

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Eight years ago one of us has shown that through the influence of chemical and physical factors it is possible to decrease the energy of growth of tumor-cells without killing the cells.¹ While a certain degree of injury kills the cells, a graded decrease in the action of the external agency leads to corresponding gradations in the decrease in the energy of growth of the cells. Thus it is possible to obtain tumor material which is still alive, but which gives rise to a very insignificant growth in many instances, and the initial growth of which is in many cases followed by a spontaneous retrogression. At that time we considered the possibility that such tumor material of experimentally decreased virulence might serve as a vaccine which might provide a certain protection against a second injection with more virulent material.

We tested therefore the influence of a first injection of such material upon the growth of a subsequent inoculation with tumor material. In the majority of cases both inoculations were separated by an interval of 10–20 days.

In order to obtain a more sensitive reagent indicating the presence of even a slight immunity, we used as material for the second (or sometimes third) test-injection not virulent tumor pieces, but again tumor material of experimentally (through heating) decreased energy of growth. Our results were as follows:

1. If the tumor material of experimentally decreased virulence did not give rise to tumor formation, no immunity was noticeable, even if the mice had received two or three preparatory injections

¹*Virchow's Archiv*, Bd. 172, 1903, p. 395.

at various intervals. In a number of cases the last inoculation gave rise to even larger tumors than in the control mice which had not received any preparatory inoculation. In cases in which mice were injected with a suspension of finely divided tumor material of (through heating) diminished virulence, the same lack of immunity was observed on subsequent inoculation with tumor pieces of decreased virulence. The number of mice which we treated with a preparatory injection of fine tumor suspension is however as yet relatively small and these experiments will therefore have to be continued.

2. If the preparatory inoculation with material of decreased virulence led to a temporary tumor growth, which latter was followed by a spontaneous retrogression an immunity against a subsequent inoculation with virulent tumor material was obtained in many cases. This observation is in accordance with the findings of other investigators. This immunity is however by no means absolute and it will be necessary to determine in further experiments upon what factors such gradations in acquired resistance depend.

3. In many cases mice in which a tumor has begun to grow after the first inoculation of tumor material of decreased virulence, can be successfully inoculated a second time with material of decreased virulence, and in some experiments the tumors derived from the second transplanted piece grow as well in mice in which the first preparatory inoculation had given rise to tumor growth as in such mice in which the first pieces had not given origin to tumor growth, and in such animals two tumors are growing simultaneously; but in the majority of cases we find that only one tumor grows after two successive inoculations with tumor material of decreased virulence. If the preparatory inoculation had been followed by tumor growth, the second inoculation gave frequently a negative result and vice versa. And especially if the tumor resulting from the first inoculation is growing very actively, a second inoculation with material of decreased virulence is in the large majority of cases not followed by tumor growth. This observation would therefore point to the conclusion that in a certain number of cases the growth of a tumor protects to some extent against a subsequent inoculation with material of de-

creased virulence. But in as much as in a number of experiments such an excluding action of a first inoculation was not noticeable, we are not yet ready to state positively that such an immunizing effect of a growing tumor exists. We are however inclined to believe that a number of variable factors (especially a variable energy of growth of the first and second tumors) are present and that such factors complicate the results. In further experiments we shall endeavor to analyze such variable factors.

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Supplementary report on attempts to immunize against tuberculosis.

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We have sought to employ the resistance acquired by or embodied in the serum of the healthy animal in its life struggle against a deadly infection with tuberculosis.

The depression reaction produced by injections of tuberculous serum into animals sensitised with tuberculin, a description of which we have already published has led us to this investigation.

After employing a number of methods for utilizing the serum of healthy animals which had been infected with tuberculosis, we are duplicating one which seems to have given promising results.

Method 1—Begun December 2, 1909. The result of this experiment was reported at the meeting of the American Association for the Advancement of Science, December 27, 1909.

One rabbit was given a sensitising dose of 1 c.c. tuberculin subcutaneously and beginning two days later this rabbit received the following:

Dec.		Tuberculous rabbit serum.
4,	1 c.c	" " "
" 6,	"	" " "
" 8,	"	" " "
" 10,	2 c.c.	" " "
" 14,	"	" " "
" 16,	"	" " "
" 18,	"	" " "

A rest of ten days was given the experimental rabbit which was