It appears that the abnormality in neoplastic diseases of plants is found in the rate of division rather than the character of the division. The rapid increase of cells is a response to the parasitic stimulation. In animal cancer both the rate and character of the divisions are aberrant.

This paper was read, in Boston, before the Botanical Society of America in December, 1922. A full report with three plates of figures will appear shortly.

254 (2486)

Further studies with the Dick test and active immunization with scarlet fever streptococcus toxin.

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Further studies have been made with the Dick test along the following lines:

1. Results with the test among special groups of children and adults.
2. Study of the control test with heated toxin and with toxin neutralized with convalescent serum.
3. Study of scarlet fever cases during convalescence.
4. Study of toxins produced by special strains of hemolytic streptococci.
5. Retest of a group of children actively immunized with increasing doses of scarlet fever streptococcus toxin.

1. The application of the Dick test to a group of 320 children at the Horace Mann School and at the Riverdale Country School, New York City, has shown a very high percentage of susceptible individuals in this class of children coming from the more well-to-do homes. The test showed that of 320 children varying in age from 5 to 18 years, 266 or 83.0 per cent were susceptible and gave a positive reaction. The Dick test was also given to 80 nurses at St. Vincent's Hospital, and of these 42 or 52.5 per cent showed a positive reaction. The nurses at this

hospital had been previously tested with the Schick test and 55 per cent were found susceptible to diphtheria. A group of babies were tested at the Heckscher Foundation with the following interesting results:

Age	Total tested	Dick positive	Dick negative	Per cent Dick positive
0-3 mo.	20	1	19	0.5
3-6 mo.	17	9	8	52.7
6-9 mo.	4	4	0	100.0
9-12 mo.	7	7	0	100.0
1-5 yrs.	25	20	5	80.0
Total	73	41	32	56.1

Of a group of 4570 individuals varying in age from a few weeks to over 20 years we found that 1543 or 34.4 per cent gave a positive Dick reaction. Up to 6 months the percentage of positive reactions was 44.8; from 6 months to 3 years it ranged from 64 to 71 per cent; from 3 to 5 years between 46 to 56 per cent and from 5 to 20 years between 24 to 37 per cent. In those over 20 years of age there were 18 per cent positive reactions.

2. Further study with the control in the Dick test has shown that the best solution to be used for this purpose is toxin which has been heated in its final dilution in a water bath at boiling temperature for one hour. A control consisting of neutralized toxin has one distinct disadvantage. The convalescent serum added to the toxin neutralizes not only the soluble toxin but also the action of the streptococcus protein which produces pseudo and combined reactions in certain individuals. These persons would therefore give positive reactions instead of pseudo or combined reactions. In some individuals the inhibition of the protein action on the skin in the control test is only temporary, the reaction there appearing in pseudo and combined reactors after 48 hours.

3. The routine application of the Dick test in scarlet fever convalescent patients has shown that the large majority give a negative Dick reaction after the 10th day of illness. There are a few patients, however, who give a positive reaction throughout convalescence. Some of these patients show desquamation, others do not. The question arises whether those who do not desquamate have had scarlet fever. The continued positive reaction in some of the patients who show desquamation indicates that there may be more than one toxin produced by the hemolytic

streptococci associated with scarlet fever. If only a single toxin were produced by the different strains of the scarlatinal hemolytic streptococcus only one type of antitoxic antibodies would develop during the later stages of the disease and all patients would show a negative Dick reaction to the same toxin preparation. Another point that has to be considered is the important question whether we are not dealing in scarlet fever with a variety of clinical entities which are classified and grouped as scarlet fever because of the absence up to the present time of any definite criteria except the symptomatic clinical ones.

The following two clinical cases are illustrative:

One patient, a girl 12 years of age, admitted to the Willard Parker Hospital with the history of 10 days of scarlet fever gave a strongly positive Dick reaction on the 12th and 13th days of the supposed illness, at a time when in convalescence from true scarlet fever the Dick reaction is, as a rule, either faintly positive or negative. On the 15th day of the supposed illness, 5 days after admission to the hospital, the patient developed a typical attack of scarlet. The Dick test in this patient so late in the disease indicated that she probably did not have scarlet fever before admission to the hospital.

Another patient, a girl 3 years of age, gave a strongly positive Dick reaction up to the very last day of her stay in the hospital. It is possible that the patient did not have scarlet fever. There was no desquamation, yet the patient did not develop scarlet fever during her stay in the hospital. By analogy with what is well known in diphtheria, one can assume that in the absence of a general immunity to an infectious disease, there is present in the normal mucous membrane of the nasopharynx a local resistance to infection which can be overcome by trauma, as after an operation on tonsils and adenoids, or by an intercurrent inflammation like a cold. The following case illustrates this point. One of the physicians at the Willard Parker Hospital was on duty in the scarlet fever pavilion for 3 months without contracting scarlet fever. When assigned to duty in the diphtheria pavilion he developed diphtheria and 2 days later scarlet fever. The diphtheria process evidently destroyed the local resistance to infection by the hemolytic streptococci, which were probably present for some time but could not exert their pathogenic action on the normal mucous membrane.

An interesting and significant appearance was noted at the site of the original Dick test in two patients who developed scarlet fever one week after the test. The area on the forearm corresponding to the previous reaction was very pale and surrounded by a sharply defined ring of the scarlet fever rash which was greatly intensified in redness when compared with the rest of the eruption on the forearm. During the height of the eruption a second Dick test was made over the pale area and another one a little to one side. The reaction which developed within the pale area was very slight when compared with the second reaction alongside of it. Apparently a certain amount of cellular immunity had developed at the site of the original positive Dick test. This gave rise to the appearance of the local pallor, which presented such a striking contrast to the rest of the blushed skin and also prevented the development of a good positive reaction during the first day of the disease. The ring of intensified rash making up the border which surrounded the pale area was probably due to the interaction between cells which were sensitized rather than protected by the minute antibody content within their substance and the scarlet fever toxin of the disease. These observations point to the probable local origin in the epidermis of some antitoxin production against scarlet fever.

4. Toxins produced by different strains of hemolytic streptococci, isolated from a variety of sources by Dr. Anna W. Williams and her associates at the Research Laboratory were studied for their local action on the human skin and their neutralization by scarlet fever convalescent serum. These toxins were produced by Dr. Williams according to the method suggested by Dick and Dick. A number of strains were thus investigated. Of these there were four strains, one from a case of osteomyelitis, one from a wound, one from a throat culture from a case of measles, and one from a normal throat, which were found to produce a toxin that could be neutralized by convalescent serum.

5. A group of 40 Dick positive children injected in an institution two months ago with 10, 25, 100 and 250 skin test doses of scarlet fever streptococcus toxin at weekly intervals gave the following results at the Dick retest made one month after the last injection: 18 of the 40 children or 45.0 per cent gave a negative reaction; 10 or 25.0 per cent gave a positive reac-

tion which was less marked than the original one and 12 or 30.0 per cent a positive reaction similar to the original one.

A second group of 143 Dick positive children injected in another institution and retested one month later showed that 104 or 72.7 per cent had become immunized; of these, 98 or 94.6 per cent gave a pseudo reaction. Of the 39 who were still positive 28 or 71.7 per cent had a combined reaction. This large number of pseudo reactors at the retest indicates that a certain amount of protein sensitiveness develops after the toxin injections. The toxin used in this work was kindly supplied to me by Dick and Dick. Purification and concentration of the toxin will eliminate most of these proteins. A similar increased protein sensitiveness I have found with the Schick retest after injections of 1/10 L+ mixtures of diphtheria toxin antitoxin.

The local and constitution reactions following immunizing injections of relative small doses of toxin vary with different individuals and depend upon the varying susceptibility of these individuals to the toxin and the protein of the toxic fluid. In a group of 30 children between 5 months and 5 years of age injected at the Heckscher Foundation with the initial dose of 100 skin test doses, 6 had slight temperature, varying between 99.6 and 100.2 and showed a diffuse scarlatiniform rash the following day. The rash lasted 24 to 48 hours. After a second injection of 250 skin test doses given a week later no local reaction at site of injection and no rash were noted. Our experience has been that, as with the diphtheria toxin-antitoxin, the younger children show much less pronounced local and constitutional reactions after injections of scarlet fever streptococcus toxin than do older children and adults.

Up to the present time we have injected with the toxin over 1000 positive Dick reactors. The dosage is as follows: For children under 12 years we give 100, 250 and 250 skin test doses; for children over 12 years, 100, 250 and 500 skin test doses. For adults the last dose could be increased to 1000 skin test doses. A dilution of the toxin is made to contain 500 skin test doses per cc. 0.2 cc., 0.5 cc. and 0.5 cc. is used for children under 12 years, and 0.2 cc., 0.5 cc. and 1.0 cc. for children over 12 years of age. The injections are given subcutaneously or intramuscularly about the middle of the outer surface of the arm and repeated at intervals of 7 days.