Measles Associated Chromosome Breakage

By

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With 2 Figures

In 1962 we reported chromosome breaks in peripheral white blood cells (1) of patients with clinical measles (rubeola). This work was part of a study on the relationship between viruses, chromosomes, and carcinogenesis. The first system studied in this project was a tumor virus, the Schmidt-Ruppin strain of the Rous sarcoma virus. This produces tumors not only in the chicken and fowl but also in a wide variety of mammals (2). When this virus was studied in the rat it was noted that chromosome breakage occurred when the tumor was studied in vivo or in tissue culture and also when the virus was added to normal rat cells in tissue culture (3). When the chromosomes of the rat tumors induced by this virus were studied in serial transplantation, new chromosome types were seen to arise. This could only occur as the result of previous breakage and reunion or healing between the broken ends of chromosomes. When rat tumors of “0” passage were put into tissue culture and serially transferred, they underwent a cellular transformation with change in morphology and growth characteristics. At the time these cellular changes took place, large numbers of chromosome breaks and rearrangements were seen. After this, the cells stabilized and behaved as a cell line. The breaks and rearrangements had not been seen in preparations made before the morphologic transformation and have not been seen since that time. Finally, when cell-free virus was added to diploid rat embryo cells in tissue culture and the first and second divisions after the addition were studied chromosomally, it was found that there was an increase in the number of breaks over the controls. On the basis of these observations it was felt that breakage was playing a role in the interaction of the cell and tumor virus.

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At this point we wanted to determine whether chromosome breakage was specific for tumor viruses or was a more general phenomenon. As a first step in this study we elected to examine the chromosomes of peripheral white blood cells of patients with measles. This decision was primarily on the basis of the relative ease of reliable clinical diagnosis and the known effect of the disease in decreasing the white blood count. When these patients were studied by serial bleedings it was found that for a short period of time, 30 to 70% of the peripheral white blood cells contained chromosome breaks. This is in contrast to 0 to 5% that is usually seen in healthy control material. This work has been confirmed in Finland by Dr. U. Gripenberg (4). Similar chromosome breaks have also been described by Dr. P. Aula (5) with clinical chickenpox. Dr. D. G. Harnden (6) in Scotland and Dr. J. Tanzer et al. (7) in France were unable to confirm these observations. The possible reasons for this disparity of observations are many. Excluding technical reasons and missing the breaks due to their short duration, both of which seem unlikely, it is possible that a second coincident virus infection either enhanced those cases in which breakage was found, or interfered with those cases in which no breakage was noted. There is also the possibility that strains of measles virus vary in their ability to induce chromosome breakage.

As a next step in these studies, observations were made on patients receiving Edmonston B vaccine. With the cooperation of Dr. Saul Krugman, New York University Medical Center, N. Y., 20 institutionalized patients were selected and divided into four groups (3, 8). Blood was obtained from these patients so that each served as his own control. Then one group of patients who were immune by virtue of previous clinical measles, and a group of susceptible patients, each received the Edmonston B vaccine. A third group, consisting of susceptible patients, received more attenuated vaccine, and a fourth group received more attenuated vaccine plus gamma globulin. The third group, those who were susceptible and received more attenuated vaccine alone, had to be eliminated due to technical reasons resulting in inadequate chromosome preparation. The total number of patients studied in this series had to remain small due to the large number of chromosome observations necessary on each patient, and there was some overlapping of the results but some generalizations in the observations can be made. First, there was chromosome breakage to a greater extent than seen in the controls in some of the patients receiving the vaccine; second, the amount of breakage was never as high as the lower level observed with the clinical disease, and third, in most cases that had either active or passive immunity the amount of breakage was the same as that seen in the controls.

In vitro studies are in progress and only preliminary data are available at the present time. We can mention briefly that work in cooperation