
EDITORIAL

Viruses and Some Blood Dyscrasias

CONSIDERABLE INTEREST has been aroused recently by the publication of two papers dealing with the possible etiologic relationship of viruses to certain blood dyscrasias. In the first, Gross¹ has proposed a new concept of viral transmission in mouse leukemia. In the other, Moolten and Ellen Clark² present evidence for a direct viral etiology in certain cases of acquired hemolytic anemia.

That viruses might be related to leukemia has long been suspected; indeed fowl leukosis and lymphomatosis are actually known to be due to specific viruses which can be passed from fowl to fowl by inoculation. In the actual fowl colony, however, the method of transmission has remained obscure. In mice having spontaneous leukemia, the incidence is extremely high in some strains as, for example, the Ak line; it has usually been assumed that the susceptibility is a matter of heredity. According to Gross, however, mouse leukemia is due to a virus infection which is transmitted "vertically," i.e., from parent to offspring either through the ovum or the spermatozoon.

Gross's concepts of "vertical" transmission are based largely on experiments with the C3H strain of mouse, in which spontaneous leukemia is rare. Mice of this strain, when inoculated with centrifuged (and presumably cell-free) extracts prepared from leukemic mice of the Ak line, failed to develop leukemia unless the injections were made within the first six days of life. The highest proportion of takes occurred if the mice were inoculated within the first twelve hours of life. Leukemia did not occur until the mice were middle aged, i.e., at about 6½ to 9 months of age. In further experiments it was shown that C3H mice inoculated with a leukemic cell *suspension* could transmit the disease to some of their offspring.

Much interest attaches to the fact that the leukemic virus might remain dormant in an inoculated mouse for many months. Further, offspring born of such an infected but nonleukemic mouse might develop leukemia. Can these observations in mice be carried over to human leukemia? Is it possible that a virus is transmitted from an infected but otherwise healthy parent, lies dormant for years, and is then activated by some extrinsic stimulus such as x-irradiation or exposure to certain chemicals? These are important matters which can only be settled in the human by exhaustive studies of family case material for a period of perhaps two or three hundred years.

Certainly familial cases of leukemia and leukosarcoma occur; until now they have been thought to be due to a familial predisposition or the inheritance of a specific gene pattern. Perhaps this orthodox view will have to be revised. Although Gross's hypotheses are revolutionary and not without certain loopholes (cf. Furth³), they are nevertheless worthy of serious consideration. One should never forget that tuberculosis was supposed to be a matter of familial predisposition until the tubercle bacillus was isolated. And it is always possible to do more with an actual pathogen than with a vague "familial predisposition."

Moolten and Clark's article is the result of their detection of viremia in a case

of hemolytic anemia. In this patient, whose history is highly suggestive of disseminated lupus, there was a marked hemolytic anemia of the acquired type and the blood showed "intense autohemagglutination." Because the Coombs anti-globulin test was found to be negative, the supposition was made that a virus might be present which could act *directly* upon the red cells causing their auto-agglutination (and presumably destruction) without the intermediary of an auto-antibody. The Newcastle disease virus was actually demonstrated. Further studies in other patients demonstrated various types of viruses in several different conditions including disseminated lupus, chronic leukemia, Hodgkin's disease, etc. In a number of these cases, hemolytic anemia, with or without a positive Coombs test, was present. From these findings the validity of the auto-antibody concept for the development of at least some cases of acquired hemolytic anemia was brought into question, and a more direct attack upon the red cell postulated. That viral diseases may actually be concerned in the development of red cell antibodies is clear from the findings in infectious mononucleosis (hetero-agglutinin) and in primary atypical pneumonia (cold iso-hemagglutinin).

It has also been shown by various technics, including that of electron microscopy that the red cell surface may become altered upon contact with a virus.^{4, 5} The speculation has even been made that the red cell thus altered may acquire auto-antigenic properties with the resultant development of auto-antibody. In Moolten and Clark's paper, auto-agglutination is emphasized as an important indication of the presence of virus and of the development of antiviral immunity. It must be said, however, that a strict definition of auto-agglutination is lacking.

There can be no doubt that the many attractive concepts presented by Moolten and Clark are not only interesting but of potentially great importance. However, the real significance of the finding of viremia in certain cases showing hemolytic anemia is still *sub judice*, to say nothing of the confirmation of these findings by other workers. Granted that viruses are present, can they really cause severe and continuing red cell destruction to the extent that occurs in severe acquired hemolytic anemia? Is it possible that the virus is simply an accelerating factor, or perhaps even an innocent bystander? Certainly, we should not make the jump from (a) viremia, to (b) hemolytic anemia without more proof than has been presented to the present. Nevertheless, concepts are always important. Even if eventually proved wrong, they often bring out new facts. In leukemia the possibility of a viral etiology offers the opportunity of some therapeutic, or even better, prophylactic attack. Let us hope that these "unorthodox" views may have some real validity.

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