OCT 8 1971

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October 4, 1971

SKM-231

Professor Joshua Lederberg
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Dear Dr. Lederberg:

It was very kind of you to send me a copy of your interesting article as well as your comments on our work. I am flattered that you chose to use our work as an introduction to your article on blood transfusion.

The article as you have written it is accurate but perhaps you might be interested in some general comments and answers to questions you pose in the memorandum.

1. Infectious nature of Australia antigen.

There is now considerable evidence that Australia antigen has the characteristics of an infectious agent. The data in favor of this hypothesis are summarized in the article (enclosed) recently published in the Journal of Experimental Medicine. The agent has been transmitted from man to man and to non-human primates. Liver tissue containing the antigen, when grown in tissue culture contains the antigen after many passages and Au is found in the tissue culture fluid. There is evidence that the particle contains a small amount of RNA although these findings have not been substantially confirmed. The other findings which support the infectious hypothesis are given in the paper.

2. "Class" stratification

We have a considerable amount of information on the "class stratification" of the prevalence of Australia antigen. In collaboration with our colleagues at the Philadelphia General Hospital and the Hospital of the University of Pennsylvania we found that the frequency of Australia antigen was some 20 times greater in the blood donors used at Philadelphia General Hospital (a city owned institution) than at the Hospital of the University of Pennsylvania (a voluntary hospital). This was to a large extent due to the fact that the blood donors for the Philadelphia General Hospital were recruited from local prison populations.

It is said that many prisoners are drug users. As a consequence of this the rate of post-transfusion hepatitis was many times greater in the Phila. General Hosp. patients than in the Hosp. of the Univ. of Penna. patients even though they are separated by only a few hundred feet. (We were able to considerably lower the frequency of post-transfusion hepatitis at PGH by our testing program. After the donor bloods had been tested for one year the frequency of post-transfusion hepatitis in Phila. General Hosp. was decreased to about 1/4 of what it had been prior to the testing program. This was due to the elimination of a large number of potentially infectious bloods which contain Australia antigen.)

During the course of our work we have tested large numbers of bloods for the U.S. Army and Air Force blood procurement programs. One of the consequences of the study, is the discovery that there is a significant increase in the incidence of Australia antigen in troops who have been in Vietnam compared to recruits. This is probably due to the massive exposure the soldiers have in Vietnam. Au is common among native Vietnamese; and drug use among U.S. troops also probably contributes to the high frequency.

3. Genetics

The genetic findings have now been supported by two studies of our own and a third by Dr. Ceppellini in Turin. The simplest explanation of the findings is that there is an inherited susceptibility to persistent infection with Australia antigen and this suceptibility factor is an autosomal recessive trait. You have expressed this view very well in your article. We have used this hypothesis for some years now but recently have proposed another kind of an explanation which, we believe, has the advantage of stimulating new studies which would not be undertaken with a conventional hypothesis. I will present it briefly here; it is discussed in more detail in the enclosed paper.

The infectious agent (virus) hypothesis has not been rejected and the serum protein polymorphism hypothesis has not been rejected. Therefore, we have made a third hypothesis which, in effect, includes both of these. This hypothesis states that Australia antigen has both the properties of an infectious agent which causes hepatitis in some people infected with it, and the properties of a serum protein polymorphism, that is the polymorphic properties are contained on the agent itself. A further implication is that the agent contains human serum proteins although not necessarily those of the host from whom the agent was isolated. We have had the temerity of assigning a name to the "class" of agents represented by Australia antigen. We have called them "Icrons" an acronym of the name of our Institute.

As you said in your article the origins of this study appeared to be quite remote from its final consequences.

We've written an account of the process of this discovery which you might find amusing to skim through. A copy of this paper is also enclosed.

I would enjoy discussing our genetic findings with you. We have some questions as to how they may relate to lysogeny, maternal transmission and other means of "infectious" and genetic transmission.

Sincerely yours,

Baruch S. Blumberg

BSB:fs

Enclosures