January 25, 1957

Vaccination of the Delayed Type

By Leo Szilard

By "vaccination of the delayed type" we shall mean a vaccination of an individual against an infectious agent (virus, bacterium, etc.) by injecting the killed infectious agent (or its surface antigens) in circumstances in which the injection evokes strong delayed type hypersensitivity to the surface antigens of the infectious agent. Pappenheimer and his co-workers have shown[1] for diphtheria toxoid and egg albumen that delayed hypersensitivity ensues against any one of these two antigens if a mixture of the antigen and an excess of the specific antibody is injected intradermally (or, together with an adjuvant, subcutaneously). I assume that delayed hypersensitivity can be evoked in this manner also against the surface antigens of infectious agents, such as polio virus, influenza virus, typhoid bacteria, etc.

It appears to me likely that the reactions which manifest themselves in the phenomenon of delayed hypersensitivity exist in nature because these very same mechanisms are involved in the defenses of the body which are active at the infected site. Thus hypersensitivity of the delayed type against the surface antigens of the infectious agent should reduce the severity and the duration of the infection. If this assumption is correct, then we must conclude that we ought to resort to "vaccination of the delayed type" in the case of diseases where ordinary vaccination with the killed infectious agent does not afford maximum protection.

In the case of polio, for instance, ordinary vaccination with a killed virus (Salk vaccine) produces circulating antibodies. In case of

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(1) Uhr, J. W., Salvin, S. B., and Pappenheimer, A.M., Jr., Journal of Experimental Medicine, Vol. 105, p. 11 (1957).

a subsequent polio infection of the intestinal tract, there is a rapid rise in the titre of the circulating antibody. Therefore, such a vaccinated individual is immune against polio in the sense that the infection cannot spread from the intestinal tract via the blood circulation to the brain. But such a vaccination does not confer on the individual resistance against the infection of the intestinal tract itself. The intensity and duration of the infection is the same for such a vaccinated individual as it is for individuals who had not been previously exposed to the virus in any way. This is in contrast to individuals who had been infected with live polio virus and who on a subsequent infection of the intestinal tract with polio virus show a resistance to this infection inasmuch as the virus will remain alive for a shorter period of time in the intestinal tract and will be shed for a shorter period of time by the intestinal tract.

We surmise that the same kind of resistance to the intestinal infection which is manifested by such persons could be conferred on an individual (who may have been rendered immune by ordinary vaccination - Salk vaccine) by giving him a polio vaccination of the "delayed type". This does not involve the use of live polio virus and could be accomplished by injecting intradermally (or together with an adjuvant subcutaneously) killed polio virus mixed with an excess of the specific antibody.

Such a vaccination of the delayed type with the killed infectious agent might prove useful also in the case of influenza and typhoid fever. It might prove useful in general in all those infections of mucous membranes in which ordinary vaccination (that leads to circulating antibodies but not to delayed type hypersensitivity) does not afford maximum protection.

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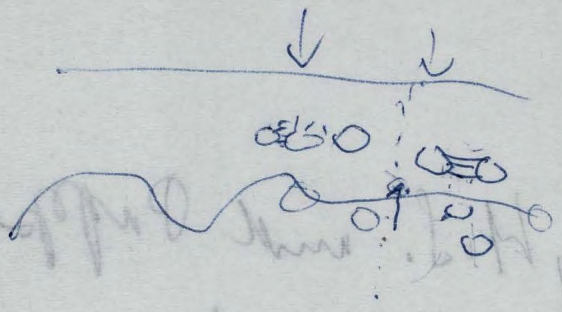

Journal of Exp. Medicine Vol 105

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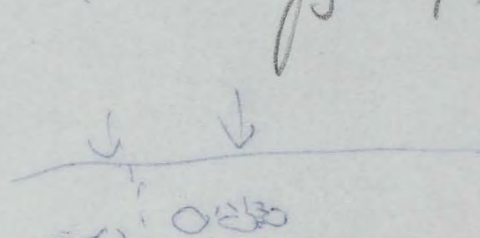

Lawrence, H.S. and Pappenheimer A.M. J. Exp. Med 1956 104 321

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Lepromatous Leprosy

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