

# ANNOTATIONS

## VACCINATION AGAINST EPIDEMIC INFLUENZA IN MAN

THE present status of vaccination against epidemic influenza, of the results so far obtained, and a discussion of the problems which still remain unsolved are presented clearly and concisely in Dr. F. G. Blake's article "An Evaluation of Vaccination Against Epidemic Influenza in Man."<sup>1</sup>

A brief survey describes the research work done in recent years on the problem of influenza vaccination and discusses some of the literature available on this subject. Starting with 1933, the year of the initial demonstration that a filtrable virus in the throat washings of patients with influenza could be transmitted to ferrets and that the serum of recovered ferrets and convalescent humans could neutralize the infecting capacity of the virus, Blake points out the most important steps in the study of the influenza virus with full reference to the original publications.

The development in the preparation of a more effective vaccine which has taken place during the last five years is described. By 1941, even though no satisfactory immunizing agent against influenza A had been found, yet the reduction in incidence observed in certain experiments was not negligible. At this time a complex chicken embryo-influenza A and canine distemper vaccine was used by Horsfall, *et al.*<sup>2</sup> on volunteers in a number of state institutions; laboratory tests showed that it stimulated the formation of considerable quantities of neutralizing antibodies against the influenza A virus. A study of

<sup>1</sup> Blake, Francis G.: An Evaluation of Vaccination Against Epidemic Influenza in Man. *Bulletin of the New York Academy of Medicine*, May, 1948, 24, p. 308.

<sup>2</sup> Horsfall, F. L., Jr.; Lennette, E. H.; Rickard, E. R.; and Hirst, G. K.: Studies on the Efficacy of a Complex Vaccine Against Influenza A. *Public Health Reports*, September 19, 1941, 56, No. 38, pp. 1863-1875.

the incidence of influenza in the epidemic which occurred four months after vaccination showed the following results: In four of the institutions where a weaker strain of the vaccine had been used there were 19 per cent fewer cases of influenza A among the vaccinated group than among the control group of same size, whereas in six other institutions there were 50 per cent fewer cases in the vaccinated group. These results also tended to confirm the theory that a high potency vaccine able to increase specific antibodies to even higher levels might effect more striking reductions in the incidence of influenza.

Attempts, therefore, followed to develop a more potent vaccine by further concentration of the virus. The new vaccines were to be tested during an epidemic expected in 1942–1943 which, however, failed to occur. Observations could, therefore, only be conducted on the protective effect of the vaccine against experimentally induced influenza A and B. In a controlled study at the Ypsilanti State Hospital in Michigan it was demonstrated that the vaccine had a significant protective effect against induced influenza A and B.

During the winter of 1943–1944 a well-controlled investigation of the prophylactic effect of influenza vaccination was carried out by the Commission on Influenza in Army Student Training Program Units in nine universities throughout the country. The students in all Units were about evenly divided into vaccinated and control groups and a considerable epidemic of influenza A appeared in all Units. Vaccination given subcutaneously shortly before or, in some cases, even after the onset of the epidemic, was found to exert a protective effect with a total attack rate of 2.22 per cent among 6,263 vaccinated persons and a rate of 7.11 per cent among 6,211 controls.

In order next to determine the effect of vaccine on influenza B, an expected outbreak of which occurred in November and December, 1945, a controlled study was conducted at the University of Michigan. It was found that in an Army Unit of 600 men vaccinated with concentrated influenza A and B vaccines, prepared from infected allantoic fluid, the incidence was 1.15 per cent, whereas in a comparable Service Unit of 1,100 men who were not vaccinated, the rate was 9.91 per cent. The evidence clearly indicated that the vaccine exerted a striking pro-

tective effect. Analogous studies made about the same time in other universities, in the Army, and in industrial groups helped to substantiate, in general, these same findings.

Blake summarizes the main prerequisites of success as follows:

. . . . (1) when a potent formalinized and concentrated vaccine, in a single dose of 1.0 cc. subcutaneously and capable of stimulating an antibody response comparable to that which develops early in convalescence, was used; (2) when the antigenic structure of the strains of virus used in the vaccine was closely similar to that of the strains causing the epidemics; and (3) when vaccination had been carried out within one to six weeks prior to the onset of the epidemic.

When, however, one or more of these conditions is lacking, vaccination is not successful. For instance, during the winter of 1946-1947, large-scale vaccinations at the University of Michigan had very little effect due to the sharp antigenic deviation of the strains in the vaccine from the prevalent epidemic strain. Moreover, in this instance, the epidemic occurred only four months after vaccination.

Despite the considerable success which has attended the recent development of vaccination against influenza A and B, Blake points out that many requirements will still have to be met before the completion of a universally effective vaccine. It will be necessary to achieve maximum antigenic effectiveness through proper concentration while avoiding excess toxicity; another aim that should be kept in mind is the reduction of the amount of egg protein for reasons of allergy and the achievement of an economic method of preparation in view of the mass production of the vaccine. Also, experiments which are now being conducted will have to determine the most successful dosage to be used which is expected to be less than the currently used 1.0 cc. As to the time and frequency of the vaccination, it appears tentatively that vaccination in fall and at yearly intervals promises the best results and that the vaccine used should contain both A and B types of virus and in each the most prevalent strains encountered in recent epidemics.

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