14478 P

Protective Effect of Vaccination Against Induced Influenza B.*

JONAS E. SALK,† HAROLD E. PEARSON, PHILIP N. BROWN, AND THOMAS FRANCIS, JR.

From the Department of Epidemiology and the Virus Laboratory, School of Public Health, University of Michigan, and the Ypsilanti State Hospital, Ypsilanti, Mich.

In the previous paper[1] evidence was presented to show that subcutaneous inoculation of vaccine containing concentrated and inactivated influenza virus, Types A and B, was followed by an increased resistance of human individuals, as measured by the febrile response, to a subsequent intranasal spray of active Type A influenza virus. The present report deals with the results of a similar study of the effect of subcutaneous vaccination upon resistance of another group of individuals in the same institution to infection with influenza virus, Type B.

The vaccine was the same material employed in the study with influenza A. The subjects were 96 physically active male residents of another ward of the Ypsilanti State Hospital, Ypsilanti, Michigan.

On December 21, 1942, 46 of the men received 1.0 cc of the vaccine subcutaneously. On April 13, 1943, 19 of the same individuals received a second injection of 1.0 cc of the vaccine and 23 men not previously vaccinated now received 1.0 cc of the vaccine. There remained 27 men vaccinated in December but not since, and 23 control subjects who had not at any time received vaccine.

On May 10, 1943, 27 days after the administration of vaccine to 2 of the groups, all 96 men received the Lee strain of influenza B virus by intranasal inhalation. The virus from the allantoic fluid of the infected hen's egg had been concentrated[2] tenfold in physiological salt solution. The material was sprayed for 5 minutes under 10 lb air pressure from a nebulizer so as to deliver approximately 0.5 cc of the virus. Oral temperatures had been recorded twice prior to the inhalation of the virus and were continued twice daily thereafter. Records were kept of signs or symptoms of illness. Material for other clinical and serological studies was collected.

In those individuals in whom evidence of infection was discerned, the incubation period was less than 24 hours and the febrile period was in only one instance longer than one day. The physical evidence of illness was also mild with chilliness, aches, cough, and malaise. The highest temperature was 102.6 F No significant complications were noted. The distribution of febrile reactions in the different groups is detailed in Table I.

In the unvaccinated group, 11 or 41%, of the 27 individuals had temperatures of 100° or more and 6, or 22%, had temperatures of 101° or above. In the 69 vaccinated individuals, 7, or 10%, had temperatures between 100° and 100.9° while none exceeded that range. There was no significant difference in the responses of the groups vaccinated 4½ months before, 4 weeks before or vaccinated twice before exposure. In this respect the results differ from those obtained with influenza virus, Type A, where the group vaccinated 4 months prior to exposure appeared less uniformly resistant than those vaccinated 2 weeks before virus was administered.

The results demonstrate that subcutaneous injection of vaccine of concentrated and inactivated influenza virus, Types A and B, is capable of exerting a protective influence, as measured by the febrile response, against

* These investigations were aided through the Commission on Influenza, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, Preventive Medicine Service, Office of the Surgeon General, United States Army.

This study was also aided by a grant from the International Health Division of the Rockefeller Foundation.

† Fellow in the Medical Sciences of the National Research Council.

[1] Francis, Thomas, Jr., Salk, J. E., Pearson, H. E., and Brown, Philip N., PROC. SOC. EXP. BIOL. AND MED., 1944, **55**, 104.

[2] Francis, Thomas, Jr., and Salk, J. E., *Science*, 1942, **96**, 499.

TABLE I.
Effect of Subcutaneous Vaccination upon Febrile Response of Human Subjects to Induced Infection with Influenza Virus, Type B.

Vaccination record	No. of subjects	Highest Temperature <99 No.	%	99+ No.	%	100+ No.	%	101+ No.	%	102+ No.	%
1. Unvaccinated	27	5	19	22	81	11	41	6	22	2	7
2. 4½ mos. before	27	12	44	15	56	2	7	0	0	0	0
3. 4½ mos. and 4 wks. before	19	4	21	15	79	2	11	0	0	0	0
4. 4 wks. before	23	12	52	11	48	3	13	0	0	0	0

induced infection with Type B influenza virus for at least one to 4 months. These data together with those in the preceding paper show that the same mixed vaccine induced an increased resistance of human individuals to infection with virus of Type A or Type B.

Further details will be reported subsequently.

14479 P

Effect of Biotin Deficiency on the Course of *Plasmodium lophuræ* Infection in Chicks.

A. O. SEELER, WALTHER H. OTT, AND MARY E. GUNDEL. (Introduced by H. Molitor.)
From the Merck Institute for Therapeutic Research, Rahway, N.J.

It has generally been assumed that malnutrition decreases the resistance of the organism to malaria. The first experimental evidence to support this view is Trager's[1,2] recently published observation suggesting that biotin deficiency increased the severity of certain avian malaria infections. Similarly, Caldwell and György have reported that biotin deficiency will prolong *Trypanosoma lewisi* infections in the rat.[3]

Since we had found, in experiments to be reported soon, that a deficiency in certain dietary factors which have not yet been chemically characterized has a pronounced effect on the course of *Plasmodium lophuræ* infections in chicks, we were interested in determining whether or not the effect of biotin deficiency on avian malaria was specific. In this communication we are reporting experiments on the relationship of biotin deficiency to the severity of *P. lophuræ* infections which, although the diets and experimental procedures used differed from those of Trager, confirm his findings on the specific effect of biotin.

Experimental. While *P. lophuræ* infections are more severe in the duck than in the chick the latter species was chosen for the following experiments because much more is known about its nutritional requirements. Because of simplicity and convenience it was decided to produce biotin deficiency for this experiment by adding dried raw egg white to a commercial chick ration. In order to be certain that the addition of egg white proteins did not in itself influence the course of the malaria, a control diet was used in which steamed egg white replaced the raw egg white. To further demonstrate whether or not biotin was the specific factor involved, 0.0001% of crystalline biotin was added to the diet containing dried raw egg white.

Twenty-five 9-day-old S.C.W. Leghorn male chicks were set out on each of the following diets:

1 Trager, W., *Science*, 1943, **97**, 206.

2 Trager, W., *J. Exp. Med.*, 1943, **77**, 557.

3 Caldwell, F. E., and György, P., PROC. SOC. EXP. BIOL. AND MED., 1943, **53**, 116.