

Virus-Inactivating Capacity of Nasal Secretions in the Acute and Convalescent Stages of Influenza.*

THOMAS FRANCIS, JR., AND I. J. BRIGHTMAN.

From the Department of Bacteriology, New York University College of Medicine.

In an earlier publication¹ it was reported that the nasal secretions of human individuals possessed the capacity to inactivate influenza virus, Type A. It was noted that considerable variation existed among individuals. Burnet, Lush and Jackson,² studying material similarly obtained, observed no significant differences in the virus-inactivating potency of secretions of different individuals. Furthermore, they observed similar effects upon different viruses. They suggested, in consequence, that the virus-inactivating substance is enzymatic in nature.

On the other hand, studies conducted in this laboratory have indicated strongly that the agent responsible for the inactivation of influenza virus is an antibody and possesses many of the characteristics ordinarily attributed to antibody.³ In a given individual, the content of virus-inactivating substance in the nasal secretions is fairly constant and uninfluenced by infections such as the common cold. Because of the similarity to antibody, it was of interest to ascertain what effect specific infection with influenza virus might exert.

During the past winter a widespread epidemic of influenza due, according to our observations, to influenza virus, Type A, was encountered. From 10 subjects, during the first 3 days of illness and again in the third week after onset, nasal secretions and samples of blood serum were obtained. These were then tested at the same time for their capacity to protect mice against infection with 1000 M.L.D. of PR8 strain of influenza virus, Type A, by means of the neutralization test. Four-fold serial dilutions of serum, ranging in final concentration from 1:4 to 1:256; two-fold serial dilutions of nasal secretions, ranging in final concentration from 1:2 to 1:16 were used. Three mice were inoculated intranasally with each serum-

* This study was conducted under a grant from the International Health Division of the Rockefeller Foundation.

¹ Francis, T., Jr., *Science*, 1940, **91**, 198.

² Burnet, F. M., Lush, D., and Jackson, A. V., *Brit. J. Exp. Path.*, 1939, **20**, 377.

³ Francis, T., Jr., *Problems and Trends in Virus Research*, University of Pennsylvania Press, Philadelphia, 1941, 41.

TABLE I.
Neutralizing Capacity of Nasal Secretions and Serum Taken During Influenza and in Convalescence.

Patient	Neutralizing titer			
	Nasal secretions		Serum	
	Acute	Conv.	Acute	Conv.
F	0	12	0	128
S	0	20	92	370
D	0	32	23	512+
Sm	0	20	32	178
B	0	6	12	370
E	5	20	32	128
G	5	32+	32	256+
L	10	12	8	32
W	0	32+	8	256+
Z	5	32+	8	512+

virus mixture. The animals were observed for 10 days, the day of each death recorded, and all survivors were sacrificed and their lungs examined for typical pulmonary lesions. The endpoint of each titration was estimated by the method of Reed and Muench.⁴ Results of these procedures are presented in Table I.

It will be seen that in 9 of 10 instances a sharp rise in the capacity of nasal secretions to inactivate the virus occurred during convalescence. A simultaneous rise in circulating antibodies was also noted. It was of interest to note that all of these patients were over 50 years of age, but possessed little or no virus-inactivating substance at the time of the acute illness. This would tend to emphasize the possibility previously suggested that only those individuals essentially devoid of inactivating substance in their nasal secretions need be considered susceptible to infection.⁵ The results of the tests serve also to support the evidence that the inactivating agent is antibody, in these instances apparently developed as a result of specific infection.

Summary. In 9 of 10 human individuals, natural infection with virus of influenza, Type A, was followed by the development of, or a sharp increase in, the capacity of their nasal secretions to inactivate the virus. Although not numerically parallel, increases in neutralizing antibodies of the blood were also observed. These results add further support to the earlier conclusion that virus-inactivating substance in nasal secretions possesses the characteristics of antibody.

⁴ Reed, L. J., and Muench, H., *Am. J. Hyg.*, 1938, **27**, 493.

⁵ Francis, T., Jr., *Bull. N. Y. Acad. Med.*, 1941, **17**, 268.