Summary. When dogs were placed on a diet deficient in nicotinic acid, the addition of nicotinic acid corrected the deficiency, while the addition of nicotinic acid and sulfapyridine failed to do so. When raw liver and sulfapyridine were added to the diet, the deficiency disappeared. It seems possible, but not proven, that sulfapyridine inhibits the action of nicotinic acid but not of preformed coenzymes.

11996

Two Outbreaks of Influenza Caused by Antigenically Different Viruses.

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Early studies on influenza suggested that the virus agents of the disease, although not antigenically identical were closely enough related for the infection to evoke a demonstrable rise in antibodies reactive against the recognized strains of the influenza virus. The first convincing indication that influenza might be due to antigenically unrelated viruses was presented by Stuart-Harris, Smith and Andrewes,[1] who found that a rise in antibodies against the usual strains of influenza virus occurred in only 33% of the cases they studied in England in 1939; although they failed to isolate the actual virus, they concluded that a number of their cases must have been caused by an agent other than the usual influenza virus. More direct evidence has recently been obtained independently by Francis and by ourselves. In February, 1940, we[2] isolated a virus (termed *TM*) from 2 cases of influenza and showed that in each instance the infection evoked an increase in antibodies against the homologous *(TM)* virus but caused no detectable increase in antibodies reactive against the *PR8*[3] strain of influenza virus. At about the same time Francis[4] isolated a strain (termed "Lee") which was also distinct from the *PR8* and from other previously recognized strains. He showed that the con-

[1] Stuart-Harris, C. H., Smith, W., and Andrewes, C. H., *Lancet*, 1940, **1**, 205.

[2] Magill, T. P., PROC. SOC. EXP. BIOL. AND MED., 1940, **45**, 162.

[3] Francis, T., Jr., *Science*, 1934, **80**, 457.

[4] Francis, T., Jr., *Science*, 1940, **92**, 405.

valescent serums from cases of influenza which had occurred in various places during the early part of 1940 and also serums from 2 cases that had occurred in 1936 had increased titers of antibodies against his *Lee* strain but not against the *PR8* strain. Francis concluded that his *Lee* strain was a new type of virus and proposed that it be termed *influenza B* to distinguish it from the older strains (PR8, WS, etc.) for which the term *influenza A* had already been suggested.[5] The relationship between Francis' *Lee* strain and our *TM* strain has not yet been determined, but since both were isolated in New York City at about the same time it is entirely possible that they are similar, if not identical. Although it is desirable that the serological properties of the two strains be compared in a future study, the important point is that the studies already made with each of the viruses have established that typical influenza can be caused by virus agents which are antigenically different than those previously described.

The present paper presents additional data in support of the general principle that clinically similar cases of influenza may be caused by viruses that are antigenically distinct. In the investigation 2 viruses were utilized: the *PR8* strain represents the older group of strains of influenza virus (*"influenza A"*), whereas the *TM* represents a virus which is antigenically distinct from the older group of strains. The 2 viruses were tested against serums obtained from cases of influenza during 2 outbreaks of the disease which occurred about a year apart (January, 1939, and February, 1940) among the nurses in The New York Hospital. All of the cases were hospitalized throughout the course of illness and hence the opportunities for clinical observation were especially satisfactory. It is important that even under these satisfactory conditions for study no consistent differences of a clinical sort were evident between the 2 groups of cases. Two samples of serum were obtained from each patient: the first within 24 hours of the time of appearance of symptoms, and the second 3 to 4 weeks later. Each pair of serums was tested against the 2 viruses: in the case of the *PR8* both protection tests and complement fixation tests were made, but in the case of the *TM* only protection tests were included because we had not yet developed a satisfactory complement fixation procedure for that virus. The results are summarized in Figs. 1 and 2 in which, for each virus, the titer of the serum obtained during the first 24 hours of illness is plotted against the titer of the serum obtained from the same person

[5] Horsfall, F. L., Lennette, R. H., Rickard, E. R., Andrewes, C. H., Smith, W., and Stuart-Harris, C. H., *Lancet*, 1940, **2**, 413.

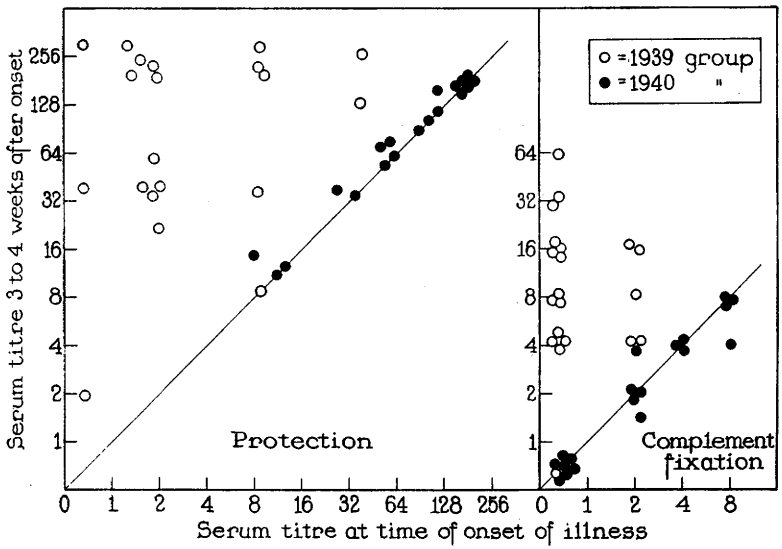

FIG. 1.
Tests with *PR8* virus.

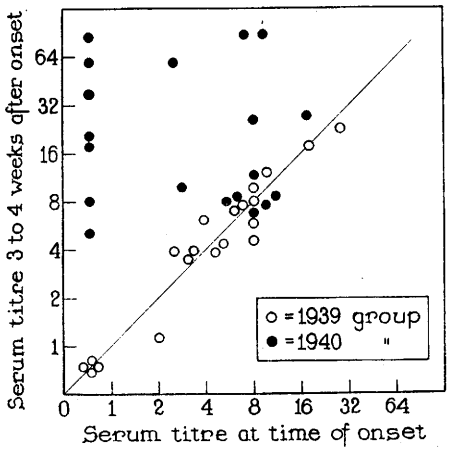

FIG. 2.
Tests with *TM* virus.

3 to 4 weeks later. The titers of the protective antibodies are expressed as the dilution of serum that would protect 50% of the mice from death;[6] all titers represent the actual dilution of serum before the addition of antigen or of antigen plus complement.

In Fig. 1 it is evident that all but one of the 20 subjects of the 1939 outbreak showed a significant increase both in protective and in complement fixing antibodies against the *PR8*, whereas none of

[6] Reed, L. J., and Muench, H., *Am. J. Hyg.*, 1938, **27**, 493.

the 19 subjects of the 1940 outbreak showed any appreciable increase in antibodies against that virus. As shown in Fig. 2, the serums from the subjects of the 2 outbreaks reacted quite differently when tested against the *TM* virus; none of the 1939 group showed any appreciable increase in antibodies, whereas most of the patients of the 1940 group showed a significant rise in titer against that virus. These results indicate that the agent involved in the 1939 outbreak must have been either identical with or closely related to the *PR8*, and the agent involved in the 1940 outbreak either identical with or closely related to the *TM*. Thus, the data furnish an example in which the influenza that occurred in the one year was due to a virus distinctly different in antigenic properties from the virus responsible for the clinically similar disease that occurred in the same institution a year previously.

11997

Excretion of Nicotinic Acid in Pellagra.*†

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The impression is given by preliminary reports from several sources[1, 2, 3] that the excretion of nicotinic acid in pellagra is "not vastly different" from that of healthy individuals, in marked contrast to the excretion of certain other vitamins in their corresponding states of deficiency. This impression is fully confirmed by the results of the present report.

Observations have been made on several patients with deficiency diseases. Among these were cases of classical pellagra; others were states which were probably due to deficiency of several factors. Ob-

* This study was conducted in collaboration with the various members of the staff of the Department of Internal Medicine. Acknowledgment should be made particularly to Dr. J. W. Weaver who administered test doses of nicotinic acid to patients.

† Acknowledgment is also made of aid from the John and Mary Markle Foundation.

1 Kühnau, W. W., *Klin. Woch.*, 1939, **18**, 1333.

2 Swaminathan, M., *Indian J. Med. Res.*, 1939, **27**, 417. (*Nut. Ab. Rev.*, 1940, **9**, 1037.)

3 Harris, L. J., and Raymond, W. D., *Biochem. J.*, 1939, **33**, 2037.