There are two possibilities, either the chemical reactions used are unreliable or the synthetic reactions of the bacteria differed under the respective experimental conditions. That the stepwise degradation used in our investigation was reliable is shown by the quantitative recovery of the C^{13} in the carboxyl group. We are at present endeavoring to determine the reliability of the chemical reactions used by Carson, *et al.*,[4] by degrading chemically synthesized propionic acid containing C^{13} in the carboxyl group.

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Repeated Attacks of Influenza.

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Recent reports[1, 2, 3] have established the principle that illnesses which on the basis of their similar clinical symptoms would be classified together as influenza can be caused by antigenically different viruses. The same principle must be taken into account when repeated attacks of influenza occur in an individual; that is, in a person who previously has had influenza a subsequent attack may be due to infection with a virus that is antigenically different from the one responsible for the earlier illness. That examples of that sort do occur will be shown by the results of the following experiments in which samples of serum obtained over a period of 4 to 5 years from persons who had had more than one attack of influenza were tested against two antigenically different viruses, the *TM* virus[1, 3] and the *PR8* strain of the virus of epidemic influenza.[4]

Patient A had 2, and Patient B had 3 attacks of influenza during the period of observation. The serums, which were 14 from each patient, included samples obtained at the time of onset of the symp-

1 Magill, T. P., PROC. SOC. EXP. BIOL. AND MED., 1940, **45**, 162.

2 Francis, T., Jr., *Science*, 1940, **92**, 405.

3 Magill, T. P., and Tyndall, M., in press.

4 Francis, T., Jr., *Science*, 1934, **80**, 457.

toms of the illnesses, samples obtained 3 to 4 weeks later, and samples obtained at reasonably regular intervening intervals. In order to make the comparison valid all of the samples from each patient were tested at the same time. Each serum dilution was mixed with an equal volume of a suspension (mouse lung) which contained between 100 and 1000 lethal doses of the respective virus per 0.03 cc, and after incubation at 37°C for ½ hour 0.06 cc of the mixture was given intranasally to mice which were under ether anesthesia. The

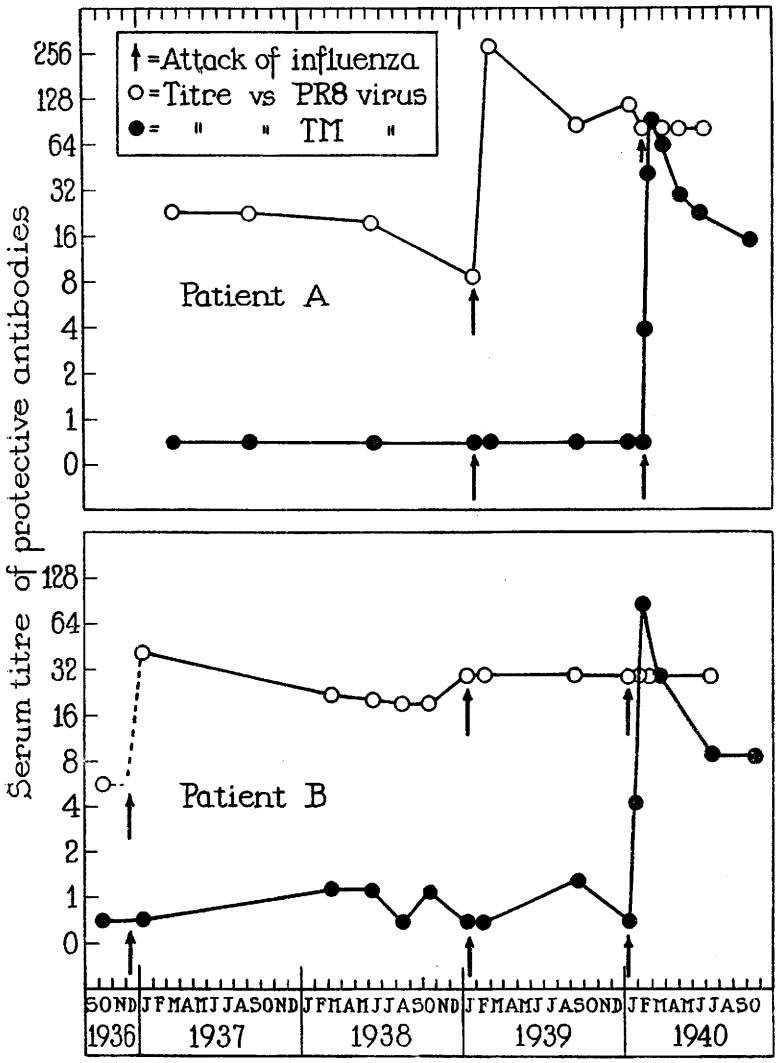

FIG. 1.

tests were terminated on the tenth day and the serum antibody titres were calculated as the dilution of serum that would protect 50% of the mice from death.[5] The results are summarized in Fig. 1 in which the serum antibody titers against the 2 viruses are plotted against the time at which the respective serum had been obtained; the serum titers are expressed as the actual dilution of serum before the addition of the virus suspension. The time of onset of each attack of influenza is indicated by an arrow.

The data (Fig. 1) show that as measured by the capacities of the serums to protect against the two viruses, the different attacks of influenza induced different antibody responses. Patient A had influenza twice: the January, 1939, illness evoked antibodies against the *PR8* but not against the *TM* while, in contrast, the January, 1940, illness evoked antibodies against *TM* but not against *PR8*. Patient B had influenza 3 times: the antibody responses to his 1936 and 1940 illnesses were similar respectively to those of Patient A's 1939 and 1940 attacks; but his 1939 attack differed from any of the others observed with him or with Patient A in that it did not cause a rise in antibodies against either the *TM* or the *PR8* viruses.

On the basis that each infection should be followed by a significant increase in antibodies against the specific causative agent or against agents closely related to it, these data would be interpreted as follows: Patient A's 1939 and B's 1936 illnesses were due to a virus identical with or closely related to the *PR8*; both Patient A's and Patient B's 1940 illnesses were due to a virus identical with or closely related to the *TM*; whereas Patient B's 1939 illness was due to some virus not closely related to either the *TM* or the *PR8*. If those deductions are correct the results presented in this paper furnish convincing examples of instances in which the subsequent attacks of a person who previously had had influenza may be explained on the basis of antigenic differences in the infecting agents.

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