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**Reactions of Monkeys to Experimental Respiratory Infections.*
I. Response to Influenza Virus A.**

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Most of our current knowledge of experimental influenza has been derived from observations made on small laboratory animals, particularly mice and ferrets. Vieuchange¹ reported certain manifestations of infection in 2 monkeys inoculated with an unfiltered mouse-lung suspension of the "W.S." strain of virus. Some 2 years ago we began a series of correlated studies—clinical, hematological, bacteriological, and immunological—in normal monkeys inoculated intranasally: (1) with the virus of influenza A, (2) with *Streptococcus hemolyticus* Group C, and (3) with the virus and streptococcus in various sequences.² Similar studies are in progress, utilizing vitamin-deficient monkeys. This communication records the reaction of normal monkeys to the virus alone.

Methods. The PR-8 strain of influenza virus used was maintained by intranasal passage in young adult white mice. The inoculum for the monkeys was prepared as follows: The lungs of infected mice were triturated in 9 volumes of buffered saline; the suspension was filtered through Berkefeld V candles and the filtrate stored at -78°C; after a period of stabilization it was titrated in mice and was retested for maintained virulence from time to time during experimentation.

Young adult monkeys (*Macaca mulatta*) were held under quarantine during a period of preliminary laboratory tests. After suitable base-line observations were completed the animals were anesthetized with ether and 3 cc of the prepared material (10,000 mouse mld) were dropped into the external nares.

Complete serial blood-cell studies, repeated tests for the presence of virus in nasal and throat washings, and serum-neutralization tests were continued over a period of several weeks.

* Recognition is herewith accorded to a grant from the Comly Research Fund in the furtherance of these studies.

¹ Vieuchange, M. J., *Acad. de med.*, Paris, 1939, **121**, 100.

² Doan, C. A., Woolpert, O. C., Merino, C., Schwab, J. L., and Saslaw, S., *Proc. Am. Soc. Clin. Invest., J. Clin. Invest.*, 1941, **20**, 452.

Results. None of the 7 monkeys thus inoculated intranasally with the influenza virus manifested clinical symptoms of infection. That invasion regularly occurred, however, was proved: (1) by consistent changes in the blood-cell equilibria, (2) by the development of neutralizing antibodies.

The blood-cell response was uniformly prompt, definite and fairly consistent. The total white-cell count characteristically fell within 24-48 hours; for example, in monkey No. 2 (Fig. 1) from 20,000 to 12,000 with granulocytes reduced from 13,400 to 6,700; the lowest granulocyte-level, 1,920, was recorded on the 6th post-inoculation day, at which time the lymphocytes had shown a reciprocal rise from 6,000 to 9,800. In another animal, No. 3, the total leucocytes were reduced from the preinoculation level of 25,000 to 17,000 and the neutrophilic granulocytes from 17,500 to 8,500 during the first 24 hours; the lowest granulocyte-level, 3,700, was recorded on the 5th post-inoculation day. The monocytes showed no significant fluctuations. The red blood cells and hemoglobin remained essentially unaltered.

In general it was observed that each time the granulocytes decreased there was a reciprocal rise in the lymphocytes, particularly striking between the 1st and 6th post-inoculation days, a phenomenon

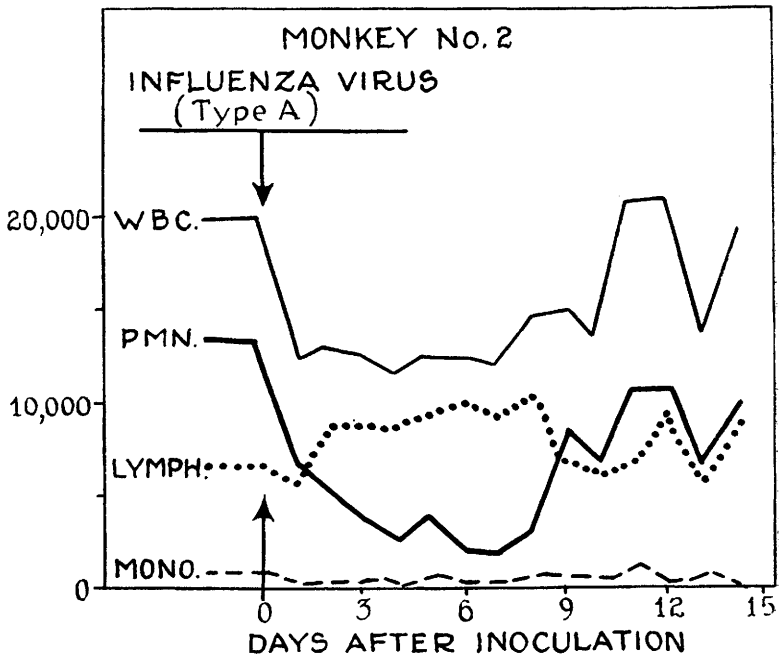


Fig. 1.

not infrequently observed in other studies of hemocytological disequilibria reported and commented upon previously.³

Virus-neutralizing antibodies, as evidenced by mouse-protection tests, were demonstrable in the serum of the six monkeys so tested, as early as the 8th day—approximately coincident with the beginning of spontaneous recovery from the granulocytopenia—and in every case by the 14th post-inoculation day. Repeated daily attempts to recover the virus from nasal and throat washings as well as from the blood were non-productive.

It may be concluded on the basis of the altered blood picture and from the specific antibody-response, that the monkey reacts characteristically to influenza A virus following intranasal inoculation. However, individuals of this species appear to be more resistant clinically than the smaller experimental animals ordinarily employed in studies of influenza, and while showing certain individual variations, they are probably more resistant to this disease, when uncomplicated, than the natural host, man. The monkey presents certain advantages over the small animals since its reactions, particularly the hematological and serological, may be more accurately followed.

13387 P

Reactions of Monkeys to Experimental Respiratory Infections.* II. Response to *Streptococcus hemolyticus* Group C.

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Comparatively few observations have been made of experimentally induced streptococcal infections of the respiratory tract in monkeys. Blake and Cecil¹ cite a sharp leucocytic rise within 24 hours following an intratracheal inoculation of hemolytic streptococcus, and in the lungs observed vascular engorgement, interstitial edema, and leucocytic infiltration. This report deals with the clinical, hematological, bacteriological, and immunological findings in monkeys inoc-

³ Wiseman, B. K., Doan, C. A., and Erf, L. A., *J. A. M. A.*, 1936, **106**, 609.

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¹ Blake, G., and Cecil, L., *J. Exp. Med.*, 1920, **32**, 401.