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 Cecil[1] 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.

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

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

ulated intranasally with *Streptococcus hemolyticus,* Lancefield Group C.

Methods. Healthy young adult monkeys *(Macaca mulatta),* selected for study, were isolated and observed for a period of 2-3 weeks during which time base lines for the various determinations were established. Animals found to be in satisfactory equilibrium were then inoculated intranasally while under deep ether-anesthesia with 3 cc of a saline suspension of living organisms (250 millions per cc). The animals were then observed daily for a period of from 3 weeks to 9 months.

Results. Clinical Characteristics. A majority of the monkeys thus studied developed distinct clinical signs of infection, including fever, anorexia, and loss of weight. Although most of the animals recovered promptly, several developed chronic foci with persistently positive throat-cultures for the Group C streptococcus.

Hematology. The first sign of invasion always appeared within 24 hours of inoculation as an acute, specific, polymorphonuclear leucocytosis. For example, in monkey No. 6 (Fig. 1), the white count rose from 17,000 to 51,000 overnight. The neutrophils usually maintained this initial high response for not longer than 24 hours, characteristically falling as precipitously as they had risen. Frequently, however, several polymorphonuclear rebounds of gradually decreasing amplitude occurred during the following 10-15 days (Fig. 1) before the previous cellular equilibrium was reëstablished, thus reflecting a successful cellular defense against the bacterial invasion. The lymphocytes showed minor reciprocal fluctuations,[2] corresponding to the polymorphonuclear peaks. The red cells and hemoglobin fell progressively with rising reticulocytes until the infection was brought under control, when spontaneous recovery followed.

Opsonocytophagic Index. Daily determinations based on a modification of Huddleson's method, revealed no significant increase in the opsonocytophagic index for Group C streptococci during the entire acute episode.

Antistreptolysin-titers. In only one monkey did the antistreptolytic level rise (from 10 units on the 5th to 200 units on the 15th day of infection), the remaining animals showing no significant variations.

Precipitin-titers. As a rule, in the monkeys exhibiting low antistreptolysin titers, little or no demonstrable precipitin was evident. In this group when a positive precipitin reaction occurred it ap-

[2] Woolpert, O. C., Schwab, J. L., Saslaw, S., Merino, C., and Doan, C. A., PROC. SOC. EXP. BIOL. AND MED., 1941, **48**, 558.

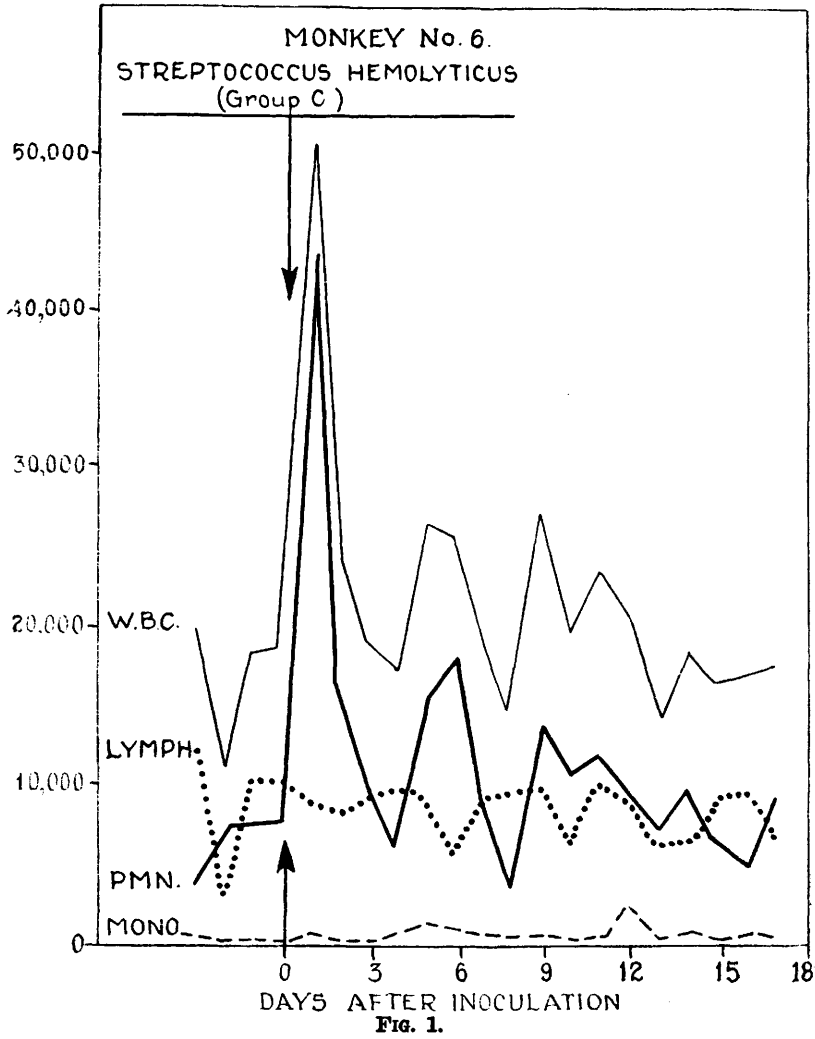

FIG. 1.

peared only with undiluted antigen, and not before 5 days after inoculation, when weak reactions were occasionally observed.

Bacteriological. Throat cultures were taken daily and revealed hemolytic streptococci on most of the examinations during the period of acute invasion. The streptococci isolated were typed by Lancefield's method to insure identification and to exclude possible spontaneous contamination by other strains from human contacts. Blood cultures were negative for streptococci in all instances.

Summary. The response of monkeys to primary intranasal inoculation with *Streptococcus hemolyticus,* Group C, was characterized

chiefly by a prompt but fleeting polymorphonuclear leucocytosis with occasional minor recurrent granulocytic elevations, followed by a transitory anemia. The opsonocytophagic index, antistreptolysin and precipitin titers were not significantly affected. Clinical manifestations of disease were mild but definite, and it is concluded that the cellular reaction, aided, if at all, only in slight degree by humoral factors, was the principal demonstrable defensive mechanism which these monkeys mobilized in successfully opposing the initial invasion by streptococci via the respiratory tract.

13388 P

Reactions of Monkeys to Experimental Respiratory Infections. III. Response to Mixtures of Influenza Virus and Streptococcus.*

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In earlier studies[1] employing mice, a shorter survival period and a greater proportion of deaths were observed in those animals which received mixtures of *Streptococcus hemolyticus*, Group C, and influenza-A virus, than in those receiving only one agent alone. The present report records particularly the hematological reactions in monkeys in which one infection was superimposed upon the other via the intranasal route.

Methods. The preparation of inocula, the dosages employed, and the method of administration were carried out as previously described.[2, 3] When the two agents were given simultaneously the concentrations were so adjusted that 3 cc of the mixture contained the full dosage of each agent.

Results. Clinical Characteristics. All monkeys receiving both agents, in whatever order, survived the infections and manifested only minimal clinical evidences of disease, except monkey No. 3

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

1 Schwab, J. L., Blubaugh, F. C., and Woolpert, O. C., *J. Bact.*, 1941, **41**, 59.

2 Woolpert, O. C., Schwab, J. L., Saslaw, S., Merino, C., and Doan, C. A., PROC. SOC. EXP. BIOL. AND MED., 1941, **48**, 558.

3 Schwab, J. L., Saslaw, S., Woolpert, O. C., Merino, C., and Doan, C. A., PROC. SOC. EXP. BIOL. AND MED., 1941, **48**, 560.