

**Reactions of Monkeys to Experimental Respiratory Infections.
IV. Response to Re-inoculation with *Streptococcus hemolyticus*.***

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The various reactions of *Macaca mulatta* to primary intranasal inoculation with *Streptococcus hemolyticus*, Group C, alone or in conjunction with the virus of influenza A, have been described in preceding communications.^{1, 2, 3} A study of the same phenomena on reinfection with the same strain of hemolytic streptococci is the basis of this report.

Methods. Eight monkeys were inoculated intranasally with streptococci 2 to 3 months previously. Six had survived also exposure to influenza A virus incurred either shortly preceding or just following the streptococcal episode. Before reinoculation, the recovered monkeys were observed and studied intensively over a control period of at least 1 to 2 weeks. *Streptococcus hemolyticus*, Group C, was then administered intranasally under ether-anesthesia in the same dosage (750,000,000 organisms in 3 cc saline) as was used for the primary inoculations.

Three monkeys, not included in the above group but having apparently recovered from a primary inoculation with hemolytic streptococci, redeveloped positive throat cultures for Lancefield Group C streptococci some 46 to 56 days after inoculation. Coincident with the spontaneous exacerbation of a latent autogenous focus or due to reinfection from others in our monkey colony, certain symptoms and signs appeared.

Results. Only 2 of the 8 reinoculated animals in the first group presented recognizable clinical evidences of disease. Symptoms and signs suggestive of renal damage appeared 2 weeks after reinoculation (95 days after primary inoculation) in one animal, and 4 days after reinoculation (108 days after primary inoculation) in another.

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¹ Woolpert, O. C., Schwab, J. L., Saslaw, S., Merino, C., and Doan, C. A., *Proc. Soc. Exp. Biol. and Med.*, 1941, **48**, 558.

² Schwab, J. L., Saslaw, S., Woolpert, O. C., Merino, C., and Doan, C. A., *Proc. Soc. Exp. Biol. and Med.*, 1941, **48**, 560.

³ Merino, C., Doan, C. A., Woolpert, O. C., Schwab, J. L., and Saslaw, S., *Proc. Soc. Exp. Biol. and Med.*, 1941, **48**, 563.

General malaise, anorexia, hypertension, edema of the face, legs, and perineal region, and albuminuria, with pus cells, red cells and casts in the urinary sediment were found. Identical phenomena were noted in all 3 of the monkeys showing the spontaneous re-appearance of Group C streptococci in their respective throat cultures. Experimental reinoculation of these 3 monkeys with Group C streptococci 2 months after subsidence of the acute spontaneous renal manifestations, failed to elicit any further constitutional signs.

Throat cultures from those monkeys which became acutely ill following reëxposure to *Streptococcus hemolyticus*, remained consistently positive for this organism, while streptococci were found only irregularly and transiently in the throats of other animals. Blood cultures were negative in all instances. The antistreptolysin titer rose significantly in 4 of 8 animals tested. The precipitin level also showed a sharp rise and the titer was best maintained in those

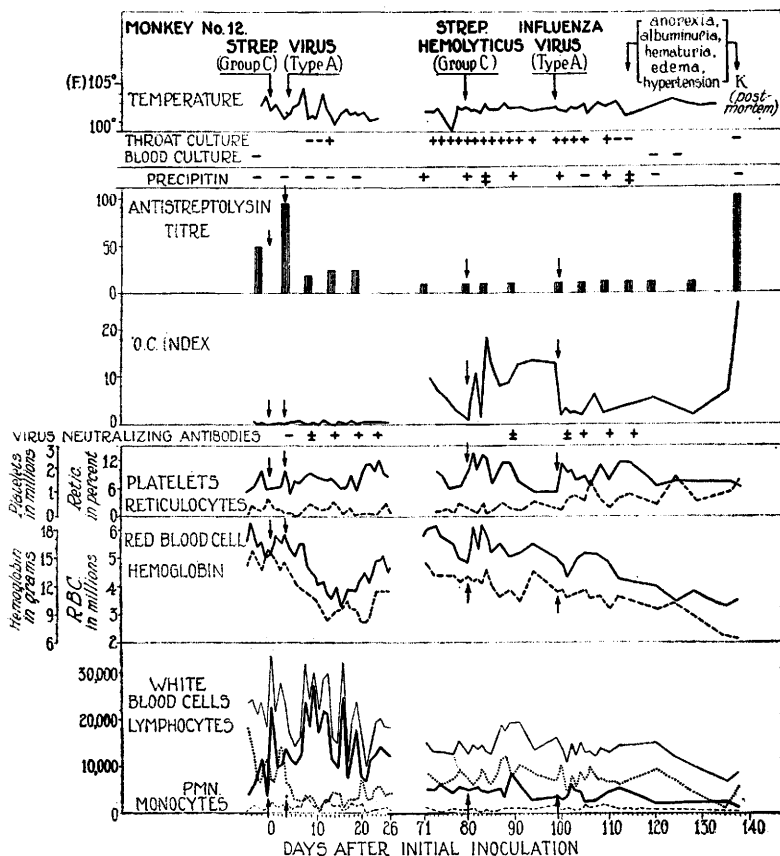


FIG. 1.

monkeys which handled the reinfections most effectively. Most noteworthy was the marked increase in opsonocytophagic index evoked by reinoculation with streptococci. On the other hand, *the granulocytosis which has proved to be one of the most characteristic responses to primary streptococcus infection² was wholly lacking in all reinoculated animals.*

Fig. 1 summarizes and correlates the pertinent data in one representative individual in this reinoculated series. In monkey No. 12, neutrophilecytosis with reciprocal lymphocytopenia, continued throughout the first 20 days of acute reaction to the original streptococcal inoculation, the superimposed influenza virus having little if any granulocyte-inhibiting influence. The dominance of the streptococcal element in this syndrome is further indicated by the progressive hemolytic anemia that developed during the first 12 to 20 days, beginning erythrocyte-recovery coinciding with subsidence of the granulocytosis. Specific precipitins and the opsonocytophagic index for Group C streptococci were essentially negative. By the 71st day all cellular equilibria had been reestablished and monkey No. 12 was in good clinical condition. Intranasal reinoculation with hemolytic streptococci was done on the 80th day. In sharp contrast to the earlier phenomena, no granulocytosis occurred, *but* a prompt and significant compensatory increase in the opsonocytophagic index was noted. This high opsonic index persisted until it was suddenly inhibited or neutralized when the influenza virus was once again instilled into the nares. Granulocytes, lymphocytes, red cells, and hemoglobin fell steadily thereafter. By the 108th day there appeared signs of renal damage with hypertension (systolic 185 mm, diastolic 140 mm Hg) albuminuria (100 mg %), hematuria, casts and edema.

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Lack of Immunity to Latent Virus.

GUSTAVE FREEMAN. (Introduced by G. F. Dick.)

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The apparent failure to encounter immune mice in the spontaneous mouse infections described by Dochez, *et al.*,¹ and us^{2, 3}

¹ Dochez, A. R., Mills, K. C., and Mulliken, B., *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **36**, 683.

² Gordon, F. B., Freeman, G., and Clampit, J. M., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **39**, 450.

³ Freeman, Gustave, *Arch. Path.*, 1940, **29**, 505.