

monkeys which handled the reinfections most effectively. Most noteworthy was the marked increase in opsonocytaphagic 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 infection*² 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, neutrophilcytosis 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 opsonocytaphagic 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 opsonocytaphagic 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.

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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.

suggested this attempt to produce evidence of immunity experimentally. It is of particular interest because the host-virus relationship seemed to be latent until provoked experimentally. The virus then grew highly virulent, killing all mice that became sick. None of the surviving mice appeared to be immune to the latent virus.

Approximately 400 mice obtained at different times from a Missouri breeder were observed for varying periods of time up to 14 months. These stock mice appeared to be well although they were known to carry the virus. None of these mice died spontaneously with pneumonitis.

Mice were anesthetized with ether and inoculated intranasally with 1:20 suspension of infected lung emulsion in saline. Lungs of sick mice were cultured on blood agar plates and 30% ascitic fluid agar, aerobically and anaerobically. Occasional colonies appeared from lungs of moribund animals but no organisms grew consistently enough to have etiological significance. Pleuropneumonia-like organisms^{4, 5} were sought particularly since these have confused work with viruses in mice.

Groups of mice were inoculated by various routes in an attempt to immunize them. The survivors were reinoculated intranasally with virus 30 days after the initial attempts in order to test for immunity. The results are seen in Table I.

During one period of observation about 50% of the stock mice became ill and died with the disease after intranasal inoculation of sterile physiological saline. Animals that did not die after such treatment were found, nevertheless, to be susceptible to the disease by inoculation with virus. At other times saline seldom affected the mice. They were all susceptible to the disease, however, when inoculated with virus.

The disease is propagated by the passage of lungs of stock mice intranasally in series, the disease appearing usually within the first 3 passages. Groups of 3 were passed in this manner. One animal of each group was used to inoculate the succeeding group of three until

TABLE I.

Route	No. of mice	Surviving 30 days	Surviving reinoculation intranasally
Intracranial	6	6	0
Subcutaneous	6	6	0
Intraperitoneal	6	6	0
Intranasal	6	0	—
" (saline)	6	2	0

⁴ Klieneberger, E., *J. Hyg.*, 1938, **38**, 458.

⁵ Sabin, A. B., *Science*, 1939, **89**, 228.

TABLE II.

Dilution	Days alive								Survivors reinoeculated (43rd day)	Days alive after reinoeculation				Survivors
	2	3	5	7	8	10	13	14		15	2	3	4	
1-20	4	2								0				—
10-2	2	2	1						1	0				—
10-3			2	2	1					1	1			0
10-4				2	1	2	1			0				—
10-5								1	1	4	2	1	1	0
Saline										6	4	1	1	0

the disease occurred uniformly in all inoculated animals. The survivors were inoculated subsequently with known virus and succumbed to the disease. None proved to be immune.

Mice were inoculated with graduated dilutions of virus. Survivors of the sublethal doses were available for testing. These animals were reinoculated with lung emulsion of the lowest dilution 43 days after the original inoculations. The results are recorded in Table II.

Uninoculated cagemates of sick and moribund mice did not contract the disease. These animals, nevertheless, demonstrated no immunity to virus inoculation.

Large quantities of virus were injected subcutaneously and intraperitoneally into rabbits weekly for 8 weeks. Antiserum was mixed with virus for 30 minutes and inoculated intranasally one week after the last injection. The activity of the virus was not neutralized. Neither was previous intraperitoneal injection of antiserum effective in protecting mice against the virus.

This report describes the unusual immunological phenomenon of an invariably fatal clinical infection caused by a virus that lies dormant in the same host until stimulated by serial passage of lung emulsion or of physiological saline inoculated intranasally. No evidence of immunity to the latent virus has been demonstrated.

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Effect of Iodoacetate and Malonate on Respiration of Sea Urchin Sperm.

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Since Lundsgaard¹ discovered that iodoacetate in small concentrations inhibited the fermentation of glucose by yeast without