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Protective Antibody in Guinea Pigs Recovering from Experimental Pneumococcus Infection.

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In the course of observing various reactions associated with spontaneous survival of guinea pigs infected experimentally with pneumococcus Type I the appearance and rise of protective antibody in the blood has been studied. The animals were infected by intra-abdominal injection of 0.25 cc of an 18-hour serum-dextrose-broth culture of pneumococci. Under these conditions and without treatment 47 of 100 animals survived. The day of recovery of the animals has been considered as being identical with the day a negative culture of the peritoneal exudate was obtained. Only surviving animals were studied, since the majority which did not survive, died before the fourth day.

Blood was taken from the heart of the guinea pigs at various intervals and the serum separated. The tests were carried out by determining the number of minimal lethal doses of a virulent Type I pneumococcus which could be neutralized by 0.5 cc of the serum when mixtures of the culture and the serum were injected intraäbdominally into mice.

It was not possible to take blood from the guinea pigs for testing of protective titer at daily intervals so that there are of necessity some intervals which have not been thoroughly explored, but the studies are probably sufficiently detailed to warrant certain conclusions.

Forty-two of 47 guinea pigs which survived the infection are considered here. Serum for antibody-titration was obtained from all animals before infection. Only one animal showed the presence of antibodies; they were no longer demonstrable by the fifth day of infection and did not reappear during the period of observation (through the 24th day).

In Table I is shown the relation between the appearance of antibodies and the recovery from infection as measured by the negative peritoneal culture. In only a very few cases was blood taken for testing antibodies on the second day after infection, and in no animals were protective antibodies demonstrable. In 2 animals antibodies were demonstrable on the third day, in 5 animals on the fourth day, in 13 animals on the fifth day, and 2 on the sixth day, in 6 on the

TABLE I.
Day of Recovery and Day of Appearance of Protective Antibody.

Day of appearance of antibody / Day of negative culture	3	4	5	6	7	8	After 8	Negative	Total
1			2					1	3
2		3				1			4
3	1		1				1		3
4		2	5		4		2		13
5			4			3	1	1	9
6	1			1	1	1			4
7			1	1	1	1			4
8							1		1
9								1	1
Total	2	5	13	2	6	6	5	3	42

seventh day, in 6 on the eighth day, in 5 after the eighth day, and in 3 antibodies were not demonstrable at any time.

If one observes the general trend of the appearance of antibodies, it will be noted that few animals show antibodies before the fifth day, and that more animals have antibodies appearing on the fifth than on any other day; after the fifth day antibodies appear in considerable numbers of the animals. It may be assumed that the tendency is for the antibodies to appear regardless of the duration of the infection but that their appearance is affected by the continuance of the infection. This point is brought out if one considers the animals in which antibodies appear before or on the day of recovery; in the animals which recover early (before the fifth day) only 3 (13%) show antibodies by this time, while in the group recovering later (on or after the fifth day) 9 (50%) show antibodies before or on the day of recovery.

There is a possible relationship between the early appearance of antibodies (by or before the fifth day) and early recovery (by or before the fourth day). It need not be assumed that this relationship is between cause and effect, but it is quite possible that the early subsidence of the infection and diminution of the specific antigen in the invaded host permits the antibody to become evident.

In only a limited number of animals (3) is antibody demonstrable before recovery and then in the cases in which recovery was not before the sixth day. In 9 animals the antibody was demonstrable on the day of recovery. Thus in 12 animals (29%) antibodies were demonstrable before or coincident with recovery. In 21 of the 42 animals antibodies were demonstrable either before recovery, on the day of recovery, or on the first day after recovery.

In Table II is shown the range of the protective titer of the serum from the guinea pigs.

TABLE II
M.L.D.'s Neutralized.

	0	10	100	1000	10,000	100,000
3-5th day	20	13	5	1	—	1
6-9th "	6	5	5	3	14	5
10-19th "	6	2	2	5	7	6
20-33rd "	18	3	6	9	6	1

Relatively few animals show a high titer at any time, but there is evident the tendency towards reaching a maximal titer in the second or third week, followed by a fall in later periods. Many of the animals that had shown antibodies in the early periods do not possess these in their serum at later periods; at least 15 animals out of 33 which were studied over a sufficient period of time had lost their antibodies before the 33d day after infection and recovery.

In general these results concerning the appearance of antibodies in guinea pigs are in agreement with those observed in pneumococcal infection in human beings. It is not possible to predict the outcome of the infection through observation of the appearance of antibody or the level of antibody-titer.

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Mononuclear Leucocytes in Blood of Guinea Pigs Experimentally Infected with Pneumococcus.

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In view of the importance attached by many observers to the rôle of mononuclear cells in recovery from infection and especially the concepts advanced by Robertson and his coworkers[1-4] in pneumococcal infection in dogs, the changes in the mononuclear cells in the circulating blood have been studied in guinea pigs that died and that recovered spontaneously from experimental pneumococcal infection. The animals were infected by intraäbdominal injection of 0.25 cc of an 18-hour dextrose-serum-broth culture of Type I pneumococcus. Of 100 animals so infected 47 survived the infection. In this study

1 Robertson, O. H., and Uhley, C. G., *J. Clin. Invest.*, 1936, **15**, 115.
2 Robertson, O. H., and Loosli, C. G., *J. Exp. Med.*, 1938, **67**, 575.
3 Robertson, O. H., and Coggeshall, L. T., *J. Exp. Med.*, 1938, **67**, 597.
4 Robertson, O. H., *J. A. M. A.*, 1938, **111**, 1432.