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.

TABLE I.

Mononuclear Counts in Animals Dying After the Second Day or Surviving the Experimental Pneumococcal Infection.

	0 hr	6 hr	1 day	2 day	3 day	4 day	5 day	6 day	7 day	8 day	9 day
Died bet. 2d and 3d day	350	300	288	121							
" " 3d and 4th "	350	225	342	148	645						
" " 4th and 5th day	266	400	118	457	608	1080					
" after 5th day	740	280	182	194	251	579	434	2608			
Group C	400	284	237	217	485	722					
Negative on 8th or 9th day	388	359	350	1387	905	651	464	987	701		1853
" " 7th day	342	234	440	169	1195	332	556		729		646
" " 6th "	451	371	258	481	1081	527	414	588		416	113
" " 5th "	392	361	131	369	311	828	480	309	414	611	1348
Group D	393	341	258	586	514	608	485	623	493	494	1181
Group E	308	261	293	229	591	588	409	311			727

of the mononuclear leucocytes 14 animals that died from 60 hours to 30 days after infection (Group C), 18 that recovered at 5 to 9 days after infection (Group D), and 14 that recovered on the fourth day (Group E) are considered. Recovery was assumed to have occurred on the day a negative culture was obtained from the peritoneal exudate.

At 6 hours after infection there was a decrease in the number of circulating mononuclears and this decrease was usually still evident or may have been more marked at 24 hours. The changes were observed in all groups regardless of whether death or survival follows (Table I).

In Group C, in those animals that died before the third but after the second day, the mononuclears continued to decrease after 24 hours; this change was concomitant with a decrease of total cells and of neutrophils.[5] Those animals that died on the fourth day showed a further decrease on the second day; however, on the third day these latter animals (which died within the next 24 hours) showed a distinct increase in the mononuclear cells. Other animals dying later than the fourth day, showed an increase at the second day and there was a tendency towards an increased number of cells in later days. In general if death was delayed beyond the third day, the number of mononuclears increased even though the animals died.

In Group D an increase in mononuclear cells occurred on the second day but was quite irregular as to magnitude in the different subgroups. From the second day onwards there was a tendency for the number of mononuclears to remain fairly high, but there was a considerable degree of variation in the different subgroups. There was no regularly observable rise in mononuclears in all of the smaller groups on the day before the negative culture; however, in the animals that became negative on the fifth day a rather sharp and distinct rise was observed on the fourth day; this is all the more striking since the mononuclears had remained at a fairly low level up to this day.

In Group E, in which all animals showed a negative culture on the fourth day, the count remained low on the second day and rose rather sharply on the third day, that is, just before recovery, remaining at about the same level on the date of the negative culture. Subsequently the mononuclear count fell.

Reviewing all 3 groups it appears that the mononuclears tend to follow a certain curve regardless of the outcome of the infection. Within the first 24 hours the counts are low, generally lower than

[5] Fleisher, M. S., and Rich, G. T., to be reported.

before the start of the infection. On the second day the count rises, although the counts in the non-surviving animals tend to lag behind. By the third day the mononuclears in all animals or groups increase to a greater or less degree regardless of what the outcome will be, and this increase is usually maintained. In those animals that develop a negative culture on the fourth or fifth day the mononuclears usually remain low (at about the same level as before infection) up to the day before the negative culture, and on this date these cells show a definite increase.

It may then be assumed that changes in the number of mononuclear cells in the circulating blood during the earlier periods of the infection (during the first 24 hours) cannot be associated with and will not serve to predict the eventual outcome of the infection.

As regards the relationship of the increase of the mononuclears just before recovery the fact that a rise in these cells occurs at this same general period in most groups regardless of the outcome, raises doubt as to the interpretation of this reaction. It may be noted, however, that reaction of the mononuclears in animals recovering may be one of two types: (1) In the group that recovered on the fourth or fifth day there may be a definite association with an increase in the number of mononuclears as shown by the earlier low level and the sharp rise just before recovery; (2) in those animals that do not recover until after the fifth day, there does not appear to be any association between a rise of the mononuclears and immediate processes of recovery. If the mononuclear leucocytes are of importance in recovery from pneumococcal infection, it seems possible that their rôle is more definite in the first type of reaction, while in the second type of reaction they are less important.

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Serum Amino Nitrogen Concentration in Different Parts of the Vascular System.

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During investigations on amino nitrogen transport in the body a few studies were made on the amino nitrogen level in blood as it courses the vascular system. The observations were on dogs under