STUDIES IN THE BLOOD CYTOLOGY OF THE RABBIT

V. Consecutive Lymphocyte and Monocyte Observations on Groups of Normal Rabbits

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Previous papers of this series have contained the results of repeated blood examinations on 5 groups of normal male rabbits with respect to the erythrocyte and hemoglobin determinations (1), the total white cell contents (2), and the neutrophile (pseudo-eosinophile), the basophile, and the eosinophile cell counts (3). The purpose of these experiments was to obtain information on the general character or trend of the spontaneous variations described by the cellular constituents of the peripheral blood over prolonged periods of time, and the data obtained have, in each instance, been presented on the basis of the consecutive weekly mean values of each group. In the present paper, the results on the non-granular cells—the lymphocytes and the monocytes—are reported.

Materials and Methods

A description of the materials and methods employed in these experiments and of the method of analyzing the results obtained has been given in the paper dealing with the observations on the erythrocytes and hemoglobin (1). Suffice it to say here that the period of time covered by the experiments extended from October, 1927 to July, 1929, and in the majority of cases, the blood was examined at weekly intervals. The numbers of examinations were: Group I, 35; Group II, 13; Group III, 8; Group IV, 29; Group V, 26. Each of the first 4 groups comprised 10 and the last, 5 normal male rabbits. The supravital neutral red technic was used in making the differential white cell counts and 100 cells were counted in each specimen.

RESULTS

The consecutive lymphocyte and monocyte determinations on 5 groups of normal rabbits are given in Tables I to V in the form of mean

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TABLE I

Group I-10 Rabbits. Consecutive Values for Lymphocytes and Monocytes

	Lym	phocytes		Monocytes		
Date	Mean values	Standard deviation	Coeffi- cient of variation	Mean values	Standard deviation	Coeffi- cient of variation
1927-28	per cmm.	per cmm.	per cent	per cmm.	per cmm.	per cent
Oct. 24*	2253 ± 185	867	25.97	987 ± 83	388	39.31
Nov. 1	1861 ± 92	431	23.16	1092 ± 139	650	59.52
Nov. 8**	1929 ± 165	772	40.02	1153 ± 104	487	42.24
Nov. 15	2560 ± 105	491	19.18	1085 ± 83	389	35.85
Nov. 22	2005 ± 169	794	39.60	1409 ± 185	869	61.67
Nov. 29	2984 ± 210	983	32.94	1209 ± 174	817	67.63
Dec. 6	2781 ± 238	1117	40.17	1073 ± 114	533	49.67
Dec. 13	3171 ± 399	1871	59.00	1178 ± 127	596	50.59
Dec. 20	2209 ± 166	778	35.22	1231 ± 127	595	48.33
Dec. 27	2554 ± 197	922	36.10	864 ± 77	362	41.90
Jan. 3	2945 ± 333	1559	52.94	1045 ± 52	245	23.44
Jan. 10	3425 ± 256	1202	35.09	967 ± 73	341	35.26
Jan. 17	3429 ± 352	1648	49.11	1025 ± 102	480	46.83
Jan. 24	3511 ± 285	1336	38.05	967 ± 58	270	27.92
Jan. 31	3444 ± 284	1332	38.68	1023 ± 81	380	37.15
Feb. 7	3501 ± 263	1235	35.28	1100 ± 106	497	45.18
Feb. 14	3070 ± 225	1056	34.40	1201 ± 134	627	52.21
Feb. 21	4671 ± 496	2324	49.75	1218 ± 148	693	56.90
Feb. 28	2507 ± 151	708	28.24	1145 ± 101	474	41.40
Mar. 6	2934 ± 183	859	29.28	1117 ± 76	354	31.69
Mar. 13	2532 ± 221	1037	40.96	1183 ± 138	648	54.78
Mar. 20	2563 ± 166	779	30.39	1084 ± 83	389	35.89
Mar. 27	3044 ± 217	1015	33.34	1112 ± 104	488	43.88
Apr. 3	3322 ± 335	1571	47.29	1181 ± 127	595	50.38
Apr. 10	3966 ± 337	1578	39.79	1027 ± 123	576	56.09
Apr. 17	3734 ± 245	1149	30.77	1107 ± 121	569	51.40
Apr. 24	3073 ± 288	1352	44.00	933 ± 134	627	67.20
May 1	4165 ± 316	1483	35.61	933 ± 93	438	46.95
May 8	3358 ± 251	1178	35.08	1092 ± 87	407	37.27
May 15	3775 ± 190	891	23.60	1071 ± 100	468	43.70
May 22	3624 ± 169	792	21.85	1245 ± 110	516	41.45
May 29	4182 ± 324	1521	36.37	1410 ± 294	1377	97.66
June 5	4602 ± 205	959	20.84	1543 ± 169	790	51.20
June 12	4455 ± 473	2219	49.81	1270 ± 117	546	42.99
June 19	3376 ± 292	1371	40.61	1106 ± 114	536	48.46
Mean	3186 ± 83	731	22.94	1125 ± 16	139	12.36
Minimum	1861			864		
Maximum	4671			1543		

* October 24 and 26.

** November 4 and 9.

	Lymp	hocytes		Monocytes			
Date	Mean values	Standard deviation	Coeffi- cient of variation	Mean values	Standard deviation	Coeffi- cient of variation	
1928	per cmm.	per cmm.	per cent	per cmm.	per cmm.	per cent	
Mar. 29	2210 ± 173	809	36.61	573 ± 35	165	28.80	
Apr. 3	3313 ± 262	1227	37.04	677 ± 101	474	70.01	
Apr. 10	3073 ± 287	1347	43.83	844 ± 89	416	49.29	
Apr. 17	3429 ± 286	1342	39.13	1076 ± 154	724	67.29	
Apr. 24	3067 ± 203	950	30.97	853 ± 102	476	55.80	
May 1	3257 ± 231	1081	33.19	680 ± 64	299	43.97	
May 8	3215 ± 216	1012	31.48	777 ± 83	388	49.94	
May 15	2605 ± 247	1158	44.45	721 ± 126	590	81.83	
May 22	3960 ± 284	1331	33.61	1028 ± 101	475	46.21	
May 29	3758 ± 365	1713	45.58	843 ± 97	455	53.97	
June 5	3864 ± 252	1180	30.54	796 ± 70	329	41.33	
June 12	3236 ± 244	1144	35.35	1063 ± 110	517	48.64	
June 19	3526 ± 222	1040	29.50	1166 ± 66	310	26.59	
Mean	3270 ± 87	465	14.22	854 ± 32	173	20.26	
Minimum	2210	1		573	1]	
Maximum	3960			1166			

TABLE II

Group II-10 Rabbits. Consecutive Values for Lymphocytes and Monocytes

Group III-10 Rabbits. Consecutive Values for Lymphocytes and Monocytes

	Lymŗ	hocytes		Monocytes			
Date	Mean values	Standard deviation	Coeffi- cient of variation	Mean values	Standard deviation	Coeffi- cient of variation	
1928	per cmm.	per cmm.	per cent	per cmm.	per cmm.	per cent	
Sept. 20	1971 ± 268	1254	63.62	712 ± 113	529	74.30	
Sept. 28	2454 ± 287	1345	54.81	780 ± 88	414	53.08	
Oct. 10	2178 ± 82	385	17.68	739 ± 80	373	50.47	
Oct. 19	2497 ± 142	667	26.71	813 ± 103	482	59.29	
Nov. 2	2009 ± 167	784	39.02	797 ± 101	472	59.22	
Nov. 9	2352 ± 151	708	30.10	820 ± 64	300	36.59	
Nov. 16	1883 ± 110	516	27.40	733 ± 89	415	53.69	
Nov. 22	2348 ± 181	850	36.20	895 ± 112	525	58.66	
Mean	2212 ± 53	220	9.95	786 ± 13	55	7.00	
Minimum	1883			712		l	
Maximum	2497			895			

values, together with the probable errors of the means, the standard deviations, and the coefficients of variation. The curves in Text-figs.

	Lym	phocytes		Monocytes			
Date	Mean values	Standard deviation	Coeffi- cient of variation	Mean values Standar deviation		Coeffi- cient of variation	
1928-29	per cmm.	per cmm.	per ceni	per cmm.	per cmm.	per cent	
Nov. 27	2616 ± 173	812	31.02	546 ± 39	183	33.56	
Dec. 4	2713 ± 153	717	26.44	499 ± 45	212	42.47	
Dec. 11	2319 ± 182	854	36.84	452 ± 55	256	56.63	
Dec. 18	2168 ± 211	991	45.72	790 ± 171	801	101.35	
Dec. 26	2160 ± 186	871	40.31	362 ± 49	229	63.24	
Jan. 2	1563 ± 82	383	24.48	456 ± 60	280	61.40	
Jan. 8	2040 ± 172	807	39.55	490 ± 90	422	86.08	
Jan. 15	1955 ± 84	394	20.13	563 ± 48	224	39.80	
Jan. 22	1839 ± 160	751	40.81	704 ± 87	406	57.72	
Jan. 29	2470 ± 154	720	29.15	591 ± 73	342	57.84	
Feb. 5	1873 ± 144	676	36.09	546 ± 70	330	60.34	
Feb. 13	2036 ± 108	505	24.80	826 ± 148	693	83.89	
Feb. 19	1907 ± 146	686	35.97	893 ± 101	474	53.08	
Feb. 26	2038 ± 139	651	31.96	1066 ± 100	468	43.87	
Mar. 12	2007 ± 142	668	33.29	1006 ± 92	431	42.81	
Mar. 19	2189 ± 129	604	27.58	857 ± 74	346	40.40	
Mar. 26	2290 ± 199	934	40.76	635 ± 66	310	48.85	
Apr. 2	1561 ± 185	869	55.70	856 ± 94	443	51.74	
Apr. 9	2530 ± 168	787	31.09	1066 ± 98	460	43.15	
Apr. 16	2765 ± 233	1092	39.50	709 ± 57	269	37.95	
Apr. 23	2971 ± 200	939	31.62	916 ± 99	462	50.44	
Apr. 30	2301 ± 183	857	37.23	619 ± 88	413	66.63	
May 7	2574 ± 146	686	26.64	699 ± 46	216	30.95	
May 14	2514 ± 150	668	26.55	622 ± 62	276	44.34	
May 21	1672 ± 93	413	24.71	565 ± 36	159	28.19	
May 28	2523 ± 169	752	29.78	479 ± 58	259	54.11	
June 4	1960 ± 172	763	38.94	678 ± 62	276	40.77	
June 11	1920 ± 153	682	35.53	509 ± 44	196	38.50	
June 18	2609 ± 205	860	32.94	530 ± 42	176	33.18	
Mean	2210 ± 45	363	16.40	673 ± 24	190	28.20	
Minimum	1561			362			
Maximum	2971			1066			

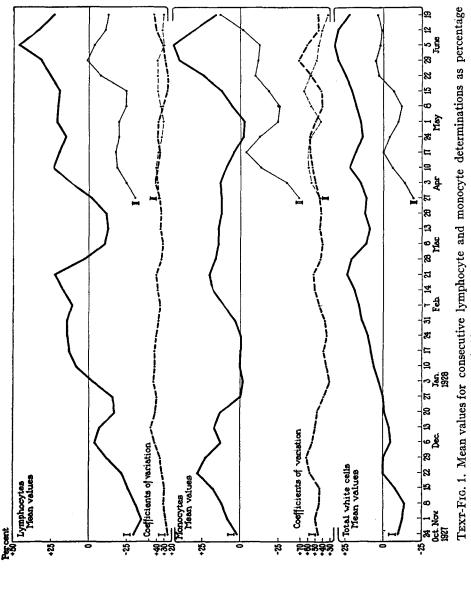
TABLE IV Group IV-10 Rabbits. Consecutive Values for Lymphocytes and Monocytes

1 and 2, illustrating the mean values, have been drawn in the form of the percentage deviations of the smoothed means from standard values (1, 4); similar curves for the total white cells (2) have been included to facilitate convenient comparisons with their fluctuations. The other curves in the text-figures represent the smoothed coefficients

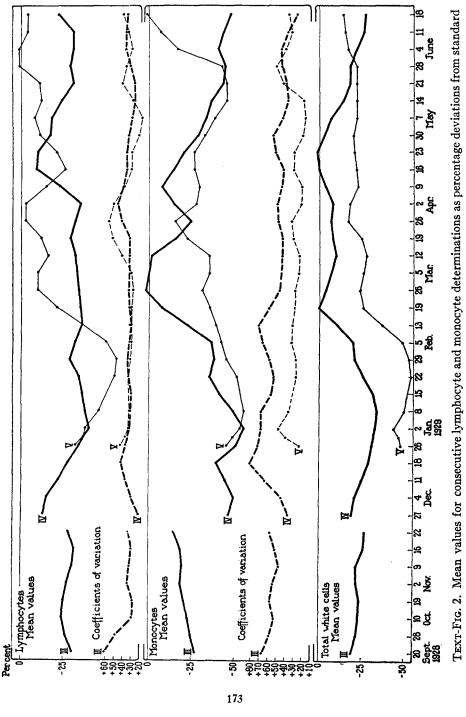
	Lym	phocytes		Monocytes			
Date	Mean values	Standard deviation	Coeffi- cient of variation	Mean values	Standard deviation	Coeffi- cient of variation	
1928-29	per cmm.	per cmm.	per cent	per cmm.	per cmm.	per cent	
Dec. 29	2310 ± 95	314	13.59	631 ± 92	305	48.34	
Dec. 31	1650 ± 206	683	41.39	350 ± 34	113	32.29	
Jan. 3	2127 ± 386	1279	60.13	588 ± 65	215	36.56	
Jan. 10	1676 ± 130	431	25.72	309 ± 26	86	27.83	
Jan. 24	1135 ± 107	353	31.10	544 ± 60	200	36.76	
Jan. 31	1503 ± 90	299	19.89	505 ± 46	153	30.30	
Feb. 7	1198 ± 139	460	38.40	591 ± 44	146	24.70	
Feb. 15	2147 ± 211	698	32.51	605 ± 69	227	37.52	
Feb. 21	2304 ± 146	485	21.05	618 ± 47	156	25.24	
Mar. 1	2941 ± 328	1087	36.96	723 ± 71	234	32.37	
Mar. 8	2820 ± 156	517	18.33	639 ± 47	146	22.85	
Mar. 15	2387 ± 167	552	23.13	561 ± 67	223	39.75	
Mar. 22	2610 ± 214	710	27.20	816 ± 148	492	60.29	
Mar. 29	3092 ± 396	1314	42.50	905 ± 133	441	48.75	
Apr. 5 ,	3038 ± 133	440	14.48	671 ± 132	436	64.98	
Apr. 12	2668 ± 114	377	14.13	635 ± 54	179	28.19	
Apr. 19	1990 ± 226	749	37.64	875 ± 73	242	27.66	
Apr. 26	2357 ± 208	688	29.19	523 ± 60	199	38.05	
May 3	2927 ± 160	529	18.07	788 ± 31	101	12.82	
May 10	2700 ± 117	388	14.37	563 ± 31	101	17.94	
May 17	2886 ± 139	459	15.90	524 ± 32	106	20.23	
May 24	2219 ± 184	610	27.49	547 ± 85	283	51.74	
May 31	3580 ± 605	2006	56.03	531 ± 56	184	34.65	
June 7	2913 ± 176	584	20.05	880 ± 60	198	22.50	
June 14	2913 ± 173	572	19.64	1023 ± 107	353	34.51	
June 21	2944 ± 260	861	29.25	1007 ± 125	414	41.11	
Mean	2424 ± 80	607	25.04	652 ± 23	176	26.99	
Minimum	1135			350			
Maximum	3580		İ	1023			

TABLE VGroup V—5 Rabbits. Consecutive Values for Lymphocytes and Monocytes

of variation of the means. The standard values used in this comparison of mean values are: lymphocytes, 3050 per cubic millimeter; monocytes, 1000 per cubic millimeter; total white blood cells, 9560 per cubic millimeter.



TEXT-FIG. 1. Mean values for consecutive lymphocyte and monocyte determinations as percentage deviations from standard values. 1927-28.





DISCUSSION AND SUMMARY

The results of these experiments will be discussed in chronological order. It will be noted that the observations on Group II were made during the spring of 1928 at which time Group I was still being examined, and that Groups IV and V were followed during the winter and spring months of 1928 and 1929.

Group I was examined at weekly intervals from October 24, 1927 to Tune 24, 1928 (Table I). From the curves in Text-fig. 1, which illustrate the lymphocyte and monocyte mean values in the form of percentage deviations from standard values as given above, it will be seen that the mean numbers of lymphocytes were considerably increased above their low initial level by the end of the experiment. This change was accomplished gradually and in a fairly consistent fashion with the exception of a minor drop of the values in December and June and an abrupt and pronounced fall at the end of February and the first half of March. In the case of the monocytes, the general level of which was continuously above the standard value, no such sustained increase of mean values was observed. The curve representing these cells contains 3 major upward swings which occurred in November, in February and March, and in May. During certain periods, as in October and November, and again in May and June, the lymphocyte and monocyte curves follow the same general trend. At other times, however, this parallel relationship did not hold. In January, the lymphocyte curve describes a sharp rise while the monocyte curve is stationary and in February, March, and April, when an abrupt fall of the lymphocyte curve is followed by a pronounced rise, the monocyte curve describes a slight but protracted decline. It will be seen by the curve in Text-fig. 1, that the total white cell count was considerably increased during the experiment, and a comparison with the lymphocyte curve shows that its fluctuations are frequently reflected in those of the total white cells. Although the coefficients of variation of the lymphocyte means (Table I) are of a high order of magnitude, the curve of the smoothed values (Text-fig. 1) is quite regular. The monocyte coefficients (Table I) are slightly higher than those of the lymphocytes and their smoothed curve (Text-fig. 1) is more irregular.

Group II was examined from March 29 to June 19, 1928 (Table II). The curves representing its lymphocyte and monocyte means (Text-fig. 1) bring out clearly the lower numerical levels of both classes of cells as compared with those of Group I. In the case of the lymphocytes the general forms of the curves of Groups I and II are very similar but with the monocytes, the resemblance is less striking.

The lymphocyte and total white cell curves are, on the whole, much alike. There are certain portions of the latter curve, however, which resemble the monocyte more than the lymphocyte curve, as for example, that covered by the last two observations. The coefficients of variations of the lymphocyte and monocyte means of Group II (Table II) are of the same order of magnitude as those of Group I and their smoothed curves (Text-fig. 1) present the same general appearance.

Group III was examined from September 20 to November 22, 1928 (Table III). From the curves in Text-fig. 2, it will be seen that the levels of both the lymphocyte and the monocyte mean values were of the same order as those of Group II rather than those of Group I. Only minor changes in the values of Group III were observed. The monocyte curve describes a gradual comparatively slight rise while the lymphocyte curve shows no clearly defined trend. The total white cell curve describes a slight downward trend and it is almost a mirror image of the monocyte curve. With the exception of the first two points of the lymphocyte curve, the curves of the smoothed coefficients of variation of the lymphocyte and monocyte means (Text-fig. 2) are comparable to those of Groups I and II.

Group IV was examined from November 27, 1928 to June 19, 1929 (Table IV). The general level of the lymphocyte mean values was comparable to the results in Groups II and III and to the first quarter of the findings of Group I. During December, the trend of mean values was decreasing as shown by the falling curve (Text-fig. 2); during January, February, and March, a low level was fairly constantly maintained; in April, an abrupt increase occurred and this was succeeded by a second decrease. The curve representing the monocytes (Text-fig. 2) shows first that the general level of mean values was usually lower than that of Group I and was more comparable to those of Groups II and III. From very low levels in December and early January, the pronounced upward swing of the curve in February, March, and April indicates the increase of monocytes during this time, and its subsequent descent illustrates the eventual drop in the numbers of these cells. The general trend of the lymphocyte and the monocyte means is similar in the beginning and during the last third of the experiment, but during much of the time, the increase of monocytes was accompanied by practically no change in the level of lymphocyte mean values. In general form, the total white cell curve (Text-fig. 2) has many points of resemblance with the monocyte as well as with the lymphocyte curve.

The coefficients of variation of the lymphocyte means (Table IV, Text-fig. 2) which are on the whole quite uniform, are of a similar order of magnitude to those of the other groups. The coefficients of the monocytes (Table IV, Text-fig. 2) are somewhat more variable and tend to be slightly higher than those of the other groups.

Group V was examined from December 29, 1928 to June 21, 1929 (Table V). The mean lymphocyte values as shown by the curve in Text-fig. 2 were on the whole higher than those of Group IV examined during the same months, but they did not equal the high levels of Group I examined the previous year. In its first portion, the curve representing these findings resembles that of Group IV, but its rise was initiated in February and from then onward to the end of the experiment, a comparatively high level prevailed. The rise of the Group IV curve, which was of short duration, occurred in March and April. In respect to the maintenance of higher values in the spring months, Group V resembled Groups I and II. The monocyte curves of Groups IV and V are, on the whole, similar in general form until the end of the experiment (Text-fig. 2); during June, the curve for Group V describes an abrupt and marked rise while that of Group IV continues its downward trend. The general level of the Group V mean values was slightly lower than those of Group IV. It will be noted by comparing their respective curves, that the movements of the lymphocyte and monocyte mean values are generally similar in direction during the first two-thirds of the experiment. In April and May, however, the lymphocyte curve is rising while the monocyte curve is falling; in June the lymphocyte curve is stationary at a high level while the monocyte curve shows an abrupt rise. On the whole, the general contour of the total white cell curve of Group V (Text-fig. 2) resembles the lymphocyte more than the monocyte curve. During April and May, however, when its level continues to be quite regularly maintained, the lymphocytes are rising and the monocytes

are falling; in June, when it is undergoing a gradual and comparatively slight rise, the lymphocytes are high and the monocytes are very high.

The coefficients of variation of the lymphocyte means of Group V (Table V, Text-fig. 2) are entirely comparable to those of Group IV; those of the monocyte means (Table V, Text-fig. 2) on the other hand, are considerably smaller and are generally more uniform. As far as general level is concerned, the monocyte coefficients of Group V are the lowest of any of the 5 groups.

There are certain features of these results which merit special attention. In the first place, the general levels of both lymphocyte and monocyte mean values during 1927-28 were on the whole higher than in 1928–29, as was found with the red cells and hemoglobin (1), the total white cells (2), and the neutrophiles, the basophiles, and the eosinophiles (3). Secondly, the parallelism shown by two groups examined during the same months with respect to the direction of a change in the level of mean cell values and the time of its occurrence, which was characteristic of the other cells and of the hemoglobin content, was less pronounced in the case of the lymphocytes and monocytes. With Groups I and II, the lymphocyte curves are very similar but those of the monocytes are less alike; with Groups IV and V, the monocyte curves up to their last periods have a general resemblance to each other while the lymphocyte curves are frequently dissimilar. Thirdly, the general trend of cell level shown by the lymphocytes was one of increasing values in the late winter and spring months while lower values prevailed in the fall and winter. In the case of the monocytes, a similar but less consistent trend toward higher numerical values was observed and in addition to a late winter and spring rise, there was some indication that higher counts were characteristic of the early winter months (Group I, November; Group III, rise of curve from a lower September to a higher November level; Group IV, fall of curve from a higher November to a lower December level). Fourthly, the period of greatest irregularity in the lymphocyte mean values occurred in the late winter and spring months of both years; with the monocytes, on the other hand, this feature was observed in the fall and early summer months of the first year and during the late winter, the spring and the early summer months of the second year.

The significance to be attached to the major changes in the levels of lymphocyte and monocyte mean values is indicated by the following examples of the ratios of the differences of various means to their probable errors.

Group	Lymphocytes			Monocytes				
number	Dates of mean values		Ratio	Dates of me	Ratio			
I	Oct. 24	June 19	3.26	Oct. 24	June 5	2.94		
	Feb. 21	May 20	4.03	May 1	June 5	3.16		
	Mar. 20	June 5	7.72					
II	Mar. 29	May 22	5.26	Mar. 29	June 19	7.91		
III	Sept. 20	Oct. 19	1.74	Sept. 20	Nov. 22	0.92		
IV	Nov. 27	Jan. 2	6,61	Dec. 26	Feb. 26	6.34		
	Jan. 2	Apr. 23	3.45	Feb. 26	June 18	4.96		
	Apr. 23	June 11	2.46	Feb. 26	Mar. 26	3.59		
v	Dec. 29	June 14	3.06	Dec. 26	June 21	2.43		
	Jan. 24	Mar. 8	8.92	May 17	June 14	4.46		
(Apr. 19	June 7	3.23		-			

The question of the numerical relationship of lymphocytes and monocytes in the peripheral blood has received much attention. In so far as the results on these groups of normal rabbits are concerned, the present findings indicate that a constant and consistent relationship between these cells does not obtain over long periods of time. This feature of the observations may be best appreciated by comparing the respective curves representing the consecutive weekly mean values of these cells (Text-figs. 1 and 2). In certain portions, both curves show similar changes in level during the same weeks, indicating that both classes of cells have undergone analogous numerical changes (Group I, November, May, June; Group IV, January, April, May; Group V, February, April). In other portions, however, the curves move in opposite directions (Group I, December, January, April; Group II, June; Group III, October; Group IV, December, February; Group V, May, June). It is evident, however, that before final conclusions on the lymphocyte-monocyte numerical relationship can

be drawn, the results of experiments of this type must be analyzed from the standpoint of the individual animal.

CONCLUSIONS

Consecutive weekly observations on the lymphocyte and monocyte counts of the peripheral blood were made on 5 groups of normal rabbits, a total of 45 animals, during a period of 20 months from October, 1927 to July, 1929. Individual groups were examined 8 to 35 weeks. The results are analyzed on the basis of the mean group values of each week.

In the case of the 4 groups followed 13 to 35 weeks, there was a general tendency for the lymphocyte mean values to become increased; with the group observed 8 weeks, the level of mean values showed little change. The general trend of the monocyte mean values was also in the direction of higher levels but it was less pronounced than that of the lymphocytes.

The period of greatest irregularity in the mean values of the lymphocytes was in the late winter and spring months of both years. With the monocytes, periods of fluctuating values occurred in the fall of 1927, the spring and early summer of 1928, and in the late winter, spring, and early summer of 1929.

There was a certain degree of parallelism in the case of two groups examined during the same months with respect to the direction and time of occurrence of a change in the level of lymphocyte and monocyte mean values.

The general levels of lymphocyte and monocyte mean values in the groups examined during 1927–28 were higher than in the groups of 1928–29.

The results based upon the trends of mean group values obtained from consecutive weekly observations showed no evidence of a consistent numerical relationship between lymphocytes and monocytes.

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