

STUDIES IN THE BLOOD CYTOLOGY OF THE RABBIT

II. CONSECUTIVE ERYTHROCYTE AND HEMOGLOBIN OBSERVATIONS ON GROUPS OF NORMAL RABBITS

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(Received for publication, April 14, 1930)

In the first paper of this series dealing with the blood cytology of the rabbit, the results of 1110 blood counts on 174 normal male rabbits were considered primarily from the standpoint of the numerical variations of the various classes of cells and of the hemoglobin content in individual determinations (1). Other phases of this investigation have included repeated observations on groups of normal and diseased rabbits for extended periods of time. In the case of normal animals, the study was undertaken chiefly for two reasons. Firstly, information was desired concerning the character of the spontaneous fluctuations in the numbers of blood cells under prolonged conditions of undisturbed indoor life with the idea that eventually some relationship might be found between these variations and certain environmental conditions, as was demonstrated with the weights of organs and the amount and degree of change of the total sunlight (2). Secondly, it was considered essential to have information of this nature as a background for whatever changes might be found in association with certain subacute or chronic experimental conditions, as for example, *Treponema pallidum* infection. Five groups of rabbits, 4 of 10 and 1 of 5 animals, were followed 35, 13, 8, 29, and 26 weeks respectively, covering a period of 20 months from October, 1927 to July, 1929. The group examinations numbered 111, in which 973 individual counts are represented.

The results of this study which have been analyzed statistically, will be reported in the present and subsequent papers. For the time being, the principal interest centers in the consecutive mean values of the various classes of cells considered from the standpoint of the trends

of numerical levels shown by each animal group. In the present paper, the erythrocytes and the hemoglobin content are considered; other papers will deal with the total white cells and their division into granular and non-granular cells (3), with the neutrophils (pseudo-eosinophiles), the basophiles, and the eosinophiles (4), and with the lymphocytes and the monocytes (5). The results will ultimately be analyzed from the standpoint of the relationships of the various classes of cells as shown by their correlation coefficients and in addition, they will be referred to in connection with the relation of the pre-inoculation blood picture to the reaction of the host to disease agents.

Materials and Methods

The rabbits employed were representative of those used in other experiments carried out in this laboratory; all were male animals approximately 6 to 8 months old. The ordinary brown and grey type predominated but the type described as the Flemish cross or mixture was also represented and there were a few black animals. Each rabbit was separately caged in a well lighted (sunlight), well ventilated room; the diet throughout the period of observation consisted of hay, oats, and cabbage.

The results reported are based upon 111 group examinations carried out at weekly intervals; in a few instances, the counts were made at shorter or longer intervals. The total number of individual blood counts was 973. The observations were made on 45 rabbits comprising 4 groups of 10 and 1 group of 5 animals:

Group	Number of rabbits	Number of examinations	Number of counts	First count	Last count
I	10	35	350	Oct. 24, 1927	June 20, 1928
II	10	13	130	Mar. 29, 1928	June 19, 1928
III	10	8	80	Sept. 20, 1928	Nov. 22, 1928
IV	10	29	283	Nov. 27, 1928	June 18, 1929
V	5	26	130	Dec. 29, 1928	June 21, 1929
	45	111	973		

A uniform routine with respect to the time and the method of collection and examination of the blood was followed as previously described (1). In the case of Group I, half of the animals were examined on one day and half on the following day of each week; all animals in each of the other groups were examined on the same day. The differential white blood determinations were made with the supravital neutral red technic; 100 cells were counted in each specimen.

In the case of Group I, additional specimens (10 cc.) of blood were taken for

chemical examination. During the first 2 months of the experiment, this procedure was carried out at weekly intervals; from January to April, the period was extended to 2 weeks, and the last bleeding on May 17 was made 4 weeks after the preceding one. These bleedings always followed the blood counts by 1 or 2 days in order that as long a time as possible would elapse before the next blood count.

In the analysis of results, absolute numbers of cells per cubic millimeter of blood have been used. The curves obtained by plotting the actual group means were smoothed by the formula $\frac{a + 2b + c}{4}$, the initial value of each curve being represented by $\frac{2b + c}{3}$ and the final value by $\frac{a + 2b}{3}$. The coefficients of variation of the means have also been smoothed by this formula. The smoothed mean values have been compared, in the form of percentage deviations, with the mean numbers of cells found in 1110 normal blood counts (1). For convenience, certain figures used in this comparison as so-called standard values differ slightly from the actual results obtained, as shown in the following tabulation:

	Actual values	Values used
	<i>per cmm.</i>	<i>per cmm.</i>
Red blood cells.....	5,198,000	5,200,000
Hemoglobin.....	63%	63%
White blood cells.....	9562	9560
Neutrophiles.....	4341	4340
Basophiles.....	950	950
Eosinophiles.....	214	215
Lymphocytes.....	3045	3050
Monocytes.....	1000	1000
Total granular cells.....	5504	5505
Total non-granular cells.....	4045	4050

It should be pointed out that the results of the first 3 groups of animals here reported representing 560 counts, appear among the 1110 counts of the above tabulation; the 413 counts of the 4th and 5th groups, on the other hand, are not included in the large group.

The figures as given include all data. No count has been omitted because of the occurrence of such conditions as snuffles or ear canker in certain animals at some time during the period of observation, but these instances will be referred to in the discussion of the results.

RESULTS

The results pertaining to the consecutive weekly erythrocyte counts and the hemoglobin contents obtained in 5 groups of normal rabbits

TABLE I

Group I—10 Rabbits. Consecutive Values for Erythrocytes and Hemoglobin

Date	Red blood cells (000 omitted)			Hemoglobin		
	Mean values	Standard deviation	Coefficient of variation	Mean values	Standard deviation	Coefficient of variation
1927-28	per cmm.	per cmm.	per cent	per cent	per cent	per cent
Oct. 24*	5420 ± 192	901	16.62	54 ± 2.1	10	18.52
Nov. 1	5539 ± 42	199	3.59	49† ± 0.4	2	4.08
Nov. 8**	4991 ± 79	372	7.45	55 ± 1.4	7	12.73
Nov. 15	5039 ± 92	433	8.59	59 ± 1.3	6	10.17
Nov. 22	5204 ± 130	611	11.74	52 ± 1.3	6	11.54
Nov. 29	5351 ± 76	355	6.63	63 ± 1.3	6	9.52
Dec. 6	5323 ± 229	576	10.82	63 ± 2.1	10	15.87
Dec. 13	5075 ± 143	670	13.20	60 ± 1.4	7	11.67
Dec. 20	5032 ± 170	799	15.88	60 ± 1.4	7	11.67
Dec. 27	5296 ± 118	555	10.48	59 ± 1.4	7	11.86
Jan. 3	5286 ± 129	605	11.45	57 ± 2.3	11	19.30
Jan. 10	4889 ± 115	540	11.05	64 ± 1.4	7	10.94
Jan. 17	4859 ± 182	851	11.81	61 ± 1.4	7	11.48
Jan. 24	5513 ± 126	591	10.72	67 ± 1.4	7	10.45
Jan. 31	5399 ± 176	825	15.28	64 ± 1.7	8	12.50
Feb. 7	5474 ± 145	679	12.40	68 ± 1.3	6	8.82
Feb. 14	5204 ± 153	719	13.82	68 ± 1.3	6	8.82
Feb. 21	5336 ± 156	730	13.68	71 ± 1.3	6	8.45
Feb. 28	5312 ± 178	834	15.70	74 ± 1.0	5	6.76
Mar. 6	5158 ± 101	475	9.21	69 ± 1.7	7	10.14
Mar. 13	5451 ± 155	725	13.30	63 ± 1.3	6	9.52
Mar. 20	5024 ± 116	544	10.83	67 ± 1.3	6	8.96
Mar. 27	5229 ± 200	936	17.90	72 ± 2.1	10	13.89
Apr. 3	4838 ± 134	628	12.98	66 ± 1.9	9	13.64
Apr. 10	5273 ± 96	451	8.55	68 ± 2.1	10	14.71
Apr. 17	5455 ± 83	388	7.11	64 ± 1.0	5	7.81
Apr. 24	5050 ± 180	844	16.71	58 ± 1.9	9	15.52
May 1	5310 ± 148	696	13.11	64 ± 1.4	7	10.94
May 8	5560 ± 117	549	9.87	66 ± 2.3	11	16.67
May 15	5188 ± 110	515	9.93	66 ± 1.7	8	12.12
May 22	5335 ± 205	962	18.03	66 ± 2.1	10	15.15
May 29	5597 ± 162	761	13.60	64 ± 1.0	8	12.50
June 5	6080 ± 205	959	15.77	66 ± 1.3	6	9.09
June 12	5730 ± 110	518	9.04	68 ± 1.9	9	13.24
June 19	5779 ± 111	522	9.03	69 ± 0.8	4	5.80
Mean	5303 ± 30	263	4.96	64 ± 0.7	6	8.59
Minimum	4838			52		
Maximum	6080			74		

* October 24 and 26.

** November 4 and 9.

† Mean of 5 specimens.

TABLE II

Group II—10 Rabbits. Consecutive Values for Erythrocytes and Hemoglobin

Date	Red blood cells (000 omitted)			Hemoglobin		
	Mean values	Standard deviation	Coefficient of variation	Mean values	Standard deviation	Coefficient of variation
<i>1928</i>	<i>per cmm.</i>	<i>per cmm.</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Mar. 29.....	4912 ± 87	407	8.29	66 ± 1.3	6	9.09
Apr. 3.....	4899 ± 69	323	6.59	65 ± 1.4	4	6.15
Apr. 10.....	4842 ± 62	289	8.84	66 ± 1.0	5	4.55
Apr. 17.....	5105 ± 163	762	14.93	64 ± 1.7	7	10.94
Apr. 24.....	5197 ± 83	387	7.45	60 ± 1.7	7	11.67
May 1.....	5169 ± 139	653	12.63	64 ± 1.7	7	10.94
May 8.....	5348 ± 119	558	10.43	63 ± 1.3	6	9.52
May 15.....	5047 ± 85	400	7.93	63 ± 1.7	6	9.52
May 22.....	5242 ± 96	450	8.58	66 ± 1.7	7	10.61
May 29.....	5270 ± 107	500	9.49	63 ± 1.7	7	11.11
June 5.....	5648 ± 116	523	9.26	69 ± 1.3	6	8.70
June 12.....	5329 ± 123	575	10.79	61 ± 1.3	6	9.84
June 19.....	5151 ± 90	421	8.17	64 ± 1.7	8	12.50
Mean.....	5166 ± 39	209	4.05	64 ± 0.4	2	3.13
Minimum.....	4899			60		
Maximum.....	5648			69		

TABLE III

Group III—10 Rabbits. Consecutive Values for Erythrocytes and Hemoglobin

Date	Red blood cells (000 omitted)			Hemoglobin		
	Mean values	Standard deviation	Coefficient of variation	Mean values	Standard deviation	Coefficient of variation
<i>1928</i>	<i>per cmm.</i>	<i>per cmm.</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Sept. 20.....	5039 ± 34	161	3.20	70 ± 1.7	8	11.43
Sept. 28.....	5129 ± 51	239	4.66	56 ± 1.0	5	8.93
Oct. 10.....	5075 ± 23	106	2.09	70 ± 1.0	5	7.14
Oct. 19.....	5116 ± 23	107	2.09	71 ± 1.7	8	11.27
Nov. 2.....	5108 ± 51	240	4.70	56 ± 1.0	5	8.93
Nov. 9.....	5108 ± 32	151	2.96	66 ± 1.4	7	10.61
Nov. 16.....	5091 ± 41	191	3.75	65 ± 1.0	7	10.77
Nov. 22.....	5252 ± 33	153	2.91	68 ± 1.3	6	8.82
Mean.....	5115 ± 15	62	1.21	65 ± 1.4	6	9.23
Minimum.....	5039			56		
Maximum.....	5252			71		

TABLE IV
Group IV—10 Rabbits. Consecutive Values for Erythrocytes and Hemoglobin

Date	Red blood cells (000 omitted)			Hemoglobin		
	Mean values	Standard deviation	Coefficient of variation	Mean values	Standard deviation	Coefficient of variation
<i>1928-29</i>	<i>per cmm.</i>	<i>per cmm.</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Nov. 27.....	5694 ± 141	660	11.59	68 ± 2.1	10	14.83
Dec. 4.....	5274 ± 107	502	9.52	64 ± 1.4	7	10.28
Dec. 11.....	5549 ± 127	595	10.72	67 ± 1.9	9	13.33
Dec. 18.....	5375 ± 53	247	4.60	61 ± 1.2	6	9.50
Dec. 26.....	5285 ± 83	389	7.35	69 ± 1.7	8	11.31
Jan. 2.....	5274 ± 107	504	9.55	64 ± 2.0	9	14.68
Jan. 8.....	4839 ± 65	306	6.32	55 ± 1.2	6	10.18
Jan. 15.....	4860 ± 62	291	5.98	59 ± 1.3	6	10.61
Jan. 22.....	4810 ± 44	206	4.27	59 ± 1.9	9	15.11
Jan. 29.....	4941 ± 68	317	6.42	54 ± 1.0	5	8.25
Feb. 5.....	4705 ± 69	322	6.84	58 ± 1.2	6	9.81
Feb. 13.....	5028 ± 57	266	5.29	60 ± 1.1	5	8.60
Feb. 19.....	4914 ± 86	405	8.24	61 ± 1.3	6	10.18
Feb. 26.....	5034 ± 53	247	4.90	60 ± 1.2	6	9.16
Mar. 12.....	4897 ± 52	244	4.98	63 ± 1.6	8	11.85
Mar. 19.....	4943 ± 66	311	6.28	60 ± 0.9	4	7.05
Mar. 26.....	4875 ± 61	284	5.83	59 ± 0.8	4	6.75
Apr. 2.....	4820 ± 35	165	3.42	60 ± 1.2	5	9.00
Apr. 9.....	4774 ± 55	256	5.35	58 ± 1.1	5	8.68
Apr. 16.....	4849 ± 62	292	6.02	62 ± 1.4	7	10.50
Apr. 23.....	4874 ± 49	229	4.69	61 ± 1.1	5	8.75
Apr. 30.....	4806 ± 33	155	3.22	64 ± 1.1	5	7.94
May 7.....	4907 ± 40	189	3.86	64 ± 0.7	3	5.06
May 14.....	4816 ± 28	123	2.55	62 ± 1.6	7	11.34
May 21.....	4808 ± 40	177	3.68	64 ± 1.4	6	9.91
May 28.....	4843 ± 65	287	5.92	59 ± 1.7	8	13.05
June 4.....	4843 ± 56	249	5.14	66 ± 1.8	8	11.82
June 11.....	4936 ± 38	171	3.46	63 ± 2.4	11	17.00
June 18.....	4888 ± 47	197	4.03	56 ± 1.4	6	10.16
Mean.....	4981 ± 31	245	4.93	61 ± 0.5	4	5.75
Minimum.....	4705			54		
Maximum.....	5694			69		

observed 8 to 35 weeks are presented in Tables I to V in the form of group means, together with the probable errors of the means, the standard deviations, and the coefficients of variation. The series of

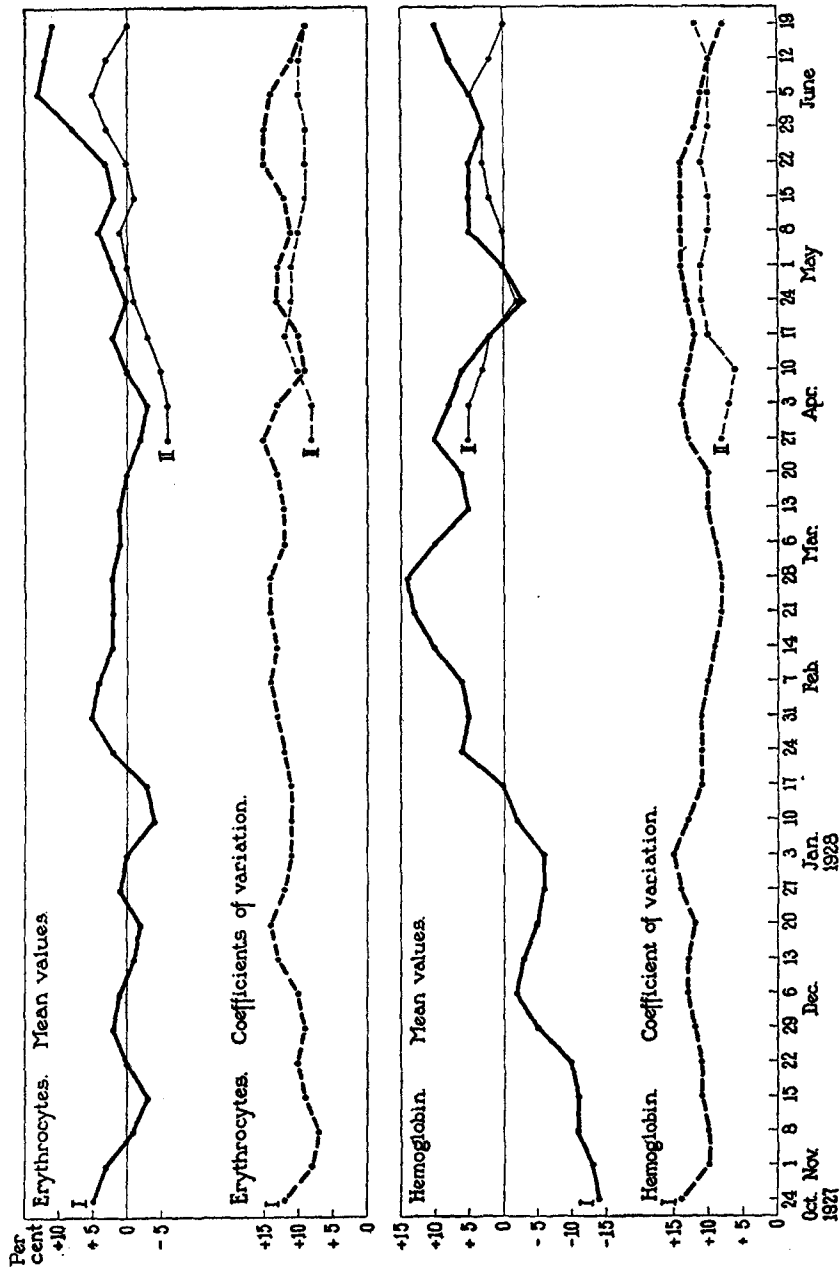
TABLE V

Group V—5 Rabbits. Consecutive Values for Erythrocytes and Hemoglobin

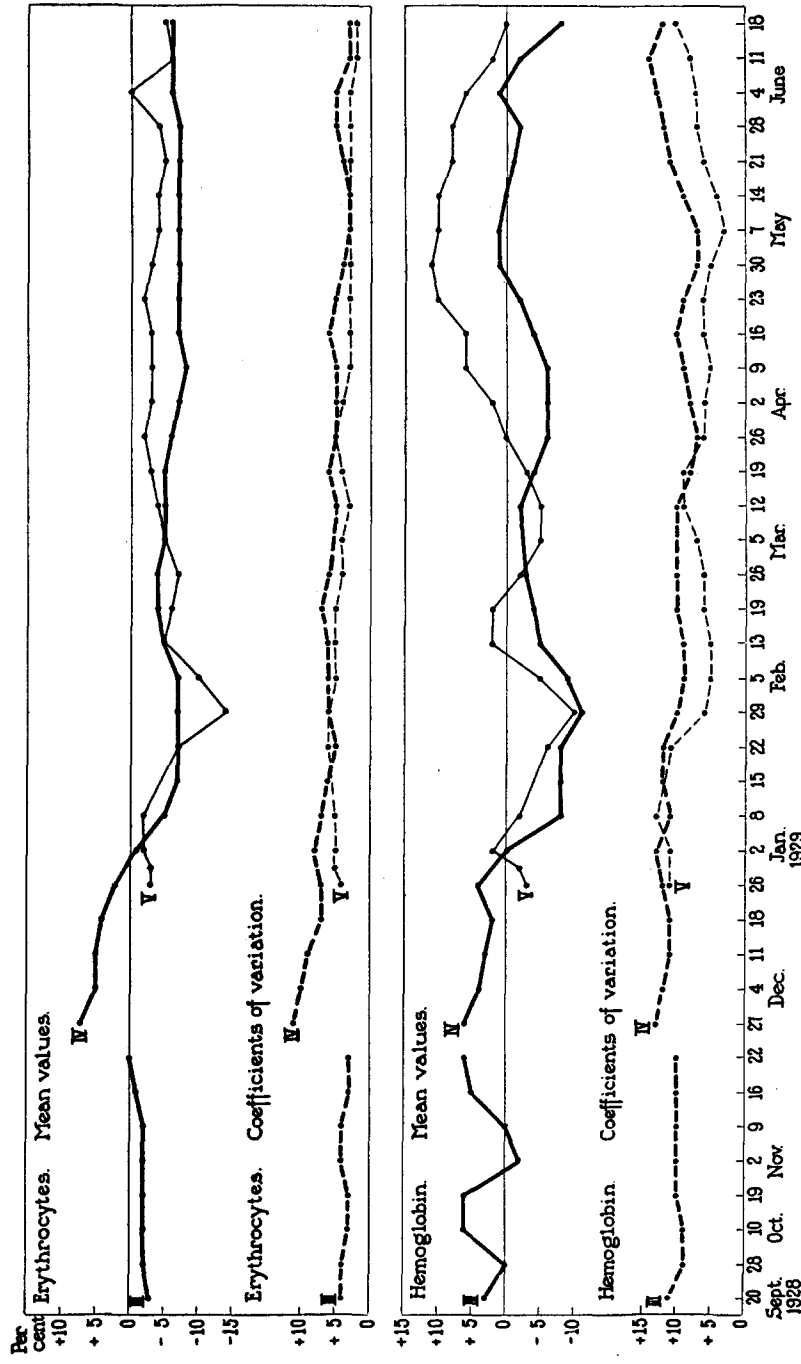
Date	Red blood cells (000 omitted)			Hemoglobin		
	Mean values	Standard deviation	Coefficient of variation	Mean values	Standard deviation	Coefficient of variation
<i>1928-29</i>	<i>per cmm.</i>	<i>per cmm.</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Dec. 29.....	5100 ± 57	190	2.73	60 ± 1.8	6	10.00
Dec. 31.....	4920 ± 90	297	6.04	62 ± 2.4	8	12.90
Jan. 3.....	5224 ± 84	279	5.34	64 ± 1.5	5	7.81
Jan. 10.....	5108 ± 65	214	4.19	64 ± 3.3	11	17.19
Jan. 24.....	4904 ± 82	271	5.53	57 ± 1.8	6	10.53
Jan. 31.....	4384 ± 97	323	7.37	56 ± 0.6	2	3.57
Feb. 7.....	4592 ± 75	249	5.42	58 ± 0.9	3	5.17
Feb. 15.....	5216 ± 54	178	3.41	67 ± 0.9	3	4.48
Feb. 21.....	4730 ± 106	352	7.44	64 ± 1.2	4	6.25
Mar. 1.....	4850 ± 35	117	2.41	61 ± 0.6	3	4.92
Mar. 8.....	4894 ± 78	258	5.27	61 ± 1.2	4	6.56
Mar. 15.....	5072 ± 37	124	2.44	58 ± 1.8	6	10.34
Mar. 22.....	4990 ± 47	156	3.13	61 ± 1.8	6	9.84
Mar. 29.....	5228 ± 86	286	5.47	64 ± 0.9	3	4.69
Apr. 5.....	4940 ± 58	192	3.89	62 ± 1.2	4	6.45
Apr. 12.....	5078 ± 50	164	3.23	69 ± 0.9	3	4.35
Apr. 19.....	5030 ± 33	108	2.15	66 ± 1.2	4	6.06
Apr. 26.....	5078 ± 57	189	3.72	70 ± 1.5	5	7.14
May 3.....	5128 ± 32	105	2.05	71 ± 0.9	3	4.23
May 10.....	4882 ± 60	198	4.06	68 ± 0.6	2	2.94
May 17.....	4984 ± 39	130	2.61	70 ± 0.6	2	2.86
May 24.....	4966 ± 49	161	3.24	67 ± 1.5	5	7.46
May 31.....	4952 ± 42	138	2.79	67 ± 1.5	5	7.46
June 7.....	5050 ± 42	140	2.77	70 ± 1.5	5	7.14
June 14.....	4756 ± 29	96	2.02	60 ± 1.2	4	6.67
June 21.....	5010 ± 33	108	2.16	64 ± 2.1	7	10.94
Mean.....	4964 ± 25	188	3.79	64 ± 0.5	4	6.25
Minimum.....	4384			56		
Maximum.....	5228			71		

curves in Text-figs. 1 and 2 are drawn as percentage deviations of the smoothed means from the standard values given above; other curves represent the smoothed values of the coefficients of variation of the means.

By using mean values to describe the results obtained, the trends or



TEXT-FIG. 1. Mean values for consecutive red blood cell and hemoglobin determinations as percentage deviations from standard values. 1927-28.



TEXT-FIG. 2. Mean values for consecutive red blood cell and hemoglobin determinations as percentage deviations from standard values. 1928-29.

changes characteristic of the group as a whole are shown. It is this feature of the results rather than the variations of individual animals which at present we wish to emphasize.

DISCUSSION AND SUMMARY

In discussing the results of repeated observations on the erythrocytes and hemoglobin content of the peripheral blood of normal rabbits over long periods of time, it will be convenient to consider in chronological order the findings obtained in each of the five groups.

Group I, comprising 10 rabbits, was examined weekly from October 24, 1927 to June 21, 1928 (Table I). The mean numbers of red cells in 35 examinations were found to be comparatively constant.

The fluctuations in the curve of the percentage deviations of the smoothed means from a standard value of 5,200,000 cells per cubic millimeter (Text-fig. 1) do not vary more than 5 per cent above or below this figure until May and June when the curve rises to the 10 to 13 per cent level. In general, the curve describes 3 major swings, each occupying a period of approximately 3 months. From the October level of 5 per cent above the base line, there is an irregular fall to 4 per cent below it on January 10. During the succeeding 3 weeks, the curve rises abruptly to its initial level and very gradually descends to slightly below the base line (March 27 and April 3). During the last 3 months the curve rises to the highest levels observed although at its termination, its trend is again downward. The coefficients of variation for the red cells means (Table I) are fairly uniform, the curve of the smoothed values varying about the 10 per cent level (Text-fig. 1). The most irregular portion of the curve is its last quarter and this phase accompanied an augmentation of mean values. It will be noted that the changes in the trend of the red cell means at the end of January and the first of April are, in both instances, preceded by similar changes in the coefficient curve, at a 2 or 3 weeks' interval.

The range of mean hemoglobin values of Group I (Table I) was considerably greater than that of the erythrocyte means. The curve of these values in terms of the percentage variations of the smoothed means from a standard of 63 per cent fluctuates within a total range of 28 per cent, that is, 14 per cent above and below the base line (Text-fig. 1).

This curve can be divided into 3 major swings which, however, are not parallel with those of the red cells. From an initial low level the curve rises to 14 per cent above the base line by the end of February; the trend of the red cell curve in the

opposite direction ended the middle of January and for the next 3 observations, the direction of both curves is upward. From the end of February to the last of April, the hemoglobin curve is generally falling, while in May and June its general movement is again in an upward direction. In March, both the hemoglobin and red cell curves are falling and from the middle of April to the end of June both are rising. The coefficients of variation of the hemoglobin means (Table I) are comparable as far as order of magnitude is concerned, to those of the red cell means. From the curve representing the smoothed coefficients (Text-fig. 1) it will be noted that small values prevailed during January and February in which months the means were considerably increased. In like manner, the second period of higher hemoglobin mean values in May and June was characterized by a steady decline of the coefficient curve.

The second group of 10 rabbits (Group II) was examined during the last 3 months of the observation period of Group I (Table II). The values for the mean numbers of erythrocytes and for the mean hemoglobin contents occupy slightly lower levels than those for Group I (Text-fig. 1), but it will be noted that the curves representing these values are remarkably like those of Group I in general outline, the only important exception being in the case of the hemoglobin means during the last 2 weeks' observations.

It should be noted that in the corresponding portion of the curve representing the coefficients of variation of these means, an abrupt upward turn occurs indicating that the sharp fall in the mean values is due to certain individual findings and is not characteristic of the group as a whole. The coefficients of variations of both erythrocyte and hemoglobin means of Group II (Table II) are generally somewhat smaller than those of Group I as is illustrated by the curves shown in Text-fig. 1.

The third group of 10 rabbits (Group III) was examined in September, October, and November of 1928. The erythrocytes and the hemoglobin means, together with their coefficients of variations are given in Table III and the curves representing these values appear in Text-fig. 2.

In the case of the red blood cells, the means were extremely regular at a level slightly below the standard value while the curve of their smoothed coefficients of variation is steadily maintained at the 3 to 4 per cent level. The hemoglobin means, on the other hand, were less uniform and their curve describes several fluctuations which, however, are of a much smaller magnitude than those of Group I. In contrast to these variations, however, the curve of the smoothed coefficients of variation of these means is almost a straight line at the 10 per cent level, a value slightly smaller than that which generally obtained in Group I.

Examination of the fourth group of 10 rabbits was begun in November, 1928 and of the fifth group comprising 5 rabbits in December, 1928; both groups were observed to the end of June, 1929. The erythrocyte and hemoglobin means and their coefficients of variations are given in Tables IV and V, and the curves illustrating these values in Text-fig. 2.

In the case of Group IV, the red cell curve which shows practically no irregularities, describes during the first 2 months' observation a steady downward trend from an initial 7 per cent above to 7 per cent below the standard value; during the remainder of the experiment this low level is almost perfectly maintained. The curve of the smoothed coefficients of variation of the red cell means has a similar form; from an initial 11 per cent level, it falls to 5 per cent at the end of the second month and to 3 per cent in June.

The hemoglobin means of Group IV were much less uniform than the red cell values as was the case with the previous groups; the fluctuations of the curve representing these values (Text-fig. 2) vary between 6 per cent above to 11 per cent below the base line. During the first 2 months, the direction of the curve is downward, parallel to that of the red cells, but from this time onward, while the red cell means continue at a fairly constant level, the general trend of the hemoglobin means is upward. The rise is interrupted in March and again in June; on the first occasion there is also a fall in the number of red cells but on the second, the red cell level is unchanged. The smoothed coefficients of variation of the hemoglobin means for Group IV vary from 7 to 14 per cent (Text-fig. 2). Their curve is fairly stationary at the 11 to 12 per cent level during the first 2 months' observations; in subsequent months somewhat lower and more irregular values obtain, and in May and June a rise to 12 and 14 per cent is observed.

The curve representing the erythrocyte means of Group V differs but little from that of Group IV as shown in Text-fig. 2. It begins in December at approximately the same level which Group IV occupies at this time and ends at the same level in June. There is an initial abrupt fall to 14 per cent below the base line (end of January) which is followed by a sharp rise, and from then onward, a fairly constant level is maintained at 5 per cent below the standard value. During January and February, the general level of the curve is slightly lower than that of Group IV while in March, April, May, and June, the relation is reversed. On the whole, the curve is uniform and contains but two irregular portions, one the end of January when the downward trend is prolonged to the lowest level observed in any of the 5 groups, that is, 13 per cent below the standard value, and the other the first of June at which time there is a sharp but temporary upward movement. The curve representing the smoothed coefficients of variation of the red cell means which is extremely uniform (Text-fig. 2) occupies a general level slightly below that of Group IV. It describes a gradual fall from 6 to 2 per cent.

In the case of the hemoglobin content, the mean values of Group V were somewhat higher than those of Group IV, but the direction of the variations observed

was essentially the same (Text-fig. 2). The curves representing these values are similar in general contour with parallel fluctuations but those of Group IV are somewhat more pronounced, their extremes being 10 per cent below and 11 per cent above the standard value. The level of the curve representing the smoothed coefficients of variation of the hemoglobin means of Group V is generally lower than that of Group IV, as was the case with the red cells (Text-fig. 2); the fluctuations in magnitude vary from 3 to 13 per cent. The general trend of this curve is similar to that of Group IV.

The great majority of the rabbits in these experiments were in excellent physical condition and gained in weight during the period of observation. There were two deaths, both in Group IV, which occurred toward the end of the experiment. Both animals had had marked snuffles and at autopsy, an extensive purulent exudate was found in the nasal passages and sinuses and in one rabbit, there was also a chronic diffuse interstitial nephritis. Snuffles and ear canker of various grades which were observed in certain rabbits will be referred to in a subsequent paper in connection with the discussion of the observations on the neutrophile cells (4).

There are certain features of these consecutive observations on the peripheral blood of normal rabbits which may now be briefly considered. In the first place, the weekly range of variation of the erythrocyte mean counts was considerably smaller than that of the hemoglobin means, a result which indicates that under the conditions of these experiments, the hemoglobin was the more labile of these two blood constituents. The technic employed may have contributed to this finding in that the error involved in a colorimetric method may be greater than in one of cell enumeration. With each specimen of blood, at least 3 hemoglobin readings were made and the mean value used; and in addition, duplicate readings with another instrument have always checked with those of our own. Secondly, it was found that a brief or a more sustained alteration in the erythrocyte means was not necessarily accompanied by a shift of the hemoglobin level in the opposite direction. In certain instances, such a change was observed, but in others, both values moved in the same direction and in still others, the hemoglobin means pursued a more or less protracted rise while the numbers of red cells were maintained at a fairly stationary level. Thirdly, the most irregular results with respect to both red cell and hemoglobin means were found in Group I and in addition,

their standard deviations were on the whole, of a higher order of magnitude than those of the other groups (Tables I to V). The examinations on Group I were not all made on the same day, half the animals being examined on one day and half on the following day; in the case of the other groups, all animals were examined on the same day. As has been mentioned in the section on Materials and Methods, the rabbits of Group I were also subjected to additional bleedings for purposes of chemical examination. Although this procedure was carried out most frequently in the first 2 months of the experiment, there is no striking difference in the order of magnitude of the standard deviations of the means nor in the coefficients of variations during this period as compared with later months (Table I). It is probable, therefore, that the greater irregularities of mean values and the higher standard deviations noted in Group I were related to the divided time of the blood counts themselves or to some other factor rather than to the additional bleedings for chemical examination.

In the present consideration, the major changes in mean values as observed over several weeks or months have been emphasized rather than fluctuations occurring in comparatively brief periods. Analysis of the results from the standpoint of the ratio of the difference of the mean values to their probable errors indicates that the major changes observed in both the red cell and hemoglobin levels are of statistical significance, as shown by the following examples:

Group number	Red blood cells			Hemoglobin		
	Dates of mean values		Ratio	Dates of mean values		Ratio
I	Jan. 10	Jan. 24	3.65	Oct. 24	Jan. 10	2.94
	Apr. 3	June 19	5.44	Apr. 24	June 19	5.24
II	Mar. 29	May 8	2.96	Mar. 29	Apr. 24	2.73
	Apr. 3	June 12	3.05	Apr. 24	June 5	4.09
III	Sept. 20	Nov. 22	4.53	Sept. 20	Nov. 2	7.00
IV	Nov. 27	June 18	5.38	Nov. 27	June 18	4.80
	Feb. 26	Apr. 30	3.68	Dec. 11	Jan. 22	2.96
V	Dec. 29	Feb. 7	5.40	Jan. 24	Apr. 19	4.09
	Feb. 21	Apr. 26	3.25	Apr. 26	June 14	5.26

A striking feature of these results is the degree of parallelism shown by two groups of animals examined over the same period with respect to the fluctuations of erythrocytes and hemoglobin mean values. The curves in Text-figs. 1 and 2 show that the trend of values for one group of animals is almost always reflected in a similar trend for the other group.

Finally, these observations make it clearly evident that the results obtained on the groups of rabbits examined in one year may not be entirely similar to those obtained on other groups followed for similar periods in another year. In the case of both the erythrocytes and the hemoglobin, the mean values during 1927-28 were generally higher than those of 1928-29. Furthermore, there was a definite trend on the part of both red cell and hemoglobin means toward higher values in the spring and early summer months of the first year which were not observed in the following year. In the fall and early winter months of both years, on the other hand, the red cells tended toward smaller values; this was also the case for the hemoglobin in the second but not in the first year.

CONCLUSIONS

Observations are reported on the consecutive weekly erythrocyte counts and the hemoglobin contents of the peripheral blood in 5 groups of normal rabbits, comprising 45 animals, during a period of 20 months from October, 1927 to July, 1929. The duration of individual group examinations varied from 8 to 35 weeks. The results are analyzed on the basis of the weekly mean values of each group.

On the whole, the erythrocyte values were quite uniform within a narrow range of variation, while the hemoglobin content was comparatively irregular within a wider range of variation. The major changes in the levels of mean values of both the red cells and the hemoglobin, however, were found to be statistically significant.

The directions or trends in the levels of the erythrocyte and hemoglobin mean values did not necessarily move in opposite directions.

The general levels of the erythrocyte and hemoglobin mean values were not identical for two consecutive years, those of 1927-28 being higher than those of 1928-29.

The fluctuations of both red cell and hemoglobin mean values

observed in one group of animals were also usually observed in another group examined during the same months.

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