STUDIES OF THE LYMPHATIC TISSUE.

III. Experimental Studies of the Relation of the Lymphatic Tissue to the Number of Lymphocytes in the Blood in Subcutaneous Infection with Staphylococci.

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Plates 25 and 26.

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In two papers published elsewhere the cellular structure of the secondary nodules (1) and their embryological development in human beings (2) have been described. It was found impossible to accept the conception formulated on Flemming's original theory that Flemming's secondary nodules are the places of formation of the lymphocytes of the blood, or to accept even a modification of this theory without some doubt.

If the conception of Hellman (3, 4) and his pupils is correct, that Flemming's secondary nodules represent "reaction areas" to "toxic" irritations of low intensity, it should be possible to induce a development of them experimentally by such irritations so that they could be studied in all stages of their development. The origin of the lymphatic hyperplasia which appears upon "toxic" irritation furthermore should be demonstrable. Finally, by simultaneous counts of the lymphocytes in the blood, a relation might be found between possible lymphocytosis and the morphological changes in the lymphatic organs.

Such experiments have so far not been reported in the literature (*cf.* also Whitney (5)). The secondary nodules have indeed not been studied experimentally at all save by experiments in which destruction of secondary nodules by x-ray (Heineke (6)), benzene (Selling (7)), or by arsenic (Wätjen 8, 9)) was followed.

Material and Method.

These experiments concern the relation of subcutaneous infection to changes of the lymphatic tissue, mainly in the regional lymph nodes, and a comparison of the latter with the number of lymphocytes in the blood. The experiments were made with rabbits. For producing the infection staphylococci of low virulence were chosen. They were injected under the skin of one hind foot, because in rabbits the regional lymph nodes are united in one popliteal lymph node, the lymph node of the other leg forming a suitable control. Especial emphasis was laid on as constant experimental conditions as possible. In order to exclude mistakes which might be caused by differences in development of the lymphatic tissue (Hellman (10)) and by the different numbers of leucocytes (Lindberg (11))

TABLE I.

The Leucocyte Counts in Relation to Rabbit Color.

Color	No. of rabbits	Total amount of leucocytes (maximum-minimum)	Polymorphonuclear leucocytes	Lymphocytes	Monocytes	Mast cells
Black and mainly black.....	13	10,894 (6,675–13,925)	36	60	3	1
Half black and half white.....	4	8,030 (6,950–9,225)	37	61	1.5	0.5
Gray and brown.....	5	6,880 (5,850–7,425)	40	58	1.5	0.5
Mainly white.....	3	5,183 (4,650–5,925)	40	57	2.5	0.5
Albinos.....	3	4,584 (2,900–5,700)	43	51	5.5	0.5

at different ages, only animals of nearly equal ages were used. If the ages were not known, animals of the same weight were taken, which Hellman found (10) may be done with young animals of the same race. Rabbits of 1,000 to 1,500 gm. were chosen since they were at the age in which lymphatic tissue is well developed and diseases are, for the most part, still absent. Some older animals were studied for comparison. Only animals as nearly alike as possible in color were used in each series, because it has been found that such animals with dark fur as were used had more leucocytes as well as more lymphatic tissue than lighter animals. All were males.

The leucocyte counts of 28 normal animals weighing about 1,000 gm. each, have been collected (Table I). The counts were repeated several times under as constant conditions as possible. The blood was always taken between 11 and 12 a.m., and from each animal at the same time each day in order to avoid the diurnal variation which has been described by Sabin, Cunningham, Doan and Kindwall

(12) and by Tschishikow (13). As the animals had not been fed since early morning digestive influences on the blood count are improbable. The absence of pathological lesions was determined by autopsy. The difference between the counts of the light and the dark animals refers especially to the lymphocytes. There is also to be noted a difference in the weight of the lymphatic organs in 13 animals (Table II). Especially marked is the difference in the weights of the peripheral lymph nodes and of the thymus. The weight of the mesenteric lymph nodes seems to be rather less in dark animals than in light ones. It is difficult, however, to decide how much is due to the lymphatic tissue because the ratio between the cells and the sinus portion, the quantity of which is determined by the

TABLE II.

*Relative Weights of Lymphatic Organs and Thymus in Light and Dark Animals.**

	Color	No. of rabbits	Weight	Axillary, cervical and popliteal lymph nodes together	Pancreas Aselli	Spleen	Thymus
			gm.				
I	White and gray	3	600	0.44	1.80	0.54	0.73
II		1	750	0.67	1.67	0.33	0.93
III		1	970	0.31	2.37	0.52	0.72
IV		1	1,175	0.30	1.40	0.39	0.70
I	Black and mainly black	1	590	0.43	0.60	0.25	1.19
II		2	760	0.64	1.05	0.36	1.41
III		1	980	0.61	2.04	0.41	1.12
IV		3	1,210	0.56	1.56	0.34	1.25

* The weights of the organs have been divided by the kilo weights of the rabbits

regional relation to the intestine, is extremely variable. The weight of the pancreas Aselli of the rabbits is also difficult to measure accurately because it is imbedded in a very varying quantity of fat, which cannot be excluded in weighing, because it cannot easily be separated from the lymph nodes. The irregularity in the weight of the spleen is probably not significant being due in the main to the varying content of the blood.

For all series the same pipettes and counting chambers were used. Two to three counts were made always and in the differential 400 to 600 leucocytes were counted in two smears.*

* In the differentiation of lymphocytes from monocytes and histiocytes in blood smears, all mononuclear cells which were not recognized with certainty as monocytes or histiocytes, were counted as lymphocytes.

Beside the popliteal lymph nodes the axillary, retroperitoneal, mesenteric lymph nodes, the lymph nodes of the intestine and the spleen were studied. The organs were fixed, cut and stained, as described in a previous paper (1).

Protocols.

Series 1 consisted of six rabbits of one brood, about 6 months old, of brown-black color. They were injected subcutaneously with 1 cc. of a 48 hour broth culture of *Staphylococcus aureus* of especially low virulence (obtained from the surgical clinic in Freiburg) diluted with equal parts of saline solution. At 2, 4, 6, 9, 12, 18, 21 and 29 days after injection leucocyte counts were made on all animals still living. R 15 was killed after 2 days, R 14 after 4, R 16 after 6, R 12 after 14, R 13 after 21 and R 11 after 29 days.

Series 2 consisted of eight rabbits of about 1,300 to 1,400 gm. They were injected subcutaneously with 1 cc. of a 48 hour broth culture of *Staphylococcus aureus* diluted with saline solution in equal parts. The leucocytes of these animals were counted beforehand, and after the injection only when the animals were to be killed. R 78 was killed after 1 day, R 76 after 2, R 72 after 3, R 79 after 5, R 71 after 7, R 73 after 14, R 70 after 28 and R 76 after 42 days. R 72 showed septicemia (streptococci) at autopsy and R 70 bronchopneumonia (*Bacillus lepisepticus*) and were consequently excluded from further studies.

Series 3 consisted of five rabbits about 2 years old and of dark color. Infection and the counting of leucocytes were managed as in series 2. R 6B was killed after 3 days, R 7B after 5, R 3B after 7, R 11B after 14, R 10B after 35 days. R 6B showed bronchopneumonia of both sides and pleurisy at autopsy, and R 7B fresh and R 3B older pneumonic areas in the lungs. R 6B and 7B were excluded from further study, whereas 3B was used for comparison.

Series 4 consisted of five rabbits about 1,200 gm. in weight, of black-brown color. Staphylococci were injected as in series 2 and 3, but the leucocytes were not counted, because this series was used only for studying the histological changes during the first days after injection. R 159 was killed after 1 day, R 160 after 1½, R 161 after 2, R 162 after 2½ and R 163 after 3 days.

RESULTS.

The results of the experiments will be considered together because those of the four series agree closely. At the site of injection a hemorrhagic inflammation first developed. On the 7th day in all series small abscesses were found at the same site, the contents of which in series 1 and 2 thickened after 14 days and consisted after 35 days of only a small amount of pus. In the old animals of series 3, however, the abscess increased in size from the 7th day onward and after 42 days (R 77) embraced a large part of the leg.

The regional popliteal lymph nodes in all cases were swollen markedly from the 1st day onward and were often about 5 times the size of the lymph node of the other leg. The color of the regional node of the infected leg was normal.

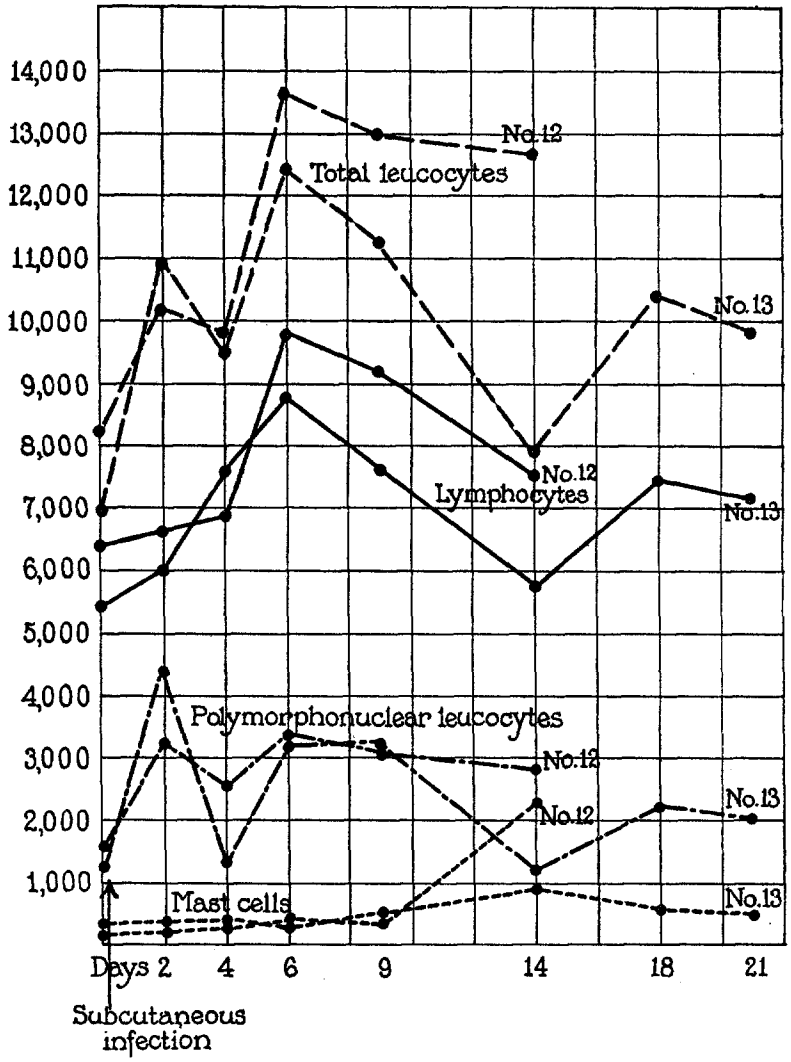
TABLE III.

Changes in the Leucocyte Count after Subcutaneous Infection with Staphylococci (Series 1).

Rabbit No.	Time after injection	Total leucocytes	Polymorphonuclear leucocytes		Lymphocytes		Mast cells	
			Per cent	Absolute	Per cent	Absolute	Per cent	Absolute
15	Control	9,250	28	2,590	69	6,382	2.5	231
	2 days	10,800	34.5	3,726	62	6,696	2	216
14	Control	9,700	31	3,007	66	6,622	2	194
	2 days	10,000	34	3,400	63	6,300	1	100
	4 "	9,000	27.5	2,475	71	6,390	1	90
16	Control	8,800	17.5	1,540	80	7,040	2.5	220
	2 days	10,450	34	3,553	63	6,583	1	104
	4 "	11,700	20	2,340	78	9,126	1	117
	6 "	11,000	24	2,640	72	7,920	2	220
12	Control	8,250	19	1,567	78	6,435	2	165
	2 days	10,200	32	3,264	65	6,630	2	204
	4 "	9,850	26	2,561	70	6,895	3	295
	6 "	13,650	25	3,412	71.5	9,760	3	409
	9 "	13,000	24	3,120	71	9,230	2.5	325
	14 "	12,700	22	2,794	59	7,493	18	2,286
13	Control	6,950	18	1,251	78.5	5,456	3	208
	2 days	10,950	40	4,380	55	6,022	3.5	383
	4 "	9,500	14	1,330	80	7,600	4	380
	6 "	12,450	26	3,237	70.5	8,777	3	373
	9 "	11,250	28	3,150	68	7,650	4	450
	14 "	7,900	15	1,185	72	5,688	10	790
	18 "	10,400	21.5	2,236	72	7,488	5	520
	21 "	9,800	21	2,058	73	7,154	5	490
11	Control	10,950	14	1,533	82	8,979	3	328
	3 days	11,800	30	3,540	67	7,906	2	354
	29 "	11,000	16	1,760	81	8,910	2	220

Leucocyte Counts.—In Table III are given the leucocyte counts of all rabbits of series 1. In Text-fig. 1 curves are drawn of the counts

of R 12 and 13 of this series. The highest point of polymorphonuclear leucocytosis is probably not expressed in Text-fig. 1 (series 1) be-



TEXT-FIG. 1.

cause it apparently occurs before the 2nd day, as was shown by series 2 and by a further experiment. The number of lymphocytes at first

decreased and had already reached the lowest point before the 2nd day. They then increased slowly and reached the highest point in series 1 at the 6th to 9th day and in series 2 at the 7th day. They then decreased again and, as with the other leucocytes, were found normal in number in all instances after the 3rd week. There was a mast cell leucocytosis at the 14th day in series 1 and 2.

While series 1 and 2 behaved in the same way the number of leucocytes in the old animals showed marked differences. Whereas the normal proportion of polymorphonuclear leucocytes to lymphocytes on the average was 25:75 in the first two series, it was 51:49 in the old animals (series 3). The number of lymphocytes in them always remained below the number of polymorphonuclear leucocytes. The highest point of the polymorphonuclear leucocytosis and of the lymphocytosis occurred later than in the young animals and the mast cell leucocytosis was apparently wanting.

Histology of the Lymph Nodes.—The histological changes in the regional lymph nodes agreed very closely in the different series. During the first 2 or 3 days a purulent hemorrhagic lymphadenitis was the outstanding pathological change. It is well known (*cf.* Kankaanpää (14)), so it need not be described again. The changes in the lymphatic tissue and especially in the secondary nodules which predominated from the 3rd day onward merit detailed description.

The secondary nodules which are normally present (Fig. 1), showed regressive changes in all series during the first few days. Polymorphonuclear leucocytes and hemorrhages often occurred in them. The nuclear fragments increased in number. The boundaries of the secondary nodules were lost. In a few nodules reticular centers appeared. In a few animals a number of Flemming's secondary nodules also appeared, but were regressively changed later. At the same time, at the margin of the cortex new small solid secondary nodules were formed.

In this period (the first 2 to 3 days) the proportion between medulla and cortex changed in favor of the medulla, owing chiefly to the accumulation of fluid in the sinus but partly to purulent hemorrhagic lymphadenitis. But in the days following an enormous enlargement of the cortex took place starting in series 1 on the 4th day (R 14 and R 16), and in series 2 and 4 on the 2nd day (R 76, R 79, R 162 and R 163). Shortly before the highest point of the lymphocytosis was reached the cortex occupied so large a part of the lymph nodes that in most instances only few central sinuses could be found (Fig. 3). The cortex consisted especially of small lymphocytes and contained a number of well developed veins into which

numerous lymphocytes migrated (Fig. 6). In the margin of the cortex smaller and larger solid secondary nodules were found.

The transition between the two pictures just described is shown in Figs. 4 and 5. Fig. 4 (R 78) shows an enlarged lymph node with an hemorrhagic purulent lymphadenitis. The cortex contains larger and smaller solid secondary nodules, few transition forms and also two small pseudo-secondary nodules.

Fig. 5 shows a further phase. On one side, some transition forms are still found, the centers of which contain many polymorphonuclear leucocytes. On the other side, some solid secondary nodes are seen, which are smaller than the transition forms. The largest part of the cortex, consists, however, of one enormous pseudo-secondary nodule which invades the tissue in all directions. On its external margin single small solid secondary nodules are found.

This pseudo-secondary nodule consists especially of small lymphocytes and contains distinct veins and reticular fibres. Everywhere large cells with karyokinetic figures are seen often connected with the walls of the vessels (Fig. 7) and penetrating the tissue. These cells have large round nuclei with fine networks of chromatin and large nucleoli. The protoplasm is broad and intensely basophil. Stained by the method of Schridde these cells contain very small or moderately sized, more or less, round mitochondria in the arrangement described by Schridde (15, 16). These cells are described by Marchand (17) as proliferating endothelial (reticular) cells. They differ from the so called lymphoblasts by their finer chromatin structure, by the very insignificant thickening of the nuclear wall and by their much broader and much more basophilic protoplasm. From these cells all transitions to small lymphocytes as well as to reticular cells are found. So called lymphoblasts, such as are found in Flemming's secondary nodules, are however, missing entirely. No myeloid cells are to be seen.

In the hyperplasia of the lymphatic tissue not only does the cortex take part, but there is also in the medullary cords an intense proliferation of lymphocytes (Fig. 5). There are many karyokinetic figures. Solid secondary nodules appear later.

Only when lymphocytosis reached its highest point in the blood stream did Flemming's secondary nodules appear. In series 2 they began to appear after 7 days (starting with R 71) but in series 1 only after 14 days (from R 12 on), for in this series no lymph nodes were available for study between the 7th and 9th days. The first of Flemming's secondary nodules to be seen lie partly in the margin of the cortex and mostly have large marginal zones, but some lie also in the inside of the cortex and in the medullary cords, where marginal zones are sometimes lacking. The light centers are at first of varying sizes but are generally small. They are typically built and often have central capillaries or arterial precapillaries.

When the number of lymphocytes in the blood began to fall, Flemming's secondary nodules grew in number and size and only when the number of lymphocytes again reached normal, did they reach their greatest development in number and size. This was reached in series 1 after 29 days (R 11) and in series 2 apparently after 28 days (R 70). The lymph nodes now seemed to consist nearly exclusively of large Flemming's secondary nodules with very large light centers rich in karyokinetic figures and distinctly limited against the narrow marginal zone. The latter was distinctly separated by reticulum from lymphoid tissue. This picture seemed to remain constant over a longer period. Our longest surviving animal (R 77) still showed this picture 42 days after the injection of the bacteria, that is to say for about 3 to 4 weeks after the ending of the lymphocytosis (Fig. 2).

In the old animals of series 3 conditions are very similar to those in the young animals. The first of Flemming's secondary nodules were found after 7 days (R 3B), and in enormous quantity and size after 15 days (R 11B) and still more so after 35 days (R 10B).

While the next more centrally lying regional retroperitoneal lymph nodes show these changes in part, the other lymphatic organs exhibit normal pictures. At the time of the most marked development of Flemming's secondary nodules in the regional popliteal lymph nodes, the secondary nodules in the other peripheral lymph nodes and in the spleen also seemed to be somewhat enlarged, but this appearance was found in its typical development only in rabbits 11B and 10B, which had both shown very large abscesses. In these animals very large Flemming's secondary nodules were found in all the peripheral lymph nodes which were studied, as well as in the spleen.

DISCUSSION.

From these experiments it can be seen that subcutaneous infection with staphylococci of low virulence results in lymphatic hyperplasia and the production of Flemming's secondary nodules in the regional lymph node. From the inflammatory irritation there first appears lymphadenitis and regressive changes of the existing Flemming's secondary nodules and transition forms which are then dissolved into lymphoid tissue. New solid secondary nodules appear at the margin of the cortex which grow, and as is shown so clearly by Figs. 1, 4, 5 and

3, lead to pseudo-secondary nodules and finally to diffuse lymphatic hyperplasia. That the pseudo-secondary nodules originate in Flemming's secondary nodules is improbable because in this case (Fig. 5) all existing secondary nodules with light centers show intense regressive changes with polymorphonuclear leucocytes and hemorrhages.

The more the lymphatic hyperplasia increases the greater is the increase in the number of lymphocytes. At the time of the greatest lymphocytosis (or shortly before) the lymph nodes still consist only of especially small lymphocytes while so called germinal centers or lymphoblasts are missing. Only when the highest point has been passed (or at the highest point) the first of Flemming's secondary nodules appear. They grow in number and size and reach their greatest development only when the lymphocytes in the blood have again decreased to normal. Here they remain quite a while. In the cases studied this remained the situation even in the last animal of the series which was killed, after the 42nd day.

In the preceding morphological and embryological studies of the secondary nodules it has been shown that Flemming's theory in its original conception cannot be accepted. These experiments show that lymphocytosis at least after subcutaneous infection with staphylococci has no relation to changes in the number and size of Flemming's secondary nodules, at least not in the regional lymph node. For at the time when the number of lymphocytes in the blood is highest, so called germinal centers are entirely wanting. The converse is also true; at the time of the highest development of Flemming's secondary nodules no increase in the number of lymphocytes in the blood can be found. The possibility that other lymphatic organs acted in a compensatory manner cannot be entirely excluded. There was at least no increase in number and no further development of Flemming's secondary nodules elsewhere to be found except those changes which were parallel with their development in the regional lymph nodes.

Against a modified Flemming's theory new doubt must be raised. If, according to the modified view, Flemming's secondary nodules are thought of as reserve depots of young lymphocytes it can be inferred from these experiments that whatever increase in formation of the nodules took place amounted to no more than an excess incident to the process of regeneration. But even this possibility seems to disappear

because Flemming's secondary nodules were changed regressively before the beginning of lymphocytosis, and the growth of the pseudo-secondary nodules took place without so called lymphoblasts, as they are found in Flemming's secondary nodules.

While no relation between lymphocytosis and Flemming's secondary nodules could be found, these showed on the other hand, a certain relation to the development of the abscesses. In each series Flemming's secondary nodules appeared only when abscesses were formed. They increased with the thickening of the abscesses in number and size. The greatest development in Flemming's nodules was found in the two animals with the largest abscesses (R 10B and R 11B).

There remains for discussion the question of how the lymphocytosis here comes about anatomically and which cells are responsible for the formation of small lymphocytes. The fact that the development of the pseudo-secondary nodules which leads to diffuse lymphatic hyperplasia is parallel with the increase of lymphocytes in the blood, makes it likely that pseudo-secondary nodules are responsible in this situation as in embryonic life for the formation of lymphocytes. This conception is supported by the observation that just at the time of greatest lymphocytosis enormous quantities of lymphocytes can be seen to migrate into the veins of the hyperplastic lymphatic tissue. The pictures which are familiar in lymphatic leucemia bear evidence of the correctness of this view. For in this disease Flemming's secondary nodules are almost entirely missing and the anatomical picture is one of diffuse lymphoid hyperplasia.

Is there a basis in these studies for drawing an inference as to the mother cells of the lymphocytes? In this connection it is necessary to speak only of some observations that were made in connection with growing pseudo-secondary nodules. Large cells were seen coming from the vascular walls. That these are rapidly multiplying is shown by their great number and the number of karyokinetic figures. These cells have been identified as being the proliferating endothelial (reticular) cells of Marchand (17). We find all transitions between these cells and the small lymphocytes as they are missing in Flemming's secondary nodules. We also find transitions to differentiated reticular cells. So called lymphoblasts, however, are missing here. It appears therefore to be reasonable to sup-

pose that the small lymphocytes are derived from Marchand's proliferating endothelial (reticular) cells.

To judge from transitional pictures genetic relations apparently exist also between lymphocytes on the one hand and histiocytes and monocytes on the other. Masugi (18) has recognized as the common mother cells of the latter the resting mesenchymal cells which are in no special stage of irritation and which exist as resting histiocytes of the connective tissue, as resting pulp cells, as resting reticular cells or as resting reticulo-endothelial cells. Pictures like Fig. 8 which shows a lymph node with a very narrow cortex and medullary cords, also point in this direction. Secondary nodules and pseudo-secondary nodules are entirely missing. And, nevertheless, an intense production of lymphocytes takes place. With high power (Fig. 9) the sinuses are seen to contain many small lymphocytes and cells which are in the stage of division and which are very similar to the cells here in question. All transitions between them are observed. It appears to be entirely reasonable to derive the small lymphocytes in these lymph nodes from resting reticulo-endothelial cells.

SUMMARY.

1. On subcutaneous infection of rabbits with staphylococci of low virulence there appears at the place of injection first a hemorrhagic-purulent inflammation and later a localized purulence. In the regional lymph nodes there is lymphatic hyperplasia, and in the blood a lymphocytosis.

2. In the regional lymph nodes there is first a regressive change of Flemming's secondary nodules and of transition forms. Then follows lymphatic hyperplasia, starting apparently from solid secondary nodules and progressing by way of pseudo-secondary nodules to a diffuse lymphoid hyperplasia. The increase of lymphocytes in the blood parallels this development.

3. Only after the highest point of the lymphocytosis has been reached or passed do we find the first Flemming's secondary nodules, which thereafter increase in number and size while the number of lymphocytes in the blood falls, and reach their maximum development when the number of lymphocytes in the blood is again normal. Therefore, the original conception of Flemming that the site of forma-

tion of the lymphocytes of the blood is in Flemming's secondary nodules, cannot be accepted.

4. The lymphocytes of the blood originate in the pseudo-secondary nodules as in embryonic life. The mother cells of the lymphocytes would appear to be Marchand's proliferating endothelial (reticular) cells.

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EXPLANATION OF PLATES.

PLATE 25.

FIG. 1. Popliteal lymph node (rabbit). Normal popliteal lymph node with a number of solid secondary nodules (*a*) and transition forms (*b*). Longitudinal section. Iron-hematoxylin-eosin. ×15.

FIG. 2. Half popliteal lymph node. (R 77). 42 days after subcutaneous infection. The lymphatic tissue consists almost entirely of large Flemming's secondary nodules with only very narrow marginal zones. Longitudinal section. Iron-hematoxylin-eosin. ×15.

FIG. 3. Popliteal lymph node (R 76). 2 days after subcutaneous infection. Lymphatic hyperplasia. On the margin of the cortex a number of solid secondary nodules (*a*). Cross-section. Iron-hematoxylin-eosin. × 15.

FIG. 4. Popliteal lymph node (R 78). 1 day after subcutaneous infection. The cortex contains smaller and larger solid secondary nodules (*a*), few transition forms (*b*) and also two small pseudo-secondary nodules (*c*). Longitudinal section. Iron-hematoxylin-eosin. × 15.

FIG. 5. Popliteal lymph node (R 161). 2 days after subcutaneous infection. On the one side there are still some transition forms (*a*) with polymorphonuclear leucocytes in their centers. On the other side some solid secondary nodules (*b*). The largest part of the cortex consists of a pseudo-secondary nodule (*c*). Proliferating medullary cords (*d*). Longitudinal section. Iron-hematoxylin-eosin. × 15.

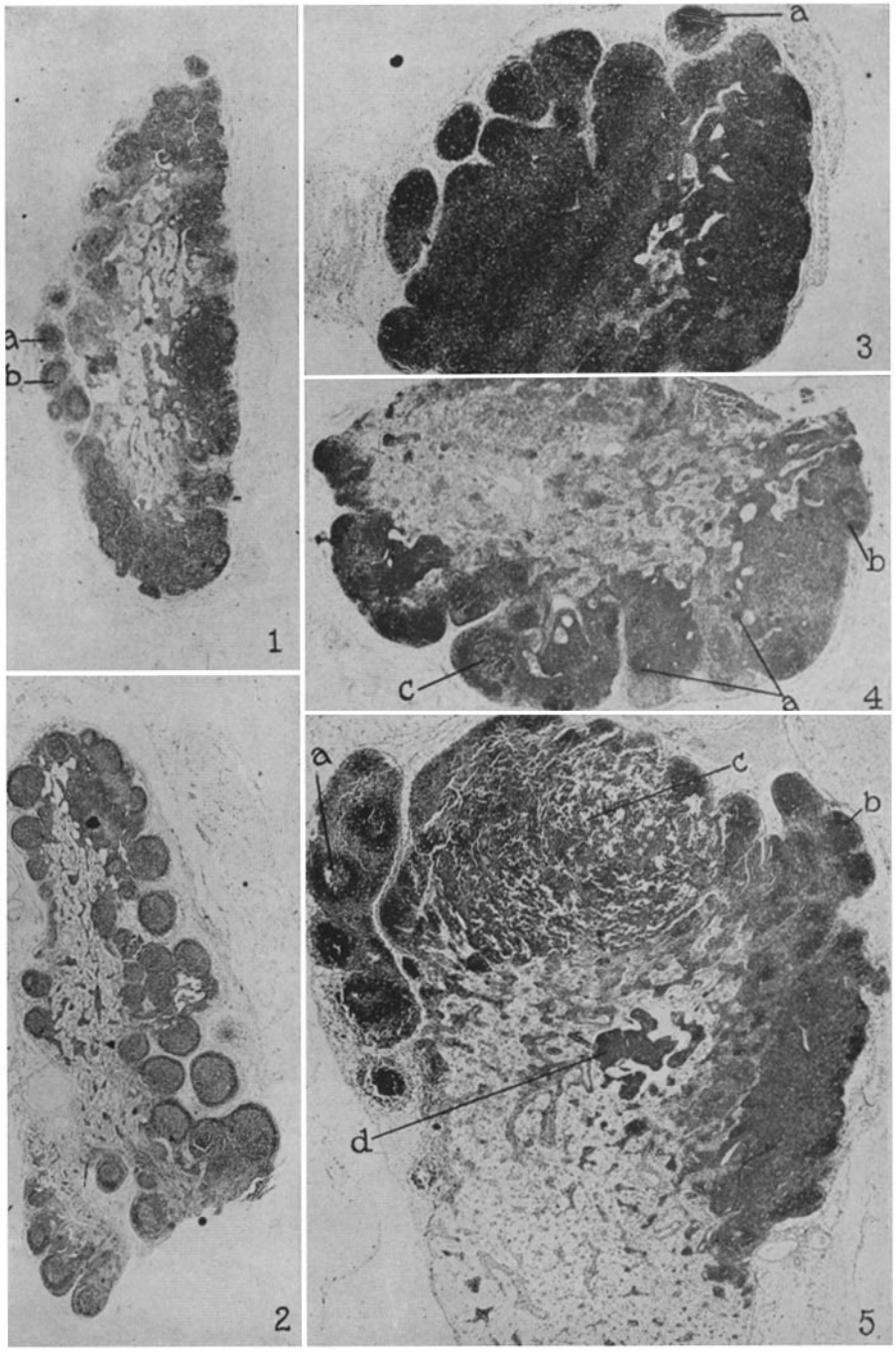
PLATE 26.

FIG. 6. Part of the cortex of Fig. 3 × 600. Many lymphocytes can be seen migrating into a vein (*a*). From the wall of the vessel some large cells have arisen (*b*).

FIG. 7. Part of the pseudo-secondary nodule of Fig. 5 × 600. From the walls of the vessels large cells have arisen (*a*) often with karyokinetic figures (*b*). From these all transitions to small lymphocytes can be seen (*c*).

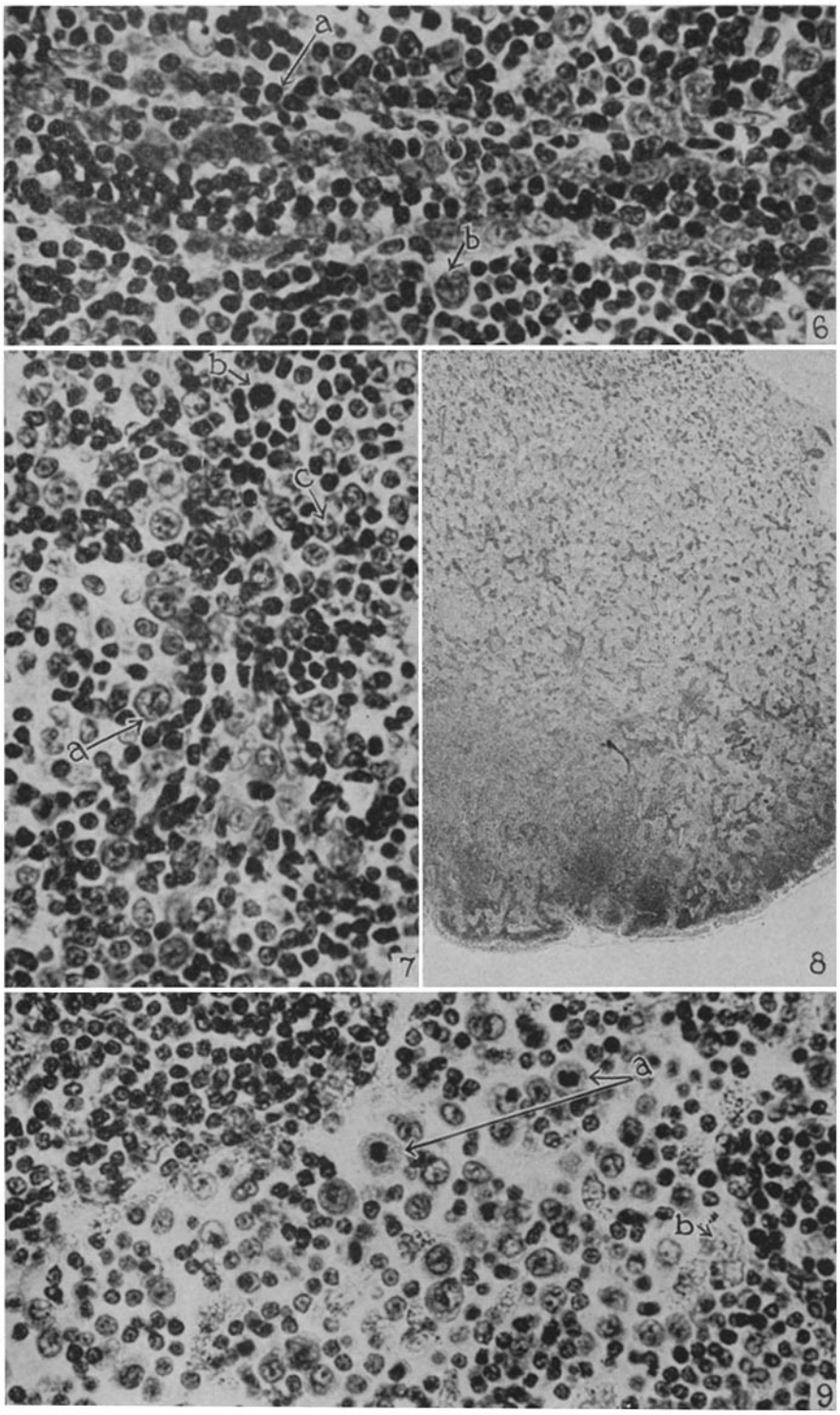
FIG. 8. Mesenteric lymph node (rabbit) with very narrow cortex and medullary cords. There are many lymphatic cells in the sinuses. Iron-hematoxylin-eosin. × 15.

FIG. 9. Part of Fig. 8 × 600. There are in the sinuses many small lymphocytes and large cells which are in the stage of division (*a*). Everywhere there is a large amount of pigment (*b*).



Photographed by Louis Schmidt.

(Ehrich: Lymphatic tissue. III.)



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