EXPERIMENTAL STUDIES ON THE CHIEF SOURCE OF BLOOD LYMHOPCYTES IN ADULT RABBITS*

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The significance of the various lymphoid organs as a source of lymphocytes has been studied by different methods. Using radioactive tracers, Andreasen and Ottesen[1] (1945) determined the rate of desoxylibose nucleic acid formation in the different lymphoid organs of the rat and found the thymus to be of highest mitotic activity. This was confirmed also in the rat by the more direct method, viz., by counting the mitotic figures in suspensions of lymphocyte nuclei prepared from the different lymphoid organs (Andreasen and Christensen,[2] 1947). More recently Horii and Tamaki[3] (1951) estimated the number of the lymphocytes produced per unit of time by the mesenterial, iliac and popliteal lymph nodes of the basis of determination of the total number of lymphocytes entering and leaveing the nodes via the afferent and efferent lymphatics. These investigators found the mesenterial lymph nodes to be of highest lymphocytopoietic activity.

Besides the above mentioned methods, the application of the classical one, the extirpation of the lymphoid organs in question, must be considesed. However, presumably because of technical difficulties involved, only few experiments of this type have hitherto been reported. So far as the writer is aware, Sanders and Florey[4] (1940) are the first who succeeded in removing a large part of the organized lymphoid tissues in the rat and rabbit without stopping the growth of the operated animals. Later Andreasen and Gottlieb[5] (1947) published similar experiments on the rat. The latter investigators reported that subtotal lymphadenectomy was followed by a marked and prolonged lymphopenia, but made no reference to the effects of removal of individual lymphoid organs.

The experiments reported here were designed to analyse the effects of removal of chief lymphoid organs such as the mesenteric lymph nodes, vermiform appendix and spleen on the level of the blood lymphocytes in the rabbit, with the aim to determine, if possible, the relative importance of these organs as the source of the blood lymphoctes.

MATERIAL AND METHOD

The animals employed were healthy adult rabbits of both sexes weighing about 2.5 kg.

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In a series of 8 rabbits *(total extirpation group)*, chief lymphoid organs such as mesenterial lymph nodes, vermiform appenedix and spleen, as well as several small lymph nodes, i.e., anterior gastric, portal, pancreatic and mesocolic nodes, were removed at one seance under laparotomy. The popliteal nodes had been extirpated on the preceding day. The total weight of the removed lymphoid organs amounted to approximately 80 per cent of that of the entire lymphoid organs (see Table 1).

TABLE I

The weights of lymph node[1] and lymphoid organs in 3 adult rabbits weighing about 2.5kg

Organ	weight in Gm			
	No. 1	No. 2	No. 3	Average
Large mesenterial nodes[2] (pancreas Aselli)	2.45	1.68	2.03	2.05
Other lymph nodes[3]				
Posterior thoratic	0.12	0.17	0.20	0.16
Para-aortic	0.05	0.02	0.03	0.03
Pelvic	0.06	0.10	0.30	0.15
Anterior gastric, portal and pancreatic	0.14	0.10	0.40	0.21
Cervical (Superficial and deep)	0.20	0.16	0.16	0.17
Axillary (Anterior and posterior)	0.15	0.15	0.55	0.28
Inguinal	0.21	0.05	0.10	0.12
Popliteal	0.16	0.14	0.18	0.16
Total	1.09	0.89	1.92	1.30
Lymphoid organs				
Thymus	0.52	1.10	1.02	0.88
Vermiform appendix	7.60	4.70	5.70	6.00
Spleen	0.60	1.26	0.90	0.92
Total	8.72	7.06	7.62	7.80

1 Pretracheal, para-xiphoid, renal and caudal nodes were not weighed because of their small size.

2 Small lymph nodes of mesocolon were included in the large mesenterial mass of nodes (Pancreas Aselli).

3 The nomenclature is the same as used by Sanders and Florey (1940).

Another series of 11 rabbits were divided into two groups ; in one group of 7 rabbits the mesenterial nodes and above mentioned small nodes were extirpated *(lymphadenectomy group)*, and in another group of 4 rabbits the vermiform appendix and spleen were removed *(appendectomy and splenectomy group)*.

In the rabbit, the mesenterial nodes aggregate in the root of the mesentery in a large mass called pancreas Aselli, the weight of which amounted to about one and a half of the sum of all the other lymph nodes as shown in Table I. Since many mesenterial vein pass through this mass of nodes and become confluent to the portal vein in or behind this mass, special care must be taken to avoid any injury to these veins during the operation. Accordingly, a small potion (about 1/5) of this mass lying behind the portal vein was left; instead, other small easily removable nodes such as gastric, portal, pancreatic and mesocolic nodes were extirpated. Although thus the operation of removal of the mesentrial nodes was performed

as carefully as possible to prevent hemorrhage, about half of the operated animals died from unknown causes within several days. Such animals were not included in the present study.

None of the other operations presented any difficulty. Sterile technique was employed in all operative procedures. Thymedectomy was not performed in the present experiments, because in the adult rabbit the thymus has undergone age involution to a large extent and therefore has a minor significance as a lymphocytopoietic center.

In every animal which survived the operation blood examinations were carried out at successive intervals. The blood samples were taken from the marginal vein of the ear. The animals were autopsied 2 to 8 weeks after the operation. The tissues to be examined were fixed in Zenker-formal, and the sections were stained with hematoxylin and eosin or eosin-azur II.

Results

1. *Total extirpation group* (Tables II, III and Fig. 1)

In this group, the mesenterial lymph nodes (pancreas Aselli), vermiform appendix and spleen, as well as other several small lymph nodes, were removed at one seance[1]. In all of 8 rabbits which survived the operation, blood examinations were performed.

The characteristic feature of the post-operative blood picture was a marked and persistent lymphopenia. The post-operative lymphocytes counts varied from 9

Table II

Changes in the blood picture after removal of the chief lymphoid organs

Animal No.	Wt. (Kg) Sex	Time Interval	R B C x 10^4	H B %	W B C	Lympho-cytes	Remarks
1	1.9 ♀	Before	500	61	7,100	5,820	Removed lymphoid organs:
		〃	459	58	6,500	4,680	Popliteal nods 0.14 gm
		〃	460	60	6,500	5,070	Mesenterial mass 0.8 gm
							Vermiform appendix 4.7 gm
		1 day			4,900	1,320	Spleen 1.26 gm
		2 days	370	50	5,200	1,560	
		4 〃	360	44	4,800	1,540	
	1.3	7 〃	407	54	4,800	2,400	
		2 wks	490	66	6,000	2,700	
		3 〃	539	78	4,600	2,480	
	1.5	4 〃	600	78	6,000	3,600	
20	3.1 ♂	Before	630	70	17,500	13,830	Removed lymphoid organs:
		〃	650	75	17,000	11,560	Popliteal nodes 0.2 gm
		〃	647	69	17,000	11,900	Mesenterial mass 1.4 gm
							Vermiform appendix 8.9 gm
		1 day			23,000	1,900	Spleen 0.7 gm
		2 days			19,000	2,300	
		3 〃	491	59	12,000	4,800	
		4 〃			12,000	4,680	
	2.6	7 〃	528	61	12,000	3,600	
	2.6	2 wks	598	68	11,000	2,640	
	2.7	3 〃	571	70	8,100	2,430	
	2.8	4 〃	660	76	8,000	3,200	
	3.1	5 〃	618	70	12,000	4,680	
	3.2	6 〃	670	77	8,000	4,400	

1 The popliteal nodes had been extirpated on the preceding day, but the effect of removal of these nodes may be neglected because of their small size (see Tlable I).

TABLE II *(Continued)*

Animal No.	Wt. (Kg.) Sex	Time Interval	R B C x 10^4	H B %	W B C	Lympho-cytes	Remarks
23	2.5 ♀	Before	590	64	11,000	4,950	Removed lymphoid organs:
		〃	570	65	10,400	4.060	Popliteal nodes 0.3 gm
		〃	620	70	10,600	4,130	Mesenterial mass 2.1 gm
							Vermiform appendix 9.0 gm
		1 day			15,100	2,000	Spleen 1.3 gm
		3 days	444	55	4,600	1,660	
		4 〃			10,000	3,000	
	2.2	5 〃			9,500	3,040	
		6 〃			9,500	2,190	
		7 〃	631	64	11,000	2,310	
		2 wks			8,000	1,760	
	2.5	3 〃			5.400	1,350	
	2.4	4 〃	642	78	7,000	1,960	
	2.5	5 〃	662	81	7,000	2,170	
26	2.7 ♀	Before	480	75	11,600	9,050	Removed lymphoid organs:
		〃	530	79	7,700	5,930	Popliteal nodes 0.15 gm
		〃	512	75	11,000	8,400	Mesenterial mass 2.9 gm
							Vermiform appendix 4.5 gm
		1 day			11,000	2,700	Spleen 0.6 gm
		2 days			6,460	1,870	
		3 〃			7,000	2,140	
		4 〃			8,200	1,440	
	2.5	5 〃	329	55	10,200	1,890	
		7 〃			10,040	2,460	
	2.4	2 wks			7,000	2,380	
		3 〃			5,460	2,240	
		4 〃			7,900	2,600	
	2.6	5 〃			7,200	2,100	
27	2.6 ♂	Before	449	74	8,600	6,020	Removed lymphoid organs:
		〃	450	70	10,000	5,600	Popliteal nodes 0.19 gm
		〃	488	74	10,000	5,850	Mesenterial mass 1.4 gm
							Portal nodes 0.18 gm
		1 day			11,300	1,190	Vermiform appendix 7.0 gm
		2 days			10,100	1,210	Spleen 1.1 gm
		3 〃			6,900	2,070	
		4 〃			9,000	2,030	
		5 〃			8,400	2,352	
	2.1	7 〃	510	75	7,220	2,440	
		2 wks			9,300	1,580	
		3 〃			4,700	1,500	
		4 〃			4,440	1,600	
	2.3	5 〃	481	74	4,620	1,680	

to 60% of the pre-operative values on the next day of operation (averaging 34%), 29 to 77% on the 7th day (averaging 49%), 27 to 71% at the end of the 4th week (averaging 43%) (see Table III). The normal blood lymphocyte level was not re-established during the course of 6 post-operative weeks in an any instances.

The total leucocyte level showed a considerable rise on the next day of operation, due to a non-specific post-operative granulocytosis which subsided rapidly. A second less prominent peak of similar nature was then observed on the 7th day. Thereafter, the total leucocyte count was decreased below the pre-operative level and ran almost parallel to the lymphocyte count (Fig. 1). The absolute number

of pseudoeosinophiles did not fall below the intial level throughout the experimental period. The number of erythrocytes and hemoglobin content indicated a moderate anemia during the first 2 to 3 weeks, but showed somewhat higher values than the pre-operative levels after 4 weeks. The post-operative reduction in body weight gradually recovered by the end of the 5th week (see Table II).

TABLE III

Per cent changes of the lymphocyte counts (A) and the total white cell counts (B) after removal of the chief lymphoid organs in 8 rabbits.

A. Lymphocyte counts

Time Interval	No. 1	No. 4	No. 14	No. 15	No. 20	No. 23	No. 26	No. 27	Average
Before	115	122	111	106	116	120	108	103	113
〃	92	98	84	74	97	98	71	96	89
〃	100	100	100	100	100	100	100	100	100
Operation									
1 day	26	49	25	60	9	48	32	22	34
2 days	31				19		22	21	23
3 〃		31	44	50	40	40	26	35	38
4 〃	30		29	44	40	73	17	35	38
5 〃			47	57		74	23	40	48
6 〃					38	53			46
7 〃	47	77	53	54	30	56	29	42	49
2 wks	53	43	34	29	22	43	28	28	35
3 〃	49	41			20	33	33	26	34
4 〃	71	52			27	47	31	27	43
5 〃					39	53	25	29	37
6 〃		52			37				45

B. Total white cell counts

Time Interval	No. 1	No. 4	No. 14	No. 15	No. 20	No. 23	No. 26	Ne. 27	Average
Before	105	145	120	114	102	102	103	86	110
〃	100	104	98	83	100	98	70	100	94
〃	100	100	100	100	100	100	100	100	100
Operation									
1 day	76	217	174	217	138	142	100	113	147
2 days	80				112		50	101	85
3 〃		76	78	60	71	43	64	69	66
4 〃	74		66	79	71	94	75	90	78
5 〃			85	86		90	93	84	88
6 〃					77	90			84
7 〃	74	214	108	156	71	102	91	111	115
2 wks	92	105	97	130	65	76	64	93	92
3 〃	71	66			48	51	48	47	55
4 〃	92	86			47	66	72	44	67
5 〃					71	66	65	46	62
5 〃		83			47				60

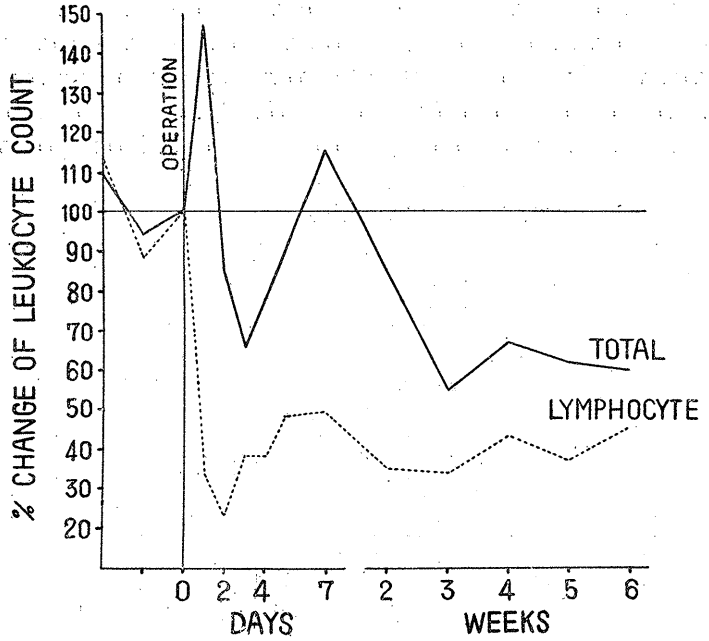

Fig.1. Per cent changes of the total white cell counts and lymphocyte conuts after removal of the mesenterial mass of nodes, popliteal nodes, vermiform appendix and spleen (average 4 to 8 rabbits).

2. *Lymphadenectomy group* (Tables IV-VII and Fig.2)

This group comprises 7 rabbits in which only the mesenterial mass of nodes (pancreas Aselli) was removed. In 4 out of 7 animals, however, the second operation (removal of the spleen, vermiform appendix and popliteal nodes[2] was performed on the 7th day after the first operation.

It was found that the removal of the mesenterial mass of nodes alone may also be responsible for a marked fall of the blood lymphocyte level. However, the size and weight of the removed mesenterial mass of nodes showed a considerable individual variation, and according to this the effect of its removal on the blood counts differed to a large extent. Data of blood examinations on 2 rabbits showing a marked difference are given in Thbles IV and V. Percent changes of the lymphocyte counts after the first and second operations are summarized in Table VI, and some typical curves are recorded in Fig.2.

An interrelation between the organ-body weight ratios for the removed mesenterial mass of nodes and the degree of fall of the post-operative lymphocyte counts is shown in Table VII. The table indicates that the greater the relative weight of the removed mesenterial mass of nodes, the more pronounced was the post-operative

2 The effect of removal of the popliteal nodes may be neglected because of their small size (see Table 1).

TABLE IV

Changes in the blood picture after removal of the mesenterial mass of nodes in the rabbit No. 10, in which the second operation was performed at 7 days after the first operation

wt. (Kg) Sex	Time Interval	R B C x10⁴	HB %	W B C	Lympho-cytes	Remarks	
2.3 ♂	Before	520	69	16,400	14,430		
	〃	500	75	11,000	9,240		
	〃	510	75	13,000	10,900		
	Lymphadenectomy (Mesenterial nodes)						
	1 day			18,000	2,700	Mesenteral mass	2.3 gm
	2 〃			6,000	1.350		
	4 〃			6,800	1,630		
	5 〃			4,200	1,550		
	6 〃			5,700	1,830		
	7 〃			5,000	1,900		
	Splenectomy + Appendectomy + Lymphadenectomy (Popliteal nodes)						
	1 days			22,000	1,540	Spleen	1.3 gm
	2 〃	400	56	7,000	1,000	Vermiform appendix	9.4 gm
	3 〃			9,800	1,960	Popliteal nodes	0.2 gm
	4 〃			10,000	950		
	5 〃			11,000	880		
2.0	2 wks			6.200	2,480		
	3 〃			4,000	1,840		
1.9	4 〃	570	74	4.800	2,600		
	5 〃			3,300	1,800		
1.9	6 〃			4.100	2,710		
	7 〃			5.000	2,450		
2.0	8 〃	640	66	7.000	2,800		

TABLE V

Changes in the blood picture after the removal of mesenterial mass of nodes in the rabbit No. 22, in which the second operation was performed at 7 days after the first operation

Wt. (Kg.) Sex	Time Interval	R B C x10⁴	HB %	W B C	Lympho-cytes	Remarks	
4.25 ♂	Before	530	75	8,700	5,570		
	〃	590	76	8,000	3,520		
	〃	580	76	7,000	3,780		
	Lymphadenectomy (Mesenterial nodes)						
	1 day			14,000	2,800	Mesenterial mass	2.0 gm
	2 days			9,000	2,520		
	3 〃			7,630	2,590		
	4 〃			8,960	3,580		
	5 〃			8,750	3,940		
	6 〃			9,100	3,730		
	7 〃			9,450	3,500		

Splenectomy + Appedectomy + lymphadenectomy (Popliteal nodes)						
	1 day			16,000	1,150	Spleen 2.2 gm
	3 days	470	59	12,500	1,750	Vermiform appendix 4.2 gm
4.2	4 〃			8,900	2,500	Popliteal nodes 0.45 gm
	5 〃			10,000	2,500	
	6 〃			10,000	2,600	
	7 〃	560	63	8,300	2,800	
	2 wks			10,000	1,200	
4.0	3 〃			6,000	2,000	
3.9	4 〃	620	73	9,000	2,250	

TABLE VI

Per cent changes of the lymphocyte count after removal of the mesenterial mass of nodes in 7 rabbits, in 4 of which the second operation was performed at 7 days after the first operation

Time Interval	No. 6	No. 7	No. 8	No. 9	No. 10	No. 11	No. 12	Average
Before	121	115	107	101	132	101	147	118
〃	92	78	82	85	85	93	93	84
〃	100	100	100	100	100	100	100	100
Lymphadenectomy (Mesenterial mass)								
1 day	65	41	66	48	25	28	74	50
2 days	108			47	12	23	67	51
3 〃	90			68		34	69	65
4 〃		47	73		15	37	95	53
5 〃	110	37	63	50	14		104	63
6 〃	114			75	17		99	76
7 〃			116	43	17	41	93	62
Splenectomy + Appendectomy + Lymphadenectomy (Popliteal nodes)								
1 day				41	14	25	30	28
2 days					9	49		29
3 〃					18	39	46	34
4 〃				19	9	34	66	32
5 〃				13			66	40
6 〃				39			69	54
7 〃				37	8	53	74	43
2 wks				41	23	38	32	34
3 〃				42	17	34	53	37
4 〃				48	24	43	60	44
5 〃				45	17	48		37
6 〃				68	25	39		44
7 〃				68	23	28		40
8 〃				47	26	31		35

TABLE VII

Comparison of the organ-body weight ratio for the removed mesenterial mass of nodes and the per cent changes of the post-operative lymphocyte counts (the pre-operative values being expressed as 100%)

Animal No.	Organ-Body Weight Ratio for Mesenterial Mass of Nodes	% Changes of the Number of Blood Lymphocytes after 1–2 Days	% Changes of the Number of Blood Lymphocytes after 5–7 Days
No. 6	1/4860	65–108 %	110–114 %
No. 7	1/1850	41 〃	37 〃
No. 8	1/3060	91 〃	63–116 〃
No. 9	1/1370	47–48 〃	43–75 〃
No. 10	1/1100	12–25 〃	12–17 〃
No. 11	1/1370	23–28 〃	41 〃
No. 12	1/2130	67–74 〃	93–104 〃

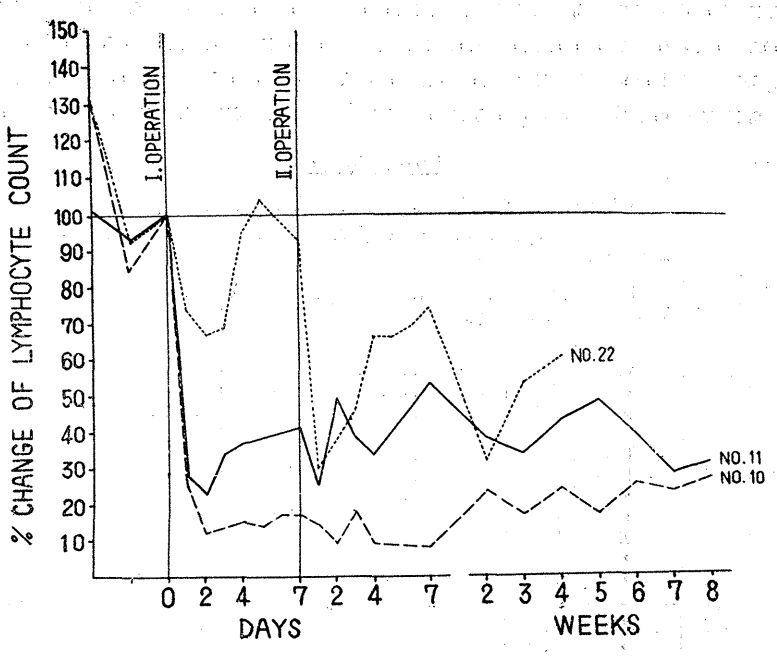

Fig. 2. Per cent cnanges of the lymphocyte counts after removal of the mesenterial mass of nodes in the rabbits Nos. 10, 11 and 22. In each, the second operation (extirpation of the vermiform appendix, spleen and popliteal nodes) was performod at 7 days after the first operation.

lymphopenia during the course of the first 7 days, so long as the weight of this mass was greater than 1/2000 of the body weight. It should be noticed here that

if the relative weight of the removed mesenterial mass of nodes was below this level, the operation was followed by no significant reduction of the lymphocyte counts during the first 7 post-operative days. This implies that the continuity of the lymphatic pathway interrupted by the removal nodes has been rapidly re-established.

The effect of the second operation (removal of the spleen, vermiform appendix and popliteal nodes) on the lymphocyte level is also noteworthy. In the rabbits which had developed a severe lymphopenia after the first operation, the second operation failed to alter significantly the blood lymphocyte level (see Tables IV, VI and Fig.2). In contrast, in the rabbits without such an initial lymphopenia the second operation was followed by a remarkable reduction of the lymphocyte counts (see Tables V, VI and Fig.2). These facts indicate that the mesenterial mass of lymph nodes together with the vermiform appendex and spleen represents the chief source of the blood lymphocytes, the latter organs being auxiliary to the former.

3. *Appendectomy and splenectomy group* (Tables VIII, IX and Fig. 3)

In none of 4 animals, in which merely the vermiform appendix and spleen had been removed, were either the lymphocyte counts or the total leucocyte counts significantly altered during the course of 7 post-operative weeks, with the exception of a non-specific post-operative granulocytosis and a concomitant severe lym-

TABLE VIII

Changes in the blood picture after removal of the spleen and vermiform appendix

Animal No.	Wt. (kg) Sex	Time Interval	RBC x10⁴	HB %	W B C	Lympho-cytes	
30	2.2 ♂	Before	680	79	11,600	7,310	Removed lymphoid organs:
		〃	730	85	10,100	5,560	Spleen 1.5gm
		〃	730	86	10,000	6,200	Vermiform appendix 9.2gm
		1 day			11,200	3,140	
		2 days			10,000	4,400	
		3 〃			10,700	5,030	
	2.0	7 〃	690	75	7,500	4,280	
		2 wks	700	74	9,800	5,000	
		3 〃	670	78	10,600	5,410	
	2.1	4 〃	730	76	9,900	5,050	
31	2.2 ♂	Before	710	85	9,000	5,220	Removed lymphoid organs:
		〃	730	82	8,500	4,370	Spleen 1.4gm
		〃	750	85	8,000	4,560	Vermiform appendix 5.5gm
		1 day			15,200	2,280	
		2 days			7,600	4,640	
	2.1	3 〃	690	74	8,700	4,260	
		7 〃	710	70	8,500	5,610	
	2.2	2 wks	600	70	8,500	4,590	
		3 〃	650	71	7,100	5,110	
	2.3	4 〃	710	70	7,700	4,080	

TABLE IX

Per cent changes of the lymphocyte counts (A) and the total white cell counts (B) after removal of the spleen and vermiform appendix in 4 rabbits

A. Lymphocyte counts

Time Interval	No. 28	No. 29	No. 30	No. 31	Average
Before	117	126	118	115	119
〃	100	85	90	96	93
〃	100	100	100	100	100
			Operation		
1 day	43	79	51	50	56
2 days	122	77	71	102	93
3 〃	72	86	81	93	83
4 〃	132	54	80		89
5 〃		107			
7 〃	105	94	69	123	98
2 wks	96	154	81	100	108
3 〃	88	78	87	112	91
4 〃	92		81	90	88
5 〃	87	124			106
6 〃	34	127			81
7 〃	71	67			69

B. Total white cell counts

Time Interval	No. 28	No. 29	No. 30	No. 31	Average
Before	102	103	116	112	108
〃	97	100	101	106	101
〃	100	100	100	100	100
			Operation		
1 day	296	168	112	190	192
2 days	129	115	100	95	110
3 〃	138	101	107	108	114
4 〃	129	106	96		110
5 〃		105			
7 〃	113	90	75	106	96
2 wks	102	116	98	106	106
3 〃	153	85	106	89	108
4 〃	166		99	96	120
5 〃	92	122			107
6 〃	92	95			94
7 〃	87	80			84

phopenia which appeared on the next day of operation and subsided rapidly. It is worthy of notice that in this group of animals a severe lymphopenia also occurred during the first 2 days. (Fig. 3). Since this lymphopenia subsided rapidly within a few days, it is probably caused by some non-specific factors associated with the operation, and is by no means due to the reduction in the amount of lymphoid tissue. The lymphopenia which was observed in the other groups during the first few post-operative days also seems to be non-specific in nature.

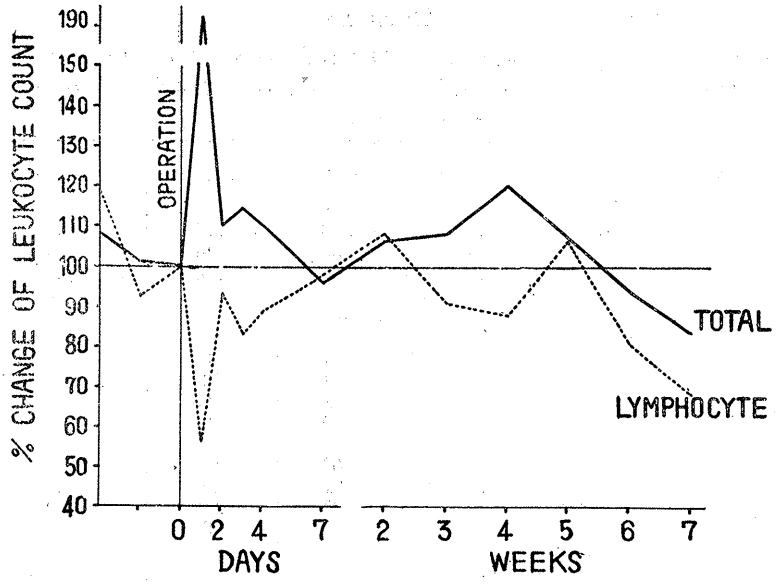

Fig. 3. Per cent changes of the total white cell counts and lymphocyte counts after removal of the vermiform appendix and spleen (average 4 rabbits).

4. *Compensatory mechanism in response to the removal of the chief lymphoid organs*

It is generally agreed that following complete removal of one lymph node in abult animals, no new formation occurs at its site, but that partial removal may be followed by an increase in size of the fragment remaining (Sanders and Florey,[4] 1940; Turner and Hall,[6] 1943; Furata,[7] 1947). The absence of newly formed nodes at the sites of total extirpation was also confirmed in the present experiments. Although small portions of the mesenterial mass of nodes remaining behind the portal vein showed a marked hyperplasia with the formation of many active secondary nodules of Flemming type, no indication of such hyperplasia was observed in the other remaining nodes and lymphoid tissues including peyer's patches, with the exception of peribronchial nodules of the lung. Thus, compensatory hyperplasia on the part of the remaining lymphoid organs and tissues took place only to a small extent.

In the liver, on the other hand, there appeared masses of newly formed lymphoid tissue along the branches of the portal system by the end of the 4th week, which may be considered to be compensatory to the reduction of the lymphoid tissue. Detailed description and discussion on the new formation of lymphoid tissue in the liver will be made in another paper.

Discussion

A number of facts indicate that the pronounced and persistent fall of the

circulating lymphocyte level, which definitely occurred following the removal of the chief lymphoid organs, is in causal relation to the reduction in the amount of lymphoid tissue: (1) The observed lymphopenia took place without any other remarkable alterations in the blood picture except for a transient post-operative granulocytosis which is non-specific in nature. (2) Appendectomy combined with splenectomy alone did not significantly alter the blood lymphocyte level. (3) The degree of reduction of the blood lymphocytes depends to some extent upon the relative weight of the mesenterial mass of nodes, when only this mass has been removed.

It should be noticed here that in the rabbits that have a mesenterial mass of nodes smaller than 1/2000 of the body weight, the removal of this mass was followed by no significant fall of the lymphocyte level. This implies that the continuity of the lymphatic pathway interrupted by the removal of the mesenterial nodes has been rapidly re-established. Clark and Goodman[8] (1948) also reported that after removal of the mesenterial nodes in dogs, there was rapid re-establishment of anatomical and functional continuity of the interrupted mesenteric lymphatics. Therefore, the factors associated with the interruption of the mesenteric lymphatic drainage which may influence the blood lymphocytes level, can be excluded.

In the rabbits, the mesenterial mass of nodes has generally been considered to be the most important source of lymphocytes because of its considerably large size, but without any other substantiating evidence. By comparing the total number of the lymphocytes entering and leaving the nodes per unit of time via the afferent and efferent lymphatics in the rabbit, Horii and Tamaki[3] (1951) have demonstrated that the lymphocytopoietic activity of the mesenterial nodes is definitely higher than that of any other lymph nodes. The experiments reported here present further evidence. Namely, it has been shown that so long as the mesenterial mass of nodes is well developed and its relative weight above 1/2000 of the body weight, the removal of this mass alone may be responsible for a marked reduction of the blood lymphocytes, and that the subsequent extirpation of the vermiform appendix and spleen on the 7th day does not further alter the lymphocyte level. This indicates that the mesenterial mass of nodes is the more important source of the blood lymphocytes than any other large lymphoid organs.

However, the fact must be taken into consideration that when the mesenterial mass of nodes is too small in size to induce a perceptible lymphopenia after its removal, the subsequent extirpation of the vermiform appendix and spleen on the 7th day is followed by a remarkable reduction of the blood lymphocytes, although appendectomy combined with splenectomy alone is ineffective in this respect. In such cases, the mesenterial mass of nodes together with the vermiform appendix and spleen should be considered to be the chief source of the blood lymphocytes, the latter two organs being auxiliary to the former.

Summary

In adult rabbits, chief lymphoid organs such as the mesenterial lymph nodes, vermiform appendix and spleen, as well as other several small lymph nodes, were removed. The total weight of the removed lymphoid organs amounted to approximately 80 per cent of that of the entire lymphoid organs. In the rabbit the mesenterial lymph nodes unite in a large mass called pancreas Aselli, the weight of which is about one and a half of the other lymph nodes.

Simultaneous extirpation of the chief lymphoid organs mentioned above and other several small lymph nodes resulted in a marked drop of the number of the blood lymphocytes, down to 30 to 40 per cent of the pre-operative values, and such a pronounced lymphopenia persisted for several weeks. No other remarkable alterations were observed in the blood picture, except for a post-operative non-specific granulocytosis which subsided rapidly. The continuity of the lymphatic pathway interrupted by the removal of the mesenterial nodes has been rapidly re-established.

Removal of the mesenterial mass of lymph nodes alone was responsible for a marked fall of the blood lymphocyte counts, so long as this mass was well developed and its weight greater than 1/2000 of the body weight. But when the relative weight of this mass was below this level, the removal of this mass was followed by little or no reduction of the blood lymphocytes.

Appendectomy combined with splenectomy alone caused no significant drop of the blood lymphocyte counts. However, when the mesenterial mass of nodes was too small in size to induce a perceptible lymphopenia after its removal, the subsequent extirpation of the vermiform appendix and spleen on the 7th day produced a remarkable reduction of the blood lymphocytes.

These findings indicate that, in the rabbit, the mesenterial mass of lymph nodes represents the chief source of the blood lymphocytes together with the vermiform appendix and spleen, the latter organs being auxiliary to the former one.

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