Quantitative Study on the Postnatal Growth and Involution of the Thymolymphatic Tissues in the Albino Rat*

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There is a considerable volume of literature on the normal age changes in the thymus (Hammar, 1905; Söderland and Backman, 1909; Watanabe, 1927; Kato, 1943; Andreasen, 1943; Kano, 1955; Ito, 1957; Ito, 1957; Takami, 1958; Kawasaki, 1959; Santisteban, 1960) and other lymphoid organs (Groll and Krampf, 1920; Hellman, 1930; Grieshammer, 1937; Hwang, Lippincott and Krumbhaar, 1938; Krumbhaar and Lippincott, 1939; Österlind, 1940; Andreasen, 1943; Andrew, 1946; Andrew and Andrew, 1948; Gyllensten, 1950; Osogoe et al. 1953; Awaya, 1956; Imamura, 1959; Santisteban, 1960). Among the most valuable investigations in this field may be mentioned the report of an analysis of Andreasen (1943), who had followed the growth and involution of the thymolymphatic tissues by quantitative determination of the DNA-P content of individual organs of normal rats at different ages. In this report he had shown that there occurred a progressive development in the thymus, lymph nodes and spleen up to the end of the 3rd and 4th months of age and that this was followed thereafter by an involution which is most pronounced in the thymus. Many other investigators, including Andreasen, have also found that the thymolymphatic tissues of the experimental animals involute in the earlier stages of the life (about 3 or 4 months of age).

Experiments involving neonatal thymectomy in some of the laboratory animals have firmly established the paramount role of the thymus in ensuring both the normal development of the lymphoid system and the capacity to respond immunologically (Archer and Pierce, 1961; Miller, 1961, 1962; Martinez et al., 1962; Janković, Waksman and Arnason, 1962; Arnason et al., 1962; Arnason, Janković and Waksman, 1962; Dameshek, 1962; Burnet, 1962; Good et al., 1962; Dalmasso et

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al. 1963). Thus, an increasing interest is being shown in the thymus as possibly the "master gland" controlling the development of the anatomic integrity of the lymphoid tissues such as lymph nodes and spleen. It appears to be a logical step at this stage of research to investigate further the normal age changes in the thymus and other lymphoid organs and try to clarify their mutual relationship in their postnatal development as well as regression.

The purpose of the present experiment is to examine this problem from a quantitative view point by the method described by A w a y a in 1962. The method, though employing simpler technique yet essentially equal in its dependability to the DNA method (A n d r e a s e n, 1943 ; M o n d e n, 1959), makes it possible to undertake quantitative assessment of hemopoiesis in normal rats at different ages.

MATERIAL AND METHODS

One handred and twenty rats of a subline of the Wister strain were used as material. The animals were bred in our laboratory under identical environmental conditions. Breeding animals were frequently inspected, pregnancies and births were recorded. At 28 days of age, the young were weaned and the sexes were segregated. They were fed on uniform diet consisting of unpolished rice, pressed barley and dried small sardines with a small quantity of cod liver oil and minerals, supplemented once a week with cabbage or other vegetables. Water was given ad libitum.

The rats were divided into twelve age groups of 1, 2, 3 and 4 weeks and 2, 3, 4, 5, 6, 8, 12 and 18 postnatal months, each groups containing five males and five females. The animals were sacrificed by a stroke in the head and thymus, mesenteric lymph nodes and spleen were removed from each animal. The total number of nucleated cells in individual organs was estimated by A w a y a's method, descrided in 1962. The principle of this method follows : A small segment—approximately 20 mg of lymphoid organ is placed in 2 ml of N/4 HCl solution for 2 to 3 hours ; the tissues are then dispersed in the solution with fine needles and the suspension of nuclei obtained. Samples are taken for hemocytometer count. From the count thus obtained numbers of nucleated cells per unit weight and per organ are estimated. At the same time, histological studies of section were also made of these organs.

RESULTS

Age changes in body weight (Table 1, Figure 1).

The body weight, in both sexes, showed a rapid increase from 2 to 8 months of life, showing a gradual slowing down till the 12th month of life, after which there was found a gradual decrease. In all the age groups beyond the 4th postnatal week, the males registered bigger weight than the opposite sex, especially after the 4th month.

Table 1. Body weights of the albino rats at different ages. Means±Standard errors.(n=5).

Age and Sex		Body weight (g)
1 week	♂	9.4±0.5
	♀	9.1±0.5
2 weeks	♂	17.4±1.1
	♀	20.3±0.8
3 weeks	♂	26.0±0.3
	♀	28.0±1.0
4 weeks	♂	35.0±1.8
	♀	34.0±2.6
2 months	♂	124.0±8.5
	♀	100.0±4.4
3 months	♂	156.0± 9.9
	♀	156.0±13.6
4 months	♂	242.0±18.8
	♀	169.0±11.8
5 months	♂	262.0±6.9
	♀	206.0±6.0
6 months	♂	295.0±12.0
	♀	222.0± 9.7
8 months	♂	408.0±22.3
	♀	264.0± 8.9
12 months	♂	450.0±34.9
	♀	297.0±19.1
18 months	♂	328.0±34.7
	♀	269.0±10.5

Quantitative estimation of age changes in the thymolymphatic tissues.

The relative values were expressed as values per 100 grams body weight. The absolute and relative growth and involution in each organ were studied.

1. Thymus (Table 2 and Figures 2, 5 and 6).

In either sex the curves for the averages of absolute organ weight were found to rise abruptly at the 2nd month of age, reaching the maximum in the 3rd month in females and in the 4th month in males. After reaching the maximum, the curves showed a progressive fall in both sexes. The curves for the averages of the number of nucleated cells per unit weight showed the values to be kept at a high level in both sexes (3.18 to 3.99 × 10^6/mg) between 1 week and 6 months of life, beyond which there was noted a gradual fall towards the 18th month. The average values for the number of nucleated cells per organ were rather low till the 4th week, but increased rapidly in the 2nd month and reached the maximum figure in the 3rd month in females and in the 4th month in males. Thus, the curves showed similar variations to those of the absolute weight.

The curves for both the relative weight and the relative number of nucleated cells per organ showed a similar form, although presented clearly in the latter (Figures 5 and 6). The maximum values were reached in the 2nd and 3rd weeks in females and males, respectively ; from this stage on the curves fell off markedly with increasing age. Thus, the growth and involution of the thymus differed markedly from those of the mesenteric lymph nodes and spleen, which will be described later on. The curves further showed that the mean relative weights and numbers of nucleated cells in females were greater than in males except at 3 weeks of age (Figures 5 and 6). Thus it is seen that there is a distinct sex difference in the relative growth and involution of the thymus.

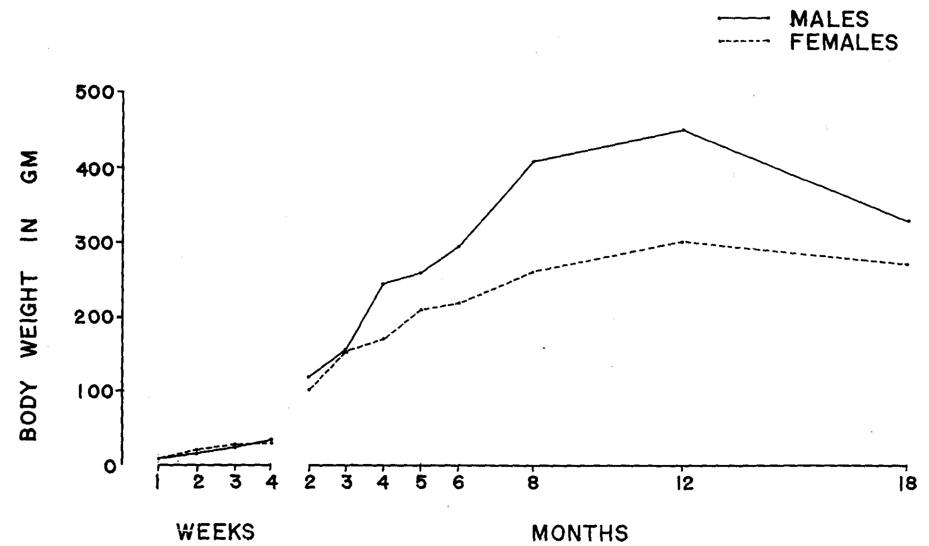

Fig. 1. Age changes in body weight in male and female albino rats of a modified Wistar strain.

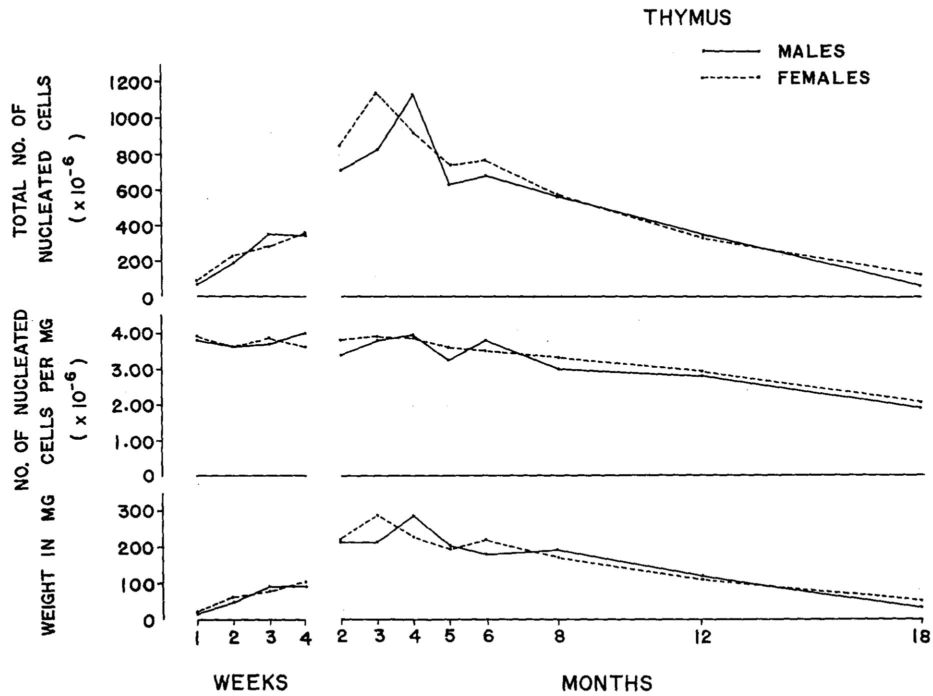

Fig. 2. Age changes in organ weight, cellular density (number of nucleated cells per mg) and total number of nucleated cells in thymus of male and female albino rats of a modified Wistar strain.

Table 2. Organ weight and total number of nucleated cells in the thymus of albino rats at different ages. Means±Standard errors. (n=5).

Age and Sex	Weight		Number of nucleated cells		
	absolute (mg)	relative (mg/100 g body wt.)	per mg ($\times 10^{-6}$)	per organ ($\times 10^{-6}$)	per 100 gm body wt. ($\times 10^{-6}$)
1 week ♂	19. 0±2. 3	204. 6±17. 8	3. 80±0. 12	72. 3±6. 3	767. 6±50. 9
1 week ♀	21. 2±2. 2	231. 1±13. 8	3. 92±0. 18	83. 7±11. 2	916. 2±83. 0
2 weeks ♂	54. 4±4. 3	312. 7±12. 6	3. 56±0. 15	191. 2±9. 6	1107. 5±36. 6
2 weeks ♀	64. 4±5. 9	315. 2±20. 2	3. 57±0. 39	234. 2±37. 5	1145. 2±162. 0
3 weeks ♂	94. 0±5. 5	351. 5±30. 8	3. 81±0. 28	370. 0±69. 9	1394. 1±222. 1
3 weeks ♀	76. 0±8. 9	268. 5±27. 5	3. 79±0. 14	284. 0±24. 8	1006. 5±80. 3
4 weeks ♂	86. 0±4. 4	249. 0±9. 2	3. 99±0. 22	344. 8±23. 8	993. 2±61. 7
4 weeks ♀	97. 1±6. 2	284. 3±11. 3	3. 58±0. 12	348. 7±29. 2	1018. 9±57. 6
2 months ♂	215. 0±11. 4	175. 2±9. 2	3. 38±0. 14	707. 4±55. 6	576. 6±40. 5
2 months ♀	224. 0±8. 7	225. 6±16. 0	3. 78±0. 16	848. 4±57. 7	852. 8±71. 7
3 months ♂	216. 0±18. 1	140. 3±15. 4	3. 81±0. 39	817. 5±90. 8	533. 9±76. 6
3 months ♀	292. 0±15. 3	191. 2±16. 4	3. 90±0. 33	1137. 2±118. 1	762. 4±132. 4
4 months ♂	291. 0±35. 9	122. 1±16. 3	3. 85±0. 12	1126. 5±154. 4	472. 2±68. 6
4 months ♀	236. 0±37. 6	147. 6±33. 1	3. 82±0. 19	912. 3±175. 7	573. 2±148. 4
5 months ♂	201. 0±27. 2	77. 5±12. 0	3. 18±0. 16	622. 9±56. 1	239. 3±25. 3
5 months ♀	198. 0±28. 5	97. 6±15. 7	3. 57±0. 38	727. 8±171. 9	360. 6±89. 6
6 months ♂	182. 0±13. 9	61. 3±2. 0	3. 76±0. 28	675. 8±43. 5	229. 5±15. 8
6 months ♀	222. 0±21. 3	99. 5±6. 4	3. 53±0. 21	768. 2±39. 7	348. 3±21. 9
8 months ♂	186. 0±22. 9	46. 0±5. 8	2. 97±0. 13	560. 1±81. 8	137. 9±20. 5
8 months ♀	173. 0±17. 6	65. 4±5. 7	3. 29±0. 11	564. 1±41. 5	214. 1±14. 3
12 months ♂	115. 0±27. 7	24. 5±3. 8	2. 84±0. 23	336. 6±89. 6	71. 3±13. 8
12 months ♀	106. 0±14. 3	36. 4±5. 2	2. 88±0. 23	334. 9±70. 3	116. 1±27. 9
18 months ♂	32. 3±9. 8	9. 4±2. 1	1. 92±0. 34	57. 7±17. 1	17. 5±3. 7
18 months ♀	50. 0±10. 7	18. 4±3. 7	2. 07±0. 39	115. 8±35. 9	42. 7±12. 9

2. Mesenteric lymph nodes (Table 3; Figures 3, 5 and 6).

The curves for the average values of the absolute weight showed in both sexes an abrupt rise in the 2nd month and reached their maximum at the 4th month. After this period a slight sex difference appeared. The curve for females ran fairly horizontally till the 6th month, after which a downward curve continued to the 18th month. In males, there was an abrupt fall at the 5th month after which no further rise appeared in the subsequent course of curve. The curves for the average values of number of nucleated cells per unit weight are shown in figure 3. These values were smaller than those in the thymus (2.76×10^6/mg, even at the maximum). The curve for females showed a gradual rise up to the

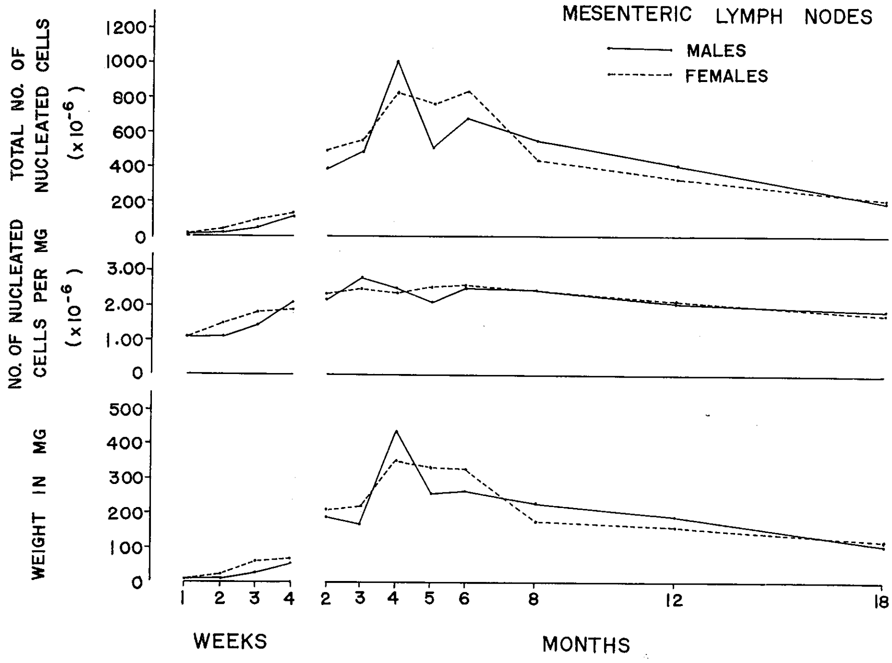

Fig. 3. Age changes in organ weight, cellular density (number of nucleated cells per mg) and total number of nucleated cells in mesenteric lymph nodes of male and female albino rats of a modified Wistar strain.

4th week and maintained this value till the 8th month of age. In males, on the other hand, the curve showed a distinct apex in the 3rd month : thereafter a temporary fall took place in the 5th month, the value again rising close to the maximum level. After the 8th month the curves for both sexes delined somewhat. The average values for the total number of nucleated cells contained in the whole of this organ are shown in Table 3 and Figure 3. In both sexes, the values were very low till the 4th week of life but rose abruptly in the 2nd month reaching their maximum in the 4th month. The subsequent segments of the curves were almost of the same form as those for the absolute weights except that there was a more distinct decrease in the 5th month in males.

The curves for both the relative weight and the relative number of nucleated cells per organ are illustrated in Figures 5 and 6. The curves for both were essentially identical. The curves rose gradually from 3 to 4 weeks and reached the maximal level in the 4th month after an initial transient fall in the 3rd month. After the 4th month the curves for both sexes declined. Thus, the relative growth of the mesenteric lymph nodes was distinctly different from that of thymus. The mesenteric lymph nodes still kept on growing till the age of 4 months, whereas the

Table 3. Organ weight and total number of nucleated cells in the mesenteric lymph nodes of albino rats at different ages. Means±Standard errors. (n=5).

Age and Sex		Weight		Number of nucleated cells		
		absolute (mg)	relative (mg/100 g body wt.)	per mg (×10⁻⁶)	per organ (×10⁻⁶)	per 100 gm body wt. (×10⁻⁶)
1 week	♂	5.0±1.1	53.4±13.0	1.07±0.12	5.5±1.5	58.8±17.3
	♀	6.9±2.2	74.2±21.9	1.09±0.10	7.3±2.5	77.1±24.5
2 weeks	♂	10.2±2.1	60.3±13.4	1.11±0.58	11.0±2.4	65.2±5.2
	♀	24.1±5.7	116.6±26.4	1.49±0.26	37.8±10.6	181.0±48.0
3 weeeks	♂	32.0±4.6	121.0±13.7	1.56±0.11	50.0±8.7	190.9±29.0
	♀	59.0±16.9	204.3±54.1	1.81±0.10	103.3±28.1	355.9±86.5
4 weeeks	♂	56.0±14.5	154.9±31.3	2.08±0.15	114.4±31.2	315.9±67.4
	♀	67.8±7.6	201.8±27.3	1.92±0.52	131.8±22.6	383.8±52.7
2 months	♂	186.0±30.3	151.9±24.3	2.19±0.14	402.1±63.4	325.2±44.8
	♀	208.0±38.9	203.4±33.1	2.35±0.13	503.6±111.0	490.8±31.4
3 months	♂	174.0±8.1	113.6±8.6	2.76±0.22	486.3±61.7	316.3±43.1
	♀	224.0±21.6	144.8±14.0	2.52±0.10	562.4±55.6	365.0±38.3
4 months	♂	431.0±106.9	193.9±61.1	2.52±0.11	1045.8±223.0	466.2±129.2
	♀	354.0±39.5	218.1±34.7	2.43±0.22	830.7±64.1	503.7±54.8
5 months	♂	260.0±38.5	98.4±12.7	2.11±0.07	554.8±96.2	209.5±32.1
	♀	330.0±76.2	156.8±31.3	2.56±0.41	769.5±119.0	368.9±46.0
6 months	♂	264.0±30.9	91.3±13.2	2.53±0.31	678.4±37.0	239.0±49.9
	♀	330.0±12.7	148.9±3.3	2.57±0.22	844.4±67.3	383.0±35.1
8 months	♂	228.0±41.7	54.9±7.9	2.51±0.18	562.1±96.6	135.0±16.7
	♀	183.0±8.0	69.4±2.0	2.41±0.07	441.7±22.9	167.4±6.1
12 months	♂	194.0±15.4	43.9±4.6	2.06±0.14	407.4±59.2	91.8±14.5
	♀	157.0±5.8	53.7±3.7	2.17±0.10	339.2±11.9	116.3±11.7
18 months	♂	112.0±17.6	36.0±7.4	1.86±0.10	208.5±93.3	68.1±16.2
	♀	122.0±12.1	45.2±9.5	1.79±0.16	214.2±20.6	79.3±6.4

thymus, after reaching its height of growth at 2 or 3 weeks, underwent a rapid involution (see Figures 5 and 6). As seen in the thymus, a distinct sex difference in relative growth of the mesenteric lymph nodes in all ages was observed.

3. Spleen (Table 4, Figures 4, 5 and 6).

As seen in Figure 4 the curves for average weight of the spleen differed in several respects from those observed in the preceding two organs. The curves for males showed a progressive rise till the 6th month when the organ attained its maximum weight. This was followed by a fall in the 8th month which again came near its maximum weight after 12 months of age. The curve for females

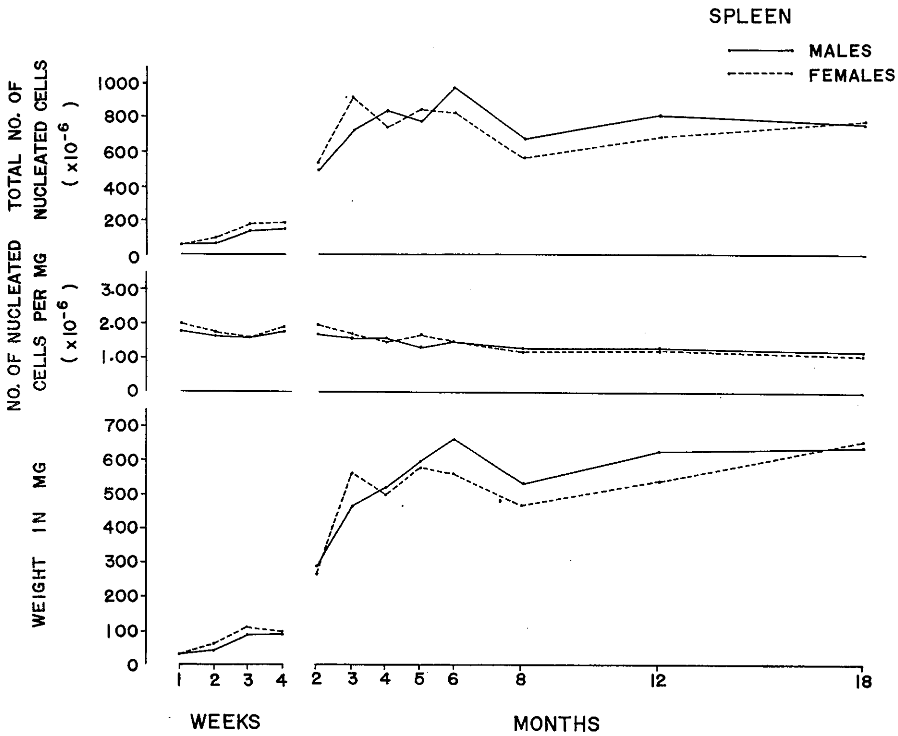

Fig. 4. Age changes in organ weight, cellular density (number of nucleated cells per mg) and total number of nucleated cells of spleen of male and female rats of a modified Wistar strain.

presented a rather irregular form but there was no essential difference from curves for the males: the maximal value was reached in the 5th month of age. The average values of the number of nucleated cells per unit weight in both sexes were maintained at high level from the 1st week to the 6th month of age except in the 5th month in males when a low value was obtained. After this period there occurred a gradual decrease towards the 18th month of age. The higher values in the first 4 weeks, however, were not due to proliferations of lymphocytic series, but chiefly to normoblast proliferations in the red splenic pulp, as will be described later. The values for number of nucleated cells per milligram of spleen were much smaller than those of the preceding two organs (1.98×10^6/mg even in the highest). As seen in Figure 4, the average values for the number of nucleated cells per organ remained still low during the first 4 weeks of age, but rose abruptly from 2 months, reaching maximum in the 3rd (females) or 6th (males) months. From these maximal points the curves showed a slight fall with some irregularities towards the 18th month. Thus, the absolute growth of the spleen in both

Table 4. Organ weight and total number of nucleated cells in the spleen of albino rats at different ages. Means±Standard errors. (n=5).

Age and Sex		Weight		Number of nucleated cells		
		absolute (mg)	relative (mg/100 g body wt.)	per mg ($\times 10^{-6}$)	per organ ($\times 10^{-6}$)	per 100 gm body wt. ($\times 10^{-6}$)
1 week	♂	31. 6±1. 9	335. 0±8. 9	1. 76±0. 15	56. 0±6. 9	498. 9±70. 0
	♀	27. 6±2. 4	302. 5±15. 4	1. 96±0. 17	53. 3±5. 1	589. 1±50. 3
2 weeks	♂	44. 8±5. 4	258. 9±30. 9	1. 65±0. 20	73. 4±11. 0	530. 6±69. 8
	♀	60. 3±6. 5	295. 0±25. 9	1. 68±0. 09	101. 7±12. 7	495. 3±47. 4
3 weeks	♂	93. 0±13. 8	354. 2±42. 6	1. 56±0. 02	153. 6±23. 2	580. 9±70. 2
	♀	112. 0±8. 3	401. 0±34. 9	1. 58±0. 08	177. 9±17. 3	632. 3±56. 9
4 weeks	♂	87. 8±8. 9	250. 8±24. 2	1. 85±0. 17	156. 9±12. 4	449. 2±22. 9
	♀	98. 1±18. 0	304. 7±81. 2	1. 92±0. 04	188. 8±36. 1	588. 8±162. 7
2 months	♂	294. 0±44. 2	236. 6±29. 2	1. 69±0. 09	502. 2±97. 1	404. 2±67. 5
	♀	266. 0±37. 4	261. 7±26. 6	1. 98±0. 12	543. 6±105. 2	531. 3±61. 9
3 months	♂	468. 0±36. 8	307. 8±37. 6	1. 57±0. 06	734. 2±49. 6	485. 1±64. 5
	♀	562. 0±134. 1	349. 8±57. 7	1. 67±0. 10	920. 5±274. 3	577. 3±87. 2
4 months	♂	522. 0±48. 5	220. 0±25. 9	1. 59±0. 12	843. 5±129. 6	359. 2±65. 6
	♀	504. 0±44. 0	299. 6±17. 8	1. 51±0. 10	745. 9±49. 2	449. 2±35. 1
5 months	♂	596. 0±40. 8	226. 8±12. 0	1. 33±0. 09	785. 8±52. 3	300. 3±22. 7
	♀	576. 0±131. 3	274. 4±56. 2	1. 66±0. 25	850. 3±121. 4	408. 3±48. 3
6 months	♂	662. 0±296. 2	225. 5±33. 1	1. 52±0. 10	989. 9±129. 1	338. 8±46. 1
	♀	560. 0±33. 8	251. 8±7. 5	1. 51±0. 06	842. 5±53. 4	380. 1±20. 1
8 months	♂	534. 0±30. 9	131. 0±3. 2	1. 29±0. 08	683. 3±38. 2	168. 0±8. 8
	♀	466. 0±28. 2	176. 1±10. 8	1. 22±0. 05	574. 2±58. 0	218. 0±21. 9
12 months	♂	631. 0±33. 4	141. 6±7. 2	1. 30±0. 09	825. 6±83. 9	182. 2±5. 9
	♀	541. 0±63. 3	186. 8±29. 5	1. 30±0. 08	706. 6±102. 3	241. 7±40. 6
18 months	♂	638. 0±33. 9	201. 9±24. 7	1. 21±0. 08	774. 7±67. 6	249. 3±46. 3
	♀	657. 0±71. 1	245. 1±26. 8	1. 17±0. 13	791. 2±159. 1	291. 8±52. 2

sexes was observed to be most vigorous between 3 and 6 months of age.

The curves for both the relative weight and the relative number of nucleated cells per organ of spleen are shown in Figures 5 and 6. The curves for both showed that these values kept on at high level during the first 3 months of age, and the maximum values were attained in the 3rd week in either sex. From the 4th month on, the curves fell off markedly with increasing age. Since the larger values in this organ in the age of the first 4 weeks is chiefly due to normoblast proliferation in the red pulp, the relative growth of the lymphatic tissues of the spleen is considered to be most vigorous between 2 and 3 months of age. Thus, the growth of spleen, as described in the preceding lines, is also distinctly different

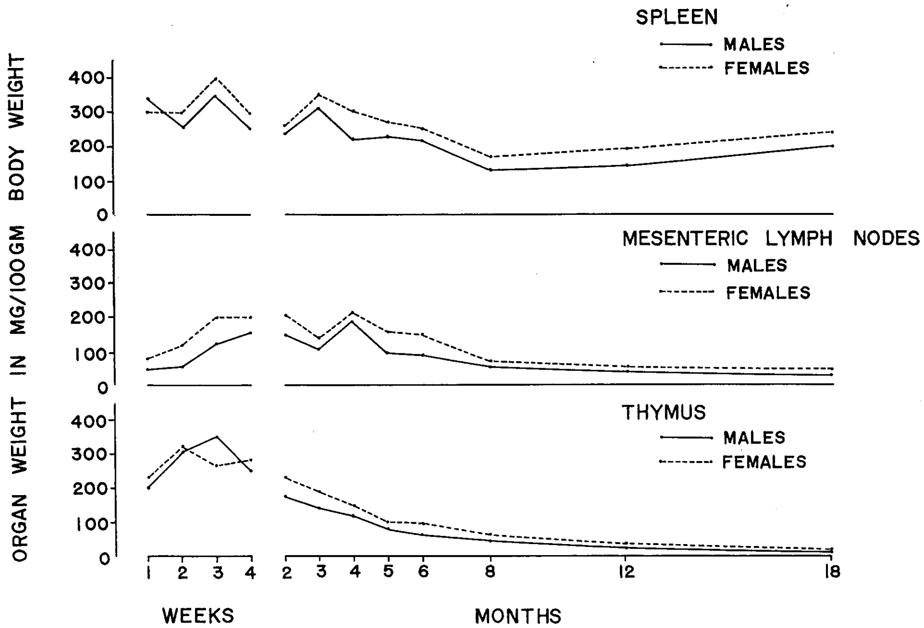

Fig. 5. Age changes in the relative weights (milligrams per 100 grams of body weight) of the thymus, mesenteric lymph nodes and spleen of male and female albino rats of a modified Wistar strain.

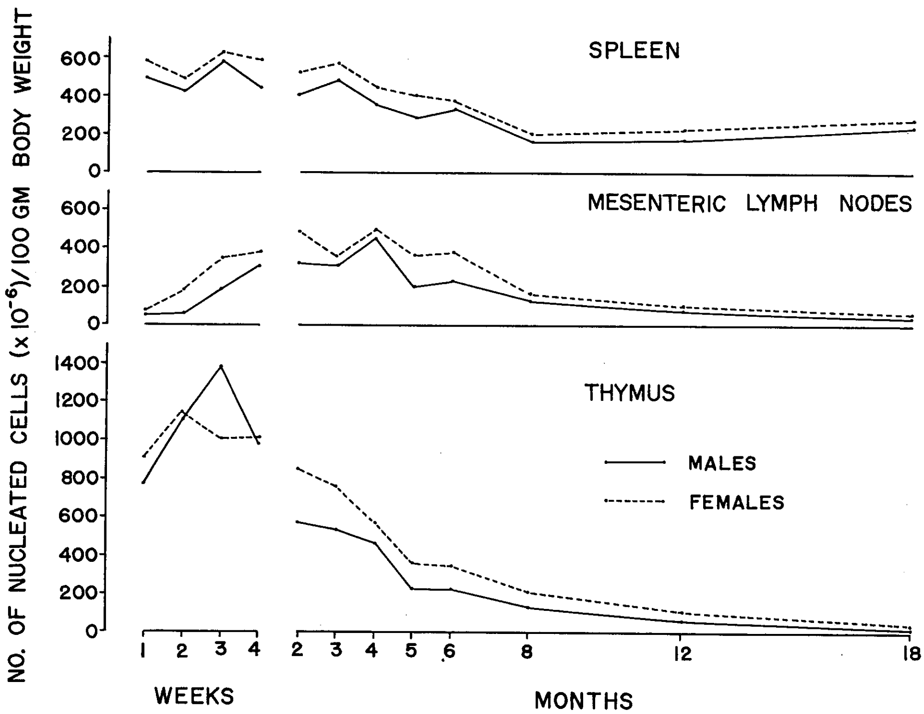

Fig. 6. Age changes in the relative total number of nucleated cells ($\times 10^6$ per 100 grams of body weight) in the thymus, mesenteric lymph nodes and spleen of male and female albino rats of a modified Wistar strain.

in this respect from that of thymus in which a more rapid involution is the rule. Also in the spleen a distinct sex difference in the relative growth were observed (Figures 5 and 6).

Histological findings. (PLATE I, II and III).

The chief histological changes in the postnatal differentiation processes in the thymolymphatic tissue were the relative enlargement of the medullary portion in the thymus and the formation of secondary nodules in the lymph nodes and the splenic white pulp, of the Flemming's types in particular. As the histological age changes in these tissues have been described elsewhere (A w a y a, 1956 ; I m a-m u r a, 1959 ; O d a, 1964), only a brief outline need be given here.

During the first 2 weeks of age the thymus was made up of lobules, each of which consisted of a predominant cortical area merging into a very small medullary portion. In the 3rd week there was observed a more normol appeaing archtecture with a relatively marked enlargement of the medullary portion, while other lymphatic tissues were still very imcompletely developed. With advancing age there occurred a more gradual involution accompanied by a cortical thinning with a medullary enlargement and a reduction in the parenchyma by an increase of fat in the connective tissues between the lobules (Figures 7–10). Since the thymus, from the quantitative views presented here, begin to regress at the age of the 3rd week, the relative enlargement of medullary protion herein presented might be regarded as a sign of the physiological age involution.

In the mesenteric lymph nodes, no nodular masses were discernible during one week. From the 2nd week on, solid secondary nodules (G r o l l and K r a m p f, 1920) and pseudo-secondary nodules (E h r i c h, 1929) made their appearance. The Flemming's secondary nodules began to occur as immature secondary nodules (A w a y a, 1956 ; I m a m u r a, 1959) from the 2nd week on, rapidly growing in size and number, reaching their full maturity between 2 and 4 months of age. In later stage, the Flemming's secondary nodules gradually underwent involutionary changes, which were characterized by a progressive increase in percentage of half-active and inactive forms (A w a y a, 1956 ; I m a m u r a, 1959). (Figures 11–16).

In the spleen, the differentiation of secondary nodules was somewhat delayed, but it proceeded in a manner similar to that of the maturation and involution of the preceding paragraph (Figures 17, 18). Up to 4 weeks of age, active myelopoiesis, erythropoiesis especially took place in the red splenic pulp. The fact that at the age of the first 4 weeks there is a greater number of nucleated cells per unit weight of spleen might be due to the active erythropoietic function of this organ during this age.

Thus, formation and maturation of Flemming's secondary nodules in the mesenteric lymph nodes and spleen took place actively from 2 to 4 months of age, when the greater magnitude of absolute as well as relative growth in these organs was observed from the quantitave data presented here.

DISCUSSION

The absolute growth in the organs under discussion was concluded in the 3rd or 4th month of age (in the 6th month in the male spleen), beyond which a progressive involution set in (Figures 2, 3 and 4). This fact fairly well agrees with the observations of Andreasen (1943), who made an extensive quantitave investigation on the same organs. Looking into their relative growth, however, the patern of the postnatal development was more characteristic of the individual organs, thymus in particular (Figures 5 and 6). At the ages of the 2nd week in females and the 3rd week in males, the relative growth of the thymus reached its maximum which was followed by progressive involution through the rest of the period studied. This fact offers distinct contrast to the relative growth of the mesenteric lymph nodes and the spleen. The mesenteric lymph nodes and the lymphatic tissue in the spleen initiated their development in the 2nd or 3rd weeks and their relative growths became most vigorous in 3 and 4 months of age. This fact implies that the thymus undergoes a very rapid "physiological" involution while the mesenteric lymph nodes and spleen still keep on growing. The results of the quantitative estimation presented here are almost mutually confirmatory with the histological findings in these organs in response to aging.

Recent work from several laboratories has established the fact that the thymus plays an essential role in maturation of immunological function and in the development of the anatomic integrity of the lymphoid tissues such as lymph nodes and spleen. Animals thymectomized at birth show a marked diminution of lymphocytes in their blood and tissues and present well marked defects in immune responses (Archer and Pierce, 1961; Miller, 1961, 1962; Martinez et al., 1962; Janković, Waksman and Arnason, 1962; Arnason et al., 1962; Arnason, Janković and Waksman, 1962; Burnet, 1962; Good et al., 1962; Dalmasso et al., 1963). These animals often develop a wasting syndrome with failure of body growth and early mortality (Good et al., 1962; Waksman, Arnason and Janković, 1962; Parrott and East, 1962, 1964; Sherman, Adner and Dameshek, 1962, 1963). The results presented here support the views of the reports referred to above regarding the thymus function.

Thus, it is our opinion that the thymus is fully developed at the 2nd or 3rd week of age, beyond which a rapid physiological involution takes place, and that this phenomenon may be closely related with further growth of other lymphatic tissues. Further work on this problem is at present in progress.

Finally, some mention must be made of the sex differences of the growth and involution in the thymolymphatic tissues. On the basis of per unit of body weight, the organ weights and the total number of nucleated cells in individual organs were found to be greater in females than in males throughout the period studied, although there were no sex differences in absolute growth. This indicates that the growth and involution of lymphatic tissues is influenced by sex factors. The endocine control of thymus and other lymphoid organs will be discussed elsewhere.

SUMMARY

In the present study, the postnatal growth and involution of the thymolymphatic tissues of the albino rats at different ages were studied chiefly by means of the quantitative analysis. The chief results are as follows :

1. The absolute growth of the thymus reached its maximum in the 3rd month in females and in the 4th month in males. The mesenteric lymph nodes, in both sexes, reached its maximum development in the 4th month, and the spleen in the 3rd month in females and in the 6th month in males (Figures 2, 3 and 4).

2. Looking into the relative growth, the thymus after reaching its maximum at the 2nd or 3rd weeks, underwent a rapid involution, while the mesenteric lymph nodes and spleen intiated their development in this period and were still growing in the 3rd or 4th months (Figures 5 and 6). This suggests that a rapid involution of the thymus may be closely related with further growth of the other lymphatic tissues.

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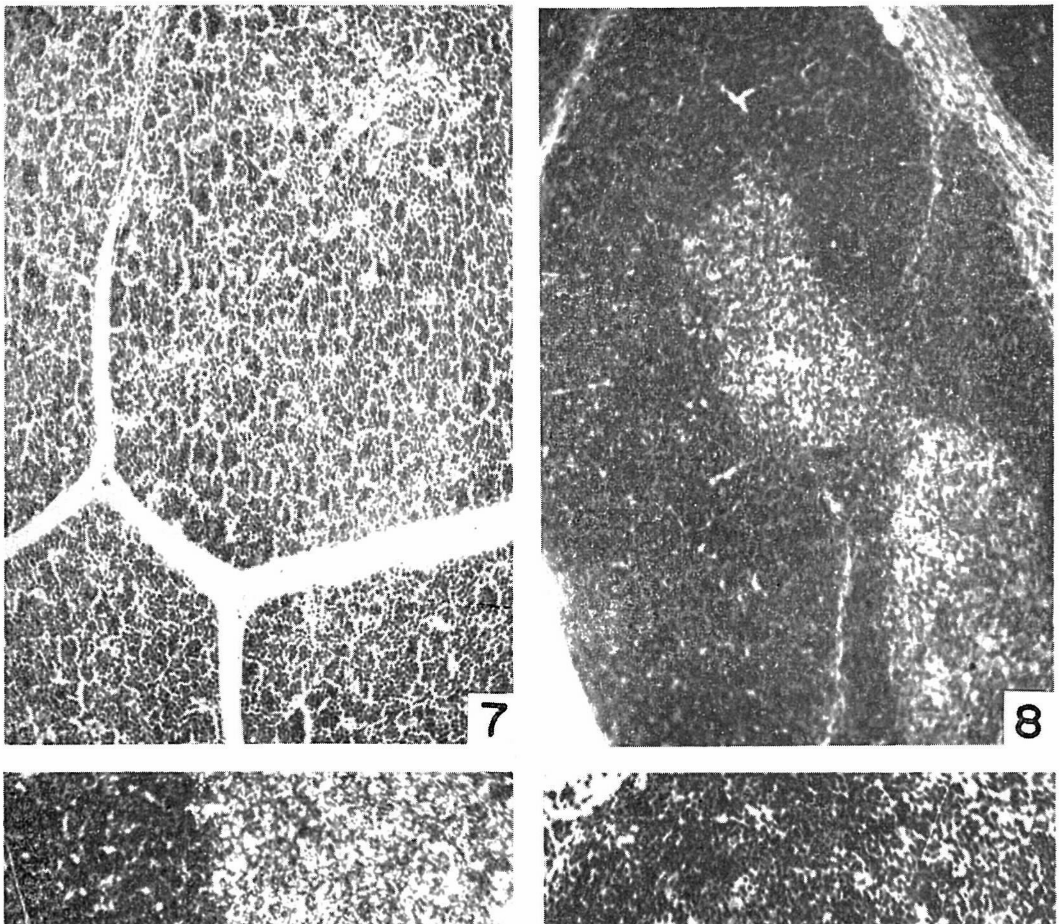
EXPLANATION OF PLATE 1.

Fig. 7. Thymus of a 1-week-old rat. Note four lobules, each of which consists predominantly of a cortical area merging into a very small portion of medulla. The greater majority of cells are thymocytes or small lymphocytes. Rat No. 76, ♀. ×100.

Fig. 8. Thymus of a 3-week-old rat. Note a cortex filled solidly with lymphocytes and a slightly enlarged medullary portion showing beginning age involution. Rat No. 33, ♀. ×70.

Fig. 9. Thymus of a 3-month-old rat. Note a relative enlargement of the medullary portion, showing further advaced age involution. Rat No. 93, ♀. ×70.

Fig. 10. Thymus of a 18-month-old rat. The atrophic parenchyma surrounded by fat and connective tissues, showing high grade age involution. Rat No. 18M-1, ♀. ×100.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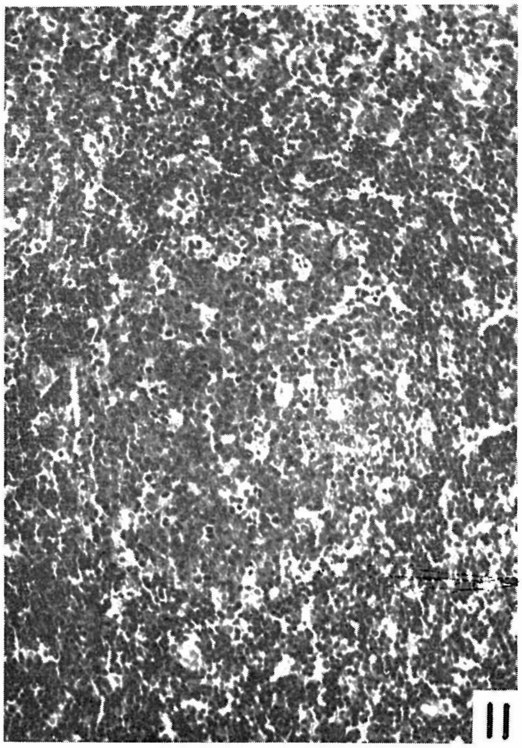
EXPLANATION OF PLATE 2.

Fig. 11. An active form of a mature secondary nodule of the FLEMMING type. Mesenteric lymph node cortex of a 3-month-old rat. Note the pale-staining center composed of densely packed, medium-sized lymphocytes with many mitotic figures. Rat No. 92, ♀. ×140.

Fig. 12. A half-active form of a mature secondary nodule of the FLEMMING type. Mesenteric lymph node contex of a 4-month-old rat. Note that the pale-staining center is half active and half non-active. Rat No. 4M-2, ♂. ×140.

Fig. 13. Two non-active froms of mature secondary nodules of the FLEMMING type. Mesenteric lymph node cortex of a 12-month-old rat. The centers are mainly composed of reticular cells and devoid of proliferating lympocytes. Rat No. 12M-8, ♂. ×100.

Fig. 14. An immature secondary nodule without outer zone of small lymphocytes (bare germinal center of CONWAY), consisting nearly of medium sized lymphocytes. Mesenteric lymph node cortex of a 3-week-old rat. Rat No. 33, ♀. ×200.



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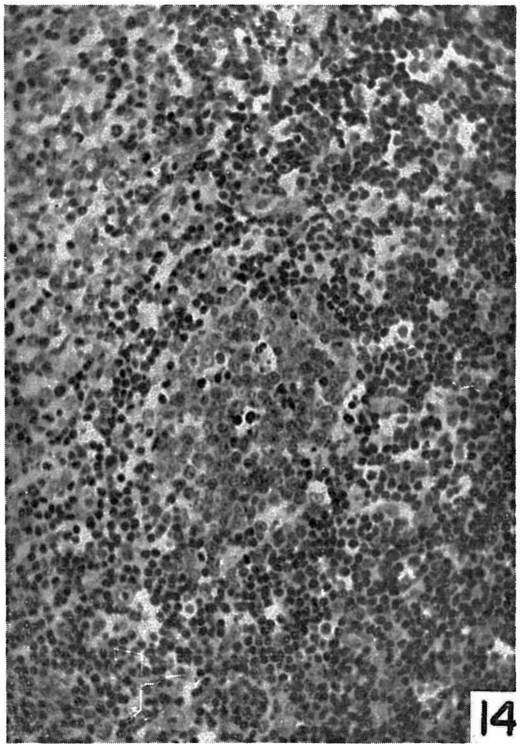

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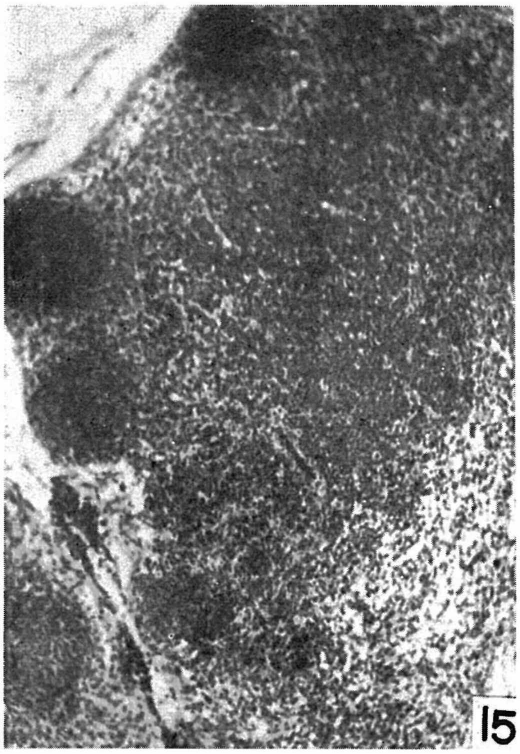
EXPLANATION OF PLATE 3.

Fig. 15. A pseudo-secondary nodule with several solid secondary nodules. Mesenteric lymph node of a 3-week-old rat. Rat No. 31, ♀. ×100.

Fig. 16. A post-capillary vein with extraordinarily large, oval endothelial cells (in the center of the figure). It contains some small lymphocytes. Greater magnification of the central portion of Fig. 15. ×400.

Fig. 17. Periarterial lymphoid sheaths seen in an early stage of development of splenic white pulp. Spleen of a 4-week-old rat. Rat No. 7, ♂. ×70.

Fig. 18. A germinal center just developing in the periarterial lymhpoid sheath. The same spleen as Fig. 17. ×200.



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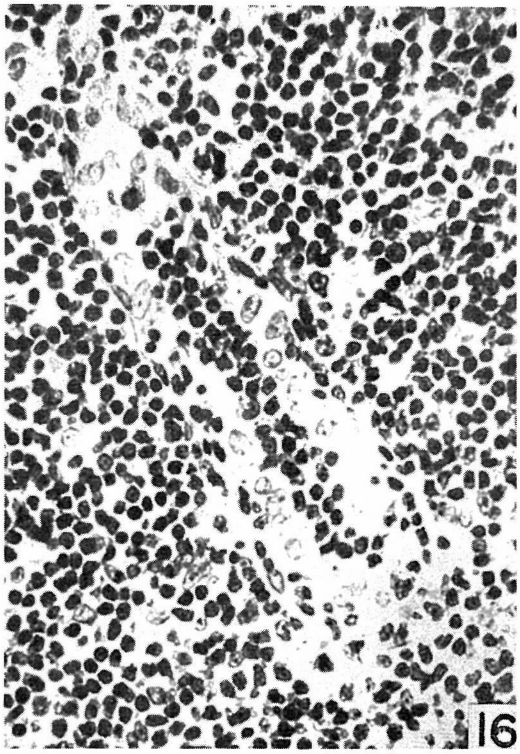

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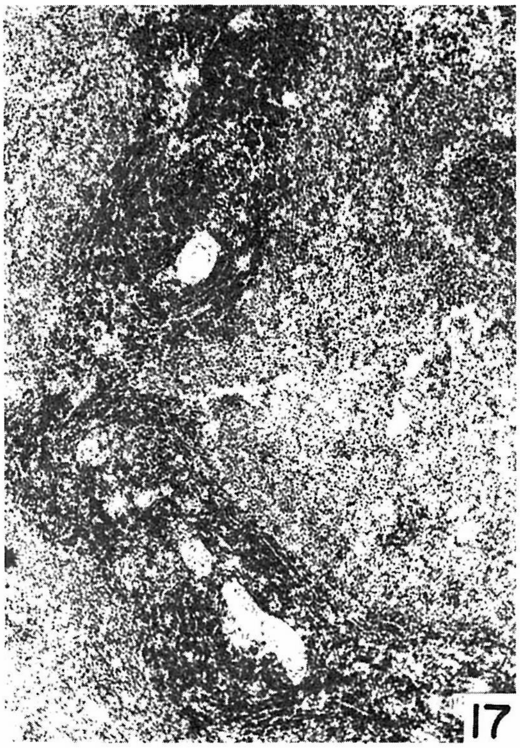

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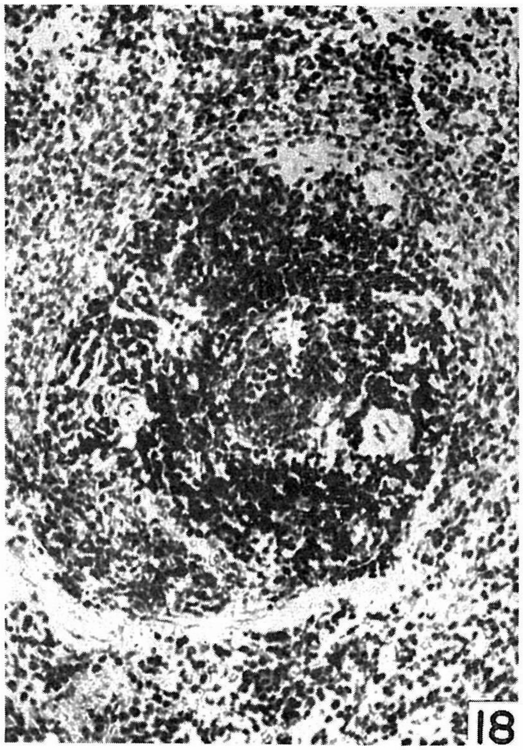

18