Thymic Lymphopoiesis and Cell Loss in Newborn Mice

By W. D. Michalke, M. W. Hess, H. Riedwyl, R. D. Stoner and H. Cottier

The role of the thymus as one of a controlling organ in the development of immunity has been advocated in recent years based on both clinical and experimental observations. The mechanism(s) whereby the thymus might directly or indirectly exert its influence on the lymphoreticular tissue throughout the body are not clearly understood.

In view of the massive number of lymphocytes being produced constantly within the thymic cortex of young mammals, it is essential to determine the ultimate fate of these cells. Metcalf and associates postulated that an overwhelming majority of thymic lymphocytes disintegrate within the thymus. Results from studies in newborn and young to adult animals indicate, however, an extensive migration of lymphocytes out of the thymus. The existence of some degree of thymic lymphocyte migration has been shown by regional labeling of the thymus with tritiated thymidine, followed by autoradiographic and radiochemical analysis of peripheral lymphoid organs. Autoradiographic studies using 3H-thymidine as a cell marker indicate that in young adult mice thymic lymphoid cells migrate from outer cortical zones into perivascular lymph channels near the cortico-medullary junction within 2 days and then disappear from this site. Most of these cells probably leave the organ by lymphatic vessels. Further studies on the magnitude of migration of thymic lymphocytes are especially needed in intact animals during the perinatal period since thymectomy performed at this stage of ontogenesis has been found to be more effective in depressing immunologic capacities than at a later age. For a meaningful assessment of this process more data are needed on the following parameters measured as a function of time prior to and after birth: 1) thymic weight; 2) percentage of thymic lymphoid cells in DNA synthesis; 3) DNA synthesis time and generation time of thymic lymphoid cells; and 4) percentage of thymic cells disintegrating per unit time. The first in a series of studies on Swiss albino mice indicated that: a) the increment of thymic weight, as a function of age, decreases sharply approximately one and a half day prior to birth, and b) the relative number of DNA synthesizing lymphoid...
cells in the thymus reaches a peak on days 3 and 4 after birth, without a concomitant increase in organ weight.

In the present study the labeling index and labeling intensity of mitotic figures are examined in two day old mice as a function of time after a single i.v. injection of \(^{3}\)H-thymidine. This combined analysis\(^{15}\) has been shown to require the least number of assumptions in evaluating autoradiographically the proliferative pattern of lymphoid cells using tritiated thymidine as a DNA precursor. DNA synthesis and generation times are compared to the thymic growth rate in the neonatal period as reported previously,\(^{14}\) and an estimate is given for the rate of cellular loss.

**Materials and Methods**

A total of 80 two day old specific pathogen-free, Swiss albino mice (Hale-Stoner strain) of both sexes were used in this study. At the end of the second day after birth each animal was given a single intraperitoneal injection of 1.0 mc./Gm. body weight of \(^{3}\)H-thymidine (Schwarz Bioresearch, Inc., Orangeburg, N.Y.; specific activity 1.9 c./mM, diluted in buffered 0.7 per cent saline, pH 7.4, to contain 200 \( \mu \)c./ml.).

Mice were killed under ether anesthesia in groups of two animals per time interval 10, 20, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 90, 100 and 110 minutes, 2, 23i and 3 hours, then each hour through 24 hours after administration of \(^{3}\)H-thymidine. One thymic lobe was fixed in buffered formalin for histologic examination and autoradiography. The other lobe was minced with sharp scissors in a drop of normal mouse serum. Within 8 ± 2 minutes after initiation of ether narcosis, smears were prepared with a fine brush, dried quickly and fixed for 10 minutes in absolute methanol. The fixed and air-dried preparations were dipped in liquid NTB\(_2\) photographic emulsion (Kodak, Rochester, N.Y.) in the darkroom, air-dried and stored at 4 C. in light-tight boxes with CaCl\(_2\) as desiccant. Autoradiographic exposure time was 51 days. The developed preparations were fixed, stained through the film with Giemsa solution buffered at pH 6.0 and mounted with a coverslip.

Lymphoid cells in mitosis were classified according to their morphologic and tinctorial characteristics as described previously.\(^{16}\) In particular the cell size was registered from the smallest size of cells in mitosis (grade 2) to the largest sizes (grade 6). Cells of size grade 1 were not found in mitosis. The various phases of mitosis (prophase, metaphase, anaphase and telophase) were recorded separately. Examples of the different types of mitotic figures are shown in Figure 1.

**Autoradiographic Analysis**

For each mouse killed an average of 100 mitotic figures was counted. The number of grains over the nuclear chromatin was registered in smear preparations. Corrections for background were made by counting in each autoradiographic preparation the number of grains in 200 cell free fields with a surface comparable to that of the average size of nuclear chromatin in mitotic figures.

**Results**

In contrast to the findings on the lymphoid cell population of the thoracic duct in calves,\(^{17}\) it was not possible in smears of the newborn mouse thymus to differentiate clearly two or more separate lines of lymphoid cells on the basis of the degree of cytoplasmic basophilia. The vast majority of thymic lymphoid cells in newborn mice have a very thin cytoplasmic rim and, for a given size class, show a comparable degree of cytoplasmic basophilia. There-
Fig. 1.—Examples of thymic lymphoid cells in mitosis (cell sizes 2-5): Prophase (5), metaphase (4), anaphase (3) and telophase (2). (Autoradiographs of smear preparations, Giemsa; yellow filter; enlargement × 2000).
Fig. 2.—Variation of the labeling index of all thymic lymphoid cells in mitosis, and of two groups of different sizes (2 to 6: small to large), as a function of time after a single i.p. injection of $^3$H-thymidine. The curves show a remarkable coincidence.

Therefore, mitotic figures of thymic lymphoid cells could only be classified according to their size.

The per cent labeled mitoses (MLI = mitotic labeling index) of all, and of two groups of thymic lymphoid cells with different nuclear sizes are represented in Figure 2 as a function of time after injection of $^3$H-thymidine. After correction for background, no labeled mitotic figure was found in the samples obtained from mice sacrificed up to 40 minutes after administration of the tritiated precursor. Then the MLI-curve (MLI as a function of time after injection of $^3$H-thymidine) for all grade sizes starts to rise and reaches an abortive first peak at 65 minutes. The grain numbers of the labeled mitotic figures at these early time intervals are very low, in fact near the background level. The steepest rise of the MLI occurs between 80 and 110 minutes from 14.6 per cent to 82.6 per cent; at the 100 minutes interval 100 per cent of prophases were labeled. From 2 to 8 hours following injection of $^3$H-thymidine the MLI oscillates between 90 per cent and 100 per cent. A sharp drop of the curve from 92.7 per cent to 55.7 per cent is noted between the 8 hour and 9 hour interval. Thereafter, no second, equally high peak of the MLI curve is observed although the values remain on a plateau of 64–72 per cent from the 11 hour to the 16 hour interval. A higher peak of 88 per cent is reached at 17 hours, followed by a drop of the curve to 56.8 per cent at 18 hours.

If the MLI is recorded separately for mitotic figures belonging to size grades 2 and 3 and compared to that of size grades 4–6, both as a function of time after injection of $^3$H-thymidine, a remarkable coincidence of the two
curves is found (Fig. 2). It should be noted, however, that mitotic figures of size grade 6 were very rare, and the curve obtained may not be representative of the largest dividing cells.

In Figure 3 the variation of the MLI of all lymphoid mitotic figures with 3 and more, 5 and more, 7 and more, and 9 and more grains are shown as a function of time after administration of \(^{3}\)H-thymidine. On this diagram the periodicity of the descending slopes of the first and the abortive second peak, at 8 to 9 hours and 17 to 18 hours respectively, is more clearly visible. In addition, this graph demonstrates that many labeled mitotic figures are covered by only few grains.

Individual grain counts as well as the median grain count per labeled mitotic figure (MGC/LMF) are represented in Figure 4 at hourly intervals as a function of time following injection of \(^{3}\)H-thymidine. When this curve is compared with MLI curves (Fig. 2 and 3), the following may be noted: during the first peak of the MLI curve between 2 and 8 hours after injection of \(^{3}\)H-thymidine a corresponding plateau with peaks at 5 hours (median grain count per labeled mitotic figure: 23) and 8 hours (median grain count per labeled mitotic figure: 21) is observed in the MGC/LMF curve. During the abortive second peak of the MLI curve, from 11 hours to 17 hours after injection of \(^{3}\)H-thymidine, the corresponding MGC/LMF values oscillate between 7 and 11 grains, i.e., approximately half the labeling intensity found during the first peak of the MLI curve.

The initial variation of the MLI as a function of time after injection of \(^{3}\)H-thymidine is shown in Figure 5 in more detail. Between the 90 minute and

Fig. 3.—Variation of the labeling index of thymic lymphoid mitotic figures with different degrees of labeling intensity, as a function of time after a single i.p. injection of \(^{3}\)H-thymidine.
the 110 minute interval the curve rises from 11.1 per cent to 82.6 per cent, i.e., by 71.5 per cent. If we extrapolate the tangent of this steep part of the slope to the zero and 100 per cent lines, a time interval of approximately 27 minutes is obtained. If, on the other hand, the MLI values at 100 and 110 minutes are used for construction of the tangent, the resulting time is 44 minutes.

No attempt was made to evaluate the labeling index and intensity of mitotic figures in autoradiographic preparations of histologic sections. The
THYMIC LYMPHOPOIESIS AND CELL LOSS

latter served to localize the relative number of dividing cells in relation to various zones of the thymus. It became evident that most mitotic figures are located in the outer half of the cortex and very few (less than 5 per cent) in the medulla. This indicates that the great majority of mitotic figures counted represent cortical and not medullary lymphoid cells.

During the observation period the overall mitotic index in smears corresponded to that reported earlier (1.0–1.7 per cent14). The mitotic index of larger lymphoid cells (size grades 2-6) varied between 3 and 7 per cent. No systematic drop of the mitotic index was noted during the 24 hours following injection of 3H-thymidine.

In all smears a small percentage of cells was disrupted. The labeling index of disrupted cells was considerably higher than the overall labeling index of all thymic lymphoid cells.

DISCUSSION

The interpretation of results is based on the following assumptions:

a. The availability time of 3H-thymidine, after intraperitoneal injection, is short for thymic lymphoid cells.

b. The proliferating thymic lymphoid cells are capable of incorporating 3H-thymidine into macromolecular DNA during DNA synthesis.

c. Labeled DNA is stable until cell death.

d. A dose of 1µc./Gm. body weight of 3H-thymidine does not interfere markedly with the physiologic proliferative activity of thymic lymphoid cells.

There is no evidence at present that the above assumptions are incorrect. In two day-old mice more than 90 per cent of all dividing lymphoid cells are located in the cortex, thus our data relate mainly to cortical elements.

Duration of G2. (Phase in the generative cycle between the end of DNA synthesis and onset of mitosis).

Since no labeled mitoses were found in samples taken from mice sacrificed 10, 20, 30 and 35 minutes after i.p. injection of 3H-thymidine while large lymphoid cells in interphase were labeled almost immediately, the shortest duration of G2 (phase in the generative cycle of cells between the end of DNA synthesis (S) and onset of prophase) is approximately 35 to 48 minutes. A time period of up to 8 minutes should be added to the interval between injection of 3H-thymidine and the appearance of the first labeled prophase (at 40 minutes) because smears were dried and fixed within an average time of 8 minutes after sacrifice of the animals and the MLI curve is based on killing time. It is probable that development of cells through the cell cycle did continue to some extent until the smears were dried. The value of 35–48 minutes represents a minimum duration of G2 for a small group of cells with a short transit time from the completion of DNA synthesis to the onset of morphologically detectable mitosis (M). These may not necessarily be the fastest moving elements since

1) DNA synthesis could have been prolonged without a change in the total time for S + G2 + M and/or

2) early prophase may have been particularly well detected in these cells.
It was not possible to relate this small group of cells with an apparently short 
G2 phase to any particular nuclear size. Further studies are necessary to 
examine their localization within the cortex and medulla. The duration of G2 
for the majority of all lymphoid cells is most probably longer than 35–48 
minutes; if a straight line through the MLI values at the 90 and 110 minute 
intervals is extrapolated to the zero line, a value for G2 of 86–94 minutes is 
obtained. Autoradiographic inefficiency or incomplete correction for back-
ground may also have influenced the variation of the MLI as a function 
of time after injection of 3H-thymidine. However, the low median grain count per 
labeled mitotic figure did not influence appreciably the steepest slope of the 
MLI curve as shown in Figure 3.

**Duration of M (mitosis).**

Evaluation of mitotic time by extrapolating the tangent of the steepest 
slope of the first ascending part of the MLI curve to the zero and 100 per cent 
lines is subject to a number of assumptions and gives only approximate 
values. With these restrictions in mind, mitotic time for the majority of cells 
may be 27–44 minutes or less. A better assessment of mitotic time by measuring 
the prophase-telophase time\(^1\) will be reported later. Based on the present 
data the total duration of G2 + M could be as short as 62 minutes for a small 
group of cells, whereas 113–138 minutes is a reasonable estimate for the ma-
jority of cells. This value is higher than that reported for thymic lymphoid cells 
of 2 month-old AKR mice (G2 + M : 1.3 hours\(^1\)).

**Duration of S (DNA synthesis).**

Duration of S phase can be estimated on the basis of the variation of MLI 
as a function of time after injection of 3H-thymidine in two ways:

1) by measuring the time interval between the point where on the first ascend-
ing slope the MLI curve reaches 50 per cent and the point where the 
extrapolated line of the descending slope crosses 50 per cent. By this ap-
proach, a duration of the S phase of approximately 7 hours (Fig. 2) may 
be estimated from our data for the majority of cells.

2) by measuring the time that elapses between the appearance of the first 
labeled mitotic figures (or: where the extrapolated tangent of the steepest 
ascending slope of the MLI curve crosses the zero line) and the reap-
pearance of a considerable percentage of unlabeled mitotic figures (or: 
where the extrapolated tangent of the steepest descending slope of the 
MLI curve crosses the 100 per cent line). According to these methods 
DNA synthesis time for the majority of cells would be 6¾–7½ hours, 
probably close to 7 hours.

Again, the value of approximately 7 hours for the duration of S phase in 
proliferating thymic lymphoid cells is higher than that reported for 2 month 
old AKR mice (5¾ hours\(^1\)).

**Generation Time and Duration of G1 (phase in the generative cycle 
between the end of mitosis and the onset of DNA synthesis).**

As discussed previously\(^1\) it is hazardous and, for practical purposes, almost
impossible to determine the generation time of lymphoid cells by trying to establish a mean grain count halving time for initially labeling types of lymphoid cells since the mean grain count of interphase cells is not a single exponential but a very complex function of time after injection of $^3$H-thymidine. A combined evaluation of the labeling index (MLI) and the mean grain count per labeled mitotic figure (MGC/LMF) represents a better method for estimating the generation time of lymphoid cells. In the present study, the MLI as a function of time after injection of $^3$H-thymidine did not follow a curve with two consecutive peaks of equal height, the second peak being abortive and reaching only 64–88 per cent. A clear-cut periodicity of the ascending slopes of the two consecutive peaks is therefore difficult to visualize. However, a periodicity is more easily seen in the descending slopes of the two consecutive peaks (Fig. 3) which are approximately 9¾ hours apart. This finding together with the fact that the MGC/LMF, as a function of time after administration of the labeled precursor, falls from a first peak around 5–8 hours to approximately half the values in the period from 14 to 17 hours may be considered as good evidence in support of a generation time of 9¾ hours for the majority of cells. This is longer than the mean cell cycle time reported for thymic lymphoid cells in 2 month old AKR mice (6.8 hours for large, 8.2 hours for medium lymphoid cells$^{19}$). A direct estimate of the duration of G$_1$ is not possible on the basis of present results. If the above estimates for the duration of S + G$_2$ + M are subtracted from the proposed generation time of 9¾ hours, little time is left for G$_1$. It may be recalled that the availability time of $^3$H-thymidine should be subtracted from the calculated duration of S-phase in favor of G$_1$.

**Generation Time of Thymic Lymphoid Cells of Different Size.**

The data obtained from our study do not allow the conclusion that larger lymphoid cells have a shorter generation time than medium size elements. The MLI as a function of time after injection of $^3$H-thymidine gives practically superimposable curves for lymphoid cells of size grades 2 + 3 vs. 4–6. This finding differs from results reported for thymic lymphoid cells of adult AKR mice$^{19}$ or rats.$^{20}$ It should be remembered, however, that very few cells of size grade 6 were found. Therefore, a shorter or longer generation time for the very largest lymphoid cells cannot be excluded on the basis of the present data.

**Comparison of Estimated DNA Synthesis and Generation Time of Proliferating Thymic Lymphoid Cells with Changes of Thymic Weight.**

As reported previously$^{6,14}$ the mean thymic weight of Hale-Stoner mice at the end of day 2 after birth (7.7 mg.) increases by 1.7 mg. or 22.05 per cent to the end of day 3 after birth (9.4 mg.). The growth process of the mouse thymus after birth can be characterized by a regression line based on measured organ weight$^{14}$:

from the regression coefficient

$$b = 0.07682$$

the growth rate is calculated as follows:
\[
\log (\text{weight} \cdot 10) = a + 0.07682 \ t \\
(\text{t = time in days})
\]

or expressed in natural logarithms (\(\log x = 0.4343 \ln x\))

\[
\ln (\text{weight} \cdot 10) = a' + 0.17689 \ t.
\]

Therefore

\[
\text{weight} = k_1 e^{0.17689 t} \\
(\text{k}_1 = \text{a constant})
\]

with a growth rate of 0.17689 per day.

Between 48 hours and 72 hours after birth (observation period) the initial labeling index for all thymic lymphoid cells after injections of \(^3\text{H}-\text{thymidine}\) increases from 12 per cent (end of the second day after birth) to 19 per cent (end of the third day after birth\(^4\)). Based on the generation time (9.5 hours) and the DNA synthesis time (7 hours) obtained from the present study, it may be estimated that the duration of S is 75 per cent of the generation time. If we compare these values with the above overall initial labeling indices after injection of \(^3\text{H}-\text{thymidine}\), it may be postulated that 15.85 per cent of all thymic lymphoid cells actively proliferate at the end of day 2 after birth, and 25.11 per cent at the end of day 3. A theoretical increase in number of thymic lymphoid cells during this period can be calculated based on these values if the assumption is made that no cell dies or leaves the organ. Such a situation may be compared to a simple birth process where a dividing cell gives off two daughter cells. In a constantly expanding population the number of individuals at a given time (\(N_t\)) depends on the number of individuals present at the beginning (\(N_0\)) and on a constant rate of population increase (\(\lambda\)):

\[
N_t = N_0 e^{\lambda t}
\]

If we assume a mean growth fraction ( = fraction of cells in proliferation) of 20 per cent and a generation time of 9.25 hours for the majority of cells, the following rate of increase is obtained:

\[
N_{0.25} = N_0 = 0.2 \ N_0
\]

Under these conditions the increase in number of individuals during one generation time is 0.2 \(N_0\) (= the number of cells in proliferation at the beginning since this fraction is able to double between time zero and 9.25 hours):

\[
N_{0.25} = 1.2 \ N_0 = N_0 e^{0.25 \lambda}
\]

Therefore

\[
\lambda = 0.0197 \approx 0.02 \text{ per hour}
\]

e.g. an hourly increase of 2 per cent.

Under the assumption of a simple birth process and a constant birth rate (Yule-Furry-process) the increase in number of thymic lymphoid cells between day two and day three after birth can be expressed as follows:

\[
N_{24} = N_0 e^{0.0197 \cdot 24} = N_0 e^{0.4728} = 1.60 \ N_0 \quad (\text{A})
\]

if no cell death occurs and no cell leaves the organ.

Since the initial labeling index of thymic lymphoid cells following injection of \(^3\text{H}-\text{thymidine}\) increases in an approximately linear fashion from the second to the third day after birth\(^4\), it seems preferable to assume a simple birth process with a linear change in the birthrate:
Birthrate on day 2 (growth fraction 15.85 per cent):
\[ \lambda_2 = \frac{1}{t} \ln \frac{1.1585}{9.25} = 0.016 \]
Birthrate on day 3 (growth fraction 25.11 per cent):
\[ \lambda_3 = \frac{1}{t} \ln \frac{1.2511}{9.25} = 0.024 \]
Linear change in the birthrate as a function of time:
\[ \lambda_t = 0.016 + \frac{0.008}{24} t \] (t in hours)
Therefore
\[ \int_0^{24} \lambda_t \, dt = \int_0^{24} [0.016 + \frac{0.008}{24} - t] \, dt = 24 \cdot 0.02 \]
and
\[ \int_0^{24} \lambda_t \, dt = 24 N_{24} = N_{0 \text{eo}} = N_0 e^{0.18} = N_0 \cdot 1.60 \] (B)
This result is identical to the value obtained in (A).

The difference between the experimentally observed growth process as based on thymic weight changes between day 2 and day 3 after birth and the values obtained from theoretical evaluation of the cell birth process in the same period is shown on Figure 6. For convenience it is assumed in this diagram that increase in number of lymphoid cells parallels increase in weight. In fact, the difference may even be greater than one third of the number of lymphoid cells present in the thymus at the end of day 3 after birth since a) the growth fraction and, therefore, the relative number of large lymphoid cells is greater at the end of day 3 than at the end of day 2, and b) autoradiographic inefficiency would lead to an underestimate of the relative size of the growth fraction. This latter possibility must be taken into consideration since many labeled thymic lymphoid cells have low grain counts (Fig. 4).

Theoretically, both migration of cells out of the thymus and intrathyMIC cell death could account for the difference between observed thymic weight changes and calculated thymic cell birth processes. Any influx of cells via the blood stream into the thymus, the existence and magnitude of which is unknown in newborn mice, would even increase this difference. It will be reported later that the thymus of newborn, 1 to 4 day old mice contains but very few disintegrating cells, i.e., 2.5 ± 0.25 (cortex) or 7.3 ± 0.5 (medulla) nuclear fragments per 10^4 lymphoid cells counted. This extremely low pyknotic index could not explain the calculated cell loss on the basis of cell death alone if the process of cell lysis is not assumed to be many times shorter than any comparable process known in mammalian pathology. Since the latter assumption is less than plausible, the present data are best interpreted by an extensive migration of lymphoid cells leaving the mouse thymus at this age. Thymic lymphoid cell peripheralization may be less important in older animals. The ultimate fate of thymic small lymphocytes that have reached the blood stream, probably via lymphatic channels, remains to be elucidated. If experiments based on intravenous injection of ^3H-5-uridine-
Fig. 6.—Comparison of the experimentally observed weight increase of mouse thymus between days 2 and 3 after birth with theoretically expected weight changes under the assumption that no cells die or leave the organ. The difference between the two curves (shaded area) gives an estimate of thymic cell loss.

labeled lymphocytes may be compared to physiologic conditions, thymic lymphocytes contribute only a minor fraction to the recycling lymphocyte pool. Further studies are also needed to examine the migrational behavior of cortical versus medullary thymic small lymphocytes.

**Summary**

Thymic lymphopoiesis in 2 day old Swiss albino mice (Hale-Stoner strain) was studied autoradiographically based on the variation of mitotic labeling indices and intensities after a single intraabdominal injection of $^3$H-thymidine. Best estimates for the duration of various phases of the generative cell cycle are as follows: G2 for the majority of cells: 86–94 minutes, shortest possible duration for a small fraction of cells: 35–48 minutes; mitosis: 27–44 minutes; DNA synthesis: 7 hours; generation time: 9½ hours. G1 could not be determined directly by the methods used but probably is short. The present data do not indicate different generation times for proliferating thymic lymphoid cells of unequal size although the very largest elements must be excluded from this statement because of rare occurrence. The results obtained in this study together with data on changes of thymic weight and proliferative activity in the neonatal period indicate that during the third day after birth,
a fraction corresponding to one third of all lymphoid cells present in the organ at the end of this period is lost. In view of the extremely low pyknotic index in the thymus at this age, the present data provide support in favor of an extensive emigration of lymphoid cells being the major cause of this cell loss.

SUMMARIO IN INTERLINGUA

Le lymphopoiese thymic in muses albin switze (linea Hale-Stoner) de duo dies de etate esseva studiate autoradiographicamente in terminos de variationes in le indices marcatori mitotic e del intensitates post un sol injection intra-abdominal de thymidina a tritum. Le melior estimationes del duration del varie phases del cyclo generatori cellular es le sequentes: C_2 pro le majoritate del cellulas—86–94 minutas (le plus breve duration possible pro un fraction de cellulas—35–48 minutas); mitose—27–44 minutas; synthese de acido desoxyribonucleic—7 horas; tempore de generation—9¾ horas. C_1 not poteva esser determinate directemente per le methodos usate, sed il es probable che illo es breve. Le datos hic presentate non indica differente tempores de generation pro proliferante cellulas lymphoide thymic de inequal dimensiones, ben que le elementos le plus marcatemente grande debe esser exclute ab iste assertion proque lor occurrence es rar. Le resultatos obtenite in le presente studio, insimul con datos relative a alterationes del peso thymic e del activitate proliferatori in le periodo neonatal, indica che durante le tertie die post nato un fraction correspondente a un tertio de omne le cellulas lymphoide presente in le organo al termino de iste periodo es perdite. Viste le extrememente basse indice pyknotic in le thymo a iste etate, le presente datos provide supporto pro le these de un extense emigration de cellulas lymphoide como causa major de iste perdita de cellulas.

ACKNOWLEDGMENTS

We acknowledge the valuable technical assistance of Miss C. Markwalder and Mr. R. Okula.

REFERENCES


Thymic Lymphopoiesis and Cell Loss in Newborn Mice

W. D. MICHALKE, M. W. HESS, H. RIEDWYL, R. D. STONER and H. COTTIER