PROLONGED SURVIVAL of a significant fraction of small lymphocytes was suggested by Ottesen and by Hamilton. Their findings at first seemed incompatible with the observation that lymphocytes leave the thoracic duct at a rate sufficient to replace all circulating forms within hours. However, continuous recirculation of lymphocytes between lymph and peripheral blood was then demonstrated by Gowans. This observation explained how the same population of cells could have a prolonged survival, and yet an apparently rapid turnover in the circulation. Direct measurement of the life span of small lymphocytes by isotopic DNA labeling remained a problem, however, because of the possibility of continued label transfer into newborn cells. This difficulty was overcome by continuous intravenous infusion of H-thymidine, which insured incorporation of the label into all cells newly formed by division. Under these circumstances, circulating unlabeled small lymphocytes must have originated from mitoses antedating the infusion, and their survival therefore measured lymphocyte life spans. In such studies from this laboratory 50 per cent of lymphocytes in the rat were replaced by labeled forms by the end of 1 month and 10 per cent were still unlabeled after 3 months of infusion.

This paper reports studies in which H-thymidine was given to rats for 6–9 months in an attempt to measure the maximum life span of the small lymphocyte. In additional experiments the disappearance of labeled cells was measured after 2–3 weeks of continuous H-thymidine infusion. Some of these animals then received infusions of large amounts of nonlabeled (“cold”) thymidine in order to suppress H-thymidine reutilization. It was hoped that infusions of 2–3 weeks duration would label the major portion of the precursors of peripheral blood cells in marrow and lymph nodes and that the disappearance curve after discontinuation of the radioisotope would reflect the turnover of the precursors, when reutilization was suppressed. The results did not permit such a simple interpretation. However, they provided unexpected insights regarding the distribution of life spans of small lymphocytes.
MATERIALS AND METHODS

Thymidine was administered by continuous intravenous infusion through a tail vein catheter. A specially designed, leak-proof "swivel-conduit" interposed between the electrical pump and the delivery tubing allowed the animal freedom of movement. The flow rate was 0.9 ml. per day. Female Sprague-Dawley rats, weighing 145-175 g., at the beginning of the experiments, received 0.30 μc. of H\textsuperscript{3}-thymidine\textsuperscript{*} per gm. of body weight per day, dissolved in sterile normal saline.

Heparin was added to the infusion fluid in a concentration of 10 units per ml., as a precaution against occlusion of the catheter. Penicillin, 100 units per ml., and streptomycin, 130 μg per ml., were added to prevent bacterial growth in the infusion fluid. Prior experiments had established that these additions did not alter the results.

Of the rats infused with H\textsuperscript{3}-thymidine for prolonged periods, 1 animal received thymidine for 271 days; the infusion was interrupted twice: for 2 days starting on day 90, and for 5 days starting on day 223. Another rat received an infusion for 234 days, with an interruption from day 145 to day 146. During these interruptions, the animals received the usual daily dose of thymidine in 2 intraperitoneal injections at 12-hour intervals. Other animals were infused for 189 days (interrupted from day 69-70), 123 days, 119 days, 85 days, 77 days, 57 days (interrupted from day 19-20 and 36-40), 33 days, and 28 days. Flow was continuous in all other animals which received infusions for shorter periods of time.

Most of the longer infusions were interrupted or terminated because of technical problems. In many instances, studies were then continued through the fall-off phase of labeling.

For systematic studies of the disappearance of labeled cells after discontinuation of the radioisotope, 11 animals were given H\textsuperscript{3}-thymidine for 17 days. Seven of the 11 received no subsequent "cold" thymidine. In 2 of them, the catheter was occluded, but left attached to the swivel-conduit. One animal received an infusion of sterile saline containing heparin and antibiotics. Four animals were disconnected from the infusion apparatus and kept in ordinary laboratory cages. The findings in all seven animals were similar and the results were therefore pooled as control data. The remaining 4 rats received continuous infusions of nonradioactive thymidine\textsuperscript{+} in an attempt to suppress reutilization of the label during the fall-off period. Two of the 4 received 1.9 mg. of "cold" thymidine per ml. of infusion fluid, or 1.7 mg. per day; the others received 50 mg. per ml., or 45 mg. per day. The former dose represents a 300-fold and the latter a 7900-fold excess of thymidine compared with the original radioactive infusion. The solutions were sterilized by Seitz filtration or by autoclaving; chromatographic analysis, kindly performed by Schwarz BioResearch, Inc., Orangeburg, New York, revealed no breakdown of thymidine after autoclaving.

In order to evaluate possible direct effects of nonisotopic thymidine upon leukocyte kinetics, 2 rats received infusions of cold thymidine, 1.7 mg. per day, for 20 days prior to the infusion of H\textsuperscript{3}-thymidine.

Blood for peripheral blood smears, white blood cell counts, and hematocrits was taken from the retro-orbital plexus using heparinized Pasteur pipettes. The method readily provided enough blood for smears. However, to obtain enough for total white blood cell counts often required multiple attempts and appeared unduly traumatic to the animal. Since no systematic changes in total counts were noted when sufficient blood was obtained without special effort, no attempt was made to do a total count at each sampling.

Radioautographs were prepared from the blood smears using Kodak N.T.B.-3 Emulsion with exposure for 30 days at −15 C. All smears from 1 animal were processed simulta-

\textsuperscript{*}Tritiated thymidine, 1.9 c/Mm, was obtained from Schwarz BioResearch, Inc., Orangeburg, New York.

\textsuperscript{+}Grade A reagent, Calbiochem, Los Angeles, California.
neously, except in some of the very long infusion experiments. On occasion, particularly toward the end of long term infusions, slides were exposed for 6 months so that low intensity labeling would not be overlooked. In no instance was there a significant increase in the percentage of labeled cells with the longer exposure time.

Radioautographs were read by technologists who were unaware of the specific details of experimental design. Usually a total of 200 cells was counted on each preparation. Cells were classified as granulocytes, small and large lymphocytes, and monocytes, and were reported as containing 0, 1, 2, 3, 4–5, 6–10, 11–15, 16–25, and over 25 grains per cell. For computation of mean grain counts, the "over 25" category was assumed to have a mean grain count of 30, although this was sometimes a conservative estimate.

Unlabeled smears were processed along with the experimental preparations for background correction. Only rare grains were found overlying cells, and correction for background was therefore not necessary in most instances.*

Means and standard errors were computed for per cent labeling and mean grain counts of all cell types except monocytes, which were observed only rarely. Curves were drawn from these values by the method of moving averages.7

The means and standard errors which appear in the figures often do not refer to all the animals used in a given experiment. Blood samples were not always taken on the same days during and after the H3-thymidine infusions. Furthermore, when infusions were of different durations, data were available from fewer and fewer of the original animals with increasing time. This was particularly true in the long-term tracer experiment (fig. 2). Thus, all data available for a given day after starting or stopping H3-thymidine were used to compute the means and standard errors. Isolated points in the figures indicate observations from only one animal on that day.

RESULTS

Percentage labeling of granulocytes during continuous H3-thymidine infusion is presented in figure 1. Labeled polymorphonuclear leukocytes rapidly replaced unlabeled cells and about 95 per cent were labeled by the third or fourth day. In most animals the remaining unlabeled polys disappeared between days 4 and 6. A few animals reached 100 per cent labeling only between days 7 and 17. Thereafter, with very rare exceptions, polys remained 100 per cent labeled throughout the duration of the tracer infusions. Technical factors, not understood at present, were thought to account for sporadic unlabeled cells. It appeared improbable that these were the result of prolonged storage of mature granulocytes or long delayed maturation without division of precursors produced before the start of the infusion.

An unexpected distribution of granulocyte labeling was noted on day 3; 45–56 per cent of granulocytes were labeled in 5 rats, whereas 91–100 per cent were labeled in the other 6 animals. This is indicated in figure 1 by the significantly different means of 50 per cent and 95 per cent on day 3. Periodic release of granulocytes from the marrow is a possible explanation, since blood smears were sometimes taken at different times of day. If a diurnal variation in release of granulocytes exists, it might be a sequela of diurnal variation of entry into mitosis which has been observed by Pilgrim

*As noted by others, grains in areas not occupied by cells were usually appreciable in control slides, even though grains over cells were rare. The density of these grains in experimental slides, however, did not exceed that in controls.
The labeling curve for small lymphocytes is given in figure 2. Initially, labeling was rapid with 10 per cent labeled on day 1 and 30 per cent on day 5. Thereafter, there was a progressive decrease in the rate of labeling. Ninety per cent of lymphocytes were labeled consistently only after 220 days of H³-thymidine administration, and 5-8 per cent were still unlabeled after 271 days of infusion.

Labeling of large lymphocytes was more variable, probably because of their lesser number and the necessarily arbitrary separation from small lymphocytes. In most animals, however, nearly all large lymphocytes appeared labeled by day 3 to 5. Thereafter, values fluctuated between 85 and 100 per cent, and in very few animals was 100 per cent labeling maintained consistently throughout the infusion period.

The labeling pattern of small lymphocytes following 17 days of H³-thymidine infusion is presented in figure 3. When H³-thymidine was discontinued, there was an abrupt increase in the percentage of labeled lymphocytes. This was not an artifact due to pooling of results, but was observed in each animal in the group. The subsequent, expected fall in the percentage
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Fig. 2.—Per cent labeling of small lymphocytes in rats receiving continuous H^3-thymidine (H^3-TDR) infusion. (Means do not always refer to all 30 animals. See Methods.)

Fig. 3.—Per cent labeling of small lymphocytes during and after 17 days of H^3-thymidine (H^3-TDR) infusion. Four animals received infusions of nonisotopic thymidine (TDR) to suppress label reutilization during the fall-off period. (Means do not always refer to the total number of rats in each group. See Methods.)
of labeled cells was more rapid when cold thymidine was infused (dashed line) than without such infusion (solid line). Similarly, infusion of cold thymidine following 17 days of tracer infusion greatly accelerated the fall-off in the percentage of labeled granulocytes (fig. 4).

The granulocyte turnover after 17 days of H3-thymidine infusion is further analyzed in figure 5. The dashed line is identical with the dashed curve in figure 4 and represents the disappearance of labeled granulocytes in 4 rats in which reutilization was suppressed by infusion of cold thymidine. The solid line represents the fall-off of unlabeled granulocytes during tracer infusion, a direct expression of granulocyte survival. The slower disappearance of labeled cells is accounted for by continued production of mature granulocytes from labeled precursors in the marrow. The dash-dotted line represents the disappearance of granulocytes with 16 or more grains after discontinuation of H3-thymidine in the same 4 rats in which reutilization was suppressed by cold thymidine. The disappearance of these heavily labeled cells should reflect the actual life spans of granulocytes from the last myelocyte division: having suppressed reutilization, any division of a labeled precursor should halve the grain count and thus remove the daughter cells from the “over 16” category, since few cells with more than 30 grains were observed during infusion. Similarly, unlabeled cells observed during the tracer infusion (solid line) cannot have received any contribution from the precursor compartment since DNA synthesis preparatory to division must result in labeled progeny. Therefore, the rate of disappearance of heavily labeled cells after H3-thymidine infusion was expected to be a direct coun-
Fig. 5.—The disappearance curve of unlabeled granulocytes during H³-thymidine (H³-TDR) infusion, based on the labeling data of figure 1, is contrasted with the disappearance of labeled granulocytes following 17 days of H³-TDR infusion. Reutilization of the label was suppressed by infusion of nonisotopic ("cold") thymidine (TDR).

terpart of the rate of disappearance of unlabeled cells during infusion. The observations were in accord with the expectations.

Figure 6 represents the same type of analysis for the disappearance of labeled lymphocytes in the 4 rats in which reutilization was suppressed upon discontinuation of the H³-thymidine infusion. The dashed curve (identical with the dashed line in figure 3) represents the rate of fall-off of all labeled cells, and the dash-dotted line the disappearance of the most heavily labeled cells. The solid line illustrates the fall-off of unlabeled cells during H³-thymidine infusion, and represents the actual life spans of small lymphocytes from the last division to their eventual disappearance from the blood, including an undetermined number of exits and reentries during recirculation through the nodes. The fall-off of all labeled cells (82 per cent to 35 per cent in 16 days) was similar to that of unlabeled cells (92 per cent to 50 per cent during the comparable 16-day period). This was unexpected, since continued divisions of precursors were expected to lead to a slower decline in labeled cells, as was observed for granulocytes. A possible explanation is that the overall turnover rate of small lymphocytes was too slow for daughter cell production to influence the decline in total labeling. Alternatively, a more rapid than expected fall-off of labeled cells might have been due to decreased survival of labeled as compared to unlabeled small lymphocytes, possibly on the basis of radiation damage.
Another discrepancy between lymphocytes and granulocytes was observed in the disappearance curves of the most heavily labeled cells. In contrast to granulocytes, the fall-off of small lymphocytes containing 16 or more grains (fig. 6, dash-dotted line) was initially much faster than the rate of disappearance of unlabeled cells during H³-thymidine infusion. The drop in 5 days from 28 per cent to 10 per cent of these heavily labeled lymphocytes represented a loss of nearly two-thirds, although a few such cells survived for several weeks. By contrast, unlabeled cells during the comparable 5-day period of tracer infusion fell from 85 per cent to 67 per cent, a loss of less than one-quarter. Heavily labeled small lymphocytes therefore constitute a group of cells with accelerated turnover.

The individual grain counts of labeled granulocytes and large lymphocytes during H³-thymidine infusion varied little about the mean of 18. The majority of small lymphocytes was labeled similarly, but a minority had significantly fewer grains. Thus, whereas virtually all labeled granulocytes and large lymphocytes and about 70 per cent of labeled small lymphocytes had 11 or more grains per cell, the remaining 30 per cent of small lymphocytes had only 3 to 10 grains.

The mean grain counts of small lymphocytes and granulocytes during and after 17 days of H³-thymidine infusion are shown in figures 7 and 8. The mean grain count of small lymphocytes rose rapidly during the first 10 days
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Fig. 7.—Mean grain counts of labeled small lymphocytes during and after 17 days of \(^{3}H\)-thymidine infusion. Four rats received infusions of nonisotopic thymidine to suppress reutilization of the label.

of infusion, and then fell significantly. Animals receiving infusions for longer periods stabilized at about the 17-day level. The percentage of labeled lymphocytes containing 16 or more grains followed a similar pattern. Each individual animal followed the general trend illustrated for the group.

With cessation of \(^{3}H\)-thymidine infusion, the mean grain count of small lymphocytes (fig. 7, solid line) rose briefly and then fell rapidly. The rebound in mean grain count appeared to parallel the abrupt increase in percent labeling which followed discontinuation of \(^{3}H\)-thymidine. However, when large doses of nonradioactive thymidine were given after 17 days of \(^{3}H\)-thymidine infusion, the rise in mean grain count was suppressed (fig. 7, dashed curve), even though per cent labeling increased as it did in controls (figs. 3 and 6). The rises in mean grain count and per cent labeling upon discontinuance of \(^{3}H\)-thymidine suggest release from some suppression of lymphocyte production or release during the tracer infusion. The increase in mean grain count may also have involved reutilization of radioisotope since it was abolished by the infusion of cold thymidine.

Changes in the mean grain count of granulocytes (fig. 8) suggested a similar trend, but were less striking. Moreover, whereas changes in the mean grain count of lymphocytes were similar in all individual animals, the mean grain count of granulocytes during tracer infusion declined from its peak value in only 4 of the 30 rats studied. This lack of consistency raises some doubt as to the significance of mean grain count changes in granulocytes.

Cold thymidine infusion caused no significant change in mean grain counts, except for suppression of the rebound elevation which occurred in lymphocytes upon stopping the tracer (figs. 7 and 8).

As already noted, the fall-off of per cent labeling in granulocytes and lymphocytes was accelerated by infusion of cold thymidine (figs. 3, 4). The
effects were the same whether 1.7 or 45 mg. per day were given. Cold thymidine infused for several weeks preceding the administration of H3-thymidine did not alter the subsequent pattern of label incorporation, and therefore appeared to have no direct effects upon leuкоpoiesis.

**Discussion**

The continuous infusion technic was designed to measure survival of unlabeled cells by insuring that each newborn cell becomes labeled. Thus, it circumvents complexities in the evaluation of labeled cells, such as reutilization of label, persistence of labeled cells in the circulation because of division of labeled precursors, or possible radiation damage due to tritium. As long as the total white blood cell count remains stable, as it did in the present experiments, the disappearance of unlabeled cells recorded as per cent of the total reflects the survival of cells from birth in the tissues to final disappearance from the circulation. Individual cells may, and in the case of small lymphocytes undoubtedly do, enter and leave the circulation repeatedly during this period. The only necessary assumption is the labeling of each newborn cell. The assumption is not proven for lymphocytes, but is probable by analogy with granulocytes, all of which become rapidly labeled and remain so with very rare exceptions. The contrary assumption of the production of unlabeled lymphocytes during H3-thymidine infusion would imply that some lymphocytes do not utilize thymidine for DNA synthesis, though
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it is available, or that the infused tracer does not reach some dividing lymphocytes, even though it reaches all dividing granulocytes. There is no evidence to support either alternative. Conceivably, the brief unintentional interruption of thymidine infusion in some of the experiments may have permitted production of some unlabeled cells. In the 2 animals which received the longest infusions, however, the precaution was taken of injecting H\(^3\)-thymidine every 12 hours during the interruption. This schedule results in labeling curves very similar to those obtained with continuous infusion.\(^4\) It is therefore quite unlikely that the unlabeled small lymphocytes which persisted through nine months of continuous infusion were produced after H\(^3\)-thymidine had been started.

Long survival of a proportion of small lymphocytes has recently received additional convincing support from observations by Buckton and Pike.\(^1\) These authors cultured human peripheral blood from patients who had undergone x-ray therapy 5 years previously. Mitoses in these cultures are now known to originate from small lymphocytes.\(^1\) The type of cytogenetic abnormalities observed indicated that some of the divisions must have been the first since irradiation, suggesting that some circulating lymphocytes must have persisted without division for at least 5 years.

Once the tracer infusion is stopped, reutilization of the tritium label markedly influences the disappearance of labeled cells. This is evident from the accelerated fall-off observed with subsequent infusion of cold thymidine (figs. 3 and 4). Parallel observations have been made with tritium reutilization in regenerating liver;\(^1\) in this system transferred label appears to originate from dying cells which had previously incorporated H\(^3\)-thymidine.\(^1\) Suppression of reutilization by cold thymidine implies that the transfer of label occurs at the nucleoside level, probably in the form of H\(^3\)-thymidine released during DNA degradation.

Except for suppression of the early rise which occurred with small lymphocytes, cold thymidine caused no significant change in mean grain count. This at first seems incompatible with suppression of tracer reutilization. However, Schultze has recently presented evidence that grain counts correspond quite poorly with the dosage of H\(^3\)-thymidine.\(^1\) The differences in the grain counts of individual small lymphocytes, as well as the changes in cell labeling during and after H\(^3\)-thymidine infusion, suggest that these cells are comprised of at least two populations with different rates of turnover. The fact that 30 per cent of small lymphocytes had significantly lower grain counts than the remaining small lymphocytes, and indeed all other labeled leukocytes, is consistent with the concept of two populations, although the mechanism of differential labeling is unexplained.

That these lymphocyte populations have different turnover rates is suggested by the changes in mean grain count during the tracer infusion. It was thought that the mean grain count would reach a plateau, reflecting the constant availability of tracer from the infusion as well as from disintegrating labeled cells. This was in general the case for granulocytes. The mean grain
counts of small lymphocytes, however, declined from a peak reached between 6 and 10 days after onset of infusion and stabilized at a significantly lower level at about day 17 (fig. 7). The findings suggest that cells with higher grain counts represent a population with a much more rapid turnover than the rest of small lymphocytes. This would explain the initially rapid rise in mean grain count during the first 10 days of H3-thymidine infusion; the more gradual emergence of lightly labeled cells might then cause depression in the mean grain count between days 10 and 17. The additional observation that the most heavily labeled small lymphocytes disappeared from the circulation at a faster rate than the initially unlabeled cells (fig. 6) also indicates a differentially rapid turnover of lymphocytes with higher grain counts. These findings are in accord with recent observations by Caffrey et al., suggesting the existence of two populations of small lymphocytes with different life spans.15 Some indication of the maximum size of the fast turnover population is given by the initial labeling curve, in which 40 per cent of small lymphocytes were labeled in 10 days, after which a drop in mean grain count indicated a significant influx of more lightly labeled, slow turnover cells.

There are a number of possible explanations for the rapid turnover of heavily labeled lymphocytes. Some undoubtedly die and are continually replaced by new cells from the lymphoid organs. Other heavily labeled cells recirculating through the lymph nodes may themselves divide there to yield new small lymphocytes. The small lymphocyte has been shown to be capable of mitosis in vitro and in vivo16,17 and recent observations by Fliedner et al. suggest that such cells in splenic lymph follicles do not originate from precursors in the germinal center but may be derived from other small lymphocytes in the surrounding cuff.18 The final possibility is that the different turnover rates of lymphocytes which are more or less heavily labeled may not be physiologically predetermined, but may result from radiation damage to cells containing greater quantities of radioisotope. Radiation damage to leukemic cells has recently been observed in 2 patients, one with acute lymphocytic and one with acute myelogenous leukemia, who received 0.25 μc. of H3-thymidine per g. of body weight at 12 hour intervals for 5 days. In the patient with lymphocytic leukemia both the mean grain count and the peripheral blood count of the leukemic cells decreased significantly within the 5-day period of H3-thymidine administration.19 Radiation damage would help to explain the unexpectedly rapid fall-off of all labeled small lymphocytes as compared to unlabeled forms in figure 6. It is not, however, a necessary assumption for interpretation of the data.

The temporary but marked rise in the per cent of labeled small lymphocytes after discontinuation of the H3-thymidine infusion suggests that lymphocyte production or release was suppressed during the infusion. Factors, such as stress, connected directly with the infusion procedure were not responsible, since this phenomenon was observed in all animals upon discontinuation of the radioisotope, regardless of whether they were freed from the infusion apparatus, kept attached thereto, or given a saline infusion during
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the follow-up period. Thymidine itself was not the cause of suppression, since the rebound still occurred in the presence of cold thymidine infusion; moreover, cold thymidine given prior to the tritiated compound did not affect the usual labeling pattern. A radiation effect of tritium on lymphocyte precursors might therefore be involved, although the rapidity of recovery would be quite unusual. A sudden release of labeled lymphocytes should have manifested itself in an increase in the absolute lymphocyte count. Experiments designed to test this thesis gave equivocal results, possibly because of the variability of total white cell counts from day to day and animal to animal.

Thus, interpretation remains speculative with regard to some of the changes observed upon discontinuance of the thymidine infusion. The data imply, however, great complexity in the labeling process and the need for caution in the interpretation of any H₃-thymidine data.

SUMMARY

Leukocyte labeling was studied in rats during and after continuous intravenous infusion of H₃-thymidine. The radioisotope was administered for varying periods up to 271 days. The results permit the following conclusions:

1. The median survival of small lymphocytes is about 1 month. Five to 8 per cent of small lymphocytes have a life span of more than 9 months.

2. Following the administration of H₃-thymidine, reutilization of the tracer markedly delays the fall-off of labeled cells in the peripheral blood. Reutilization probably involves H₃-thymidine released from labeled DNA during cell death, since suppression occurs with massive infusion of nonlabeled thymidine.

3. Unlike granulocytes and large lymphocytes, small lymphocytes label nonuniformly, and appear to be comprised of at least two populations with different intensities of labeling and different turnover rates. The more heavily labeled cells have the faster turnover.

4. The complexity of the labeling process indicated by the present observations must be considered in the interpretation of H₃-thymidine data. However, the survival of unlabeled cells during continuous H₃-thymidine infusion remains a valid means of measuring the life spans of circulating blood cells.

SUMMARIO IN INTERLINGUA

Le marcage del leucocytos esseva studiate in rattos durante e post le continue infusion intravenose de thymidina a tritium. Le radioisotopo esseva administrante durante varie periodos de un duration de usque a 271 dies. Le resultatos permette le formulation del sequente conclusiones:

1. Le longevitate median de micre lymphocytos es circa 1 mense. Inter 5 e 8 pro cento del micre lymphocytos ha un longevitate de plus que 9 menses.

2. Post le administration de thymidina a tritium, le reutilisation del molecula vector del isotopo relenta marcatemente le declino del radioactivitate in le sanguine perioperific. Il es probable que le thymidina a tritium que es
liberate per acido deoxyribonucleic durante le morte del cellulas es le fonte de provision de ille reutilisation, proque le massive infusion de thymidina sin marcation isotopic resulta in un suppression del evidentia de reutilisation.

3. Per contrasto con le granulocytos e le grande lymphocytos, le micre lymphocytos accepta le marca de maniera non uniforme, e il pare que lor numeros es componite de al minus duo diferente populationes con diferente intensitates de marcage e diferente rapiditates de metabolisation. Le plus pesantemente marcate cellulas es characterisate per un plus rapide metabolismo.

4. Le complexitate del processo de marcation que es indicate per le presente observationes debe esser prendite in consideration quando on interpreta observationes in studios con thymidina a tritium. Tamen, le superviventia de non-marcate cellulas durante un continue infusion thymidina a tritium remane un valide methodo pro mesurar le longevitate de cellulas sanguinee in le circulation.

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Leukocyte Labeling in Rats during and after Continuous Infusion of Tritiated Thymidine: Implications for Lymphocyte Longevity and DNA Reutilization

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