Zwischen Blut- und Sputumwerten findet sich kein messbarer Unterschied. Dies stimmt mit Befunden am Menschen nach einmaliger Injektion von ^{3}H-Thymidin überein und darf als weiterer Hinweis auf die statistische Elimination der Granulozyten gewertet werden[3]. Würden die Granulozyten ähnlich wie die Erythrozyten erst nach Ablauf eines Alterungsprozesses das Gefäßsystem verlassen, so wäre eine zeitliche Verschiebung zwischen den Messwerten im Blut und im Sputum zu erwarten.

Die dargestellte Methode kann auch bei sehr kleinen Tieren (Maus, Goldhamster) angewendet werden. In solchen Fällen ersetzt man die Dauerinfusion von ^{3}H-Thymidin zweckmässig durch Einzelinjektionen, deren Zeitabstände kürzer sind als die DNS-Synthesephase. Da ferner für alle Tiere gelten dürfte, dass der Prozentsatz markierter Granulozyten im Blut und im Sputum ausreichende Übereinstimmung zeigt, kann allein aus Mundhöhlenabstrichen die Verweilzeit der Granulozyten im Blut bestimmt werden[4].

Summary. Labelling of neutrophil granulocytes in the blood and sputum of rats was followed by autoradiography for 120 h after starting a continuous infusion of ^{3}H-thymidine*).

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[3] T. M. FLIEDNER und E. P. CRONKITE, Blood *24*, 402 (1964).
[4] Mit Unterstützung der Deutschen Forschungsgemeinschaft.
* The mean sojourn of these cells in the blood was determined to be c. 10 h.

Oscillations in the Rate of Disappearance of Labeled Triiodothyronine from Human Plasma and the Minimum Sampling Rate for their Observation

Diurnal variations (oscillations) in the concentration of plasma thyroxine have been reported by MARGOLESE and GOLUB[1] and VOLPE et al.[2], and a diurnal pattern in the rate of disappearance of labeled thyroxine from human plasma has been investigated by WALFISH et al.[3] and BUSHLER et al.[4]. The WALFISH group[3] first suggested that their observations may be related to diurnal changes in plasma volume. Later, the BUSHLER group demonstrated that the observed rhythms are *paralleled* by changes in plasma proteins, plasma PBI^{127}, I^{125}-RISA and TBG. They also showed that changes in the feeding cycle had no effect, while reversal of the sleep-waking rhythm immediately reversed the observed diurnal variations in plasma thyroxine[4]. They concluded that observed oscillations in plasma thyroxine concentration are related to the redistribution of fluid between the intravascular and extravascular pools, associated with changes from upright to recumbent positions.

We investigated the rate of disappearance from the plasma of ^{125}I-labeled triiodothyronine (T3) in two[5] recumbent patients. Our objective was to determine whether the rate of disappearance of T3 from the blood exhibits oscillatory behavior, a phenomena which would be related to the temporal pattern of binding, distribution and/or metabolism of T3, and, if it does, how often we must sample the blood to observe these oscillations.

Materials and methods. Two euthyroid patients, A (hypertensive) and B (anemic), were given 20 mg of methimazole approximately 2 h prior to the injection of 500 µCi of ^{125}I-T3 (from Amesham) to prevent recycling of ^{125}I. The administration of 10 mg of methimazole was repeated about every 6 h for the duration of the experiment. Sampling was begun 4 h after injection of the tracer in patient A and after 2 h in patient B. Blood samples were taken for 3 days. For patient A, sampling occurred every 4 h on the first day, every 2 h the second day, and every 6 h the third day. This ordering was mixed in patient B, who was sampled every 2 h on the first day, every 6 h the second day and every 4 h the third day. ^{125}I-PBI was determined in a well-type scintillation counter. The corrected data points for all 3 days are plotted on rectangular coordinates in Figure 1 with straight lines connecting the points. In Figure 2, the vertical and horizontal graph scales of Figure 1 have been magnified to illu-

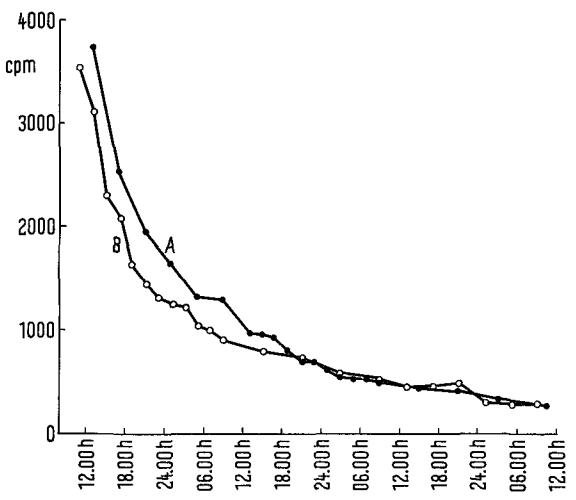

Fig. 1. ^{125}I-PBI activity in 2 patients A and B, beginning 4 h after injection of 500 µCi of ^{125}I-T_3. Blood samples were taken every 2, 4 or 6 h for 3 days, staggered as described in the text. 20 mg of methimazole was administered 2 h prior to the ^{125}I-T_3, to prevent recycling of ^{125}I, followed by 10 mg every 6 h thereafter.

[1] M. S. MARGOLESE and O. J. GOLUB, J. clin. Endocr. Metab. *17*, 849 (1957).
[2] R. VOLPE, J. VALE and M. W. JOHNSTON, J. clin. Endocr. Metab. *20*, 415 (1960).
[3] P. G. WALFISH, A. BRITTON, P. H. MELVILLE and C. EZRIN, J. clin. Endocr. Metab. *21*, 582 (1961).
[4] V. BUSHLER, P. DECOSTRE, S. REFETOFF and L. J. DEGROOT, (Abstract) Proc. Ann. Meeting American Thyroid Assoc., Washington, D.C., 9–12 October 1968, p. 45.
[5] Technical difficulties prevented studies in more than 2 patients. Fortunately, the results for each patient show the same effects.

strate ^{125}I-PBI plasma activity in greater detail for the 2-h sampling periods for each patient, the second day samples from patient A and the first day samples from patient B; and the data points have been connected by smooth curves. The 4-h sampling period data, for patient A only, has similarly been recorded in Figure 3. Radioactivity of the 4-h samples taken on the third day in patient B was insufficient for a reliable representation of the curve.

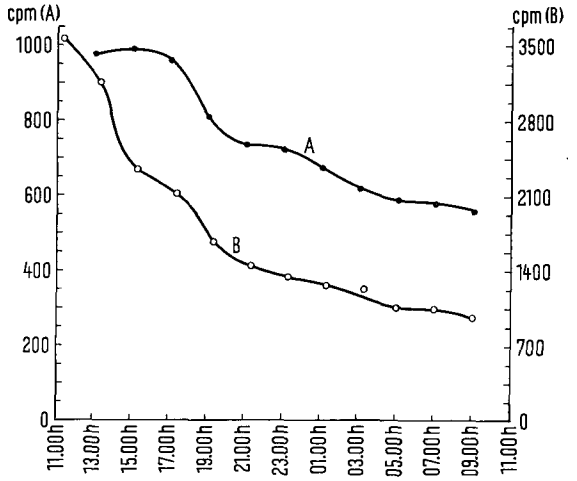

Fig. 2. ^{125}I-PBI activity as in Figure 1, but magnified and abbreviated to illustrate only the 2-h sampling period data in patients A and B.

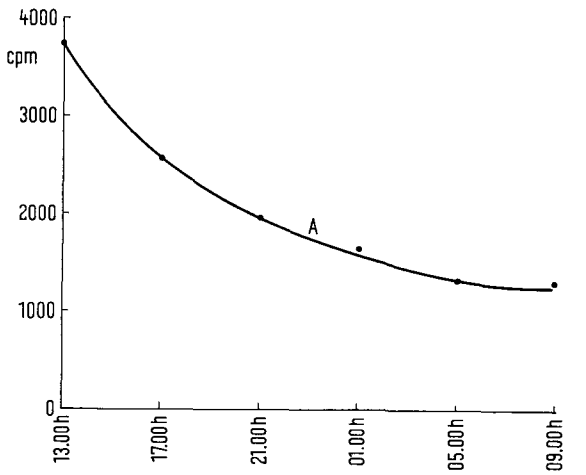

Fig. 3. ^{125}I-PBI activity as in Figure 1, but for only the 4-h sampling period data in patient A.

Results. The overall character of curves A and B in Figure 1 is grossly exponential, as expected. The important result is illustrated in the amplified curves in Figures 2 and 3. Both curves A and B in Figure 2 exhibit relatively smooth and well-defined oscillatory variations of several percent about an approximately exponential decay function, while the curve A in Figure 3 shows no significant variations. This difference is further emphasized by comparing curves A only in Figures 2 and 3, since they represent data taken from the same subject. The data suggests that the pronounced variations exhibited on the second day of sampling (every 2 h) in subject A were unobservable on the first day because the 4-h sampling period was too great.

Conclusions. Oscillations in the rate of disappearance of labeled-T3 have been observed in this experiment. A 4-h sampling period is insufficient to demonstrate this behavior; and sampling every 2 h appears to be an approximate upper limit on the sampling period. A more detailed knowledge of the character of these oscillations may be obtained by sampling more often than every 2 h during time intervals when the variations are largest. Curve A in Figure 2 suggests that sampling every hour during the mid-day would be desirable.

The results about T3 reported here are not necessarily incompatible with reports that thyroxine (T4) concentration may not be diurnal, as discussed in the introduction. Although T3 and T4 are almost the same species, to within a single atom, their dynamics of distribution, binding and metabolism are sufficiently different[6] for one to be observedly diurnal and the other not. Another possibility is that diurnal variations may exist in T4 disappearance which are too small to measure by currently available techniques.

Résumé. Des oscillations dans la réduction du taux de triiodothyronine (marquée ^{125}I) ont été observées dans le plasma humain. On a trouvé qu'une période d'échantillonage de 4 h était insuffisante pour révéler ces oscillations. Une période de 2 h constituerait une limite supérieure adéquate.

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[6] J. Robbins and J. E. Rall, in *Hormones in Blood*, 2nd edn. (Eds. C. H. Gray and A. L. Bacharach; Academic Press, New York 1967), pp. 383–491.

[7] Reparto Medicina Nucleare, 11° Clinica Medica, Università di Roma (Italia).

The Generation Time of Human White Blood Cells taken from a Mother and her Daughter

As described by Painter and Drew[1] the duration of S, G_2 plus mitosis, G_1 and of the generation time (T) can be estimated by plotting percentage of labelled metaphase cells between ^{3}H-thymidine pulse labelling and harvest.

In the experiments presented, leukocyte samples from blood of a 44-year old female donor and her 8-year old daughter were cultured as described by Herzog and Steffenson[2] and labelled as described by German[3]. The results are presented as mitotic index curves illustrated in

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[2] R. Herzog and D. Steffenson, Cytogenetics *7*, 471 (1968).
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