two had had one episode of peritoneal dialysis at least a week before. Mean blood urea nitrogen (BUN) at the time they were studied was 113 mg/100 ml, mean creatinine was 14 mg/100 ml, and mean CO_2 was 17.9 mm/l (normal 22.5–27 mm/l). The mean BUN of fourteen non-uremic controls was 14.5 mg/100 ml.

Four ml of heparinized blood was collected in a plastic syringe from each subject. Then latex particles (Difco, 0.81 μm diameter), suspended in normal saline at 10-fold dilutions, were added to 1 ml aliquots of the blood in 0.05 ml amount. This resulted in a concentration of 7×10^4, 7×10^3, and 7×10^2 latex particles/mm³ blood. An NBT test was done on each of the blood-latex dilutions and on an unstimulated sample of blood by adding 0.1 ml of blood to 0.1 ml of NBT solution (0.2% General Biochemical NBT in physiologic saline, diluted with an equal volume of phosphate-buffered saline, pH 7.35) and incubating at 37 °C for 1 h on an agglutination tray in a moist chamber. Coverslip slides were prepared and counterstained with Wright-Giemsa stain. For each coverslip, the percentage of 100 PMN's which contained latex particles was counted, and the percentage of 100 PMN's which contained black cytoplasmic granules or clumps of reduced NBT was tabulated as the 'NBT score'. An NBT score below 10% is considered normal for uninfected patients[5].

The uremic patients had unstimulated NBT scores similar to the controls. The mean was 7.2% for the uremic group and 7.5% for the control group. After stimulation of the PMN's with increasing concentrations of latex, latex engulfment was higher for the uremic patients than for controls (Figure 1). The stimulated NBT scores for both groups were elevated after phagocytosis, uremic scores being slightly higher (Figure 2). Mild acidosis and initially high or rising values of BUN caused no impairment of the PMN's activity.

Our studies suggest that both latex particle engulfment by the PMN and subsequent NBT reduction are not only unimpaired in patients with an average BUN over 100 mg/100 ml and mild acidosis, but may actually be increased, depending on the number of particles introduced. Since whole heparinized blood was used for these studies, it is apparent that the patient's own uremic serum had no deleterious effect on phagocytic ability or intracellular enzyme activation. From this study, it would appear that untreated uremic patients with varying degrees of mild acidosis have normal phagocytic ability of their PMN's.

Zusammenfassung. Nachweis, dass neutrophile Leukozyten von Urämikern verglichen mit Gesunden eine unveränderte Fähigkeit zu Phagocytose und Reduktion von Nitroblau Tetrazolium besitzen.

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Changes Induced by the Acute Administration of Iodide on Secretion of Iodinated Components by the Rat Thyroid Gland Perfused in situ

Several investigations have shown that administration of large quantities of stable iodide to patients with thyrotoxicosis causes an amelioration of the disease by decreasing thyroid secretion[1–5]. The mechanism of this action is uncertain. There are conflicting data whether large doses of iodide have any inhibitory effect on thyroid secretion in euthyroid individuals with a normal rate of secretion and whether administration of thionamide drugs is necessary to demonstrate an inhibitory effect of iodide[3–13].

Because of the difficulty in obtaining precise quantitative data on changes in the secretion of iodinated components in vivo for reasons previously outlined[14], we felt that the technique of single-pass perfusion with nonradioactive blood in prelabeled rat thyroid glands[14] might provide useful information relative to this problem. We considered that the data would be of value only if positive effects were obtained since the in situ perfused thyroid deteriorates after 1–2 h. Data in man have indicated that it requires 1–2 days of iodide administration before thyroid secretion is inhibited[3]. Similar observations have been made in mice[15]. Methimazole was added to the perfusate in some experiments because thionamides may have some potentiating effect on iodide inhibition of secretion.

Materials and methods. Adult male Sprague-Dawley rats weighing approximately 300 g were fed a low-iodine diet of approximately 30 μg ^{127}I/kg for 1 week. 150 μCi carrier-

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free ^{131}I-was injected i.p. 24 h before carrying out single-pass perfusion studies with non-radioactive citrated beef blood containing 12 mU/ml of TSH[16]. Effluent was collected from the thyroid vein at intervals. All perfusion techniques were performed as previously described[14,17]. During the first 45 min of perfusion, no iodide was added to the entering perfusate, during the last 45 min, 10^{-3} or $10^{-4}M$- $M^{127}I^-$ was added. In some groups, $10^{-3}M$ methimazole (MMI) was present in the perfusate during the entire period of perfusion.

For each rat, 4 collections of effluent from the left inferior thyroid vein were made for 10-min periods, 2 before and 2 during perfusion of stable iodide. The first collection period began 15 min after starting the perfusion to allow wash-out of radioactivity in the vascular system. Immediately after collection, the blood was transferred to hematocrit tubes containing approximately 1–2 mg MMI. The tubes were centrifuged, the radioactivity of each sample was determined, and an aliquot of each plasma sample was individually chromatographed in butanol-acetic acid-water (BAW), and also in butanol-ethanol-ammonia (BEA) in most experiments, to determine relative distribution of the radioiodinated components[18]. The data from any sample in which the origin radioactivity in BAW was above 15% of total chromatograph radioactivity were discarded since this was taken as an indication of a deteriorating preparation[14]. However, the relative changes in absolute radioactivity in I^-, T_4 and T_3 in successive periods were similar in the samples with high origin radioactivity to those tabulated here. Statistical analysis was made by Duncan's multiple range comparison test[19].

Effect of perfusion of $^{127}I^-$ on the quantity of labeled I^-, T_4 and T_3 in thyroid effluent

Group		Time after beginning perfusion $^{127}I^-$		
		35 to 45 min	60 to 70 min	80 to 90 min
$10^{-3}M$ $^{127}I^-$ + $10^{-3}M$ MMI	I^-	58 ± 20 (4)	408 ± 139 (4)	415 ± 88 (3)
	T_4	96 ± 21	145 ± 58	215 ± 79
	T_3	87 ± 23	161 ± 59	212 ± 67
$10^{-3}M$ $^{127}I^-$ without MMI	I^-	69 ± 14 (4)	163 ± 33 (4)	236 ± 81 (3)
	$T_4 + T_3$	73 ± 8	61 ± 8	57 ± 8
$10^{-4}M$ $^{127}I^-$ + $10^{-3}M$ MMI	I^-	96 ± 19 (7)	98 ± 14 (7)	131 ± 62 (4)
	T_4	79 ± 15	69 + 22	43 ± 10
	T_3	62 ± 6	42 ± 7	43 ± 10

The number of rats sampled is indicated in parentheses. The mean ± SE of the total effluent radioactivity for each 10 min collection period is shown. The absolute radioactivity of each component in the first collection period (15 to 25 min) was arbitrarily assigned a value of 100 for each rat. The radioactivity in subsequent periods, shown here, is expressed relative to the first period. Perfusion with $^{127}I^-$ begun at 45 min. When MMI was employed, it was present throughout the entire period of perfusion. T4 and T3 are combined in the second group because chromatography was performed only in the BAW system.

Results. The distribution of total radioactivity in the thyroid effluent in the various radioiodinated components was similar in the initial collection period: I^-: 20 ± 3%, T_4: 42 ± 3%, T_3: 25 ± 2%. Detectable quantities of MIT* and DIT* were not found in any effluent sample. Absolute rates of secretion of T_4^* and T_3^* did not change significantly ($p > 0.05$) during perfusion with 10^{-3} or $10^{-4}M$ $^{127}I^-$, with or without MMI, when compared to the blood sample collected immediately before ^{127}I-administration. The T_3^*/T_4^* ratios were closely similar for all collection periods in the same rats.

The relative secretion of radioiodinated components in successive collection periods is summarized in the Table. There was a significant increase ($p < 0.05$) in $^{131}I^-$ secretion with perfusion of $10^{-3}M$ $^{127}I^-$, with or without MMI present in the perfusate. However, the increase in $^{131}I^-$ was significantly more ($p < 0.05$) during the first collection period of perfusion with $10^{-3}M$ $^{127}I^-$ (15–25 min after starting $^{127}I^-$) in the group in which MMI was present in the perfusing blood than in the group without MMI. There was a concomitant slight rise in iodothyronine* secretion in the former group and a slight drop in the latter relative to the first (pre-$^{127}I^-$) collection period. If $^{131}I^-$ was calculated as percent of total secreted radioactivity in the first post $^{127}I^-$ collection period, there was no statistical difference between the 2 groups.

There was no significant change in secretion of any radioiodinated component with $10^{-4}M$ $^{127}I^-$. The difference between the effects of the 2 concentrations of $^{127}I^-$ on $^{131}I^-$ secretion was highly significant ($p < 0.01$).

Discussion. We were unable to demonstrate a significant inhibition of iodothyronine* secretion during perfusion with $10^{-3}M$ $^{127}I^-$ under the conditions of our experiments. It is possible that the concentration of TSH which we used in the perfusate (approximately the same as the plasma TSH concentration in chronically iodine-deficient rats) may have been too large to permit detection of an iodide effect on hormone secretion[3,9–11]. However, a more probable explanation is that it takes longer than 45 min high concentration of $^{127}I^-$ can inhibit secretion[3,15].

The increase in ^{131}I-secretion caused by administration of $10^{-3}M$ $^{127}I^-$, with or without perfusion of MMI, was expected from earlier observations in our laboratory[17]. Perchlorate at a concentration of $10^{-3}M$ in the perfusate causes an even greater increase in $^{131}I^-$ secretion. This is presumably because of the well-known greater potency of perchlorate than of iodide in inhibiting iodide transport. The discharge of $^{131}I^-$ is presumably resultant in both instances from a saturation of the iodide pump and a decrease in the ability of the gland to retain an effective concentrating machanism of iodide. Thus, $^{131}I^-$ generated intrathyroidally through iodotyrosine deiodination leaves the gland rapidly whether organic iodinations are inhibited or not[17,20]

Résumé. Nous avons étudié l'effet de l'iodure 127 (10^{-3} et $10^{-4}M$) sur la sécrétion de T_4*, T_3* et $-I$* par la thyroïde de rat, prémarquée à l'iode 131 et perfusée in situ avec du sang non radioactif contenant 12 mU de TSH/ml. Il n'a pas été noté de changement significatif dans la sécrétion de T_4* ou T_3* jusqu'à 45 min après le début de l'administration d'iodure 127, qu'il y ait ou non

[16] Kindly supplied by the National Institutes of Health (NIH-TSH-B5).

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du méthimazole ($10^{-3}M$) dans le sang perfusé. Il y avait par contre une augmentation de la sécrétion d'-I* pendant la perfusion de $10^{-3}M$ d'ïodure, indiquant une décharge d'-I* pendant la perfusion de $10^{-3}M$ d'ïodure, indiquant une décharge d'-I* de provenance intra-thyroïdienne. Cet effet est similaire à celui noté auparavant pendant la perfusion de $10^{-3}M$ de ClO_4^-.

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* An asterisk indicates that only the radioiodinated component is considered.

Circadian Rhythm of Progesterone Secretion During Pseudogestation in the Rat

Accounts of studies of the endocrine function of the rat ovary, with particular reference to the secretion of progestins during pseudogestation, are given in the publications of Fajer and Barraclough[1] and Hashimoto et al.[2]. These authors, however, omit to mention the time of day at which the levels of progesterone and 20 α OH-progesterone were determined in their pseudopregnant animals.

In the light of a recently published observation by Freeman and Neill[3] to the effect that a nocturnal release of prolactin takes place in pseudopregnant rats, the present study was undertaken to find out to what extent progestin secretion displays a nychthemeral rhytm.

Material and methods. The experiments were performed on 25 female rats of strain SIV (Ivanovas, Kisslegg, Germany), weighing between 200 and 250 g, which were kept under conventional conditions in respect of temperature, humidity and lighting (light from 06.00 to 20.00 h) throughout the study. These females were mated with sterilized males and subsequently examined for the presence of a vaginal plug, to ensure that copulation had taken place. On the 7th day of pseudogestation they were divided into 4 groups. Every 6 h from 03.00 h onwards, 1 group was cannulated according to the method described by Fajer and Barraclough[1], the cannula being passed via the renal vein into the ovarian vein. To perform this operation on all the animals in 1 group took 2 h.

Blood samples of 0.5 ml were withdrawn slowly, over a period of 3–5 min, from each animal. The blood was extracted and chromatographed (3 × 10 cm migration on aluminium oxide in a cyclohexane: ethyl acetate solvent system) and the content of progesterone determined by a slightly modified version of the protein-binding assay method of Neill et al.[4]. After chromatographic separation, 20 α OH-progesterone was eluted in 5 ml of ethyl acetate and measured fluorometrically in sulphuric medium. Losses of progesterone and its metabolite due to the experimental procedures were estimated by the addition of ^{3}H-progesterone and ^{3}H 20α OH-progesterone in a ratio of 1:1.

The animals were killed after the blood samples had been taken, and the ovaries, corpora lutea and uteri were removed and weighed. The standard error of the mean was calculated according to Lord[5].

Results. The rate of progesterone secretion calculated from the blood levels determined between 03.00 and 05.00 h, 15.00 and 17.00 h and 21.00 and 23.00 h were very similar, ranging from 5.5 to 7.4 μg/h. The differences were not significant. These values may be taken as the basal rate of secretion of progesterone during this phase of pseudogestation[1]. Between 09.00 h and 11.00 h, however, an abrupt increase in the release of progesterone occurred. The mean rate of 19.4 μg/h measured during this period is significantly different from the foregoing values.

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Organ weights and production of progesterone and 20α OH-progesterone in the rat on 7th day of pseudogestation

Clock time	*n*	Body weight (mg)	Duration of cannulization (min)	Weight of ovary (mg)	Weight of corpora lutea (mg)	Weight of uterus (mg)	Blood flow (ml/h)	Progesterone (μg/h)	20 OH-Progesterone (μg/h)	Prog./20 OH-progesterone (ratio)
a) 03.00 to 05.00	5	236.8 ± 5.5	4.0 ± 2.0	39.7 ± 1.9	1.59 ± 0.07	282.3 ± 13.0	18.5 ± 6.3	6.0 ± 1.8	10.7 ± 2.3	0.56
b) 09.00 to 11.00	10	225.4 ± 3.0	3.3 ± 0.5	31.7 ± 1.5 (a–b)[a] $p < 0.01$	1.81 ± 0.08 (a–b) $p < 0.1$ n.s.	292.4 ± 16.3	13.3 ± 2.2	19.4 ± 4.2 (a–b) $p < 0.05$	6.5 ± 1.5	3.00
c) 15.00 to 17.00	5	225.6 ± 3.5	5.1 ± 1.2	31.3 ± 1.9 (a–c) $p < 0.01$	1.58 ± 0.07	260.0 ± 6.3	7.4 ± 1.4	5.5 ± 1.8	4.0 ± 1.2 (a–c) $p < 0.05$	1.37
d) 21.00 to 23.00	6	214.0 ± 14.4	4.0 ± 1.0	32.4 ± 1.0 (a–d) $p < 0.01$	1.59 ± 0.05	277.5 ± 22.9	9.2 ± 1.2	7.4 ± 1.5	3.4 ± 0.7 (a–d) $p < 0.01$	2.18

[a] Difference between values for groups indicated.