presumably through the action of cyclic 3′,5′-AMP[13], and this newly formed hormone diffuses out without being incorporated into the granular structure for storage[5].

Despite the presumed differences in the mode of secretion from the adrenal cortex and medulla, the requirement for calcium is readily evident in both structures. Thus, the question arises as to whether calcium has the same action in both endocrine organs. In vitro studies have shown that calcium is an important factor in the intra-mitochondrial synthesis of corticosteroids in response to ACTH[14,15]. The importance of calcium observed in the present studies and its relationship to adrenal mitochondria remains to be elucidated, and further studies are presently in progress to investigate this problem. However, it should be noted that in contrast to the present findings in vivo, strontium was a very poor substitute for calcium in the in vitro system[15–17].

The effects of divalent cations on the release of hydrocortisone from the perfused cat adrenal gland by ACTH

ACTH m.u./ml	Experiment	Steroid output[a] µg/50 min		Experimental as % of control
		Experimental	Control	
0.1	Ca^{+2}-free	0.11	3.59	3.1
1.0	Ca^{+2}-free	4.18	60.70	6.9
0.1	Ca^{+2} (0.2 m*M*)	17.65	37.60	46.9
1.0	Sr^{+2} (2.0 m*M*) Ca^{+2}-free	37.63	38.51	97.7
1.0	Sr^{+2} (2.0 m*M*) Ca^{+2}-free	18.53	15.44	120.0
0.1	Mg^{+2} (5.0 m*M*) Ca^{+2}-free	0.80	13.75	5.8
1.0	Mg^{+2} (15 m*M*) Locke	21.47	28.84	74.4
1.0	Mg^{+2} (20 m*M*) Locke	2.88	9.34	30.8

[a] Represents the total steroid output during a 10 min exposure to ACTH plus the next 40 min in the absence of ACTH. Control outputs were obtained in normal Locke's solution with the same concentration of ACTH as the experimental values which were obtained in the modified Locke's solution. Normal Locke's solution contained 2.0 m*M* calcium and 0.5 m*M* magnesium.

Zusammenfassung. Es wird gezeigt, dass die Freisetzung von ACTH in der durchströmten Katzennebenniere nur bei Anwesenheit von Kalzium erfolgt. Strontium, nicht aber Magnesium kann Kalzium freisetzen, während Magnesium (15 m*M*) die Freisetzung von ACTH in Gegenwart von Kalzium hemmt. Ein Vergleich zwischen Brenzkatechinamin und Kortikosteronfreisetzung wird diskutiert.

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Distribution of the Sulphur-35-Labelled Goitrogen L-5-Vinyl-2-Thio-Oxazolidone in the Rat

In earlier papers[1,2] we have demonstrated the high biological activity of the naturally occurring goitrogen L-5-vinyl-2-thio-oxazolidone (VTO). This substance we have been able to isolate from the seeds of cruciferous weeds growing abundantly in the endemic goitre districts of Finland and from the milk of the same districts[2,3]. In these papers the necessity of studying the distribution of this substance and its possible accumulation in the body, especially in the thyroid during long-term feeding, has been pointed out. This preliminary communication is concerned only with the distribution and delay of this compound in the body after one single dose.

Material and methods. The radioactive sulphur-35-labelled L-5-vinyl-2-thio-oxazolidone (L-VTO-S35) was prepared by the chemists of the Radiochemical Centre, Amersham, England, starting from the DL-aminobutenol (L-amino-3-buten-2-ol and 2-amino-3-buten-1-ol), separation of the L-isomer by resolution of its D-α-bromocamphor-π-sulphonate and heating of this substance with potassium hydroxide and carbon disulphide-S35, exactly as described by ETTLINGER[4]. The synthesis of the intermediate, DL-aminobutenol, was performed by Mr. A. ARSTILA, who primarily prepared 3,4-epoxy-1-butene (butadiene-1,2-oxide), which on aminolysis furnished the amino-butenols[5]. The purity of the substance was checked by IR-spectrophotometry.

L-VTO-S35 was given to rats as i.p. injection in 0.5 and 1.0 ml, respectively, of distilled water. The dose used was about 50 and 100 µg of VTO with a radioactivity of 11 and 22 µCi, respectively. The animals were killed under ether anaesthesia and the whole thyroid and suitable parts of liver and kidneys were weighed 6 h, and 1, 2, 4, 6 and 9 days after administration of the VTO dose. The radioactivity of the specimens was measured in a liquid scintillation counting equipment (Packard Tricarb) after homogenization of the tissue in

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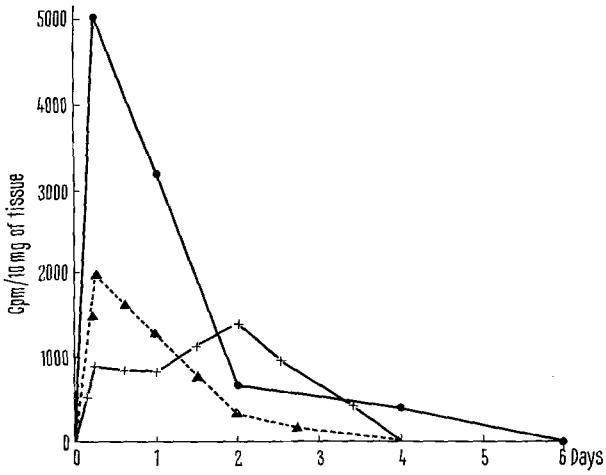

Relative concentration of radioactivity in different rat organs after one single dose of L-VTO-S35. The dose was 100 μg of L-VTO with a radioactivity of about 22 μCi S^{35}. ———, thyroid; +—+—+, liver; △--△--△, kidneys.

a tissue grinding device (Ultra-Turrax) and suspension of the homogenates in Bray's solution.

The rats used were males weighing 120–140 g, the total number of animals being 80. The rats were kept on a moderate iodine diet, containing about 4 μg/day, and in equal conditions.

Results. As can be seen from the Figure, the L-VTO-S35 seems to concentrate in the thyroid even 5-fold over the concentration in the liver or the kidneys, when calculated per weight unit. A similar result was seen also with the smaller dose of L-VTO-S35.

The radioactivity seems to remain in the thyroid up to 6 days, whereas in the liver and kidneys not more than 4 days. In all organs studied the concentration seems to be highest during the first day after the injection. In the liver the concentration remains at about the same level for 3 days.

Discussion. Like the synthetic antithyroid drugs propyl-thiouracil and methimazole[6], VTO also seems to be concentrated, especially in the thyroid. The long delay of this compound in the thyroid, up to 6 days after one single dose, makes a rather high accumulation possible, when long-term feeding is used. This could well explain the high biological activity of this substance shown earlier[1,2]. Further studies on long-term feeding with L-VTO-S35 are needed and are in progress. Our results are in accordance with the findings of GREER[7], who studied the excretion of VTO in the urine during 3 days after one single dose, and showed that during that time only 10% of the dose was excreted as VTO. As pointed out by LANGER[8], some metabolites of VTO may also be excreted into the urine.

Zusammenfassung. Nachweis mittels Radioschwefel ^{35}S, dass das in der Natur vorkommende Strumigen 1-5-vinyl-2-thio-oxyzolidon offenbar in der Schilddrüse in fünffach grösserer Konzentration gespeichert wird als in Leber und Niere.

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An Immediate Effect of Thyroxine in the New-Born Pig

There is a high level of activity of the thyroid gland in the early post-natal period of the pig's life[1], at which time the animal also shows a marked capability for heat production when exposed to the cold[2]. The highest level of free thyroxine in the pig's blood has been found in animals less than 1 day old[3,4]. During the course of several days, however, increasing amounts of thyroxine are bound, mainly to the α-globulin fraction of the plasma proteins, so that the level of free thyroxine falls. By about 8 days of age thyroxine and the thryoxine-binding protein are in equilibrium.

From this the question arises: does the increase in the thyroxine-binding capacity of globulin in any way modify the response to injected thyroxine? After about 8 days of age, thyroxine which is injected may be expected to become bound, with the result that its metabolic effect will be diminished. Before this time, however, an injection may produce an increase in free thyroxine which could result in a rapid metabolic response in spite of the high level of free endogenous hormone in the first few days after birth. It was in order to test any influence of age on the time-course of action of injected thyroxine that the present experiments were undertaken.

The rate of oxygen consumption in the pig was measured in a closed system with automatic recording which permitted observations to be made continuously for periods up to 24 h. The animal was provided with water while in the chamber but not with food; in consequence the metabolic rate in the control pigs declined continuously during the course of the experiment (see Table).

The pigs used in the experiments were of the Large White breed, a total of 51 in number, aged from 1 h to 19 days, and with a range of body weight from 0.81–3.35 kg. They were all born on the Institute farm.

Each animal was removed singly from the sow. It was weighed, the rectal temperature was measured by a thermojunction inserted 5 cm in the rectum, and the pig placed in the metabolism chamber. The chamber temperature was adjusted to 32 °C for pigs in the first few days

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