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## Effect of Sodium 5-Allyl-5-(1 methylbutyl) 2-Thiobarbiturate on Uptake of $I^{131}$ by Rat Thyroid. (20574)

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Recent observations(1,2) indicated sodium ethyl(1-methylbutyl) thiobarbiturate (Pentothal), a commonly used anesthetic agent, to reduce the $I^{131}$ uptake by rat thyroid to the extent of 89%. The reduced uptake was not found to be related to the anesthetic effect, since other anesthetics not containing a $-NH-\underset{\underset{SH}{|}}{C}=N-$ grouping did not impair $I^{131}$ incorporation into the thyroid. It was decided to test another commonly used sulfur containing anesthetic(3,4), sodium 5-allyl-5 (1 methylbutyl) 2-thiobarbiturate (Surital) to determine its effect on the $I^{131}$ trapping mechanism and particularly the chemical partition of $I^{131}$ in the thyroid gland.

*Methods.* Eight adult male rats of the Wistar strain (180-205 g) were given Surital (40 mg/kg) intraperitoneally. Sixty minutes later, each animal was given intraperitoneal injections of 2 $\mu$c of carrier-free radioiodide ($I^{131}$) contained in one ml of physiological saline. In addition, 8 male rats of comparable weight were given $I^{131}$ only to serve as controls. Four hours post administration of the $I^{131}$, the animals were sacrificed by a sharp blow on the head, the thyroids removed, stripped of adherent tissue. Mounting and radio assay technics have been described elsewhere(2). Results are expressed as counts per minute (cpm) per milligram of tissue. Thyroids from each group were pooled immediately following radio assay and digested in 3.5 N KOH for 8 hours on the water bath. The alkaline digests were fractioned with n-butanol by the method of Tong and Chaikoff(5) with minor modifications. The radioactivity of these fractions was determined under conditions of identical geometry. Counting was continued to give a statistical error of 2% or less. Results are expressed as the percentage of total recovered radioactivity from the thyroid hydrolysate.

*Results.* The data in Table I indicate that Surital markedly inhibits the uptake of $I^{131}$ by the rat thyroid. Table II shows that although the total incorporation into the inorganic, di-iodotyrosine and thyroxine fractions was much lower in the Surital treated rats than in the controls, the ratio of $I^{131}$ among these fractions is essentially the same.

*Discussion.* Obviously, the inhibition of $I^{131}$ uptake in the presence of Surital is a reaction which prevents iodide from ultimately combining with thyro-protein, (a) by in-

TABLE I. Effect of Surital on $I^{131}$ Incorporation into Rat Thyroid.*

| | cpm/mg thyroid | % controls |
|---|---|---|
| Control animals | 107.1 ± 11.8† | 100.0 |
| Surital-treated animals | 10.4 ± 1.5 | 9.7 |

* Avg of 8 animals.
† Stand. error of the mean.

TABLE II. Partition of Recovered $I^{131}$ in Alkaline Hydrolysates of Pooled Rat Thyroid Tissue.

| Thyroid fraction | Control cpm | Control % of recovered $I^{131}$ | Treated cpm | Treated % of recovered $I^{131}$ |
|---|---|---|---|---|
| Iodide | 2860 | 56.9 | 320 | 54.1 |
| Di-iodotyrosine | 1400 | 27.9 | 196 | 33.1 |
| Thyroxine | 760 | 15.2 | 76 | 12.8 |
| Totals | 5020 | 100.0 | 592 | 100.0 |

hibiting the oxidation of $I^-$ to $I_2$ or (b) by reacting with $I_2$ to form some other compound so making the iodine unavailable to thyroid cells(6). The same ratio of activities among the thyroid fractions from both groups of rats suggests that Surital does not interfere with thyroxine synthesis in the cells. Iodine has been shown to react with thioureas and thiouracil derivatives(7), the reaction being not always stoichiometric. This suggests that iodine may react with the thiobarbiturate forming a complex substance from which the iodine cannot be assimilated by the thyroid gland. The action of Surital probably follows the mechanism of action of other antithyroid drugs(6). This study suggests that clinical evaluation of thyroid status via $I^{131}$ uptake should exclude previous treatment with thiobarbiturate anesthetics.

*Summary.* 1. Surital markedly reduces the incorporation of $I^{131}$ into rat thyroid. 2. The proportion of recoverable $I^{131}$ in the inorganic and organically bound fractions of thyroid alkaline hydrolysate is essentially the same for control and Surital treated rats.

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## Incorporation of $C^{14}$-Carboxyl-Labeled Leucine by Antibody Protein.* (20575)

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An important question in the physiological behavior of proteins is whether proteins can exchange amino acids without losing their original identity. Antibody protein offers an excellent tool for this problem since such proteins can be introduced into the circulation of an animal and removed after suitable time and specifically recovered by precipitation with a homologous antigen. Heidelberger *et al.*(1), carried out an investigation of this type by feeding $N^{15}$ labeled glycine to rabbits which had been given an injection of antipneumococcus rabbit serum. Although subsequent analysis of their passively transferred antibody precipitates gave heavy nitrogen values which were slightly higher than experimental error, they concluded *a priori* that this was the result of non-specific absorption of other serum constituents which had taken up considerable amounts of the labeled glycine. When $C^{14}$ became available, Kooyman and Campbell(2) reinvestigated this problem by injecting $C^{14}$ labeled leucine into rabbits which were also given injections of several different antibodies. Their results indicated that passively transferred homologous antibody acquired considerable radioactivity after several days. However, as a result of some subsequent investigations, the question arose as to whether this activity might not be the result of absorption of non-specific serum proteins as Heidelberger *et al.* had thought possible. In view of this possibility the following investigation was carried out to repeat the previous studies with leucine but to study the problem of contamination more carefully.

*Materials and methods.* Synthesis of $C^{14}$-labeled leucine. The synthesis of leucine was

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