Release of Labelled Iodotyrosines in the Thyroid Vein of Dog

Despite the fact that the thyroid gland contains most of its iodine in the form of iodotyrosines, they could not be detected in the plasma of euthyroid human beings[1], rats[2,3], nor even in the thyroid vein of TSH-treated dogs, rabbits and cats[4]. Using neutron activation analysis of ^{129}I in the plasma of rats, equilibrated with this isotope, RHODES and WAGNER[5] found that iodotyrosines represent less than 1% of the total plasma amino acid iodine. The results of experiments to be reported show that labelled iodotyrosines can be released from the thyroid gland of dog when TSH-stimulation is applied simultaneously with an exogenous iodotyrosine overcharge.

Material and methods. The experiments were performed on 12 dogs of 12–15 kg weight. Approximately 48 h before the surgery, the animals received 250 C carrier free ^{131}I. In chloralose anaesthesia, the thyroid artery (through one of its branches) and thyroid vein were cannulated. After initial thyroid venous samples had been obtained, 20–30 U of thyrotropic hormone (TSH) was administered i.v., and blood samples were collected at the intervals thereafter. 40–50 min after TSH injection, stabile L-3-monoiodotyrosine (MIT) or stabile L-3, 5-diiodotyrosine (DIT) was infused via the cannulated thyroid artery, 0.5 ml, 5×10^{-3} in 0.1 *N* NaOH during 15 min. Chromatographic analysis of untreated plasma and its butanol extract was performed as described by TAUROG et al.[4].

Results. The scan of chromatograms of untreated thyroid venous plasma and its butanol extract showed that after TSH injection there was no peak corresponding to MIT and DIT markers at a time when labelled thyroxine and triiodothyronine had increased as much as 6–7 times. Figure 1 illustrates results obtained when stabile DIT-

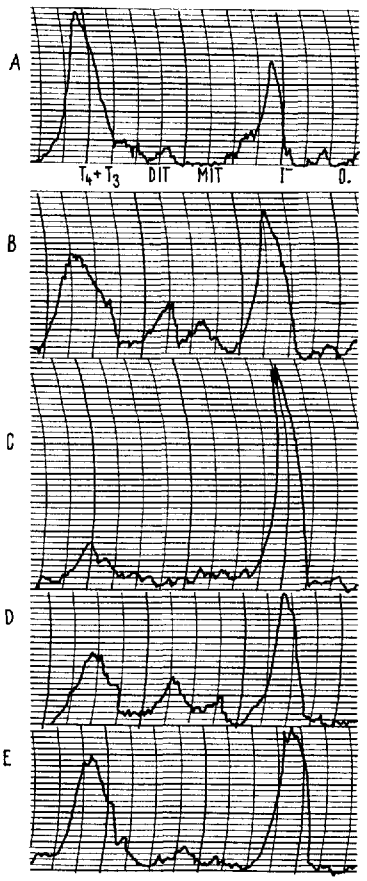

Fig. 1. Untreated plasma, radioscan-chromatogram in butanol-acetic acid. (A) Thyroid venous plasma 30 min after TSH. (B) 45 min after TSH during first DIT infusion. (C) 120 min after TSH and 15 min after first DIT infusion. (D) 137 min after TSH and during second DIT infusion. (E) 145 min after TSH and 8 min after second DIT infusion.

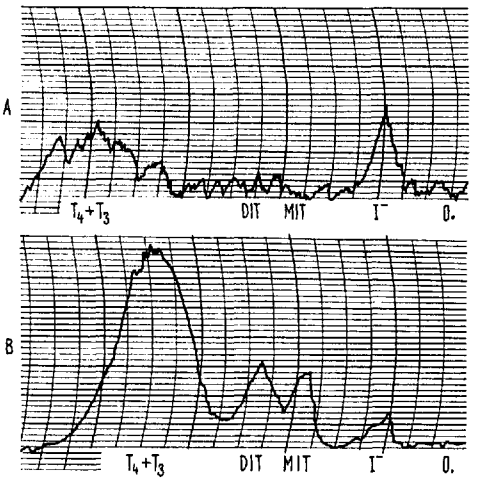

Fig. 2. Untreated plasma, radioscan-chromatogram in butanol-acetic acid. (A) Thyroid venous plasma after TSH. (B) Thyroid venous plasma after TSH and during MIT infusion.

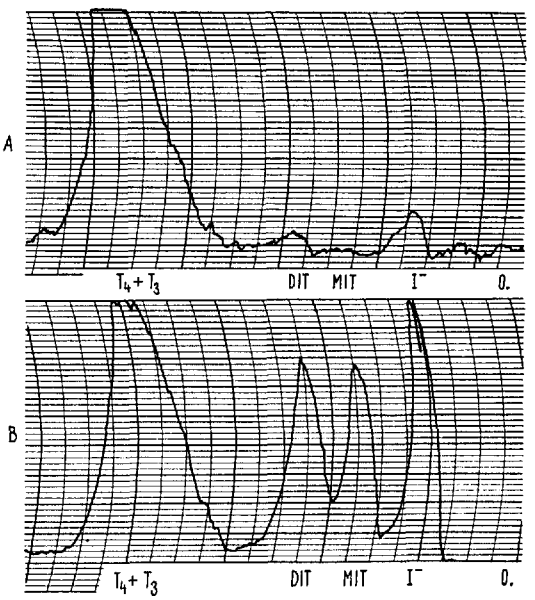

Fig. 3. Butanol extract of plasma, radioscan-chromatogram in butanol-acetic acid. (A) Butanol extract of thyroid venous plasma after TSH. (B) Butanol extract of thyroid venous plasma after TSH and during MIT infusion.

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infusion was repeated in the same dog. During the first and repeated infusion of DIT, both labelled iodotyrosines appeared in the thyroid venous plasma (Figure 1B and 1D). After DIT infusion had been stopped, both labelled iodotyrosines disappeared (1C). Similar results were obtained when MIT was infused (Figures 2 and 3). The release of labelled iodotyrosines varied in individual experiments so that in 10 dogs labelled tyrosines amounted to 22.2% (ranging from 14.6–29) of the total labelled iodine of the thyroid venous plasma.

Comments. The results of this experiment brought additional evidence that free iodotyrosines are existing in the thyroid gland[6], and in these conditions can be exchanged by the exogenous blood-born iodotyrosines. The deiodination of iodotyrosines within the gland is a very efficient process, suggested by the findings that TSH acceleration of iodotyrosine-generating hydrolysis of thyroglobulin, and simultaneous exogenous overloading with iodotyrosines are only capable of exceeding the capacity of this process. TSH alone in the conditions of this experiment has released iodide but not iodotyrosines; therefore the enzyme of dehalogenation possesses a higher capacity than the system responsible for further recycling of iodide so generated.

The infusion of only one iodotyrosine released both labelled iodotyrosines, indicating that the 2 are deiodinated by the same enzyme of the gland[7]. This 'interdischarge' between MIT and DIT shows that in these conditions, besides the isotope dilution of the free iodotyrosine pool in the gland, a substrate oversaturation of the dehalogenating system takes place and consequent release of labelled iodotyrosines[8].

Résumé. L'injection de thyréostimuline (20–30 U) suivie d'une infusion de monoidotyrosine (MIT) ou bien de diiodotyrosine (DIT) stables dans l'artère thyroïdienne provoque la libération de MIT et DIT ^{131}I-marquées dans la veine thyroïdienne chez les chiens auxquels on a injecté du ^{131}I. La TSH seule élimine la thyroxine, la triiodothyronine et l'iodure marqués, mais non la iodotyrosine. L'injection d'une seule des 2 iodotyrosines élimine les 2 iodotyrosines marquées.

N. SERAFIMOV and G. ŠESTAKOV

Institute of Physiopathology, Medical Faculty, University of Skopje (Yugoslavia), 26th January 1967.

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On the Norepinephrine Replacement by α-Methyl-Norepinephrine in the Rat Heart after Treatment with α-Methyl-DOPA

α-Methyl-DOPA (α-M-DOPA) depletes norepinephrine (NE) stores of the heart and of other tissues, whereby it is generally accepted that the released NE is replaced by equimolecular amounts of α-methyl-norepinephrine (α-M-NE), the decarboxylation and β-hydroxylation product of α-M-DOPA[1–6]. It has been shown recently, however, that a prolonged treatment with α-M-DOPA or with its metabolite α-M-NE is able to produce besides NE depletion such an accumulation of α-M-NE in adrenergic innervated tissues that the total catecholamine content of these tissues can exceed significantly their normal NE content[7,8].

The presence of α-M-NE in excessive amounts is not in agreement with the replacement phenomenon which was observed in relatively short-term experiments. Because of the importance of this metabolite (for references see MUSCHOLL[9]), it was of interest to study its action on the NE stores as well as the rate of disappearance of α-M-NE after repeated administration of α-M-DOPA or of α-M-NE itself.

Methods. Male guinea-pigs, 250–400 g body-weight, or male rats, 180–240 g body-weight, were treated with D,L-α-M-DOPA (300 mg/kg; p.o.) or with L-α-M-NE·.HCl (0.1–1 mg/kg; s.c.), once or daily for 11 days. Control animals received the same volume of saline. The cardiac catecholamines were extracted twice with 10% trichloracetic acid, adsorbed onto alumina at pH 8.4 and eluted with 0.25 *N* HCl. NE and α-M-NE were estimated differentially by using both biological and fluorometric assay procedures[10,11].

Results. In a preliminary experiment, it was shown that a single injection of α-M-NE depletes markedly myocardial NE stores in rats and guinea-pigs (Table).

In another experiment, rats were pretreated daily for 11 days with D,L-α-M-DOPA or with α-M-NE. Cardiac NE was estimated 24 h after the 1st, 2nd, 4th, and 11th (last) administration, as well as 2, 4, 7, and 10 days after the last administration. Cardiac α-M-NE was estimated concomitantly with NE after the end of the treatment period. The results are shown in the Figure. They clearly demonstrate that the hearts of treated rats regained a normal NE content after 8–10 days. At this time, however, they contained still α-M-NE in amounts which were of the same order of magnitude as those of NE. The rate of disappearance of NE from the heart was faster during

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