adrenergic blocking agents were given at doses which totally reversed the usual cardiovascular actions of intravenously injected adrenaline or noradrenaline.

It has now been observed in experiments performed under these conditions with any of the selected drugs, that subsequent applications of adrenaline to the cerebral cortex were regularly followed by hypertensive reactions. Relatively high concentrations of these compounds sometimes attenuated this effect at the beginning. But later on, the cortical response was restored, and even surpassed its previous amplitude, while intravenous adrenaline and noradrenaline administration continued to cause hypotensive actions. Such an assay is illustrated in the Figure, showing that an animal having received a dose of Regitine, sufficient to transform the cardiovascular reactions to intravenous adrenaline, maintains an important hypertensive response to the same hormone on cortical application.

One could possibly object to this kind of experiments in that the important quantities of transmitter which may 'diffuse' from the cerebral cortex into the systemic circulation, might act differently from the very small amounts introduced intravenously. But in the same experiment shown in the Figure, the administration of three times the initially injected dose of i.v. adrenaline (II) only accentuated the previously obtained reversal, and a repetition of such an injection (IV) even led, in this case, to a lethal blood pressure fall.

One could then argue that the 'diffusing' substance, passing into the jugular vein and consequently entering directly the heart, might not react like the same transmitter injected through more peripheral channels, such as the saphenous or the femoral vein. However, such a possibility has been ruled out in experiments in which rabbits pretreated with Dibenamine, and reacting indifferently by hypotensive effects to injections of adrenaline performed through the saphena, the jugularis, or even the carotid artery, unvariably responded by pressor effects to cortical applications of the same substance.

Another possible objection might be concerned with the apparent discrepancy between the amounts of adrenaline and those of its antagonistic drugs, on the one hand, and between their respective modes of administration (cortical in the first, and intravenous in the second case). However these arguments cannot be considered as particularly pertinent, for intravenous as well as cortical adrenaline produced equipressor reactions in the experiments reported. They could finally be eliminated by assays in which the transmitter and the adrenergic blocking agent were both applied to the cerebral cortex at strictly corresponding concentrations. Here again a complete dissociation has been realized.

Uni- or bilateral contacts during 5 min of a piece of filter-paper soaked in a 5% solution of Regitine, Piperazine, Dibenamine or Largactyl, resulted in a considerable enhancement of the hypertensive response to a subsequent topical application of adrenaline, whereas the cardiovascular effects of intravenous injections of the same hormone were unchanged or decreased.

Adrenaline-sensitive elements can thus be characterized at cerebral levels thanks to the fact that their affinity to so-called 'adrenergic blocking' agents differs in a specific way from that of corresponding peripheral structures.

Résumé. L'administration parentérale d'agents «adrénolytiques» de structures diverses laisse persister la réaction hypertensive à l'application corticocérébrale de l'adrénaline tout en inversant les effets cardiovasculaires habituels de cette hormone injectée par la voie intraveineuse. L'application corticocérébrale de ces mêmes agents engendre un renforcement de la réponse hypertensive à l'adrénaline corticale.

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Thyroid Hormone Synthesis During Hypothermia in Rats

Hypothermic reduction of thyroid I^{131} uptake has been shown in rats[1,2] and has persisted even after returning to normal body temperature[3]. Paper radiochromatography of the alkali hydrolysate of the gland demonstrated an organic incorporation of the iodine taken up during hypothermia[1]. The aim of the present investigation was to study the formation of iodinated amino acids in hypothermia by means of paper radiochromatography of trypsin hydrolysed gland.

Material and Methods. Eighteen male albino rats of 150–170 g weight were used. Two groups of six rats were cooled by Gjaja's method of hypoxic hypercapnia[4], one group to 18–20°C and the other to 28–31°C rectal temperature. 20 μC of carrier-free I^{131} in 0.4 ml saline solution were injected intravenously during the corresponding degree of hypothermia, and then kept for 5 h at this rectal temperature. The rats were sacrificed and each thyroid gland removed and weighed on a microtorsion balance, homogenized and hydrolyzed for 48 h at 38°C in 1 ml veronal buffer pH 8.6 with 2 mg trypsin, and $7 \cdot 10^{-4}$ propylthiouracil was added to avoid further transformation of I^{131} *in vitro*. 30 μg of monoiodotyrosine, diiodotyrosine, triiodothyronine, thyroxine, and KJ were added as carriers. Paper chromatography of the hydrolysate was carried out in a system of butanol-acetic acid-water (4:1:5), developed during 20 h, and the detection of iodine was by ceri arsenic reagent[5]. Chromatograms were cut in a segment of 1 cm and radioactivity of each determined on a well type scintilating counter.

Results and Comments. The results (Table and Figure) show that deep and light hypothermia reduce thyroid I^{131} uptake and, at in the same time, a change in the various intraglandular forms of iodine compounds occurs. Monoiodotyrosine and diiodotyrosine are present in a higher proportion in relation to the total iodine. Iodinated thyronines (triiodothyronine and thyroxine) activities were at

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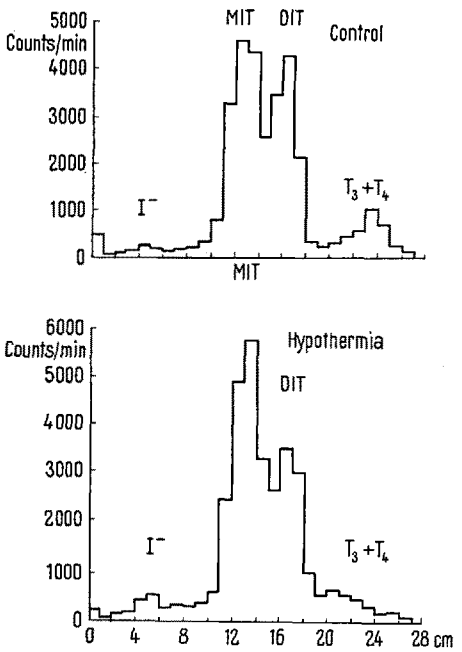
Thyroid 5 h I^{131} uptake and paper chromatographic distribution during hypothermia in rats. M ± S.E.

		Number of rats	Thyroid I^{131} uptake p. 100 dose	p. 100 of total thyroid I^{131} I^-	MIT	DIT	$T_3 + T_4$
Control		6	31.7 ± 2.05	2.4 ± 0.65	48.4 ± 1.8	38.6 ± 1.09	10.3 ± 1.23
Hypothermia	18–20°C	6	6.0 ± 2.14	4.1 ± 1.37	58.5 ± 1.45	37.7 ± 1.21	0
Hypothermia	28–31°C	6	8.25 ± 1.75	6.92 ± 0.65	51.25 ± 1.21	41.83 ± 1.34	0

I^- Inorganic iodine; MIT Monoiodotyrosine; DIT Diiodotyrosine; $T_3 + T_4$ Triiodothyronine + Thyroxine



the background level of chromatograms, with an absence of any corresponding peak in activity. These findings support the hypothesis of a hypothermic blockade of enzyme reactions concerned in the last phases of hormone synthesis, probably the coupling of iodinated tyrosines. The absence of iodinated thyronines, and higher values of iodinated tyrosines, can be explained as a result of a more severe affection of this system in hypothermia than other enzymes of thyroid hormone synthesis[6].

Zusammenfassung. Tiefe und oberflächliche Hypothermie an Ratten reduziert die Radiojodfixation der Schilddrüse. Markierte Jodtyrosine werden dedektiert, während Jodtyronine fehlen.

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Effects of Guanethidine on Salivary Glands

Like extirpation of the superior cervical ganglion[1] a 'pharmacological sympathectomy' brought about by administration of drugs such as bretylium and guanethidine can give rise to pain in the salivary gland regions during meals. This seems to be a much more common side-effect of bretylium than of guanethidine. Experiments on anaesthetized cats have demonstrated that bretylium abolishes vasoconstrictor and secretory effects of sympathetic stimulation in salivary glands, thus imitating sympathectomy. In addition, however, the drug has a muscarine-like effect on the glands, evoking a flow of saliva in doses only slightly larger than those required to produce 'sympathectomy'[2].

In the present experiments the effect of guanethidine was investigated on submaxillary and parotid glands of cats and submaxillary glands of rats. The anaesthetic used was chloralose, about 80 mg/kg given intravenously after induction with ether. The salivary ducts were exposed and cannulated. Drugs were given intravenously. Artificial ventilation was given from a pump.

In the cats the secretory responses of the submaxillary glands to sympathetic stimulation were abolished by guanethidine in doses of 0.5–1 mg/kg, i.e. doses similar to those required with bretylium. When the dose of guanethidine was slightly increased no secretion of saliva ensued, as was the case with bretylium. Very large doses had to be given to obtain a small secretory response from normal parotid (20 mg/kg) or submaxillary (40 mg/kg) glands. Doses of this order were also found to abolish for a short period the secretory effect of chorda stimulation but not that of acetylcholine or noradrenaline in submaxillary glands.

The secretory effect of bretylium is increased by previous parasympathetic denervation (parotid) or decentralization (submaxillary gland)[2]. This was found to be the case with guanethidine also, doses of 2–10 mg/kg producing secretion from parotid and submaxillary glands.

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