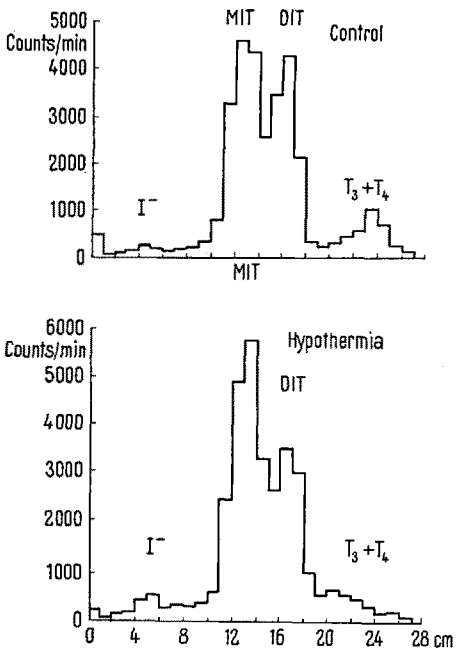
Thyroid 5 h I^{131} uptake and paper chromatographic distribution during hypothermia in rats. M ± S.E.

		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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[6] Our thanks are due to Prof. I. S. TADŽER for helpful discussion.

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.

[1] W. J. GARDNER and A. F. ABDULLAH, Amer. J. med. Sci. *230*, 65 (1955).

[2] N. EMMELIN and J. ENGSTRÖM, Lancet *1960*, 263.

Such glands were used to analyze the secretory effect of guanethidine and to compare it with that of bretylium. The secretion caused by guanethidine was not abolished by parasympatholytic agents but by dihydroergotamine; the reverse is true for bretylium. It is therefore not a muscarinic effect, as that of bretylium, but rather a sympathomimetic effect. The secretory response to guanethidine could be obtained after removal of the adrenals and acute extirpation of the superior cervical ganglion. When the sympathetic fibres had degenerated, however, as a consequence of previous excision of the sympathetic ganglion, guanethidine had no secretory effect; this operation augments the secretory effect of bretylium.

Essentially the same results were obtained in rats. Secretion could be obtained from normal glands with somewhat smaller doses of guanethidine than in cats, 5–10 mg/kg. Parasympatholytic agents did not affect the flow. It was very markedly reduced but not completely abolished by chronic sympathetic ganglionectomy or injected dihydroergotamine; it may be added that dihydroergotamine could not wholly abolish the secretory effect of injected noradrenaline in rats.

It has thus been found that guanethidine is about as potent as bretylium in producing a 'sympathectomy' in salivary glands. The secretory effect of the drug is, however, much smaller than that of bretylium. This finding might explain the fact that pain in the regions of the salivary glands during meals seems to be less common when guanethidine is used as a therapeutic agent. The secretory effects of guanethidine and bretylium on salivary glands have entirely different mechanisms. Whereas bretylium exerts a muscarinic action on the gland cells, the effect of guanethidine is dependent on the integrity of the postganglionic sympathetic fibres. The observations made are compatible with the present view that guanethidine may liberate catechol amines from the sympathetic fibres.

Zusammenfassung. Guanethidin hebt den sekretorischen Effekt der Sympathicusstimulierung von Speicheldrüsen genau so wirksam auf wie Bretylium. Ebenso wie Bretytylium kann Guanethidin eine Speichelsekretion hervorrufen, aber nur, wenn es in grosser Menge gegeben wird. Während Bretylium dabei einen Muskarineffekt hat, scheint Guanethidin durch Freisetzen von Catecholaminen an den sympatischen Nervenenden zu wirken.

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The Effect of Alkylating Agents on the Excretion of Taurine in the Urine of Rats

Following upon irradiation, increased amounts of taurine are excreted in the urine by human beings[1] and rats[2]. It would be of interest to know whether radiomimetic compounds have a similar effect, and Kostos and Koczis[3] did in fact report that colchicin caused an increase of taurine excretion in rats. Since it is questionable whether colchicine should be classified as a radiomimetic agent[4], we have investigated the effect of alkylating agents (which are well-known radiomimetic compounds) on the taurine excretion in rats. The compounds studied, di(chloroethyl)-methylamine (HN_2), tri(ethyleneimino)-phosphine sulfide (Thio-TEPA) and 1,4-di(methanesulfonyloxy)buthane (Myleran), represent three different types of alkylating agents and they all gave rise to an increased taurine excretion. The increases obtained after HN_2 and Thio-TEPA were of the same magnitude as those observed after 500 r X-rays (Table) whereas Myleran produced a smaller effect. The alkylating compounds were also used at dose levels half of those reported in the Table, but only small increases of taurine excretion were obtained, which were not significantly different from the control values. The present results thus demonstrate that radiomimetic agents may provoke metabolic disturbances of the same type as those caused by ionizing radiation.

Effect of alkylating agents and X-rays on taurine excretion: Groups of 5 (4 in case of Myleran) male rats of 250–300 g body weight were fed a synthetic diet[5] and received the compounds studied by i.p. injection. Urine was collected at 24 h intervals and its taurine content determined[6]. Values shown are means ± standard error

Treatment	Taurine excretion (μmoles/24 h) before treatment	after treatment Day 1	Day 2	Day 3
HN_2 (1.0 mg/kg)	33.5 ± 3.6	53.1 ± 17.8	80.8 ± 10.8[b]	71.8 ± 18.3
Thio-TEPA (6.0 mg/kg)	52.7 ± 6.5	66.5 ± 10.5	84.3 ± 12.4	92.7 ± 7.4[b]
Myleran (30 mg/kg)	33.6 ± 5.5	44.6 ± 8.3	57.1 ± 8.2	57.4 ± 7.1[a]
X-rays (500 r)	49.8 ± 9.3	83.8 ± 16.6	108.9 ± 17.0[a]	86.1 ± 21.4

[a] Significantly different from control value at the 5% level.
[b] Significantly different from control value at the 1% level.

Zusammenfassung. Die alkylierenden Verbindungen HN_2, Thio-TEPA und Myleran bewirkten eine vermehrte Taurinausscheidung in der Ratte.

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