line caused practically no increase in V_{Pul}. Bemegride, picrotoxin, Rec 7-0105 and DEHB showed a moderate action. Prethcamide and dimefline exerted the greatest and most lasting stimulant action on the respiration, the former acting more on the F and the latter more upon the V_T.

Experiments on rabbits with morphine-depressed respiration yielded similar results. In fact, only dimefline, prethcamide, bemegride, DEHB and picrotoxin brought the V_{Pul} back to normal or supranormal levels.

Taking account of toxicity, the widest therapeutic margin was shown by dimefline, followed by bemegride, prethcamide and Rec 7-0105.

The pneumokinetic activity of dimefline and prethcamide was confirmed in dogs and cats with barbital- or morphine-depressed respiration. Both drugs raised the HbO_2 and the blood pH in addition to the V_{Pul}.

Dimefline is, moreover, highly active in combating respiratory syncope induced by various drugs and in establishing the respiratory function in immature foetuses.

55 Immunosympathectomy as a New Approach to the Study of the Sympthetic System. R. Levi-Montalcini and P. U. Angeletti (U.S.A.).

Adult Swiss mice and albino rats were used. Injections of the antiserum were given soon after birth for 5 consecutive days at the daily doses of 0·05 ml/g of body wt. Histological examination of the superior cervical ganglia was performed in all animals used for the chemical assay of catecholamines and MAO activity.

Adrenaline and noradrenaline were measured in various organs by spectrophotofluorometric procedures. MAO was measured in the same organs by manometric technique. A marked decrease in the noradrenaline content was found in heart, spleen and other tissues of the immunosympathectomized animals. Levels of MAO activity were also found to be decreased in several organs of the same animals. The influence of the administration of various substrates on MAO activity was investigated in normal and experimental mice and rats. The results of the above experiments will be discussed with respect to mono-amine-oxidase activity and sympathetic function.

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1. Levi-Montalcini, R. and Cohen, S. (1960), *Ann. N.Y. Acad. Sci.*, **85**, 324.

56 Cholinesterase Distribution in the Sympathetic Nervous System of the Cat. F. Sjöqvist and B. Fredricsson (Sweden).

Sympathetic ganglion cells are not homogeneous with respect to their content of acetylcholinesterase (AcChE). A small number of the neurons resemble parasympathetic ganglion cells and anterior horn cells in terms of strong histochemical staining intensity for AcChE (thiocholine method). The great majority of the sympathetic ganglion cells have very little, if any, AcChE-activity.

The characteristic AcChE-rich nerve cells are predominantly found in the stellate ganglion and at the level of L6–S1. In these particular ganglia these neurons can amount to 5–15 per cent of the cell population, but in other paravertebral ganglia they are surprisingly few. They seem to be extremely rare in the prevertebral ganglia. Denervation experiments show that most of these cells in the stellate ganglion are connected with nerve fibres to the fore leg.

The results are suggestive of two functionally different types of sympathetic ganglion cells. The AcChE-rich ganglion cells are unevenly distributed in the sympathetic nervous system with an accumulation in those ganglia giving rise to the secretory and vasomotor fibres to the fore and hind foot.[1] This is of interest since the sweat glands of the cat are exclusively found in the paws and are cholinergically innervated.[2] The possible relationship between these AcChE-rich ganglion cells and postganglionic cholinergic sympathetic fibres in general will be discussed.

1. Langley (1891).
2. Dale and Feldberg (1934).

57 On the Mechanism of Action of the Ganglion-blocking Agents. D. A. Kharkevich (U.S.S.R.).

The influence of tetraethylammonium, hexamethonium, hexonium, pendiomide and mecamylamine on the interneuronal transmission of excitation in sympathetic ganglia was studied. It was found that all the drugs tested deepen the passimal (Wedensky) inhibition of the ganglia, increase the time required for transmission of nervous excitation from the pre- to the post-ganglionic fibres (latency) and prevent after-discharges. The influence exerted by ganglion-blocking agents in respect to the above parameters seemed to be fairly uniform. A different result was obtained in experiments with postactivation potentiation. Hexamethonium, pendiomide and mecamylamine decrease or totally prevent the development of potentiation; tetraethylammonium was found to be ineffective.

In view of these data, and considering the nature of postactivation potentiation it may be suggested that hexamethonium, pendiomide and mecamylamine exert a depressing action on the activity of the presynaptic endings.

In order to analyse the action of the ganglion-blocking agents on the conduction of excitation in the post-synaptic neurones, experiments with post-activation inhibition were undertaken (the latter developing as a result of interaction of the hetero-

synaptic volleys, together with recording of the bioelectric activity of the ganglia following antidromic stimulation). It was found that the ganglion-blocking agents do not increase postactivating inhibition and have no influence on the conduction of excitation during antidromic stimulation. In contrast to the ganglion-blocking agents, procaine considerably impairs conduction of excitation in the postsynaptic neurones.

From the above data it appears that the inhibition of transmission of excitation in autonomic ganglia which occurs under the influence of ganglion-blocking drugs is related not only to the selective depression of the cholinoreceptores, but may also be the result of the influence exerted by these substances on the function of the presynaptic endings.

58 Enhanced Postganglionic Responses of Sympathetic Ganglia to Stimulating Agents Following Repetitive Preganglionic Stimulation. R. L. VOLLE (U.S.A.).

Asynchronous postganglionic discharges of the feline superior cervical ganglion, *in situ*, evoked by acetylcholine (ACh), carbamylcholine, and tetramethylammonium (TMA) were monitored with conventional electrophysiological techniques. Following repetitive preganglionic stimulation with supramaximal volleys at rates ranging from 20 to 100 c/s for periods of 10 sec to 15 min, the amplitudes and time–courses of the ganglionic responses to these agents were enhanced markedly. The duration of stimulation required to produce these changes appeared to be related inversely to the frequency of stimulation. Following repetitive stimulation, carbamylcholine, administered in doses which elicited postganglionic responses lasting 20–30 sec in previously unstimulated ganglia, evoked responses which last 3–5 min. Doses of ACh and carbamylcholine which produced just detectable postganglionic firing were reduced 8- to 16-fold by this procedure of conditioning. The threshold doses of TMA, however, were not reduced; suprathreshold doses were potentiated. The enhanced responses, once induced, persisted for the duration of the experiment (up to 5 hr after conditioning stimulation). Antidromic stimulation of the postganglionic trunks of normal and chronically denervated ganglia did not result in any significant alteration of the responses of the ganglia to these agents. Furthermore, ganglionic blockade by hexamethonium, infused into the arterial supply of the ganglia before and during repetitive stimulation in amounts which blocked completely the postganglionic responses to single preganglionic volleys, did not prevent the occurrence of enhanced responses to injected stimulating agents. It is suggested from these findings that: (1) conditioning with repetitive preganglionic volleys results in alterations in the presynaptic nerve terminals as reported previously by Larrabee *et al.*[1]; and (2) the action of ACh and carbamylcholine on the ganglion is due in part to stimulation of the nerve terminals.[2]

1. LARRABEE and BRONK (1947), *J. Neurophysiol.*, **10,** 139.
2. VOLLE and KOELLE (1960), *The Pharmacologist*, **2,** 88.

59 Classification of Ganglionic blocking Agents. J. M. VAN ROSSUM (Holland).

Transmission of impulses through the ganglionic synapse is to some extent similar to transmission through the neuromuscular junction. In both cases acetylcholine (ACh) is involved, which implies that drugs may act by: (a) inhibiting the synthesis of ACh; (b) affecting the release of ACh; (c) occupying ACh-receptors whilst having intrinsic activity and thus action as an ACh-mimetic; (d) merely occupying ACh-receptors and thus acting as a competitive antagonist; (e) occupying other receptors and so acting as a non-competitive antagonist.

When studying ganglionic blocking agents on neuro-muscular preparations evidence accumulates that some may act as competitive antagonists and others as non-competitive antagonists.

Ganglionic-stimulants and -blocking agents have therefore been investigated upon the isolated guinea-pig intestine under conditions that only ganglionic effects are measured. Dose–response curves were made of the stimulants using nicotine as a standard, whereas the blockers were studied as how they affect dose–response curves of nicotine.

At least three classes of ganglionic drugs occur: Class I: the mimetics as nicotine, DMPP, pyridine-3-methyl-yl-trimethylammonium; Class II: the lytics or competitive antagonists as hexamethonium, pentapyrrollidinium and azamethonium; Class III: the non-competitive ganglionic blocking agents as pentacyne, chlorisondamine. There exists a number of intermediate compounds, e.g. mecamylamine and pempedine, which are both competitive and non-competitive.

There exists a characteristic relationship between chemical structure and the class of drug.

60 The Effect of Various Amines on Transmission through the Superior Cervical Ganglion of the Cat. S. B. GERTNER and A. ROMANO (U.S.A.).

We have recently reported that guanethidine and bretylium blocked transmission when perfused through the superior cervical ganglion. This block which could be antagonized by the perfusion of epinephrine and norepinephrine, prompted a more thorough investigation of the effects of amines on ganglionic transmission. The actions of epinephrine, norepinephrine, isoproterenol, ephedrine, phenylephrine, tyramine, dopamine, tryptamine, 5-hydroxytryptamine and various other derivatives were tested on transmission. The stability of the