catecholamines during perfusion was greatly increased by the simultaneous use of ascorbic acid, which itself did nothing to transmission. In all the experiments there was never an indication of noticeable stimulation or facilitation of transmission. All of the catecholamines blocked transmission in doses varying from 50 γ/ml upwards. With lower concentrations no effect could be observed. Epinephrine and norepinephrine appeared to be equally effective in blocking transmission; dopamine was considerably less active. Of the drugs tested, tryptamine appeared to be the most potent, often causing considerable block of transmission when perfused in concentrations as low as 10 γ/ml. It was often possible to show a transient block when the drug was given as a single injection of 25 γ into the perfusion stream. Tyramine was somewhat less active. 5-Hydroxytryptamine showed very little if any effect on transmission although sometimes a slight potentiation was noticed. The blocking action of some of the amines was potentiated if given during the perfusion of a mono-amine-oxidase inhibitor.

61 The Mode of Action of Acetylcholine on the Adrenal Medulla. W. W. Douglas and R. P. Rubin (U.S.A.).

It is commonly accepted that the sympathetic nerves innervating the adrenal medulla are cholinergic, and that acetylcholine is the physiological stimulus which effects the release of catecholamines from the adrenal medullary cells. In experiments on perfused cat's adrenals, we have obtained evidence that the action of acetylcholine involves some Ca dependent process. Thus when the adrenals were perfused with Ca-free Locke's solution the amount of catecholamine liberated by acetylcholine fell to 5 per cent or less of the control value obtained in Locke's solution containing 2·2 mM Ca. Moreover, there was a quantitative relationship between the amount of catecholamine released by acetylcholine and the Ca content of the perfusion fluid: catecholamine output was about halved when the Ca concentration was lowered to 0·5 mM, and was increased by about half when the Ca concentration was raised to 8·8 mM. It was found that Ca itself (2·2 mM) caused secretion of catecholamine when introduced after a period of Ca free perfusion: excess Ca (to 35 mM) added during perfusion with Ca containing Locke had no such effect.

These findings, that catecholamine secretion in response to acetylcholine is related to the extracellular Ca concentration and that Ca itself (in appropriate conditions) causes catecholamine release, considered along with the known ability of acetylcholine to effect permeability changes at other post-synaptic sites, lead us to propose that acetylcholine causes catecholamine secretion by promoting an influx of Ca ions into the adrenal medullary cells.

62 The Influence of Ganglion-blocking Agents on Tissue Sulphydryl-Groups Content and Analysis of the Action of Thiol Substances on Impulse Transmission in Autonomic Ganglia. S. A. Mirzoyan (U.S.S.R.).

Some reactive groups of protein bodies undoubtedly play a responsible role in the primary chemical reactions of pharmacological agents with the receptors of effector organs. The present report concerns the interaction of gangliolytics with the tissue sulphydryl groups in structural homogenate. The objects for study have been the superior cervical ganglion and the ganglia of the vagal intestinal fibres in cats. The observations have shown that following the blocking of transmission in ganglionic synapses by hexamethonium, Gangleron or pentamine, a marked decreased in tissue sulphydryl content is observed. The experiments prove that the chemical interaction of gangliolytics with tissue reactive groups is not an accidental or side effect of the examined preparations. In experiments with nicotine it has been shown that the preparation, in doses which augment the sensitivity of ganglionic cells to electrical stimulation of presynaptic fibres and facilitate transmission in interneuronal synapses, causes an increase in tissue thiol groups content. In large doses, the blocking effect of nicotine on ganglionic transmission fully spreads over the sulphydryl groups content.

Titration of the homogenate in the presence of hexamethonium, Gangleron or pentamine, shows that the interaction of these preparations with the tissue sulphydryl groups takes place also in the non-structural homogenate, and under the action of hexamethonium, Gangleron or pentamine, a decrease is noted in sulphydryl groups content.

In perfo ion experiments an antagonism is observed between the sulphydryl groups and ganglion-blocking agents in their action on sympathetic ganglia and ganglia of the vagal intestinal fibres.

Thus, gangliolytics exhibit a capacity to decrease the thiol groups content and tissue sulphydryl groups have a definite significance in the chemical sensitivity of receptors towards ganglion-blocking agents.

63 Lipid Solubility as an Important Factor for the Penetration of Drugs into the Liver. H. Kurz (Germany).

The relative rate at which various foreign organic compounds of widely different chemical and physical properties enter the liver tissue was investigated in the isolated rabbit liver. The liver was perfused from the portal vein with a drug–saline solution at constant rate. The perfusate was collected in small fractions over a period up to 5 hr. The rate of disappearance of the drug was calculated from the decrease in concentration in the perfusate. Protein-binding was eliminated by calculation. The experiments were made at a temperature near 0°C to avoid metabolic interference