unsaturated fatty acids[5–7]. In the present experiments also this was clearly confirmed as shown in Figure 1, B. When oleic acid was substituted for the tissue extracts, the liberation pattern of histamine and 5-HT has a strong resemblance to that of the tissue extracts.

Discussion. According to the present results, certain unsaturated fatty acids affect platelets to liberate not only 5-HT but also histamine. Several cytochemical and electronmicroscopical studies have indicated that platelet histamine is contained in bound state in their storage granules as 5-HT[9–13]. Further, our electronmicroscopical observations have demonstrated typical degranulation of rabbit platelets after incubation with the alkaline tissue extracts (to be published). It is highly probable, therefore, that certain unsaturated fatty acids first affect amine-containing granules in platelets which in turn cause release of 5-HT and histamine from the platelets. Similar observations have already been made in this laboratory on the nucleated thrombocytes[14–16].

Zusammenfassung. Durch In-vitro-Inkubation mit alkalischen Gewebsextrakten oder mit Oleinsäure wurde Histamin aus den Blutplättchen von Kaninchen freigesetzt.

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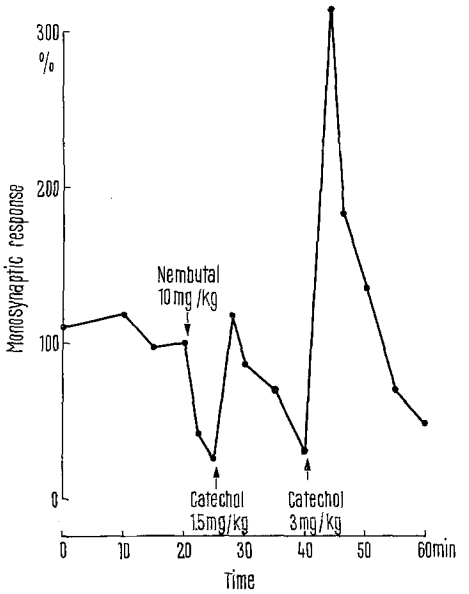
Antagonism of Barbiturate Depression of Spinal Transmission by Catechol

It is generally believed that the synapse is the major site of action of barbiturates at all levels of the neuraxis. In the spinal cord, barbiturates depress transmission across both monosynaptic and polysynaptic reflex arcs[1]. Recent neurophysiological investigations have probed into the possible mechanism of this synaptic depression. LØYNING et al.[2] have observed a decrease in potentials which represent activity in spinal afferent nerve terminals after barbiturate administration, while the firing threshold of the motoneuron remained constant. They postulated that barbiturates act mainly on these terminals resulting in decreased transmitter release and leading to reduction of synaptic potentials. Subsequently, WEAKLY[3] showed that an interference with the mechanism responsible for transmitter release could account entirely for the barbiturate-induced depression of transmission in the spinal monosynaptic pathway.

Recent work on convulsant phenols[4] has demonstrated the ability of these compounds to facilitate central synaptic transmission and produce spinal actions opposite to those reported for barbiturates. The observed facilitation induced by phenolic substances was postulated to result mainly from increased transmitter release by afferent presynaptic terminals after nerve stimulation. Phenolic substances may therefore be expected to antagonize the effects of barbiturates on synaptic transmission.

Cats (2.5–4.2 kg) were anesthetized with ether, then spinalized by a section at the atlanto-occipital junction. Ether anesthesia was terminated and artificial respiration instituted and maintained during the experiment. Carotid arteries were ligated. The lumbosacral cord was exposed by laminectomy, the dura sectioned, and all nerve roots from L_5 to S_3 were severed extradurally on one side. On the other side, L_5, S_2 and S_3 nerve roots were cut, along with the ventral roots of L_6, L_7 and S_1. The spinal cord was bathed in mineral oil at a constant temperature of 37 °C. Body temperature was also maintained close to 37 °C.

Square wave stimuli of 0.1 msec duration maximal for group I fibers were applied to the hamstring nerve and the evoked potentials measured from ventral L_7. Stimulating electrodes were also placed on the sural nerve, while all the other leg nerves were cut. Exposed nerves were covered with warm mineral oil. A filament from dorsal L_6 was used to record the dorsal root reflex. Occasionally the cut L_7 dorsal root was stimulated supramaximally and the evoked discharge recorded from L_7 ventral root.



Typical experiment showing the antagonism of barbiturate-induced depression of the spinal monosynaptic response by catechol. The hamstring nerve was stimulated and the evoked ventral root discharge was recorded from the ipsilateral L_7 ventral root. Drugs were administered i.v.

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Blood pressure was continuously monitored from a carotid artery. Gallamine (Flaxedil) was used to relax skeletal muscles. Pentobarbital (Nembutal, Abbott) and freshly dissolved catechol were administered through a cannulated antibrachial vein.

In all 15 experiments performed, there was a quantitative antagonism of the effects of pentobarbital on monosynaptic transmission. The monosynaptic response (MSR) could thus be 'titrated' to the desired size by varying the relative doses of catechol and pentobarbital. A dose of 10 mg of pentobarbital per kilogram of body weight depressed the MSR to an average of 30 $\pm$ S.E. 5.5% of control size in 7 cats. A dose of 1.5 mg of catechol/kg returned it to average control size ($n = 3$) and 2 mg/kg to 34 $\pm$ 6.75% above control size ($n = 4$). Further doses of catechol resulted in progressive increase in facilitation of evoked motoneuronal discharge (Figure). Larger doses of pentobarbital produced a stronger depression of the MSR which in turn required larger amounts of catechol to relieve. Thus when 20 mg of pentobarbital/kg was administered, a dose of 4.5 mg of catechol/kg was just sufficient to antagonize its effects. The duration of this antagonism was brief, in keeping with the usually short duration of action of catechol (15 min). However, by means of slow infusion of catechol after the initial dose, it was possible to maintain normal transmission over a prolonged period of time. Thus an initial dose of 1.5–2 mg of catechol/kg followed by continuous administration of about 0.15 mg/kg/min maintained normal transmission for at least 45 min. Results obtained after stimulation of a cut dorsal root and recording from the corresponding ventral root were essentially similar.

The barbiturate-induced depression of multisynaptic spinal responses evoked by stimulation of a skin nerve (sural) was also antagonized by catechol. The depression of the dorsal root reflex by large doses of pentobarbital was antagonized by small doses of catechol (1 mg/kg). Catechol produced no significant changes in the blood pressure of anesthetized spinal cats.

Unlike other convulsants, catechol appears to act mainly by a mechanism[4] opposite to that proposed for barbiturates. The antagonism reported here is physiological, although a common site of action is involved, namely the presynaptic terminals. This antagonism is only of experimental interest, however, since the potent peripheral and toxic actions of catechol limit its usefulness[5].

Résumé. La diminution, par le pentobarbital, de la transmission à travers les relais monosynaptiques et multisynaptiques de la moëlle épinière, est rapidement contrecarrée par l'administration intraveineuse de catéchol. Cet antagonisme est de courte durée et paraît être le résultat d'effets physiologiques contraires sur les extrémités présynaptiques afférentes.

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Antinicotinic Properties of Papaverine in Guinea-Pig taenia coli

Hirtz[1], in 1913, inferred that, in the action of papaverine, not only is a direct effect on smooth muscle involved, but also parasympathetic nerve endings are influenced. An antinicotinic action of papaverine on ganglionic and neuromuscular transmission was observed recently in this laboratory[2].

For the detection of an antispastic effect of papaverine, drugs stimulating smooth muscle by different mechanisms were used. Contractions of the taenia produced by nicotine are due to stimulation of intramural cholinergic ganglia; those produced by acetylcholine represent a muscarinic effect, while those induced by $BaCl_2$ are partly caused by its direct effect on smooth muscle, and partly explained by its effect on ganglia or nerves[3,4].

Materials and methods. The taeniae coli of the guinea-pig were suspended in Krebs solution, either in an isolated organ bath, or in a sucrose-gap apparatus. Membrane activities were recorded extracellularly[5]. The tension was measured with a mechano-electric transducer valve, or with a strain-gauge system[6].

The dose of papaverine (1×10^{-5} g/ml) used throughout the experiments was chosen from a wider range of concentrations (5×10^{-6} — 5×10^{-4} g/ml). This concentration, even when present in the perfusion fluid for 30 min, did not completely block spontaneous activity of the taenia. The concentrations of nicotine, acetylcholine and $BaCl_2$ were selected so as to produce approximately 3/4 of maximal acetylcholine contraction. The mechanical response and the maximal spike frequency increase above the spontaneous frequency level to any one of the contracting drugs, in the absence of a spasmolytic drug were considered as 100% effect. Both mechanical and electrical activities evoked by the contracting drugs in untreated and treated muscles were compared by the 'paired' t-test.

Results and discussion. Nicotine (2×10^{-6} g/ml), acetylcholine (1×10^{-6} g/ml) and $BaCl_2$ (5 mM) were in contact with the preparation for 120, 90 and 60 sec, respectively. The mechanical response evoked by nicotine was inhibited to 7.5 $\pm$ 14.5% (mean $\pm$ S.E.M.) of its control level by pretreatment with papaverine. The average spike frequency evoked by nicotine was 59.8 $\pm$ 2.8 per min. This electrical activity was depressed to 37.0 $\pm$ 5.5% by papaverine.

The contractions caused by acetylcholine were depressed to 63.0 $\pm$ 5.9% by papaverine pretreatment. The mean

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