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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[5] Acknowledgments. This work was supported by the Medical Research Fund, American University of Beirut. Nembutal was kindly provided by Abbott Laboratories. I wish to thank Miss N. Azzam for technical assistance in this investigation.

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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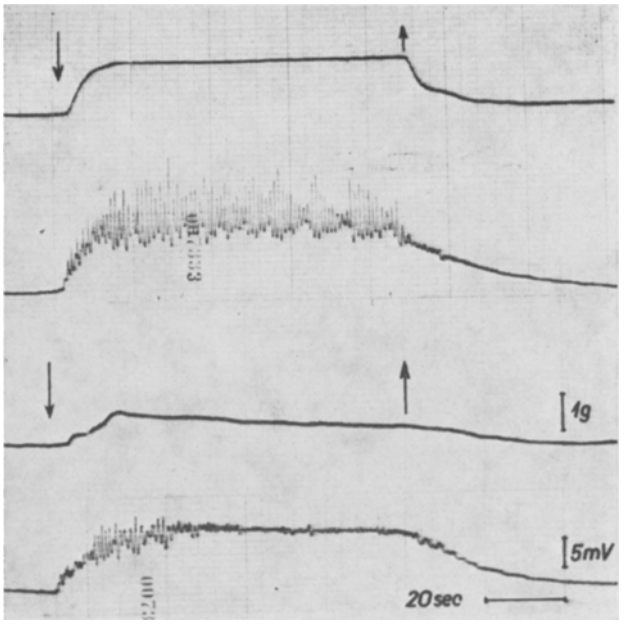

Fig. 1. The mechanical and electrical activities of taenia coli evoked by acetylcholine (1×10^{-6} g/ml) recorded by sucrose-gap method. Top tracing was taken before and bottom tracing during papaverine (1×10^{-5} g/ml) perfusion.

spike frequency induced by acetylcholine was 76.0 ± 5.1 per min, and was decreased by papaverine to $67.0 \pm 15.8\%$. Despite the presence of acetylcholine in the papaverine-treated preparation, the spikes and contractions stopped before the acetylcholine was washed out (Figure 1).

The mechanical responses elicited by $BaCl_2$ after papaverine pretreatment were inhibited to $69.5 \pm 12.0\%$. The average spike frequency induced by $BaCl_2$ was 85.3 ± 5.6 per min. Papaverine only slightly decreased ($82.0 \pm 14.2\%$) this spike frequency. The results are summarized in Figure 2.

Papaverine was used at a dose level that did not abolish the spontaneous (mechanical and electrical) activities. Shortening of the action of acetylcholine, as opposed to an unchanged duration of the action of $BaCl_2$, after papaverine, agrees with the observation that the responses to acetylcholine were depressed to a larger extent. Papaverine antagonism was maximal against the effects of

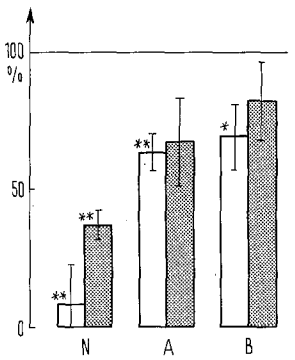

Fig. 2. The comparison of inhibitory action of papaverine on the contractures (open bars) and the spike frequencies (shaded bars) evoked by nicotine (N), acetylcholine (A) and $BaCl_2$ (B). The respective values from 6–10 experiments (mean $\pm$ S.E.M.) were significantly different from controls (100% effect) by $p < 0.05$ (*) or $p < 0.01$ (**).

nicotine. In most cases, the stimulating effect of nicotine was blocked completely. The height of the contractions was always significantly lowered. The increase of spike frequency was significantly depressed by papaverine only in case of nicotine.

Papaverine, in small doses, thus possessed a distinct antinicotinic effect. Since the mechanical responses to acetylcholine and $BaCl_2$ were also, though less significantly inhibited, papaverine may also exert a direct inhibitory effect on smooth muscle cells.

HIRTZ[1] concluded that a part of the action of papaverine involves parasympathetic nerve endings in the intestinal smooth muscle. Our results confirm the antinicotinic properties of papaverine[2], in the action of papaverine on the taenia coli of the guinea-pig.

Zusammenfassung. Mit Hilfe der Saccharosetrennwand-Methode wird nachgewiesen, dass Papaverin antinikotinisch an der glatten Muskulatur (Taenia coli) des Meerschweinchens wirkt.

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In vitro Induced Disappearance of Nucleoli in Cells Treated with LSD-25

There are some drugs influencing the phase-contrast picture of nucleoli in living cells, e.g. adenosine[1], arabinosylcytosine[2], ethionine[3], and quinacrine[4]. The drugs induce the central light zone in the nucleolus followed by the nucleolar fragmentation. The ultrastructural picture of the deeply transformed nucleolus commonly corresponds to the segregation of the organell[5]. However, the nucleoplasm of the cells treated in this way reveals the apparent rough residue of the nucleolar material distinguishable even in the light microscope.

In attempting to enlarge the extension of drugs capable of transforming the nucleolar phase-contrast morphology, influence of lysergic acid diethylamide (LSD-25) on cells of tissue culture was examined. LSD binding to DNA molecules in vitro[6], and the role of the drug in changing the ratio of nucleosides in nervous cells[7], is known well. Also the ability of the drug to make the chromosomal abnormalities in mitotic[8] and meiotic[9] cells was studied as a possible cause of the observed teratogenic[10] and mutagenic[11] effect of LSD, though some newer papers support the negative results[12–15]. The attributes of the drug including the inhibitory effect in mitotic division[16],

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