1961) at 32°C, gassed with 5% CO_2 in O_2. Contractions were recorded on smoked paper via an isotonic frontal writing lever. The tension applied to the muscle was 300 mg. The stripped vas deferens appeared relatively insensitive to agonist drugs. Noradrenaline ($5{\cdot}9\times10^{-8}$ M to $1{\cdot}2\times10^{-4}$ M) produced only small contractions and increasing the concentration up to $5{\cdot}9\times10^{-4}$ M failed to elicit a response comparable to that obtained by transmural stimulation. Adrenaline ($6{\cdot}0\times10^{-6}$ to $6{\cdot}0\times10^{-5}$ M) or acetylcholine ($2{\cdot}8\times10^{-6}$ to $4{\cdot}4\times10^{-4}$ M) acted similarly. Dopamine ($2{\cdot}6\times10^{-5}$ to $3{\cdot}7\times10^{-3}$ M), 5-hydroxytryptamine ($4{\cdot}9\times10^{-6}$ to $1{\cdot}5\times10^{-4}$ M) or histamine ($6{\cdot}5\times10^{-7}$ to $2{\cdot}0\times10^{-4}$ M) failed to contract the preparation.

Responses to noradrenaline were not facilitated by the use of the MAO-inhibitor Iproniazid ($3{\cdot}6\times10^{-6}$ to $7{\cdot}2\times10^{-5}$ M), COMT-inhibitor, Pyrogallol ($1{\cdot}6\times10^{-5}$ M) or uptake$_1$ inhibitor desmethyl-imipramine ($11{\cdot}9\times10^{-7}$ to $3{\cdot}8\times10^{-6}$ M). The preparation contracted in response to transmural stimulation at 30 Hz with 0·3 ms rectangular pulses of supramaximal voltage applied for 10 s every 3·25 minutes. Despite the insensitivity of the preparation to exogenous noradrenaline, the involvement of noradrenergic nerve fibres in the responses to transmural stimulation is suggested by the inhibitory action of guanethidine ($8{\cdot}1\times10^{-8}$ to $2{\cdot}0\times10^{-6}$ M) on these responses, and by the observations that dexamphetamine would protect against, or reverse, guanethidine-induced inhibition. In addition, desmethylimipramine ($9{\cdot}4\times10^{-9}$ M) prevented the inhibitory action of guanethidine.

However, the responses of the vas deferens to transmural stimulation were also impaired by atropine ($1{\cdot}4\times10^{-6}$ to $5{\cdot}6\times10^{-6}$ M). Dexamphetamine ($1{\cdot}1\times10^{-5}$ M) antagonized this effect of atropine, although with the higher doses of atropine recovery after dexamphetamine was not 100%. The inhibitory action of atropine was markedly reduced by prior exposure of the vas deferens to dexamphetamine ($2{\cdot}7\times10^{-6}$ M) or desmethylimipramine ($9{\cdot}4\times10^{-8}$ M).

The relationship of log dose to percentage inhibition of responses to transmural stimulation are linear for both guanethidine and atropine and the regression lines are parallel. In the presence of DMI or dexamphetamine, the regression lines are moved significantly to the right and remain parallel.

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Neuromuscular actions of lignocaine and prilocaine

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Jindal & Patel (1965) reported that lignocaine has a curare-like action on rat phrenic nerve-diaphragm preparations. Katz (1965) found that prilocaine sometimes decreased and sometimes increased the twitch tension of muscles stimulated via the motor nerve. We have examined the conditions under which prilocaine increases twitch tension and have investigated the action of lignocaine under similar conditions.

Rat phrenic nerve-diaphragm preparations were set up in 100 ml Krebs solution at 37°C as described by Jones & Laity (1965). The phrenic nerves were stimulated by

means of a constant voltage stimulator with supramaximal pulses of 100 μs duration at twelve/minute. Recordings were made on a smoked drum using a Starling spring-loaded heart lever. Two minute control recordings were made; the drug was added to the bath and the drum was stopped after a further 2 minutes. The bath was washed out 4 times during 30 minutes. Each type of experiment was repeated at least 3 times.

Prilocaine (20–80 μg/ml) and lignocaine (10–40 μg/ml) increased the twitch tension of diaphragms stimulated via their phrenic nerves.

This effect was not due to a direct action of the drug on skeletal muscle as neither drug increased the twitch tension of chronically denervated diaphragms stimulated supramaximally with pulses of 1 ms duration at twelve/minute.

It was noted that the increase in twitch tension produced in innervated diaphragms by prilocaine and lignocaine was rather less than that produced by neostigmine.

Acetylcholine was incubated with a 1 in 10 dilution of a haemolysate of human erythrocytes pretreated with prilocaine (1·5 mg) or lignocaine (1·0 mg), according to the method described by Burn (1952). When the mixture was added to a frog rectus preparation suspended in aerated Ringer solution at room temperature, a contraction resulted, whereas the same dose of acetylcholine and haemolysate failed to cause an effect. This suggested that the local anaesthetics had anticholinesterase activity, which has been confirmed biochemically using the method of Michel (1949).

Preincubation of the phrenic nerve-diaphragm preparations with mipafox (20 μg/ml) converted the increase in twitch tension produced by both drugs into a decrease, suggesting that at low concentrations, the effect of the drugs is probably the algebraic sum of their anticholinesterase and local anaesthetic actions.

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Theophylline and adenosine at the neuromuscular junction

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Adenosine reduces the output of the transmitter from the terminals of the phrenic nerve (Ginsborg & Hirst, 1971). In an attempt to investigate the possible involvement of cyclic 3′–5′ AMP in this phenomenon the interaction of adenosine (0·025–0·25 mM) and theophylline (1·8 mM) has now been studied. Adenosine increases cyclic AMP concentrations in central nervous tissue and theophylline inhibits this increase (Sattin & Rall, 1970). In our experiments the mean quantal contents of endplate potentials recorded from fibres of the rat diaphragm have been measured, and we have found that there is indeed an interaction and that the effect of 0·05 mM adenosine is abolished by theophylline. The antagonism is not due to the increase in transmitter