obtained with a concentration of 0.0012 μM, at which concentration naloxone has no agonist activity (Kosterlitz & Watt, 1968).

Recently, however, we have found that in very high concentrations (50–100 μM), naloxone causes a depression of the twitch induced by coaxial stimulation. These high concentrations reduce the responses of the longitudinal muscle also to agents which act directly on the smooth muscle cells—for example, acetylcholine, histamine and bradykinin; thus the depressant action of naloxone, unlike that of low concentrations of morphine (Paton, 1957), cannot be attributed to a reduction of acetylcholine release. Furthermore, the recovery from the antagonist action of a low concentration of naloxone has a half-time of 19 min, whereas the depressant effect of a high concentration of naloxone is fully reversed 6 min after washing out the drug.

In rabbit isolated superior cervical ganglia, in which transmission was just blocked by hexamethonium (275–550 μM), relatively high concentrations of morphine (27–130 μM) are required to depress the synaptic potential; this depression is reversed by naloxone (3–7 μM). In high concentrations (100–300 μM) naloxone itself had a depressant effect which was partly reversed by washing out the drug.

In the perfused superior cervical ganglion of the cat, morphine (130–2,700 μM) causes a decrease in the contraction of the nictitating membrane in response to stimulation of the preganglionic nerve; this effect is only partly due to a reduction in acetylcholine output. The depressant effects of morphine on acetylcholine release and on transmission are reversed 2–5 min after changing to a morphine-free Krebs solution. The block of transmission is not antagonized by naloxone which, in concentrations of 400–700 μM, blocks transmission as effectively as morphine.

On the basis of these results, it is suggested that care must be taken to differentiate specific from non-specific inhibitory actions of morphine-like compounds when these are used in high concentrations.

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The human isolated vas deferens: its response to electrical stimulation and to drugs

A. T. BIRMINGHAM, *Department of Pharmacology, King's College, Strand, London, W.C.2, England*

Both vasa deferentia were removed by vasectomy under general anaesthesia from healthy young men (aged between 33 and 41 years) and transported in cold Krebs solution to the laboratory. When suspended between parallel platinum wires (Birmingham & Wilson, 1963) in Krebs solution at 32° C bubbled with 95% oxygen and 5% carbon dioxide, electrical stimulation (0.1 msec pulse duration; maximal voltage) induced a threshold contraction at 2 shocks/sec and an increased height

of contraction with doubling of frequency up to a maximal response at 20 or 40 shocks/sec; stimulation at 80 shocks/sec usually gave a reduced contraction.

Lignocaine (1×10^{-5} g/ml.) abolished the response to electrical stimulation (20 shocks/sec; 0.1 msec) and the response returned on washing out the drug. The contractions were not diminished by ganglion blocking drugs (hexamethonium 1×10^{-5} g/ml. or mecamylamine 1×10^{-5} g/ml.) but were abolished by guanethidine (2×10^{-6} g/ml.) and this blockade was reversed by dexamphetamine (2×10^{-6} g/ml.). The threshold contraction to noradrenaline was at about 3×10^{-7} g/ml. and the maximum was achieved at about 2×10^{-5} g/ml. Tyramine ($2–8 \times 10^{-5}$ g/ml.) also contracted the human vas deferens. When examined histologically, conventional staining showed the human vas to consist of a thin, poorly defined, inner layer of longitudinal muscle fibres, a well defined middle layer of circular fibres and a thick outer layer of longitudinal fibres disposed in fasciculi well separated by connective tissue. Histochemical examination (Spriggs, Lever, Rees & Graham, 1966) showed a spare distribution of fluorescent varicose nerve terminals. The noradrenaline and adrenaline content of seven vasa was measured by the method of Brownlee & Spriggs (1965) and found to be 2.9 ± 0.46 μg/g and 0.22 ± 0.06 μg/g respectively.

Taken together, these results indicate that the human vas deferens is innervated by adrenergic postganglionic nerve fibres, but the innervation, compared with most other species that have been studied (Sjostrand, 1965), is not dense. Further analysis, of cholinergic mechanisms, suggests that if there is a cholinergic component to the innervation, it is small.

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Monoamine oxidase and catechol-O-methyl transferase activities in cat nictitating membrane and rat and guinea-pig vas deferens after sympathectomy

L. L. IVERSEN, B. JARROTT* and S. Z. LANGER, *Department of Pharmacology, University of Cambridge and A.R.C. Institute of Animal Physiology, Babraham, Cambridge, England*

Although there is considerable evidence in favour of the view that postganglionic sympathetic neurones contain the enzyme monoamine oxidase (MAO), sympathetically innervated tissues also contain variable amounts of extra-neuronal MAO activity. After sympathectomy, however, either no significant change, or falls in MAO activity ranging from 10 to 50%, have been reported in various animal tissues (Burn & Robinson, 1952; Burn, Philpot & Trendelenburg, 1954; Snyder, Fischer & Axelrod, 1965; Waltman & Sears, 1964). The greatest reductions in MAO