nergic innervation. Furthermore, the two layers may not have an equally dense noradrenergic innervation although the difference would seem to be small.

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The *in vitro* effects of vinblastine on the nerve-mediated responses of the guinea-pig vas deferens

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It has recently been shown that an intravenous injection of vinblastine causes degeneration of noradrenergic nerves after about 48 h (Bennett, Cobb & Malmfors, 1973). Thoa, Wooten, Axelrod & Kopin (1972) have suggested that an immediate *in vitro* effect of vinblastine on the guinea-pig vas deferens is the inhibition of noradrenaline release from nerves. In the present investigation we have examined the acute effects of vinblastine and vincristine on the mechanical responses of the guinea-pig vas deferens to stimulation of pre and post-ganglionic nerve trunks and nerve terminals.

Vasa deferentia and the attached hypogastric nerves were removed from guinea-pigs weighing 200-400 g. The tissues were set up in 100 ml organ baths, containing Kreb's solution at 37° C, bubbled with 95% oxygen and 5% carbon dioxide. Stimulating electrodes were arranged so that the preganglionic nerve trunks, the postganglionic nerve trunks or the intramural nerve terminals could be stimulated separately. Postganglionic nerve trunk stimulation was confirmed by the addition of a mixture of pentolinium, mecamylamine and hexamethonium (1×10^{-5} M) to the organ bath. Longitudinal contractions of the vasa deferentia in response to nerve stimulation were recorded isotonically.

With the stimulus parameters used (10 s trains of pulses at 10 Hz, 40 V strength, 0.2 ms pulse duration, applied to pre or postganglionic nerve trunks; 10 s trains of pulses at 10 Hz, 140 V strength, 0.2 ms pulse duration applied to the intramural nerve terminals), reproducible responses were obtained over a period of 6 to 8 hours.

When pre or postganglionic nerve trunks and intramural nerve terminals were stimulated alternately (every 2 min), vinblastine or vincristine (1×10^{-4} M) caused an enhancement of both responses that lasted about 30 minutes. Subsequently the response to nerve trunk stimulation (pre or postganglionic) was reduced and eventually extinguished after about 180 min when the responses to stimulation of nerve terminals were little affected. With more prolonged drug contact times (4 h or more) the responses to both nerve trunk and nerve terminal stimulation were irreversibly abolished.

The results provide little evidence for blockade of transmission through the hypogastric ganglion by vinblastine; this is in contrast to its effects on the cat superior cervical ganglion (Trifaró, Collier, Lastowecka & Stern, 1972). The responses to stimulation of nerve terminals persisted when the responses to stimulation of preterminal nerve trunks were blocked; one possible explanation for this finding is that vinblastine and vincristine interfere with action potential propagation in preterminal nerve trunks.

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