# Endogenous, possibly prostaglandin-mediated inhibition of the neuromuscular transmission in the vas deferens

Recently it was reported (Swedin, 1971) that the mechanical response of the rat and guinea-pig isolated, nerve stimulated vas deferens is divided into two separate phases when the usual 5 s period of stimulation is extended to 30 s (cf. Fig. 1). It was observed that repeated periods of prolonged nerve stimulation, either as field stimulation or via the hypogastric nerve (2–25 Hz, supramaximal voltage) depressed especially the initial, rapid phase ("twitch") of contractions of the organ (Fig. 1). Some features of this depression will be reported here.

The following findings led to the conclusion that the inhibition was induced by some substance, released together with the neurotransmitter upon nerve stimulation. (i) The inhibition was immediately abolished on washing of the organ (Fig. 1). (ii) The inhibition appeared faster and was more complete in an organ bath of small volume than in one of a greater volume (Fig. 2). (iii) The substance with its inhibiting properties could be transferred from one bath to influence an organ in another in a dose-dependent way (Fig. 2).

The inhibitory factor is probably acting at a prejunctional level, since tests with exogenous noradrenaline (0·1–2·0 $\mu$g/ml) revealed unaltered responses of the preparation after periods 30 s stimulation.

That the inhibitory agent is related to prostaglandins is supported by the following result. (i) The inhibitory agent influences both phases of contraction, the second


FIG. 1. Isolated field stimulated (5 and 30 s) guinea-pig vas deferens in 5 ml bath. 20 V, 1·5ms duration, 5 Hz. 1 min rest between stimulations. At dot washing. Number of 30 s contractions indicated above the contractions.

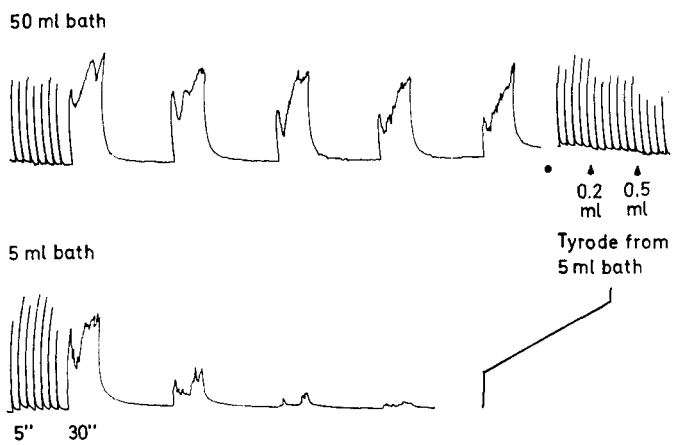


FIG. 2. A pair of guinea-pig isolated vasa deferentia in baths of different volumes. Same amplificiation. Hypogastric nerve stimulation at 25 V, 1·5 ms duration, 7 Hz. 1 min rest between stimulations. At dot washing. After four 30 s stimulations of the organ in the small bath, 0·2 and 0·5 ml of the Tyrode solution was transferred to the 50 ml bath as indicated.

phase, however, to a less extent, as do exogenously administered $PGE_1$ and $PGE_2$ (1–50 ng/ml). (ii) The ganglionic relay in the peripheral part of the hypogastric nerve was extremely sensitive to the inhibitory substance (cf. Fig. 2), and the same was found for exogeneous PG (0·1–0·4 ng/ml). (iii) Incubation of the vas deferens with an inhibitor of PG synthesis (5,8,11,14-eicosatetraynoic acid, ETA, 1–20 $\mu$g/ml) (Downing, Ahern & Bachta, 1970)| led to a partial or total abolishment of the endogeneous inhibition. (iv) Release of prostaglandin-like material, mainly resembling $PGE_2$, from the vas deferens on nerve stimulation, was established by silicic acid thin-layer chromatography (Gréen & Samuelsson, 1964).

It can be concluded from the present results that the mechanical response of the isolated vas deferens to nerve stimulation is under a dual influence from excitatory and inhibitory agents. Several experimental data support the hypothesis that the endogenous inhibition could be due to release of prostaglandins that are acting by restricting the amount of noradrenaline liberated from adrenergic nerves by stimulation (cf. Hedqvist, 1970; Wennmalm, 1971). With regard to the effectiveness of the autoinhibition described even at very low frequencies of stimulation (2–5 Hz), it is tempting to suggest that this process might play a modulating role in the nerve-induced mechanical activity of this organ in *in vivo* conditions, as recently suggested by Wennmalm (1971) for the rabbit heart. Furthermore, the results provide the first indications of an inhibitory action of PG on ganglionic neuro-transmission.

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REFERENCES

DOWNING, D. T., AHERN, D. G. & BACHTA, M. (1970). *Biochem. biophys. Res. Commun.*, **40** 218–223.

GRÉEN, K. & SAMULESSON, B. (1964). *J. Lipid Res.*, **5**, 117–120.

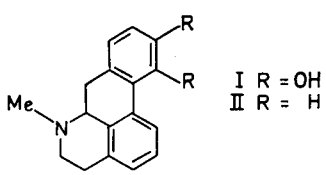
HEDQVIST, P. (1970). *Acta physiol. scand.*, **79**, *Suppl.*, 345.

WENNMALM, Å. (1971). *Ibid.*, **82**, *Suppl.*, 365.

SWEDIN, G. (1971). *Ibid.*, **81**, 574–576.

# On the dopamine-like action of apomorphine

Apomorphine (I) elicits a gnawing compulsion in rats which is due to stimulation of inhibitory dopaminergic neurons in the corpus striatum (Ernst, 1967, 1969; Ernst & Smelik, 1966; Ungerstedt, Butcher, & others, 1969). It apparently reduces the impulse flow of these neurons by a negative feedback mechanism arising from dopamine receptor stimulation, although an indirect mechanism involving the release of dopamine from central stores has also been implicated (Fekete, Kurti & Pribusz, 1970). However, pretreatment with iproniazid does not potentiate apomorphine-induced gnawing (Ernst, 1967), and apomorphine both retards the utilization of brain dopamine (Andén, Rubenson, & others, 1967) and inhibits its biosynthesis (Goldstein, Freedman, & Backstrom, 1970). It is therefore likely that apomorphine acts directly




I R = OH
II R = H