

replacement of noradrenaline in the vesicles by guanethidine might contribute to the lesser degree of blockade during a later phase of recovery.

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#### REFERENCES

- CASS, R. & SPRIGGS, T. L. B. (1961). Tissue amine levels and sympathetic blockade after guanethidine and bretylium. *Br. J. Pharmac. Chemother.*, **17**, 442-450.
- HAGGENDAL, J. (1963). An improved method for fluorimetric determination of small amounts of adrenaline and noradrenaline in plasma and tissues. *Acta physiol. scand.*, **59**, 242-254.
- KOPIN, I. J. (1968). False adrenergic transmitters. *Ann. Rev. Pharmac.*, **8**, 377-394.

#### Uterine response to adrenergic nerve stimulation in the guinea-pig

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Although there are many published reports which indicate that under certain experimental conditions stimulation of the sympathetic nerves can induce uterine contractions, the physiological importance of the adrenergic innervation of the myometrium is still unclear. In most animals, the uterus can function in the apparent absence of sympathetic innervation. However, it has been suggested that adrenergic nerves may exert a modifying influence on the myometrium, perhaps by changing its sensitivity to circulating hormones (Abrahams, Langworthy & Theobald, 1964). The present experiments were designed to study the effects of hypogastric nerve stimulation on uterine motility in the anaesthetized guinea-pig. The study had two objectives; one, to determine the effects of various frequencies of nerve stimulation on uterine motility *per se*, and two, to determine whether nerve stimulation could influence uterine sensitivity to oxytocin.

Guinea-pigs either in oestrus or immediately post partum were anaesthetized with urethane. After laparotomy the hypogastric nerves were cut below the inferior mesenteric ganglion and threaded through platinum electrodes. Intra-uterine pressure was recorded with a saline-filled catheter. Heart rate was monitored with a cardi tachometer and in some animals blood pressure was registered from the carotid artery. Nerve stimulation at frequencies between 1 and 20 Hz with rectangular pulses of 1.5 ms duration and 1.5 mA intensity for periods of 5 min caused uterine contractions. These contractions were abolished by phentolamine (5 µg/kg, intravenously). Nerve stimulation at frequencies between 1 and 6 Hz and at lower intensity, 1.0 mA, although not causing a contraction of the uterus, increased the uterine sensitivity to injected oxytocin (4 mu./kg, intravenously). This increase in sensitivity was abolished by phentolamine (5 µg/kg, intravenously) and by hexamethonium (5 mg/kg) and potentiated by propranolol (5 µg/kg). It was not accompanied by any observable changes in blood pressure or heart rate and was reproducible for many hours. Furthermore, it was much more pronounced in oestrus than after delivery (oestrus, mean increase=55%; post partum, mean increase=35%).

The frequencies of nerve stimulation at which the increase in oxytocin sensitivity was observed are within the same physiological frequency range as those thought to occur in other autonomic neuro-effector systems (Folkow, 1952). We suggest that

a possible physiological role for the adrenergic nerves might be a modulation of uterine sensitivity to oxytocin as well as to other hormones.

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#### REFERENCES

- ABRAHAMS, V. C., LANGWORTHY, E. P. & THEOBALD, G. W. (1964). Potentials evoked in the hypothalamus and cerebral cortex by electrical stimulation of the uterus. *Nature, Lond.*, **203**, 654-656.
- FOLKOW, B. (1952). Impulse frequency in sympathetic vasomotor fibres correlated to the release and elimination of transmitter. *Acta physiol. scand.*, **25**, 49-75.

#### Consequences of calcium and/or phosphorus deficient diets on various parameters of callus formation and on growth rate in young rats

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The role of calcium in the process of bone mineralization, as well as the optimum dietary requirements of this element, have been investigated extensively (Fourman & Royer, 1968; McLean & Urist, 1968). Phosphorus, which is assumed to be in excess in the diet, has attracted somewhat less interest in this respect, presumably because of very different requirements of calcium during life and the established importance of maintaining calcium homoeostasis, factors which inevitably affect bone turnover. Although the effects of phosphorus deficient diets on mineral metabolism, growth and general symptomatology of rats have been analysed (Day & McCollum, 1939), no data concerning fracture healing (callus formation) are apparently available in the literature.

Male, 5 week old rats were used. They were anaesthetized with ether and the tibia and fibula of both hind legs were fractured. Animals were randomly allocated to the different diet groups and kept in single cages. The diets (Altromin) and distilled water were supplied *ad lib*. On day 11 the animals were killed, the callus removed, and various parameters obtained by standard methods (Table 1).

TABLE 1. *Effect of calcium and phosphorus deficient diets on callus formation and growth rate in young rats*

Diet deficiency	None (Control)	Calcium and phosphorus	Calcium	Phosphorus
Number of animals	38	24	24	24
Food intake g/day	13.3±1.8 (100)	13.0±1.0 (98)	12.7±1.5 (96)	12.5±1.7 (94)
Body weight gain g/day	3.81±1.11 (100)	3.29±0.70* (86)	3.28±0.74*(86)	1.76±1.05*(46)
Callus fresh weight mg/rat	646±161 (100)	480±113* (74)	576±119 (89)	480±99* (74)
Callus dry weight mg/rat	198±41 (100)	138±27* (70)	167±25* (84)	131±24* (66)
Calcium (Callus) mg/100 mg	16.9±1.6 (100)	13.9±2.0* (82)	15.0±2.6* (89)	12.9±1.7* (76)
Phosphorus (Callus) mg/100 mg	8.6±1.0 (100)	7.2±1.0* (83)	7.8±1.3* (91)	6.6±0.8* (76)
Ratio: calcium/ phosphorus	1.98±0.1	1.96±0.08	1.9±0.06*	1.98±0.08
$\frac{\text{Calcium} \times \text{Phosphorus}}{100}$	2.97±0.60 (100)	2.04±0.57* (69)	2.43±0.76* (82)	1.78±0.45* (60)
Hydroxyproline mg/100 mg	2.88±0.39 (100)	3.04±0.32 (106)	3.06±0.35 (106)	3.41±0.47* (118)
$\frac{\text{Calcium} \times \text{Phosphorus}}{100 \times \text{Hydroxyproline}}$	0.54±0.15 (100)	0.34±0.12* (64)	0.42±0.14* (78)	0.27±0.06* (50)

Mean values±s.d. \*  $P < 0.05$ . Figures in parentheses are percentages of control value.