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Influence of calcium on responses of human isolated uterine tissue to fenfluramine

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The actions of fenfluramine on isolated human vein and gut have been described (Coupar, Hedges, Metcalfe & Turner, 1969). This communication describes its effects on human isolated uterine tissue, obtained at hysterectomy, and placed in cold Krebs-

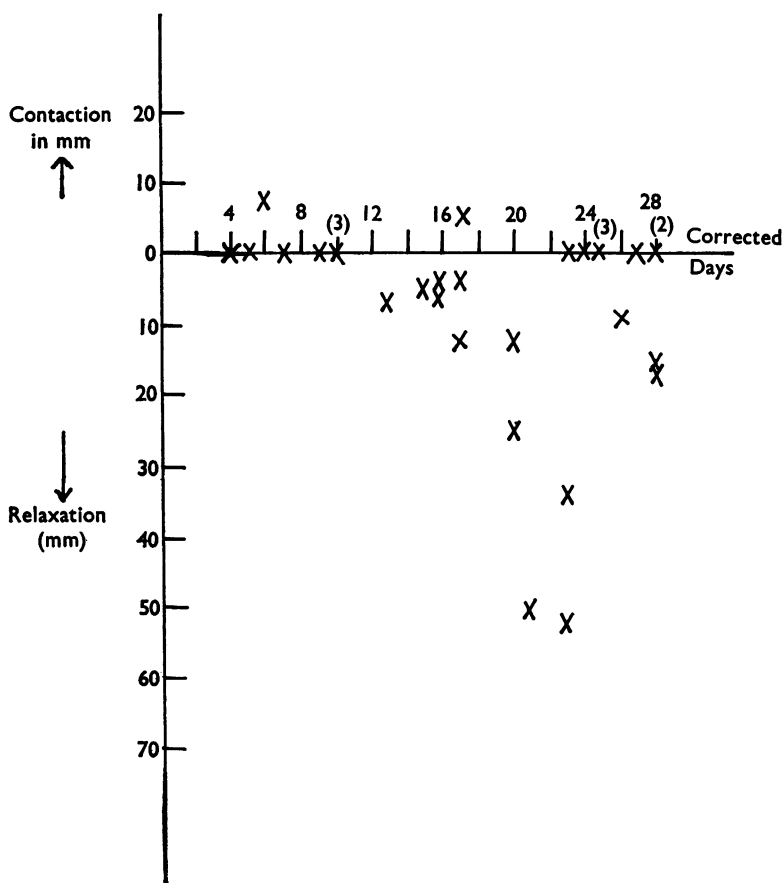


FIG. 1. Variations in response to fenfluramine on isolated strips of human uterine muscle, in 1.25 mm calcium Krebs solution, plotted against corrected day of the menstrual cycle.

bicarbonate solution within 15 minutes. A standard size strip from the lower segment (4 mm × 40 mm × thickness of specimen) was cut and set up in an organ bath in normal 2.5 mM calcium Krebs solution at 37°C, gassed with 95% oxygen containing 5% carbon dioxide. The tissue was attached to a frontal writing lever and the responses recorded on a kymograph. Magnification and tension were constant for all samples. Strips were then equilibrated for 30 min in Krebs solution containing 2.5, 1.25 or 0.625 mM calcium before the addition of drugs. Responses to 5-hydroxytryptamine, isoprenaline, and fenfluramine (20–400 µg/ml) were recorded in each calcium concentration. If no response was obtained to these or to noradrenaline the preparation was abandoned. After each experiment the tissue was returned to normal calcium Krebs solution to obtain the original responses. The maximum contraction or relaxation (mm) produced by fenfluramine was measured. The days of the menstrual cycle for premenopausal specimens were corrected to a 28-day cycle using the cycle length and the last menstrual period and assuming that 14 days elapse between ovulation and menstruation. Results for fenfluramine responses were related to the corrected cycle day for each calcium concentration.

Relaxation occurred in only one specimen in normal calcium but was seen frequently in 1.25 mM or 0.625 mM calcium during the second half of the cycle (Fig. 1). Such a difference in response was not seen with other agonists. Postmenopausal specimens showed no response to fenfluramine. Although the uterine specimens cannot be considered normal, the results suggest a relationship between the response to fenfluramine, calcium concentration and hormonal status.

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Study of the contractile and electrophysiological maturation responses of the human foetal myocardium

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Seventeen hearts from fetuses removed at therapeutic abortion between the twelfth to twenty-second week of gestation have been studied by a micro-electrode technique under physiological conditions of pH and temperature. The tissue was constantly superfused with well oxygenated (95% O₂ with 5% CO₂) Tyrode solution. Inotropic dose-response curves to varying concentrations of carbamyl choline and isoprenaline were determined using an R.C.A. 5734 force transducer.

The foetal atrial and ventricular action potentials showed a specific response typical of human tissue, characterized by a relative prolongation of repolarization when compared to the action potentials of other species of animals. Widespread pacemaker activity was observed in the atrial and ventricular myocardium; such activity is restricted to the sino-atrial region and specialized Purkinje fibres in the adult cardiac tissue.

The foetal myocardium is less sensitive than the adult human myocardium in its contractile response to both carbamyl choline and isoprenaline. There is a maturation