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 foetuses 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% O_2 with 5% CO_2) 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

in the contractile response in direct relationship to the length of gestation of the cardiac tissue. Contractile responses to carbamyl choline and isoprenaline develop before any alteration in the electrophysiological record is observed.

A study of the foetal myocardium offers normal cardiac tissue with a human electrophysiological response. The frequent finding of automaticity makes the foetal myocardium particularly useful for the investigation of the action of anti-arrythmic agents. The insensitivity of the receptor to autonomic agents allows a study of the direct effect of drugs on the membrane action potential without the influence of nervous factors.

We are grateful to Mr. J. Cobb for technical assistance. Dr. Coltart is the Mary Scharlieb Research Scholar of the University of London, 1970–71, and the Cooper and Coventson Research Scholar of St. Bartholomew's Hospital, 1970–71.

Cardio-active amines found in ox spleen extracts

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The presence of a cardio-active principle in freeze-dried extracts of ox spleen has been reported (Cobbin & Thorp, 1957), and later studies (Cobbin & Thorp, 1959, 1960; Temple, Thorp & Gillespie, 1966) suggested that its activity on cat papillary muscle was attributable to a low molecular weight base, but not to histamine, choline, acetylcholine, catecholamines, 5-hydroxytryptamine, dopamine, tyramine or a number of other cardio-active amino-acids. More recently the substance was shown to be widely distributed in mammalian tissues (Jackson & Temple, 1969) and claimed to be β-phenylethylamine (Jackson & Temple, 1970).

We have looked for the cardio-active principle in spleen extracts and have found β-phenylethylamine and several other amines which have positive inotropic actions.

Guinea-pig isolated left atria suspended in Krebs-Henseleit solution at 32°C and stimulated supramaximally at 1 Hz were used to monitor the extraction. Some extracts were also tested on isolated guinea-pig ileum in Krebs-Henseleit solution at 32°C.

Ox spleen, which was frozen immediately after its removal from the animal, was freeze-dried, defatted with chloroform and extracted with acetone. The concentrate was partitioned between methyl isobutyl ketone and water, the aqueous phase freeze-dried and extracted with ethanol and the alcoholic solution evaporated. This fraction (0·1% w/w wet tissue) caused a positive inotropic effect at concentrations between 10 and 100 μg/ml. A similar concentration caused a contraction and initiated spontaneity in the ileum; these effects were blocked fully by 100 ng/ml of triprolidine.

Separation of this alcohol-soluble extract by gradient elution on IRA 50 resin gave acidic, neutral and basic fractions, of which only the basic fraction was cardio-active. This was subjected to chromatography on Dowex 50 resin using a pyridine acetate buffer at pH 5·0 and fifteen discrete fractions isolated. Only fractions 6–9 showed positive inotropic activity and all, except 6, caused triprolidine-sensitive contractions of the guinea-pig ileum.

The following amines were identified in the fractions indicated within brackets, ethanolamine (3–5), isoamylamine (5 & 6), tyramine (5 & 6), β-phenylethylamine (7–9), histamine (7–9), putrescine (7 & 8) and cadaverine (8).