Total body retention in % of the administered dose of ^{47}Ca, ^{85}Sr and ^{226}Ra, 4 days after gastric intubation in mice: influence of $AlPO_4$ gel

Time of treatment relative to isotope intubation	Retention (% of dose)			Reduction factor = agar controls/PO_4 treated		
	^{47}Ca	^{85}Sr	^{226}Ra	^{47}Ca	^{85}Sr	^{226}Ra
1. $AlPO_4$ just before	8.0 ± 1.8	0.8 ± 0.2	< 0.3	3.3	14	>26
2. Agar just before	27 ± 8	11 ± 4	7.7 ± 5.9			
3. $AlPO_4$ just after	7.1 ± 1.2	0.8 ± 0.2	< 0.3	3.5	12	> 27
4. Agar just after	25 ± 8	11 ± 4	7.9 ± 5.5			
5. $AlPO_4$ later (1 h)	24 ± 5	9.6 ± 2.4	8.8 ± 3.7	1.3	1.5	1.7
6. Agar later (1 h)	32 ± 11	15 ± 6	15 ± 9			

Limits are the 95% fiducial limits ($x \pm ts_{\bar{x}}$), 5 to 6 mice/group.

In a second experiment, 20 μCi ^{226}Ra without other isotopes was intubated to each of 10 mice. The first group of 5 animals received 0.4 ml of phosphate gel just before the Ra intubation, the second group 0.4 ml of agar gel.

After 4 days, the Ra retention was measured in the $AlPO_4$ treated animals with a more sensitive method. The mice were killed with an overdose of ether anaesthesia, and slowly incinerated up to 520 °C. Directly hereafter, the ashes were measured in a NaI(Tl) well crystal with a 400 channel analyzer on the 186 KeV emission of ^{226}Ra; thus avoiding the interferences of all the daughter isotopes build up by the Rn-gas (= the first daughter of the whole chain) and giving a detection limit of about 10^{-5} μCi. The whole-body retention for the $AlPO_4$-treated group was 0.01% (± 0.005 at the 95% fiducial level) of the dose; in the agar-controls (measured with the GeLi detector) this was 8.0% (± 4.0).

The limiting effect of a massive quantity of aluminium phosphate gel on the intestinal uptake in mice is thus similar to that obtained in man [1] and rat [2] for ^{85}Sr and ^{47}Ca, but is very much higher for Ra than for Sr. The heavier alkaline earth thus seems to be more strongly fixed, as was observed with sodium alginate also [4]. The simultaneous administration of both ^{226}Ra and $AlPO_4$ reduced the Ra-burden 800 times in mice, while the maximal effect observed with sodium alginate [4] was a 135-fold reduction.

Résumé. L'administration presque simultanée d'un gel de phosphate d'alumine et de $^{226}RaCl_2$ réduit de 800 fois l'absorption intestinale du ^{226}Ra chez la souris. La charge corporelle en ^{85}Sr et ^{47}Ca est réduite d'environ 10 resp. 3 fois.

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Development of Human Foetal Inotropic Responses to Catecholamines

The blood pressure response of foetuses to catecholamines have been studied for many years. Mature foetal rabbits [1] and new-born dogs [2] respond the same as adult animals. Blood pressure responses in young foetal lambs, however, are less than in mature foetal lambs [3], suggesting that the pressure responses to catecholamines are not fully developed until the foetus nears term. This decreased response to catecholamines in immature foetuses has also been observed in foetuses of rabbits and guinea pigs [4], cats [5] and rats [6]. There is little information on the development of inotropic responses to catecholamines in foetuses; a previous study has shown great variations in positive inotropic responses to adrenaline and noradrenaline of a human foetal Langendorff preparation [7]. We have previously reported [8] that inotropic and electrophysiological responses of human foetal myocardium to carbamylcholine are not fully developed at 12–22 weeks gestation and that inotropic responses develop before certain electrophysiological responses. The present study was undertaken to investigate the development of inotropic responses in human foetuses to catecholamines.

Atrial and ventricular tissues were dissected from 17 human foetuses of 12–22 weeks gestation, as judged from nomograms relating crownrump length and dry weight of the excised heart to the period of gestation. A total of 30 left and right atria, 6 ventricular strips and 3 papillary

muscles dissected from the right ventricle were mounted under 1 g tension in a muscle chamber containing well oxygenated (95% O_2–5% CO_2) Krebs-bicarbonate solution at 30°C. All preparations were electrically driven via platinum wire electrodes at 120 pulses/min (1 msec duration), 10% above threshold voltage. An RCA 5734 transducer was used to measure contractions which were either photographed from an oscilloscope or recorded on a polygraph. Cumulative dose-response curves were obtained in both atrial and ventricular tissues to noradrenaline, adrenaline and isoprenaline. Figure 1 shows the mean ($\pm$SEM) percent change in contractile force for the first administration of varying concentrations of isoprenaline and noradrenaline to atria from ten foetal hearts. The response of ventricular and papillary muscles to identical concentrations of isoprenaline and noradrenaline was similar to the atrial responses. Adrenaline elicited effects on atria and papillary muscles which were intermediate between those produced by isoprenaline and noradrenaline. After the peak response to each catecholamine was obtained, $CaCl_2$(7.5 mM) was added to the muscle bath (Ca^{++} concentration of the Krebs-bicarbonate solution was 2.5 mM). In every experiment, a further increase in contractile force was observed. The maximal response to noradrenaline (3×10^{-5} g/ml) obtained was $53\pm14\%$ and after calcium it was $92\pm30\%$. The maximal response to isoprenaline (3×10^{-5} g/ml) obtained was $121\pm31\%$ and after calcium it was $193\pm57\%$ ($p<0.01$ in each case by the chi square test). Contractile responses to the same agonist 30 to 60 min after washing the tissues were variable. Tissues either responded similarly or failed to respond. In the most mature foetus studied (22 weeks gestation) isoprenaline (3×10^{-8} g/ml) caused a 100% increase in contractile force and the peak response occurred at a concentration of 10^{-6} g/ml. The results obtained with this foetus were not included in Figure 1.

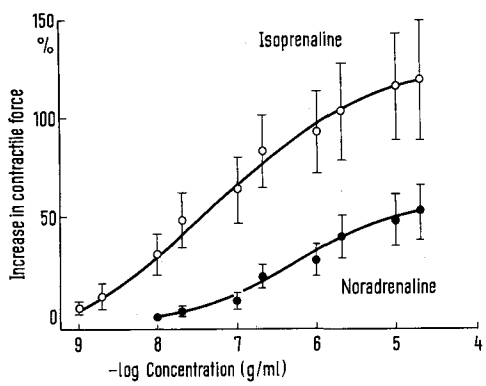

Fig. 1. Mean $\pm$ S.E.M. percentage change in contractile force to varying concentrations of isoprenaline and noradrenaline in human foetal atria.

The large standard error of contractile responses to catecholamines (Figure 1) is probably due, at least in part, to the various ages of the foetuses studied. In order to determine the influence of embryo age on the ability to respond to catecholamines, data obtained from other experiments with isoprenaline at 10^{-7} g/ml were plotted according to embryo age (Figure 2). It is apparent from Figure 2 that the ability of embryonic atria to respond to isoprenaline increases with age in the range of 12–22 weeks.

The present results show that there is a progressive development of foetal contractile responses to catecholamines from 12–22 weeks, but even at 22 weeks of age, contractile responses are not as marked as those observed in adult human atria[9]. These inotropic results are in concurrence with blood pressure responses in foetuses of other species, i.e. responses to catecholamines are less marked in young foetuses than in adults[4,5,6] and are less marked in young foetuses than in older ones[3]. Negative inotropic responses to carbamylcholine did not show a progressive development in embryos from 12–20 weeks[8].

Résumé. L'auteur a étudié la contraction du cœur fœtal au cours des différents stades de la gestation, avant et après stimulation par les catécholamines. Le tissu humain fœtal répond aux catécholamines au fur et à mesure de sa maturation.

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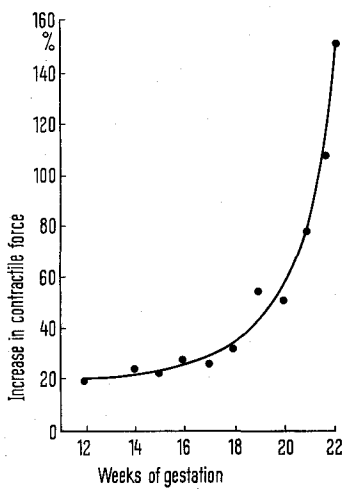

Fig. 2. The development of inotropic responses of human foetal atria to isoprenaline (10^{-7} g/ml) between 12 and 22 weeks gestation.

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