

Short communications

The effect of age on β -adrenoceptor activity in tracheal smooth muscle

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There was an age-related reduction of the sensitivity of rat and guinea-pig isolated tracheal smooth muscles to stimulation of β -adrenoceptors, but the ability of tracheal smooth muscle to relax to isoprenaline was not completely lost.

Fleisch, Maling & Brodie (1970) and Fleisch (1971) have demonstrated what they called 'ageing' of the β -adrenoceptor activity in rat, rabbit and guinea-pig aortas. It was shown that the ability of isolated aortas to relax to isoprenaline decreased with increasing age and was completely lost when rats were 3–6 months old and when rabbits were 2 years old.

We have now determined the effect of age on β -adrenoceptor activity in the tracheal muscle of rats and guinea-pigs.

Methods.—Sprague-Dawley rats and guinea-pigs of either sex were used. The rats used were 45 days (145–155 g), 98 days (250–300 g) and 210 days (400–450 g) old, while the guinea-pigs were 3 weeks (160–170 g), 4 months (570–640 g) and 27 months (900–1,100 g) old.

Tracheal chains were prepared and mounted in a modified Krebs solution containing (mm): Na^+ 137.47; Ca^{2+} 2.49; K^+ 5.93; Mg^{2+} 1.19; Cl^- 134.11; HCO_3^- 15.48; H_2PO_4^- 1.19 and glucose 11.5. The solution was aerated with 95% O_2 and 5% CO_2 and the contractions were measured isometrically with a Grass FT 03B force transducer and recorded on a Grass polygraph. The rat and guinea-pig tracheal chains were contracted with carbachol 1 $\mu\text{g}/\text{ml}$ and 0.1 $\mu\text{g}/\text{ml}$ respectively

and were relaxed by (–)-isoprenaline that was added to the bath fluid every 5 min in increasing concentrations.

Results.—Tracheal chains from guinea-pigs were more sensitive to isoprenaline than tracheal chains from rats. There were age-related reductions in sensitivity to isoprenaline in tracheal smooth muscle from both guinea-pigs and rats during the first months of life (Fig. 1a & b). Thereafter the reduction in sensitivity was not significant. Thus the differences in sensitivity to isoprenaline between 45 and 98 day old rats, and between 18 and 120 day old guinea-pigs were significant ($P < 0.001$ and $P < 0.01$, respectively), but the differences between 98 and 210 day old rats and between 120 and 800 day old guinea-pigs were not ($P > 0.05$). A reduced β -adrenoceptor activity was still present in the older animals.

Discussion.—The 'ageing' of the tracheal β -adrenoceptor activity occurred during the first months of life of the animals used in the present investigation. It might therefore be better to use the term 'maturation' instead of 'ageing'.

In contrast to the rat aorta (Fleisch *et al.*, 1970; Fleisch, 1971) the β -adrenoceptor activity was not completely lost in any of the tracheal chain preparations investigated.

Fleisch *et al.* (1970) reported a significantly decreased relaxant response to isoprenaline 0.03 mg/ml in tracheas from rats 275–420 days old as compared with tracheas from rats 41–60 days old. The relaxant responses to higher concentrations of isoprenaline (0.1–1.0 mg/ml) were not significantly decreased with increasing age in their experiments, nor was there a clear dose-response relationship. In our experiments, however, there was a good dose-response relationship for the isoprenaline-induced relaxations in the rat and guinea-pig tracheal preparations. Tracheal preparations from guinea-pigs were much more sensitive to isoprenaline than preparations from rats. There was also an age-dependent loss in β -adrenoceptor activity over a wide range of concentrations of isoprenaline in isolated tracheal preparations from rats as well as from guinea-pigs.

As isoprenaline is frequently used for clinical treatment of bronchial spasm it is of interest to know if there are any age-

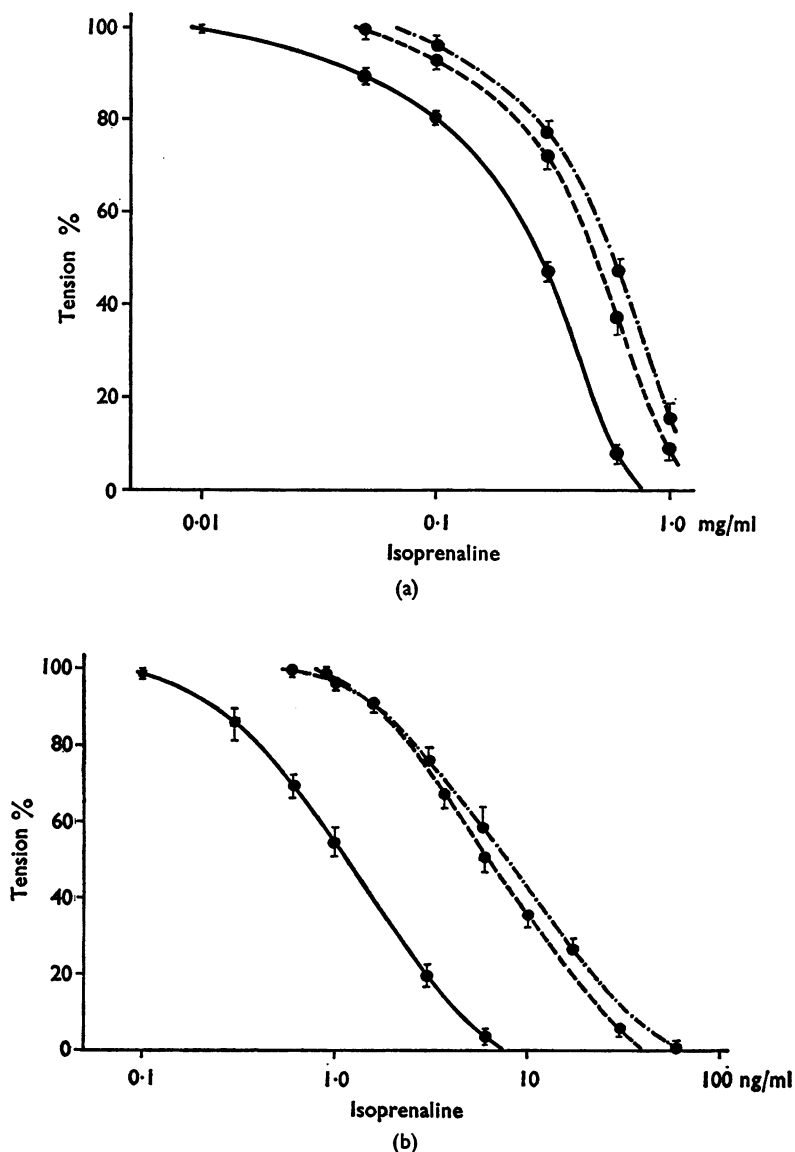


FIG. 1 (a and b). Relaxing action of isoprenaline on isolated tracheal chains from rats (a) and guinea-pigs (b) of different ages. Each curve shows mean \pm S.E.M. from 8-10 experiments. The rat tracheal chains (a) were contracted with carbachol 1 μ g/ml and the guinea-pig tracheal chains (b) with carbachol 0.1 μ g/ml. (a): \bullet — \bullet , 45 days old; \bullet — \bullet , 98 days old; \bullet — \bullet , 210 days old. (b): \bullet — \bullet , 18-22 days old; \bullet — \bullet , 120-125 days old; \bullet — \bullet , 800-810 days old.

related changes in the sensitivity of bronchial β_2 -adrenoceptors in man. In experiments on human isolated bronchial muscle none were found in preparations from patients from 21 to 72 years old (Svedmyr, personal communication). The sensitivity of bronchial β_2 -adrenoceptors may however be higher during childhood than later in life.

REFERENCES

- FLEISCH, J. H., MALING, H. M. & BRODIE, B. B. (1970). Beta-receptor activity in aorta: Variations with age and species. *Circulation Res.*, **26**, 151-162.
- FLEISCH, J. H. (1971). Further studies on the effect of ageing on β -adrenoceptor activity of rat aorta. *Br. J. Pharmac.*, **42**, 311-313.

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