*Br. J. Pharmac.* (1972), **45**, 504–509.

# The nature of the adrenoceptors in the post-partum rat uterus

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**Summary**

1. Uteri were removed from rats 0·5 h to 8 days after parturition and were suspended in Locke solution at 37° C.

2. The agonists isoprenaline, adrenaline, noradrenaline and phenylephrine produced an inhibition of the post-partum rat uterus.

3. In the presence of propranolol, the agonists noradrenaline, adrenaline, and phenylephrine had an excitatory effect on the post-partum rat uterus. This excitatory effect was blocked by phenoxybenzamine indicating that it is mediated through $\alpha$-adrenoceptors.

4. These excitatory $\alpha$-adrenoceptors could be demonstrated for 5–6 days after parturition. By the 7th–8th days their existence was no longer apparent.

5. Excitatory $\alpha$-adrenoceptors were also demonstrated in the late pregnant rat uterus.

## Introduction

The existence of inhibitory $\beta$-adrenoceptors in the rat uterus has been reported by many workers (Ahlquist, 1948, 1962; Rudzik & Miller, 1962; Levy & Tozzi, 1963; Tothill, 1967; Butterworth & Randall, 1970). However, excitatory $\alpha$-adrenoceptors have been shown to exist in the rat uterus only under certain conditions such as after oestrogen treatment (Diamond & Brody, 1966; Tothill, 1967; Paton, 1968), during natural oestrus (Butterworth & Randall, 1970) and in late pregnancy (Tothill, 1967). No data are available about the nature of the adrenoceptors that exist in the post-partum rat uterus. The present work deals with the type of adrenoceptors that exist in the post-partum rat uterus at different time intervals after parturition.

## Methods

### *Post-partum rat uterus*

Litters were removed from female rats immediately after birth so that the females were non-lactating. Uteri from 55 non-lactating albino rats were used. Uteri were removed at 0·5 h, 12 h and daily intervals up to the eighth day after parturition; 5 animals were used at each time interval. Uteri were suspended in Locke solution at 37° C in a bath of 20 ml capacity. The bathing fluid was gassed with a mixture of 95% oxygen:5% carbon dioxide and contractions were recorded isotonically on a smoked drum by means of a lever with a magnification of 10 and an optimal load. Uterine strips of suitable size were obtained from

animals killed within 3 days after parturition, otherwise whole uterine horns were used. Uteri suspended in Locke solution showed fairly regular rhythmic contractions.

The Locke solution had the following composition (g/l.): NaCl 9·0, KCl 0·42, CaCl 0·24, $NaHCO_3$ 0·5 and glucose 2·0.

*Late pregnant rat uterus*

Uteri were obtained from 15 pregnant albino rats 21 days after mating. Uterine strips of suitable size were used and were suspended in Locke solution.

*Sympathomimetic agonists*

The sympathomimetic amines tested were (−)-adrenaline bitartrate, (−)-noradrenaline bitartrate, (−)-isoprenaline sulphate and (−)-phenylephrine hydrochloride; the concentration of agonists refer to the base. Each agonist was added to the bath and was left in contact with the uterus for 3 min, followed by washing three times. An interval of at least 8 min was allowed between successive additions of agonists. The agonists were then retested in the presence of the $\beta$-adrenoceptor blocker, (±)-propranolol hydrochloride or in the presence of the $\alpha$-adrenoceptor blocker, phenoxybenzamine hydrochloride or in the presence of both antagonists. The antagonists were added at least 10 min before addition of the agonists.

## Results

*Post-partum uterus in Locke solution*

In the range of concentrations used, the agonists adrenaline (1·4–40 ng/ml), noradrenaline (40–600 ng/ml), phenylephrine (50–600 ng/ml) and isoprenaline (0·1–2·0 ng/ml) inhibited the amplitude of rhythmic contractions and in some cases this was accompanied by a relaxaton of uterine tone. In no case did any of these agonists have excitatory action. In the presence of propranolol (0·1–1·0 $\mu$g/ml), there was a reversal of the action of adrenaline, noradrenaline and phenylephrine (see Fig 1), but the action of isoprenaline was only blocked and showed no reversal. The unmasked excitatory action of adrenaline, noradrenaline and phenylephrine appeared in the majority of post-partum rat uteri (42 out of 45) removed within 0·5 h to 5 days after parturition. However, on the 6th day after parturition, the excitatory effects of these agonists tended to disappear (Fig. 2) and only one out of five uteri showed such excitatory responses. On the 7th and 8th day after parturition, none of 10 post-partum uteri showed excitatory responses. The excitatory action of adrenaline, noradrenaline and phenylephrine unmasked by propranolol, was blocked by phenoxybenzamine (0·5–1·0 $\mu$g/ml). Also in some experiments with uteri removed during the first 4 days after parturition, and in the absence of propranolol it was observed that there was potentiation of the inhibitory actions of noradrenaline (Fig. 3), adrenaline and phenylephrine after the addition of phenoxybenzamine (0·5–1·0 $\mu$g/ml).

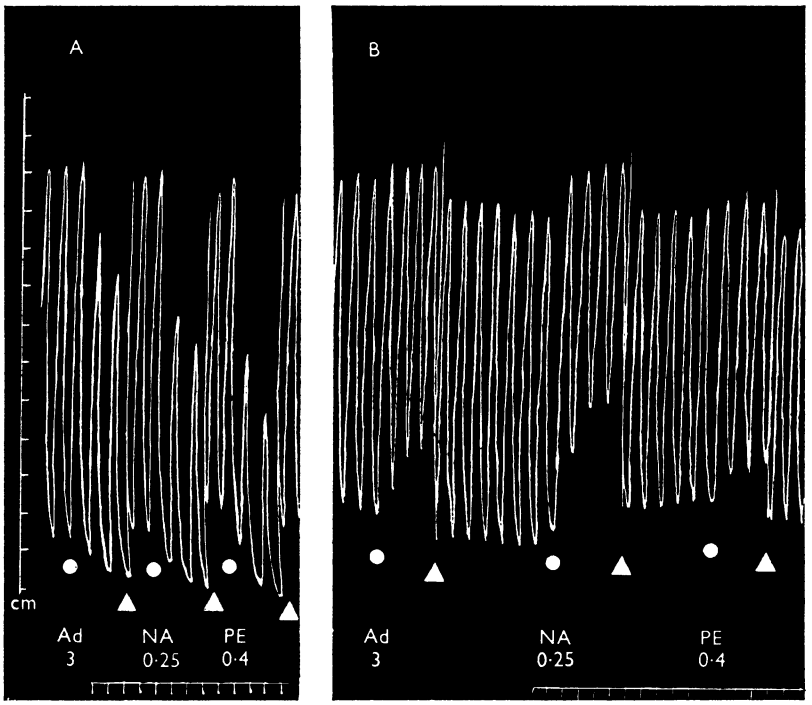


FIG. 1. Effect of adrenaline, noradrenaline and phenylephrine on the post-partum rat uterus, 36 h after parturition and suspended in Locke solution. (A) Control responses to adrenaline (Ad), noradrenaline (NA) and phenylephrine (PE). (B) Responses in presence of propranolol, 0·5 $\mu$g/ml. At (△), washing, concentration of adrenaline in ng/ml, and of noradrenaline and phenylephrine in $\mu$g/ml, time intervals in minutes. Tracing retouched.

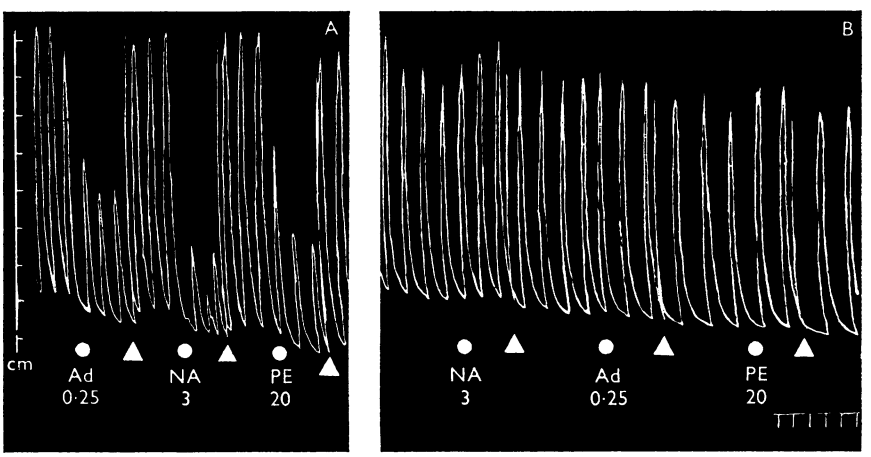


FIG. 2. Effect of adrenaline, noradrenaline and phenylephrine on the post-partum rat uterus, 6 days after parturition and suspended in Locke solution. (A) Control responses to adrenaline (Ad), noradrenaline (NA) and phenylephrine (PE). (B) Responses in the presence of propranolol 0·5 $\mu$g/ml. At (△), washing, concentrations of agonists in ng/ml, time intervals in minutes. Tracing retouched.

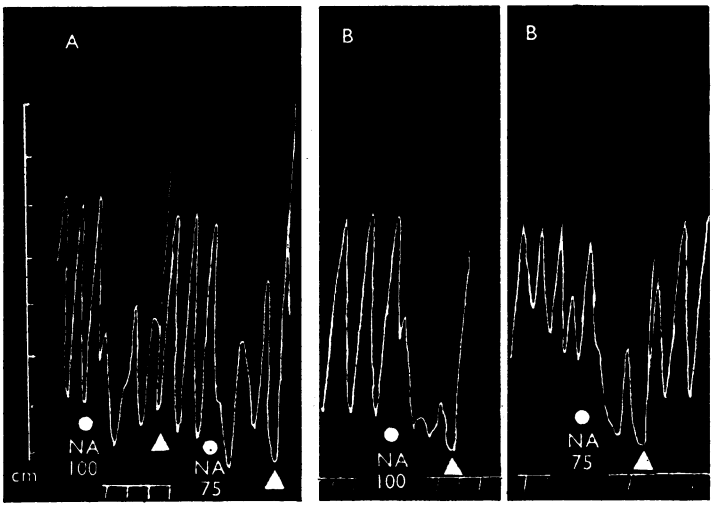


FIG. 3. Potentiation of the inhibitory action of noradrenaline by phenoxybenzamine. Post-partum rat uterus, 48 h after parturition. (A) Control response to noradrenaline (NA). (B) Responses to noradrenaline in presence of phenoxybenzamine, 1·0 $\mu$g/ml. At (△), washing, concentration of noradrenaline in ng/ml, time intervals in minutes. Tracing retouched.

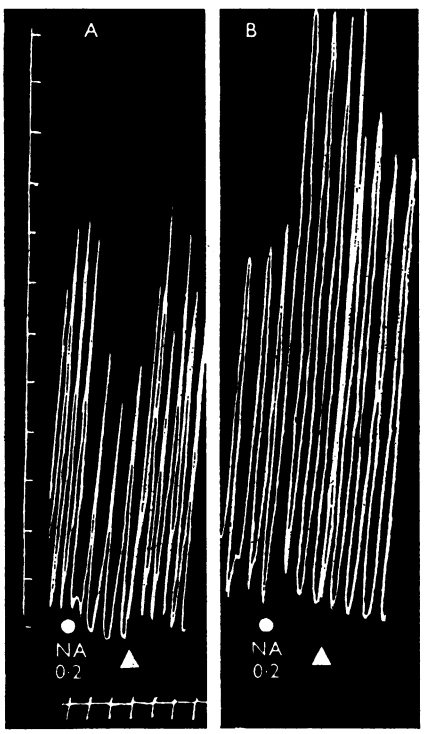


FIG. 4. Effect of noradrenaline on 21 day pregnant rat uterus suspended in Locke solution. (A) Control response to noradrenaline (NA). (B) Response to noradrenaline in presence of propranolol, 0·5 $\mu$g/ml. Concentration of noradrenaline in $\mu$g/ml. At (△), washing, time intervals in minutes. Tracing retouched.

*Late pregnant rat uterus*

Excitatory as well as inhibitory adrenoceptors were present in the late pregnant rat uterus (Fig. 4). As in the post-partum rat uterus, the excitatory effects of the sympathomimetic agonists were blocked by phenoxybenzamine (0·5 $\mu$g/ml). It was found that noradrenaline (20–100 ng/ml) in most cases elicited an excitatory effect in the absence, as well as in the presence, of propranolol.

## Discussion

The results obtained in the present work favour the view that the post-partum rat uterus possesses alpha excitatory and beta inhibitory adrenoceptors. That the four sympathomimetic amines investigated in the absence of $\beta$-adrenoceptor blockade caused mainly an inhibitory effect on the post-partum rat uterus would indicate that probably the $\beta$-adrenoceptors greatly outnumber the $\alpha$-receptors. When the $\beta$-adrenoceptors were blocked with propranolol excitatory $\alpha$-adrenoceptors were unmasked. The ability of phenoxybenzamine to antagonize the excitatory effects of adrenaline, noradrenaline and phenylephrine indicates that these excitatory effects were mediated through $\alpha$-adrenoceptors. The potentiation of the inhibitory action of adrenaline, noradrenaline and phenylephrine by phenoxybenzamine is most probably due to blockade of the $\alpha$-adrenergic excitatory receptors thus leaving the $\beta$-adrenoceptors unopposed to react with these agonists. The finding that lignocaine, a membrane stabilizer, can block the motor effects of adrenaline, noradrenaline and phenylephrine, on the rat uterus in Ringer solution (Abdel-Aziz & Bakry, unpublished observations) would indicate a membrane location of the $\alpha$-adrenoceptors similar to those found by Bowman & Hall (1970) in the rabbit intestine.

The time elapsed after parturition seems to determine whether or not $\alpha$-adrenoceptors can be demonstrated. They tended to disappear after the 5th day post-partum. The existence of excitatory $\alpha$-adrenoceptors may be linked with the predominance of oestrogen action on the uterus. Thus, it has been reported that these $\alpha$-adrenergic excitatory receptors can be found after oestrogen treatment (Tothill, 1967; Paton, 1968), during natural oestrus (Butterworth & Randall, 1970) and in the late pregnant rat uterus (Tothill, 1967). It is known that the rat uterus in late pregnancy is predominantly under the influence of oestrogen (Marshall & Miller, 1964; Knifton, 1968). The continued presence of excitatory $\alpha$-adrenoceptors in the post-partum rat uterus reported here, may be linked with a persistent effect of oestrogen on the post-partum rat uterus.

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(*Received May* 19, 1971)