

## LETTER TO THE EDITOR

### EFFECT OF SOME ANTIHISTAMINES ON THE UTERINE RESPONSE TO OESTROGEN IN RAT

Sir,

Exogenous administration of oestrogen induces pronounced hyperaemia followed by uterine oedema. Both hyperaemia and oedema have been suggested to involve, and be mediated by, histamine (8,9). The uterine histamine concentration is significantly reduced during oestrus phase of the oestrous cycle (2,8,9) as also during oestradiol-induced oestrus (3,5,8). Further, parenteral administration of histamine induces pro-oestrus and oestrus, and concurrent administration of pyrilamine maleate results in a quiescent vaginal mucosa characteristic of dioestrus and metaestrus (4). Also, like histamine, the intraluminal application of oestradiol produces hyperaemia, vasodilatation and oedema in the uterus and antihistamines block these changes (9). Recently, parenteral administration of antihistaminic drugs has been found to significantly prolong the duration of oestrous cycle (6). These findings, therefore, suggest that the action of oestrogen is possibly mediated through the local release of endogenous uterine histamine. The present work was undertaken to study the effect of antihistaminic drugs on the oestradiol-induced water imbibition in the uterus of rats.

Eightyone immature healthy female albino rats (40-60 g) were divided into 5 groups of 21(A), 20(B), 5(C), 26(D) and 9(E) animals each. Oestradiol dipropionate (10  $\mu$ g/rat) solution, prepared in arachis oil, was injected, i.p., daily, for 5 days, to all the rats except those of group A which received comparable volume of arachis oil and served as negative controls. Antihistaminic drugs (10 mg/kg) namely, mepyramine maleate, antazoline hydrochloride and diphenhydramine hydrochloride were injected, i.p., daily for 5 days in two divided doses (9.30 A.M. and 5.30 P.M.) to the rats of groups C, D and E respectively. Simultaneously, animals in group B received comparable volume (10 ml/kg) of normal saline, twice daily and served as controls. The animals were sacrificed 24 hr after the last injection of oestradiol and their uteri collected individually. The wet weight and the constant dry weight were recorded. The percent water content was calculated in terms of dry weight of the uterus. The data were statistically analysed by following the Duncan's multiple range test (7).

From the results represented in Table I, it was observed that there was significant increase in the wet weight, dry weight and water content of the uterus. Mepyramine and diphenhydramine markedly reduced the oestradiol effect; but, this reduction was not statistically significant. Interestingly, however, antazoline significantly augmented the uterine response to oestradiol.

The results indicate that the prolongation of the duration of oestrous cycle by antihistamines reported earlier (6) is, probably, not due to the blockade of uterine hyperaemia or oedema induced by the oestrogens. Possibly, the antihistamines exert their action through the mecha-

TABLE I: Effect of antihistaminic drugs on oestradiol-induced changes in the rat uterus.

Treatment	Oestradiol dipropionate				
	Arachis oil	Distilled water	Mepyramine	Antazoline	Diphenhydramine
Mean wet weight of uterus (mg)	41.46 <sup>a</sup> ±3.85	111.14 <sup>b</sup> ±7.25	89.80 <sup>ab</sup> ±14.27	166.84 <sup>c</sup> ±19.06	80.30 <sup>d</sup> ±6.66
Mean dry weight of uterus (mg)	9.02 <sup>a</sup> ±0.84	19.87 <sup>c</sup> ±1.04	19.00 <sup>bc</sup> ±1.90	23.44 <sup>c</sup> ±1.62	13.95 <sup>d</sup> ±1.23
Mean water content of uterus (mg)	32.44 <sup>a</sup> ±3.04	91.27 <sup>b</sup> ±6.54	70.80 <sup>ab</sup> ±12.40	143.42 <sup>c</sup> ±18.26	66.35 <sup>d</sup> ±5.53
Percent water content of uterus	360.04 <sup>b</sup> ±21.06	459.33 <sup>b</sup> ±23.68	372.63 <sup>b</sup> ±37.27	611.86 <sup>a</sup> ±27.40	475.67 <sup>c</sup> ±18.86
	Group A	Group B	Group C	Group D	Group E

Values bearing the same superscript in the same row are not significantly different ( $P < 0.05$ ).

nisms other than direct inhibition of water imbibition at the site of oestrogen action. In the doses used here, antihistaminics produce central nervous system depression. Incidentally, tranquilizers are known to prolong the duration of oestrous cycle in mice (1). The augmentation of uterine hyperaemic response to oestradiol by antazoline hydrochloride is an interesting observation and deserves further investigation.

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### REFERENCES

- Bhargava, K.P. and K.D. Jaitly. The effect of some phenothiazine tranquilizers on the oestrous cycle of albino mice. *Br. J. Pharmac.*, **22** : 162-165, 1964.
- Kapila, K. Histamine content of albino rat uterus during oestrous cycle and early pregnancy. *Ind. J. Physiol. Pharmac.*, **11** : 127-128, 1967.
- McKercher, T.C., L.S. Van, R.K. Bhatnagar and J.P. Burke. Estrogen induced biogenic amine reduction in rat uterus. *J. Pharmac. Exp. Ther.*, **185** : 514-522, 1973.
- Oppo, G.T. *Boll. Soc. itali. biol. Sper.*, **32** : 1365, 1956. (Cited by Spaziani and Szego, 1959; see No. 9)
- Sabir, M., N.P. Singh and V. Raviprakash. Changes in blood and uterine tissue concentrations of histamine and 5-hydroxytryptamine during oestradiol-induced oestrus in rats. *Proceedings of Symposium on Drugs and Biogenic Amines held at S.M.S. Medical College, Jaipur, p. 24. November 1-2, 1976.*
- Sambasivarao, K. and M. Sabir. Effect of some antihistaminic drugs on the oestrous cycle of rats. *Ind. J. Physiol. Pharmac.*, **21** : 2, 156-158, 1977.
- Snedecor, G.W. and W.G. Cochran. *Statistical Methods*, 6th edition, IBH Publishing Company, New Delhi, 1967.
- Spaziani, E. and C.M. Szego. The influence of oestradiol and cortisol on uterine histamine of the ovariectomized rats. *Endocrinology*, **63** : 669-678, 1958.
- Spaziani, E. and C.M. Szego. Further evidence for mediation by histamine of oestrogenic stimulation of the rat uterus. *Endocrinology*, **64** : 713-723, 1959.