Hypotensive Activity of Natural and Synthetic Estrogens in Metacorticoid Hypertensive Rats. (22815)

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Estrogens were reported some years ago to have a hypertensive action in rats(1,2); however, subsequent workers were unable to confirm such effects on the blood pressure of normal or renal hypertensive animals(3-7). On the contrary, several reports suggested an antihypertensive action of estrogens(8-10). The present paper confirms the latter in the case of the metacorticoid hypertensive rat treated with 3 natural and 2 synthetic estrogens.

Methods. The experimental animals consisted of 80 male, Sprague-Dawley rats that had received subcutaneously a 40 mg wax pellet containing 20 mg desoxycorticosterone acetate (DCA) at least 3 months previously and that had been maintained on 0.86% NaCl solution and Rockland Rat Diet *ad libitum*. Saline and food were not removed during the course of the tests. The systolic blood pressures of treated rats were estimated without anesthesia or heating using a photoelectric tensometer(11) before and 2, 4, and 6 hours after injection, and were compared to simultaneous readings from solvent-injected controls. Pressure readings on individual rats were made in ignorance of the injection the rat had received and of the previous pressure readings. Each test usually consisted of 4 treated and 4 control rats run simultaneously by one person on the same tensometer in a darkened room. The 5 estrogens listed in Table I were injected subcutaneously in a total of 40 rats as 1% solutions in corn oil at a dosage of 20 mg/kg. Injected material was always deposited at least 60 mm from the site of puncture in order to prevent leakage. The significance of *changes* in blood pressure, as compared to those in the controls, was estimated by the rank-sum method(12).

Results. The mean group blood pressures are listed in Table I. The 3 natural estrogens had a mild anti-hypertensive effect, while the 2 synthetic compounds were more potent. The fall in blood pressure after treatment with the epiestriol derivative was highly significant and reduced blood pressure to the normotensive range. From the subsequent condition of the animals and also from our experience with many other steroids, there was no reason to ascribe the hypotensive responses to a general toxic action.

The 3 natural estrogens were considerably more potent than the 2 synthetic compounds with regard to their metrotrophic, osteotrophic, and lipemic actions, as measured by uterine growth in immature mice(13), bone density in adult mice, and blood lipids in cholesterol-fed chicks, respectively.* This is in contrast to the greater hypotensive activity of the synthetic estrogens (Table I).

Summary. Three natural and 2 synthetic estrogens were compared for hypotensive activity in metacorticoid hypertensive rats. The most active compound was 16-epiestriol 3-methyl ether.

TABLE I. Effects of Estrogens in Metacorticoid Rats.

Compound	No. rats	Mean group blood pressure, mm Hg			
		Before inj.	2 hr	4 hr	6 hr
Estrone	4	188	178	176	170*
Estradiol	8	185	172	173	164*
Estriol	8	171	174	163†	160*
16-epiestriol 3-methyl ether	8	186	143‡	139‡	130‡
16-oxoestradiol 3-methyl ether	12	180	165	162*	154†
Pooled controls	40	187	183	188	188

* $P < .05$. † $P < .01$. ‡ $P < .001$.

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Some Aspects of Relationship between Antigens of *Pasteurella pestis* and *Pasteurella pseudotuberculosis.* (22816)

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Schütze(1) established that *Pasteurella pseudotuberculosis* and *P. pestis* shared a common somatic antigen. Bhagavan *et al.* (2) have recently confirmed Schütze's finding and have presented data indicating that 5 of 7 *P. pestis* antigens are shared with *P. pseudotuberculosis*. Fraction I of *P. pestis*, according to the authors, is not shared with *P. pseudotuberculosis*. Since the toxin of the plague bacillus is considered an endotoxin, as originally stated by Rowland(3), it can be postulated that as an antigen it would be located in the somatic complex. The study of plague toxin has, in fact, usually been preceded by some operation designed to rupture the cells, such as prolonged growth followed by treatment with toluene(4), alternate freezing and thawing(5,6), and neutral salt extraction of acetone-killed bacilli(7). Somatic antigens of *P. pestis* which are shared with *P. pseudotuberculosis* do not include the plague toxin (2,8,9). For this reason, the toxin of *P. pestis* may be defined as a somatic antigen which is not shared with *P. pseudotuberculosis*.

The present communication describes attempts to establish these criteria using a previously described gel-precipitin technic(10, 11) by comparing lysed and unlysed suspensions of *P. pestis* and lysed suspensions of *P. pestis* and *P. pseudotuberculosis*.

Methods and materials. (a) *Preparation of cell suspensions*: Organisms were grown on heart infusion agar (Difco) at 37°C and harvested in phosphate buffered saline at pH 7.0. Organisms used were *P. pestis* strain A1122 and *P. pseudotuberculosis* strain 1, received from Dr. S. F. Quan, Communicable Diseases Laboratory, USPHS, San Francisco, Calif. The final suspensions contained 1.97-2.00 mg total nitrogen/ml. (b) *Rupture of cells*: Suspensions described above were placed in the glass receiver tubes of the Mickle disintegrator(12). Approximately 5 g of "ballottini"(12) were added to 20-30 ml of organism suspension. The instrument was allowed to vibrate at its maximum amplitude for 15 minutes (time determined by preliminary trials to be described in the next section. (c) *Determination of patterns in 2-channel comparator cells*: The technic used was similar to that described previously(10,11), using 1:50 anti-plague serum globulin in 1% clarified agar as internal reactant(13). *Experi-*

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