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Effect of Chronic Treatment With an Estrogen-Progestogen Combination on Beta Adrenergic-Induced Thirst[1]

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THRASHER, T. N. AND M. J. FREGLY. *Effect of chronic treatment with an estrogen-progestogen combination on beta adrenergic-induced thirst.* PHARMAC. BIOCHEM. BEHAV. 8(2) 177–183, 1978. – Rats chronically administered various doses of the estrogenic agent, ethinyl estradiol, combined with the progestogen, norethynodrel, showed an estrogen-related, dose-dependent decrease in water intake in response to acute SC administration of the beta adrenergic agonist, isoproterenol (200 μg/kg of body wt). Conversely, rats receiving a constant dose of ethinyl estradiol (16 μg/kg/day) combined with norethynodrel (233 μg/kg/day) for 7 weeks drank significantly less water in response to graded doses of isoproterenol (10, 25, 50, 100 and 200 μg/kg) than controls. The slope, but not the intercept, of the regression line relating water intake to dose of isoproterenol administered was reduced significantly in the steroid-treated group. Furthermore, water intake of the treated group in response to acute administration of either epinephrine (1 mg/kg) or serotonin (1 mg/kg) was significantly less than control. These data suggest that chronic treatment with ethinyl estradiol, combined with norethynodrel, reduced beta-adrenergic responsiveness. In addition, rats treated with the same combination of ethinyl estradiol and norethynodrel showed a reduced drinking response to an osmotic thirst stimulus, i.e., IP load of 1 M NaCl solution at 1% of body wt. The fact that the response to both types of thirst stimuli was attenuated in rats receiving an estrogen combined with a progestogen suggests the possibility that treatment may have affected thirst mechanisms at the level of the central nervous system.

Thirst Isoproterenol Norethynodrel Ethinyl estradiol Serotonin Dehydration Phenylephrine

PREVIOUS studies from this laboratory showed that chronic treatment with the estrogenic agent, ethinyl estradiol, either alone or in combination with the progestogen, norethynodrel, attenuated the drinking response of rats induced by acute administration of the beta adrenergic agonist, isoproterenol [17]. Administration of norethynodrel alone did not appear to affect the response to the dipsogen. Drinking induced by acute administration of either renin or hypertonic saline was also reduced in rats chronically receiving ethinyl estradiol, either alone or in combination with norethynodrel [17]. Again, intake of the group receiving norethynodrel alone did not differ from control in response to acute administration of either renin or hypertonic saline. However, treatment with ethinyl estradiol did not affect drinking induced by dehydration [17]. These results indicated that chronic treatment with an estrogenic agent altered some component of beta adrenergic-induced thirst. The fact that thirst in response to hypertonic saline, an osmotic stimulus, was also attenuated in estrogen-treated rats seemed suggestive of an effect of the treatment at the level of the central nervous system. However, the fact that estrogen treatment did not reduce thirst following dehydration, which combines hypovolemic and osmotic stimuli, indicated that the estrogen effect could be overcome.

The purpose of the studies reported here was to determine how chronic treatment with a combination of ethinyl estradiol and norethynodrel affected the dose-response relationship between isoproterenol and water intake. In addition, the response to other thirst stimuli was examined.

METHOD

Experiment 1: Effect of Acute Administration of Isoproterenol on Water Intake of Rats Treated Chronically with Combination of Norethynodrel and Ethinyl Estradiol

A total of 42 female rats of the Blue-Spruce Farms (Sprague Dawley) strain were used in this experiment. Initially, the rats weighed between 180–200 g. They were housed in groups of 4 in wire cages in a windowless room maintained at 24 ± 1°C and lighted from 6 a.m. to 6 p.m. Tap water and finely ground Purina Laboratory Chow were available ad lib except during experimental periods.

The rats were assigned randomly to a control and 4

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treatment groups. Three treatment groups received a combination of crystalline 17-α-ethinyl-$\Delta^{1,3,5}$-estratriene-3,17-β-diol (ethinyl estradiol) via a Silastic tube implanted beneath the skin of the head, and crystalline 17-ethinyl-17-β-hydroxy-5(10)-estrene-3-one (norethynodrel) via a second Silastic tube implanted subcutaneously between the shoulder blades. One group was implanted with an 8 mm length of Silastic (No. 602–281, Dow Corning Co., Midland, MI, 0.0315 inch wall thickness) tubing containing ethinyl estradiol and a 20 mm length of Silastic (No. 602–231, 0.0095 inch wall thickness) tubing containing norethynodrel. A second group received a thinner walled 10 mm tube (No. 602–231, 0.0095 inch wall thickness) containing ethinyl estradiol and a 20 mm tube (0.0095 inch wall thickness) containing norethynodrel. The third group differed from the second group only in that the norethynodrel tube (0.0095 inch wall thickness) was reduced to a length of 10 mm. Implantation of the tubes was carried out under ether anesthesia. The tubes were palpated at weekly intervals to insure that they remained in place.

The procedure for determining dosage of steroid was as follows; after the tubes were filled with the appropriate crystalline steroid and sealed with silastic cement, they were placed in a desiccator for 72 hr and then weighed on an analytical balance. At the end of the experiment, the tubes were removed, cleaned of adhering tissue, placed in a desiccator for 72 hr and reweighed on the same balance. The average daily amount of each drug received by each rat was then calculated from the change in tube weight divided by the number of days the tube was implanted; and this value was then divided by the mean body weight of the animal during the time the tube was implanted. This method yields the dosage expressed as μg of drug/kg of body wt/day.

Dimethylpolysiloxane (Silastic) tubing has been shown to allow diffusion of certain crystalline steroids into various media at a constant rate over relatively long periods of time [2,10]. Previous experience in this laboratory has indicated that delivery of ethinyl estradiol and norethynodrel is reasonably constant over periods of up to 6 months.

A fourth treatment group received the oral contraceptive, Enovid, NM (each tablet containing 5.0 mg norethynodrel and 0.075 mg mestranol, the 3-methyl ether of ethinyl estradiol) mixed into finely ground Purina Laboratory Chow at a concentration of 7.5 mg/kg of food. The amount of drug ingested was determined from the daily food intake of the rats in this group. The control group was implanted with an empty 10 mm length of Silastic tubing.

The protocol for this and other experiments described in this report was similar and consisted of the following. All experiments were begun about 9 a.m. at which time food and water were removed; each rat was then lightly anesthetized with ether to induce reflex emptying of the bladder, injected with the dipsogen and placed in a stainless steel metabolism cage. All injections were administered subcutaneously (SC) in the loose skin of the back. The concentrations of drugs are expressed as the base and the volume injected in all experiments in which a drug was administered was adjusted by dilution with isotonic saline to approximately 0.2 ml. Distilled water was provided in infant nursing bottles containing cast aluminum fountains as described by Lazarow [11]. After 3 hr, the bottles were removed and water intake was determined by measuring the change in bottle weight to the nearest 0.2 g on a torsion balance. At the end of the experiment, gentle pressure was applied to the abdomen of each rat to induce emptying of the bladder and the urine collected was added to that voided during the experiment. Urine was collected in graduated centrifuge tubes and the volume read to the nearest 0.1 ml.

Experiment 1 was performed during the 7th week of continuous steroid treatment. A dose of 200 μg l-isoproterenol (Isuprel^{R} hydrochloride)/kg of body wt was administered and water intake and urine output were measured over the succeeding 3-hr period.

Experiment 2: Dose-Response Relationship Between Isoproterenol and Water Intake in Rats Treated Chronically with a Combination of an Estrogenic and Progestational Agent

The control group and the group implanted with an 8 mm length of Silastic tubing (No. 602–281, 0.0315 inch wall thickness) containing ethinyl estradiol and a 20 mm tube (No. 602–231, 0.0095 inch wall thickness) containing norethynodrel as described above were used in this study. Drinking studies were begun during the 8th week of steroid treatment. Doses of l-isoproterenol (10, 25, 50, 100 and 200 μg/kg of body wt) were administered SC and water intake and urine output measured during the 3-hr period following each dose. A minimum of 3 days was allowed between test doses.

Experiment 3: Effect of Acute Administration of Epinephrine, Phenylephrine and Serotonin on Water Intake of Rats Treated Chronically with an Estrogenic and a Progestational Agent

During the 12th week of steroid treatment, the drinking response to epinephrine, phenylephrine and serotonin was tested in the 2 groups of rats used in Experiment 2. The experimental protocol was carried out as described above and 3 days were allowed between tests. An acute injection of each drug was given and water intake and urine output were measured over the succeeding 3-hr period. The dosages for each test were as follows: epinephrine hydrochloride – 1 mg/kg; phenylephrine (Neosynephrine^{R}) – 200 μg/kg; and serotonin (Nutritional Biochemicals) – 1 mg/kg.

Experiment 4: Effect of Hypertonic Saline and Dehydration on Water Intake of Rats Treated Chronically with an Estrogenic and a Progestational Agent

During the 14th week of steroid treatment, drinking induced both by an osmotic stimulus and by dehydration was tested in the 2 groups of rats used in Experiments 2 and 3. In the first study, the 3-hr water intake induced by an intraperitoneal load of 1 M NaCl solution (equivalent to 1% of body wt) was determined. A dehydration study began 5 days later and consisted of a 24-hr period of water, but not food, deprivation. Following dehydration, the rats were placed in metabolism cages and water intake measured during the succeeding 3-hr period.

Data collected from the groups in the first experiment were analyzed statistically by analysis of variance [5], and comparisons of means were made using the pooled variance from the analysis of variance and the *t*-test [8]. The slopes and intercepts derived from the data of Experiments 1 and 2 were calculated by the method of least squares. The *t*-test for independent samples was used for comparisons between

TABLE 1

EFFECT OF CHRONIC TREATMENT WITH COMBINATIONS OF ETHINYL ESTRADIOL AND NORETHYNODREL ON WATER INTAKE AND URINE OUTPUT IN RESPONSE TO ACUTE SC ADMINISTRATION OF *l*-ISOPROTERENOL (200 μg/kg BODY WEIGHT)

TREATMENT GROUP	DOSE OF STEROID (μg/kg/day)	NO OF RATS	3hr WATER INTAKE* (ml/100g body wt)	3hr URINE OUTPUT* (ml/100g body wt)
CONTROL	0	9	4.55 ± 0.27	1.28 ± 0.34
ORAL				
MESTRANOL + NORETHYNODREL	5 353	8	3.74 ± 0.25	0.34 ± 0.11
IMPLANTED				
1 ETHINYL ESTRADIOL + NORETHYNODREL	16 233	10	1.64 ± 0.29‡	0.70 ± 0.12
2 ETHINYL ESTRADIOL + NORETHNODREL	46 223	6	1.22 ± 0.47‡	0.55 ± 0.34
3 ETHINYL ESTRADIOL + NORETHNODREL	56 136	6	0.84 ± 0.30‡	0.40 ± 0.17

*Mean ± one standard error.
‡Significantly different from control ($p<0.01$).

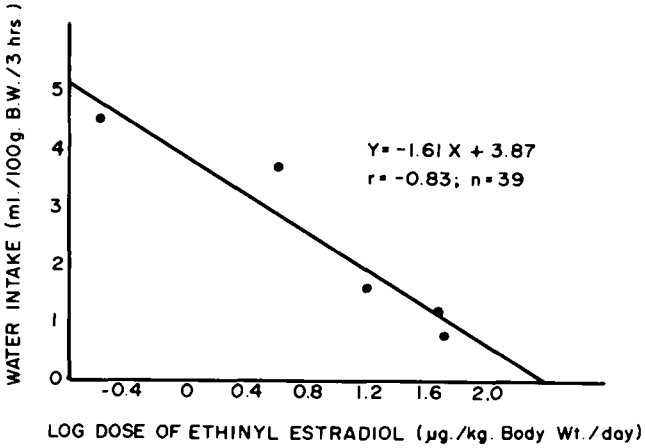

FIG. 1. Relationship between dose of ethinyl estradiol received chronically and 3-hr water intake stimulated by acute SC administration of 200 μg isoproterenol/kg of body wt.

the control and a single treated group in the other experiments. In all cases, significance was set at the 95% confidence limit.

RESULTS

Experiment 1

The 3-hr water intake stimulated by an acute administration of 200 μg l-isoproterenol/kg of body wt was measured following 7 weeks of chronic treatment with combinations of ethinyl estradiol and norethynodrel. Mean water intake of each group (expressed in ml/100 body wt/3 hr) is shown in Table 1. The 3 groups of rats receiving steroid treatment via implanted Silastic tubes all drank significantly ($p<0.01$) less water than the control group. The response of the group receiving the oral contraceptive, NM, via their food did not differ significantly ($p>0.05$) from control. A regression analysis of the logarithm of the dose of estrogen on the 3-hr isoproterenol-induced water intake suggested that combined steroid treatment attenuated the response to the beta-adrenergic agonist in a dose-dependent manner (Fig. 1). Comparison of urine output during the 3-hr period indicated no significant differences among the groups (Table 1).

The calculated doses of estrogenic and progestational agents received by each group were as follows. The group administered NM mixed into food received 5.3 ± 1.0 μg of mestranol/kg body wt/day and 353 ± 8 μg of norethynodrel/kg body wt/day; the group implanted with the 8 mm ethinyl estradiol and 20 mm norethynodrel tubes received 16 ± 2 and 233 ± 9 μg/kg/day of each drug respectively; the group implanted with the 10 mm ethinyl estradiol and 20 mm norethynodrel tubes received 46 ± 2 and 223 ± 15 μg/kg/day of each drug respectively; and the group implanted with the 10 mm ethinyl estradiol and 10 mm norethynodrel tubes received 56 ± 11 and 136 ± 10 μg/kg/day of each drug respectively.

Experiment 2

The effect of chronic administration of ethinyl estradiol and norethynodrel on the dose-response relationship between isoproterenol and water intake was determined in a group of rats implanted with Silastic tubes (receiving 16 μg of ethinyl estradiol/kg/day and 233 μg of norethynodrel/kg/day for 8 weeks), and an untreated control group. During the first study, each rat was administered a SC injection of 0.2 ml saline and water intake measured over a 3-hr period. During succeeding studies, graded doses of l-isoproterenol (10, 25, 50, 100 and 200 μg/kg of body wt) were administered and water intake and urine output measured during the next 3-hr period. The results of these tests are shown in Table 2. The drinking response of the treated group differed significantly ($p<0.01$) from the control response following each dose of isoproterenol. The equation of the line relating water intake (Y) to the logarithm of the dose of isoproterenol (X) for the control group was $Y = 1.59X + 0.62$ and the correlation coefficient was 0.68 ($n = 37$, $p<0.01$). The equation for the steroid-treated group was $Y = 0.16X + 1.00$ and the correlation coefficient was 0.12 ($n = 40$, $p>0.05$). A plot of each line and the mean group response at each dose of isoproterenol is shown in Fig. 2. The slope of the line corresponding to

TABLE 2

EFFECT OF CHRONIC ADMINISTRATION OF A COMBINATION OF ETHINYL ESTRADIOL AND NORETHYNODREL ON THE DIPSOGENIC AND ANTIDIURETIC RESPONSES TO GRADED DOSES OF *l*-ISOPROTERENOL

GROUP	NO OF RATS	DOSE OF *l*-ISOPROTERENOL (μg/kg body wt, s.c.) 0	10	25	50	100	200
		3-HOUR WATER INTAKE (ml/100g body wt.)*					
CONTROL	8	0.44±0.11	2.42±0.30	2.71±0.31	3.05±0.26	3.80±0.30	4.54±0.32
TREATED	9	0.51±0.24	1.24±0.24‡	1.19±0.23‡	1.18±0.18‡	1.21±0.18‡	1.49±0.27‡
		3-HOUR URINE OUTPUT (ml/100g body wt.)*					
CONTROL	8	1.02±0.11	1.81±0.24	2.42±0.36	1.96±0.23	1.72±0.16	2.30±0.42
TREATED	9	1.38±0.20	1.28±0.16	1.73±0.19	1.45±0.17	0.76±0.20‡	1.06±0.24†

*Mean ± one standard error.
†Significantly different from control ($p<0.05$).
‡Significantly different from control ($p<0.01$).

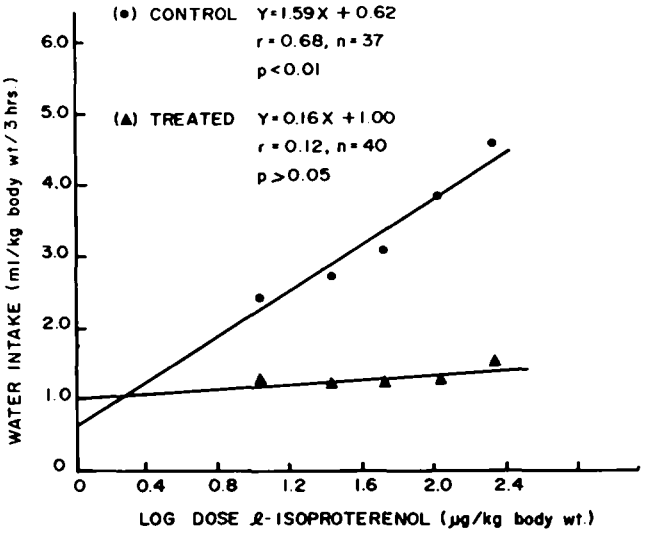

FIG. 2. Relationship between acute administration of isoproterenol and 3-hr water intake in control rats and in rats chronically receiving both ethinyl estradiol and norethynodrel.

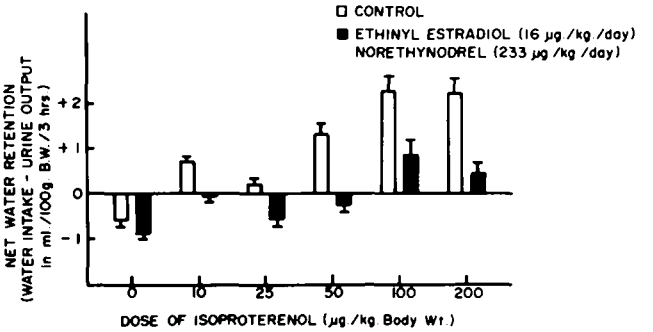

FIG. 3. Effect of chronic treatment with both ethinyl estradiol and norethynodrel on net 3-hr water retention (water intake – urine output) in rats administered various doses of isoproterenol. One standard error is set off at each mean.

the control group differed significantly ($p<0.01$) from that of the treated group. Comparison of the intercepts indicated no difference between the 2 groups.

The 3-hr urine output of the control group exceeded that of the treated group in response to both 100 ($p<0.01$) and 200 μg isoproterenol/kg ($p<0.05$), but no difference was observed following administration of 10, 25 and 50 μg of isoproterenol/kg of body wt (Table 2). One measure of antidiuresis is the net water retention (water intake minus urine output) over the course of the 3-hr period following injection of isoproterenol. The net water retention for both groups was calculated for each dose of isoproterenol and these data are shown in Fig. 3. During the control test, i.e., an acute injection of 0.2 ml saline SC, urine output exceeded water intake in both the control and the treated groups. Isoproterenol stimulated copious drinking and produced a net retention of water drunk at each dose administered in the control group. Since the volume of water drunk increased as the magnitude of the dose increased and urine output remained relatively constant (Table 2), the volume retained during each 3-hr test tended to increase directly with the dose of isoproterenol. The treated group, however, showed a net water loss in response to the 3 lower doses of isoproterenol and retention only in response to the 2 highest doses. Comparison of the effect of isoproterenol on net water exchange indicated a significant ($p<0.01$) difference between the control and the treated groups in response to all doses of isoproterenol.

Experiment 3

Water intake during 3 hr after administration of epinephrine was attenuated significantly ($p<0.01$) by chronic treatment with ethinyl estradiol and norethynodrel (Fig. 4). Urine outputs of control and treated groups during the same 3 hr period were 3.9 ± 0.7 and 3.9 ± 0.3 ml/100 g body wt/3 hr respectively ($p>0.05$).

Water intake during 3 hr after administration of serotonin was also attenuated significantly ($p<0.01$) by chronic treatment with ethynyl estradiol and norethynodrel (Fig. 4). Urine outputs of control and treated groups during the

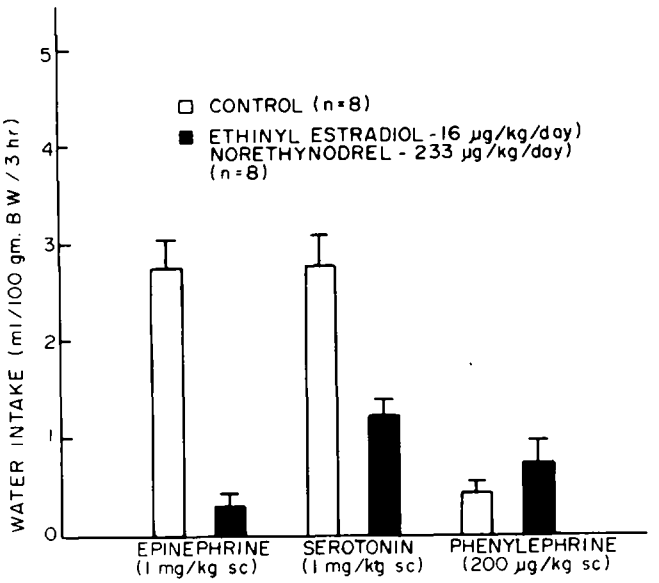

FIG. 4. Effect of chronic treatment with both ethinyl estradiol and norethynodrel on the 3-hr water intake in response to acute administration of epinephrine, serotonin and phenylephrine. One standard error is set off at each mean.

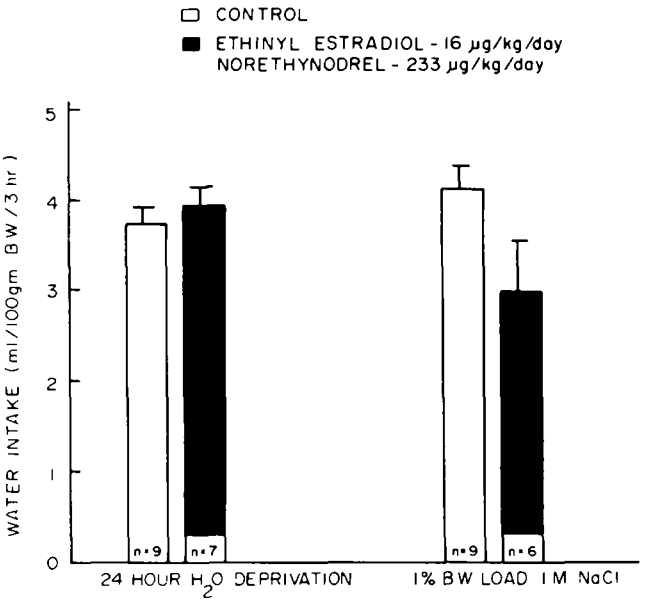

FIG. 5. Effect of chronic treatment with both ethinyl estradiol and norethynodrel on the 3-hr water intake in response to either IP administration of a load of 1 M NaCl solution (1% of body wt) or 24 hr of water deprivation. One standard error is set off at each mean.

same 3 hr period were 1.3 ± 0.3 and 0.9 ± 0.2 (SE) ml/100 g body wt/3 hr respectively ($p>0.05$).

Administration of phenylephrine failed to reveal any differences in either water intake (Fig. 4) or urine output between the steroid-treated (1.1 ± 0.3) and the control (0.8 ± 0.2 ml/100 g body wt/3 hr) group.

Experiment 4

Water intake during 3 hr after administration of an IP load of 1 M NaCl solution (1% of body weight) was attenuated significantly (p = 0.05) by chronic treatment with ethinyl estradiol and norethynodrel (Fig. 5). Urine outputs during the same 3 hr period were 2.0 ± 0.1 and 2.0 ± 0.4 (SE) ml/100 g body wt for control and steroid-treated groups respectively ($p>0.05$).

Water intake during 3 hr after return of water bottles to rats dehydrated for 24 hr was uninfluenced by steroid treatment (Fig. 5). Urine outputs during the same 3 hr period were 1.3 ± 0.1 and 1.6 ± 0.3 (SE) ml/100 g body wt for control and steroid-treated groups respectively ($p>0.05$).

DISCUSSION

Chronic treatment with ethinyl estradiol, alone or in combination with norethynodrel, attenuated the drinking response to acute administration of isoproterenol [17]. The reduced beta adrenergic responsiveness appeared to be due to the estrogen since the progestogen alone was without effect and did not alter the estrogen effect when both were administered in combination. The present studies show that there is an inverse relationship between the magnitude of the drinking response induced by an acute dose of isoproterenol and the dose of estrogen administered chronically (Fig. 1). The results of Experiment 2 show that chronic treatment with an estrogen depresses significantly the dose-response relationship between water intake and dose of isoproterenol administered. This suggests that steroid treatment alters the sensitivity of that portion of the thirst mechanism responsive to beta adrenergic stimulation.

These observations are difficult to interpret since the mechanism of beta-adrenergic thirst is still controversial. However, current studies would appear to support the hypothesis that isoproterenol stimulates a beta-receptor in the kidney to release renin which leads to generation of angiotensin II, the actual dipsogenic stimulus [3]. The facts that nephrectomy abolishes beta-adrenergic thirst [7], and that saralasin (a specific angiotensin II antagonist) has been shown to block isoproterenol-induced drinking [14], support this theory. However, it must be noted that an earlier study was unable to show a blockade of isoproterenol-induced drinking by saralasin [16]. Nevertheless, if one assumes that the renin-angiotensin system is the mediator of beta-adrenergic drinking, then rats treated with estrogenic agents should show an enhanced response to isoproterenol. This conclusion follows from the fact that estrogens elevate plasma renin-substrate concentration [6,13]. However, these studies have shown exactly the opposite, i.e., a reduced responsiveness to isoproterenol-induced drinking. Previous reports from this laboratory have also demonstrated other cases of reduced beta-adrenergic responsiveness in rats receiving chronic estrogen treatment, e.g., the increases in tail skin temperature [1], and heart rate [4] characteristically accompanying administration of isoproterenol. Thus, part of the explanation for the reduced dipsogenic responsiveness may be that chronic administration of an estrogen reduces renal secretion of renin in response to isoproterenol.

The results of Experiment 3 are in agreement with the explanation proposed above. Epinephrine has been reported to induce both drinking and diuresis in rats [12]. Moreover, in the presence of an alpha-receptor blockade, epinephrine induces drinking without an accompanying diuresis, and in the presence of beta-receptor blockade, it induces a diuresis but no drinking [12]. Epinephrine is known to stimulate

release of renin in vitro and the effect is blocked by l- but not d-propranolol [18]. Therefore, thirst induced by epinephrine may act via the renin-angiotensin system. Figure 4 shows that the control group responded to epinephrine as would be expected, i.e., copious drinking and large urine output. However, the group treated with the combination of steroids failed to show a drinking response but did increase urine output to the level of the control group. The response of the treated group was very similar to that reported to occur following administration of epinephrine in the presence of beta receptor blockade [12]. Acute administration of serotonin is also known to induce drinking and the effect is blocked by pretreatment with propranolol [12]. The response of the steroid-treated group to this amine was significantly reduced compared to the response of the control group (Fig. 4). Acute administration of an alpha-agonist has been shown to stimulate urine production and inhibit drinking [12]. Therefore, phenylephrine was administered to determine whether this particular alpha-adrenergic response was altered in rats treated chronically with contraceptive steroids. No differences were apparent with respect to either water intake or urine output between the control and the treated groups (Fig. 4).

Acute administration of isoproterenol has been reported to stimulate release of antidiuretic hormone (ADH) [15]. This may account for the observation that the water drunk following administration of isoproterenol is retained acutely [12]. It has been suggested that both the dipsogenic and the antidiuretic responses to isoproterenol are mediated by angiotensin since both of these responses to isoproterenol are blocked by saralasin, the angiotensin antagonist [14]. Acute administration of angiotensin II to rats has been shown to elevate plasma levels of ADH within 90 sec [9] Therefore, if one assumes that the isoproterenol-induced retention of water is mediated by the renin-angiotensin system, one could predict that rats treated with estrogenic agents would show a reduced antidiuretic response to a beta-adrenergic stimulus. The effect of graded doses of isoproterenol on the net volume of water retained in rats treated chronically with a combination of ethinyl estradiol and norethynodrel and an untreated control group is shown in Fig. 3. The control group showed a trend toward increasing fluid retention with increasing dose of isoproterenol. However, the treated group showed a net retention only at the 2 highest doses of isoproterenol and differed significantly from the control group in responses to all doses. This suggests that chronic treatment with a combination of ethinyl estradiol and norethynodrel attenuates the antidiuretic response to acute administration of isoproterenol. The mechanism by which steroid treatment affected the antidiuretic response to isoproterenol is not clear from these observations. However, the possibility exists that these steroids may either decrease the release of ADH in response to isoproterenol via reducing the isoproterenol-induced secretion of renin, or reduce the renal response to ADH. Further study will be required to determine whether either of these possibilities could account for the observed effect.

These results would appear to agree with the hypothesis that estrogen treatment attenuates beta adrenergic-induced release of renin. In an earlier report, it was also found that chronic treatment with an estrogen reduced drinking in response to an osmotic stimulus [17]. This study was repeated here because the finding was considered to be significant to understanding the locus of interaction of estrogenic agents in the thirst mechanism. Drinking in response to an osmotic stimulus was also significantly reduced in the present studies when the treated group was compared to the control group (Fig. 5). Thus, the response to both hypovolemic (Fig. 2) and osmotic (Fig. 5) thirst stimuli, applied singly, appear to be attenuated in rats administered the combination of an estrogenic and a progestational agent. However, the response to dehydration, which combines both hypovolemic and osmotic stimuli, was very similar in the treated and control groups (Fig. 5).

The data presented here indicate that chronic treatment with ethinyl estradiol and norethynodrel affects both hypovolemic and osmotic thirst mechanisms. While the nature of the effect cannot be determined from these data, the fact that responses to both primary thirst stimuli are affected suggests the possibility of an interaction at the level of the central nervous system. This suggestion is currently being investigated.

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