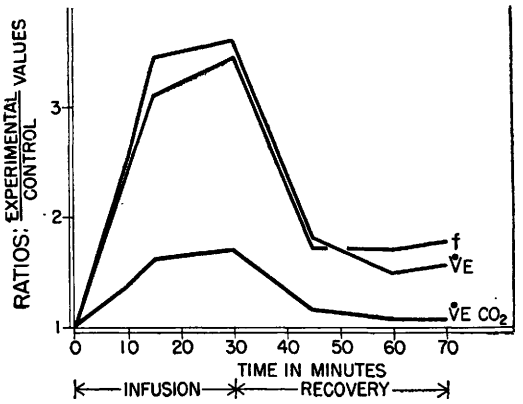

FIG. 1. Influence of venous infusion of gaseous CO_2 on breathing rate, f; minute volume expired, $\dot{V}_E$; and volume of CO_2 expired/min. $\dot{V}_E CO_2$, in relation to control values before infusion.

Cardiac outputs calculated for blood flow before, during, and after infusion are presented in Table I. Cardiac output (blood flow) was 8.7% lower during 29-30th minute of infusion than during pre-infusion measurements. This difference was not statistically significant, $t = 1.24$, $p = 0.30$. On the basis of these data, it is suggested that decreased arterial oxygen saturation during infusion of gaseous CO_2 is most likely due in part to a significant Bohr effect and not to decrease in cardiac output. Something more than the Bohr effect is needed for a complete explanation.

TABLE I. Summary of Respiratory Responses of 5 Dogs to Venous Infusion of Gaseous CO_2.

	Control	After 30 min. infusion	After 40 min. recovery
Respiratory rate	19	63	35
Tidal vol. (BTPS)	158	165	136
Resp. min vol. (BTPS)	3.0	10.4	4.7
CO_2 expired, ml/min. (STPD)	101	179	109
Arterial % HbO_2	90	78	90
" pCO_2	44	53	42
Heart rate/min.	124	113	122
Systolic blood pressure	131	116	115
Diastolic blood pressure, mm Hg	97	80	80
Cardiac output, l/min.	2.3	2.1	2.1

Summary. Cardiac output was measured in dogs before, during, and after intravenous infusion of gaseous CO_2. Slight decreases in output occurred but not great enough to indicate a significant impairment in blood flow through the pulmonary system. Infused CO_2 moves rapidly into the expired gas. Lowered oxygen saturation of blood following infusion of CO_2 can be explained in part by Bohr effect. However, this does not account entirely for level of oxygen unsaturation and something more than Bohr effect seems involved.

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Received January 30, 1959. P.S.E.B.M., 1959, v100.

Histamine Releasing Activity of Natural Estrogens.*† (24762)

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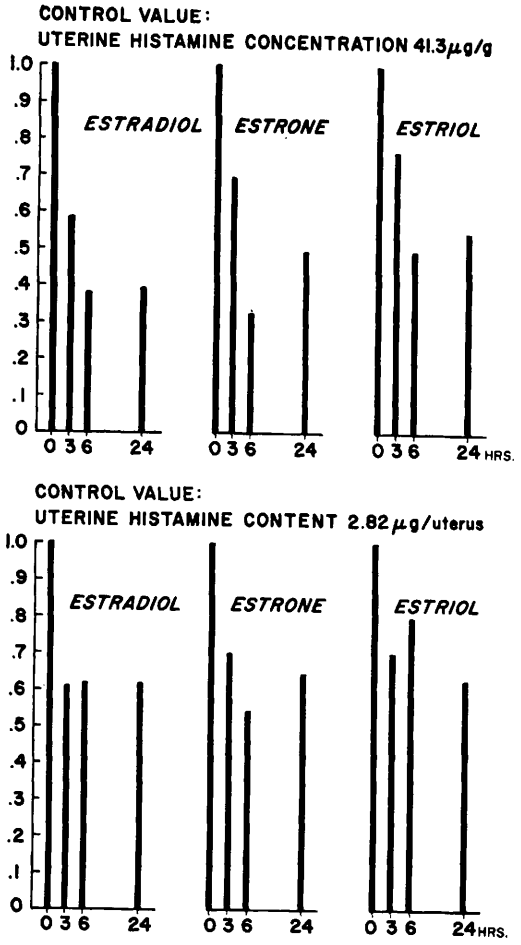
In a recent communication dealing with an estrogen-progesterone-histamine complex associated with pregnancy in the rat(1) we indicated that estradiol appeared to release histamine. Spaziani and Szego(2) reported a

* Supported in part by funds from Population Council of N. Y.

† This work was carried out at Physiological-Pharmacological Research Labs. of N. V. Organon, Oss. The author is greatly indebted to Prof. M. Tausk and Dr. G. A. Overbeek for cooperative hospitality, and to the technical staff who aided immeasurably.

‡ Sir Simon Marks Fellow, on leave to Univ. of Birmingham, England, 1957-58.



Concentration (above) and content (below) of histamine of uteri of spayed rat after single injection of 2μg estrogen in ratio to control value 1.0

FIG. 1.

drop of 6.9 μg/g to 3.7 in uterine histamine of the spayed rat after injection of estradiol. The present communication reports histamine releasing action of estradiol, estrone and estriol, as determined by bioassay of extracts of uteri of spayed rats following a single injection of estrogen.

Methods. Adult female rats were spayed. Between 120 and 125 days thereafter, a single injection of 2 μg of estrogen, in 0.1 ml arachis oil, was injected intramuscularly. At 3, 6, and 24 hr after administering the hormone, animals were killed, and uteri were removed, trimmed, weighed, and extracted in 10% TCA according to Parrat & West(3). Uteri of 5 animals were pooled, and the extracts assayed on guinea pig ileum. Two samples of 5 rats each were used for each point; bioassays were repeated. Validation of histamine was by tripelennamine inhibition. Control values were from untreated spayed rats; 3 sets, each a pool of 5 rat uteri.

Results. Fig. 1 presents reduction of uterine histamine after estrogen injection, in concentration and total content, in ratio to control value taken at 1. At the level used all estrogens behaved approximately the same.

Discussion. Other observations consistent with these findings include local tissue response to histamine which parallels general and initial response of uterine tissue to estrogens, namely, water imbibition, electrolyte shift, and increased permeability(2); depletion of tissue of mast cells by histamine releasers which parallels mast cell depletion of uterus and vagina of spayed rats and mice following injection of estradiol(4).

In light of experiments of Kraicer and Shelesnyak(5) who induced deciduomata in pseudopregnant rats by single subcutaneous injections of histamine releaser, these findings afford a basis for explaining induction of decidual cell reaction in rabbits(6) and rats by a single injection of estrogen(1). They also have some bearing on initiation of nidation during delayed implantation of lactation(7) and experimentally delayed lactation(8); and they present a basis for relating reduction of uterine histamine prior to nidation(9) to estrogen required for nidation.

It is noteworthy that the greater effectiveness of estradiol and estrone as compared with estriol in stimulating uterine tissue growth (6), a difference which does not exist with respect to initial water imbibition(10), also does not exist with respect to histamine releasing activity, at any rate not with the doses used. Studies with minimal effective doses are under way.

Summary. Uteri of spayed rats showed significant reduction in histamine content and concentration following single intramuscular injection of 2 μg of estradiol, estriol, or estrone as measured by guinea pig ileum assay of TCA extract of uteri.

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Received January 28, 1959. P.S.E.B.M., 1959, v100.

Tolerance to Blood Loss in Newborn Dogs. (24763)

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In the past it has been found that adult dogs seldom survived when 4-5% of body weight in blood was removed rapidly(1-6). Observations(7,8) that newborn animals were more resistant to respiratory hypoxia than adults suggested that tolerance to hemorrhage might also vary with age and prompted the experiments below.

Procedures. 213 mongrel dogs of various ages were anesthetized with ether, and blood removed rapidly from the heart with heparinized syringe and 19-gauge needle. Blood was weighed and hemorrhage defined in % of body weight. Hematocrit was determined by micro technic. After recovery from anesthesia, animals were given food and water *ad lib.* In surviving animals a second hematocrit was taken 24 hours later. In another group of 108 animals an intraperitoneal infusion of saline, equal to 5% or 10% of body weight, was given as pretreatment 1-4 hours before bleeding. Blood volume was determined in 14 dogs by Evans blue method of Gregerson (9).

Results. Fig. 1 shows % survival of dogs subjected to various amounts of hemorrhage. For simplification, results were presented in 2 categories: group A includes dogs 10 days and younger, group B older dogs. As shown in Fig. 1, when blood loss averaged 3.4% of body weight, survival was 52% in group A, and 57% in group B. However, when the hemorrhage averaged 5.2%, survival in group A was 22%, and in group B, 6%. Statistical tests of significance indicated the latter difference was not likely due to chance ($P = <0.001$).

In saline pretreated animals, absorption of fluid from peritoneal cavity was indicated by drop in hematocrit of about 10%. As shown in Fig. 1, saline failed to increase survival in either group A($P = >0.2$) or B($P = >0.4$) to a statistically significant degree. The results however, confirmed the finding of greater hemorrhage tolerance in younger animals.

Hematocrit changes with age have been described in detail elsewhere(10), and findings in our dogs were similar. In group A the initial hematocrit averaged 45% in those that recovered, compared to 37% in those not recovering. For group B these values were 32% and 30%, respectively. Dogs surviving 5.2% hemorrhage had a large decrease in hematocrit, the average value dropping about 50% at 24 hours.

Blood volume was not done on smallest animals because of technical difficulties, but results from 4 pups 10-16 days old showed average blood volume of 10.1% of body weight. In 10 dogs 6 weeks or older blood volume averaged 9.6% of the weight. These results are similar to those reported by others(11,12). Since blood volume was a fairly constant fraction of body weight at all ages, it was assumed that hemorrhage on weight basis imposed the same relative blood loss on all animals.

Discussion. The greater resistance of