The influence of sexsteroid hormones on the uterine response to epinephrine and to stress in the laboratory-rabbit

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Abstract

Studied the influence of sexsteroid hormones on uterine response to epinephrine and to stress-stimulation in laboratory rabbits.

Nine rabbits of different breeds were provided with electrodes to record uterine activity and ECG and simultaneously ovariectomized. Four other rabbits were ovariectomized one week after insertion of electrodes. All rabbits were fitted with a permanent indwelling jugular catheter.

Sexsteroid treatment was started 2 to 6 days after ovariectomy.

Results indicate that during estrogen domination epinephrine or stress cause an increase in uterine motility; during estrogen withdrawal stress or epinephrine cause the +— effect (initial activition followed by a period of quiescence). Estrogen — withdrawal together with progesterone-influence favours the occurrence of inhibition of uterine activity due to epinephrine or to stress.

Progesterone treatment induces total uterine irresponsiveness.

Administration of the α-adrenergic blocking agent Dibenyline® prevents both the + and the +— effect.

The β-blocking agent Inderal® potentiates the + component and prolonges the — component of the +— effect.

The pure — effect is prevented by Inderal®.

Results are discussed in the light of former findings on pregnant, parturient, post partum and post abortum does. It is concluded, that the different effects of stress and of epinephrine, observed in the latter animals, are due to changes in the ratio oestrogens/progesterone.

Introduction

From a comparative study on the influence of stress on mammalian reproduction it was concluded that stress could interfere with the normal pattern of activity of the non-gravid, the gravid and the parturient uterus, by way of a release of catecholamines from the adrenal medulla. (Naaktgeboren and Bontekoe 1976).

In vivo investigations on the effect of stress and of epinephrine administration on uterine motility in unrestrained free moving rabbits and sheep revealed that stress and epinephrine administration can have three different effects on uterine mechanical and electrical activity (Bontekoe et al. 1977). The three observed effects of epinephrine and stress were: an increase in mechanical and electrical uterine activity, (the + effect), or a decrease of both forms of activity (the — effect) or an increase followed by a period of decrease below the spontaneous level of activity (the +— effect). Moreover, in some cases stress and epinephrine administration had no effect at all. In sheep, the +— effect has not been observed. In sheep, the effects of stress and of epinephrine were related to the measured ratio of estrogens and progesterone.

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It was supposed that also in the rabbit the different reactions of the uterus to stress or to epinephrine during pregnancy, parturition and the post partum and post abortum phase, were due to fluctuations in the ratio of circulating estrogens and progesterone, although plasma steroid levels could not be determined.

The present experiments were carried out with ovariectomized rabbits in order to investigate the influence of sexsteroid hormones on the effects of epinephrine or stress on uterine motility.

Materials and methods

A. Animals and operation procedures

Thirteen rabbits of different breeds, weighing about 3,5 kg were used. Under Nembutal® (30 mg/kg bodyweight) and fluothane inhalation anaesthesia three pairs of silver-electrodes were attached to the myometrium. The method was analogous to that described by Naaktgeboren (1975) except for the fact that in addition to three pairs of myometreal electrodes two silver wires were used to record the ECG synchronously. These silver ECG wires were implanted opposite to each other, one subcutaneously dorsally, the other was attached to the peritoneum. All connecting wires were silastic-coated and were solded to a contact set, implanted in the animal's neck. Nine rabbits were bilaterally ovariectomized and provided with the silver-electrodes and ECG-wires during one operation. Four rabbits underwent two operations with an interval of one week. During the first sham-operation electrodes were fixed to the myometrium and ECG-wires were implanted. One week thereafter, these animals were bilaterally ovariectomized. All rabbits were fitted with a permanent indwelling canula in the jugular vein.

B. Recording technique

The electrical activity of the uterus was recorded; the ECG was recorded synchronously. For each trial the animal was connected to the preamplifiers of the recorder (Elema Schönander Mingograf 81). Uterine activity was recorded at a paperspeed of 2,5 mm per sec.; the amplifiers were set at 30 HZ with a time constant of 0,03 sec.

Each record was divided in periods of two minutes. Of each period the number of seconds during which the uterus displayed electrical activity was calculated. Heart rate was counted in beats per minute (B. p. m.). Records were made from sham-operated animals, from ovariectomized animals and from ovariectomized animals treated with sexsteroid hormones.

C. Sexsteroid-treatments

Sexsteroid treatment started two to six days after ovariectomy either by administering a single dose of 500 μg intramuscularly injected estradiol benzoate or by the administration of a single dose of 12,5 mg progesterone intramuscularly. Most estradiol treated does received 12,5 mg progesterone three or four days later, whereas in two cases both hormones were administered at the same time. Some animals could be treated several times. Sexsteroid treatment was only repeated when uterine activity was no longer under the influence of the preceding hormonal treatment (a. l. after 10 days). Records made on the day of treatment started one hour after treatment.

Drugs

The drugs used in the present study were: Epinephrine (levo-isomere) in a dose of 0,01 mg per kg bodyweight; Phenoxybenzamine (Dibenyline®) in a dose of 3 mg per kg bodyweight; Propranolol (Inderal®) in a dose of 0,03 mg per kg bodyweight. All drugs were administered intravenously.

Stress-stimulation

In order to stress the animals in a uniform way, only one kind of stress-stimulus was used: inhalation of tobacco smoke, blown in the direction of the nose. This stimulus has proved to be very effective. It is a strong nervous system stimulation, only exerting an influence in the conscious doe (Bontekoe et al. 1977).

Adaptation to the stimulus occurred only very occasionaly, which could be observed from the animal's behavioural reaction and from the fact that the heart rate nearly always reacted in a very characteristic way, both qualitatively and quantitatively: tachycardia followed by bradycardia (Fig. 1a and 1b). The recording of the heart rate was used as in independent parameter to detect whether the stimulus was experienced as a stressful event (see discussion).

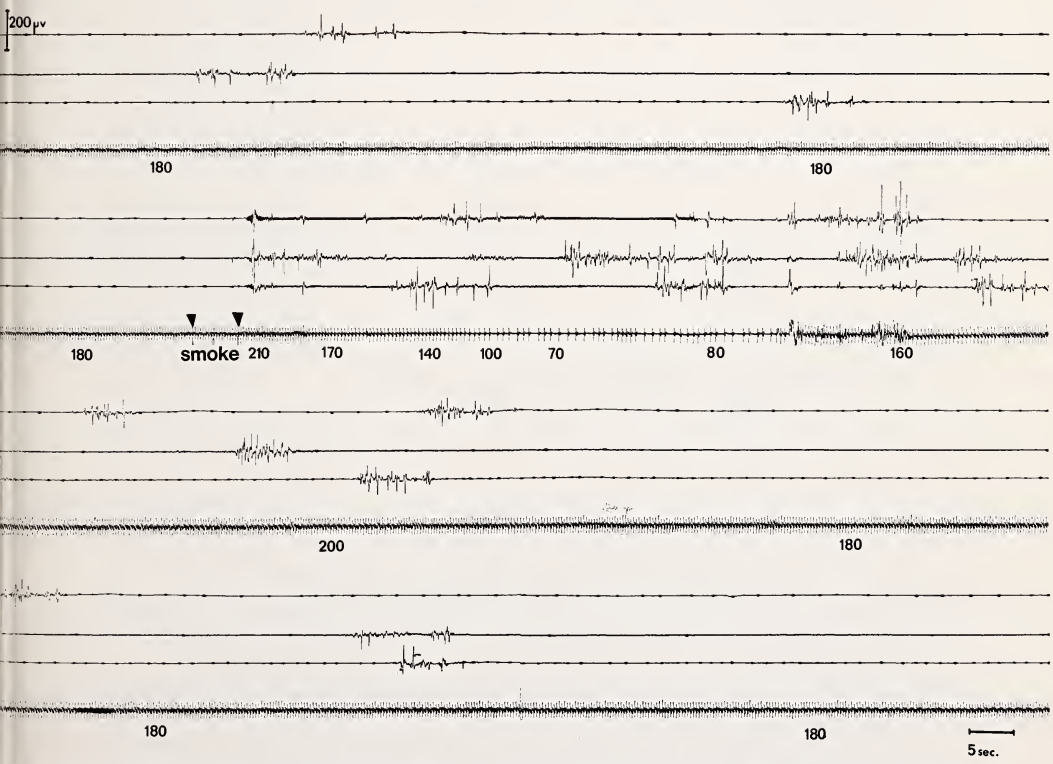


Fig. 1a. The effect of blowing smoke on uterine activity and on the heart rate in an ovariectomized doe on the first day after oestrogen treatment:uterine activity is irregular, heart rate is constant. Blowing smoke increases uterine activity (+ effect). The heart rate however reacts by an initial increase in frequency (to 210 beats per minute) followed by a dramatic decrease (to 80 beats per minute). Gradually, both heart rate and uterine activity reach their initial level

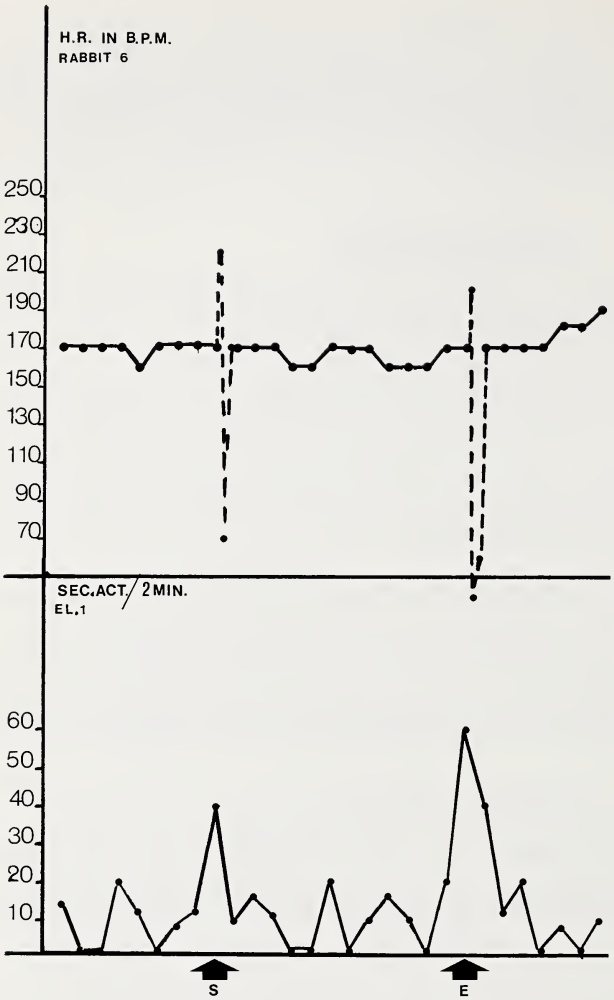


Fig. 1b. Effects of stress (blowing smoke; S) and of administration of 0.03 mg epinephrine (E) on uterine motility (lower part of the figure) and on the heart rate (upper part of the figure) in a rabbit two hours before an abortion. Uterine activity is expressed in seconds of activity per two minutes, heart rate is expressed in beats per minute. Both stress and epinephrine provoke an increase in uterine activity. The heart rate reacts with an initial increase followed by a decrease, both after blowing smoke and after administration of epinephrine

Results

A. The effect of epinephrine and of stress

1. In the sham-operated untreated does very different patterns of uterine motility occurred such as:
   a. quiescence, varying from complete rest to a more or less irregular pattern of single spikes.
   b. regular contractions with a duration of about 20 to 30 seconds, with a frequency of 2 contractions per 2 minutes, with low amplitudes (about 50 μV).
   c. Regular contractions with a much shorter duration (8 to 10 sec.), in a frequency of about 6 to 8 contractions per 2 minutes with higher amplitudes (about 120 μV).

   In these does epinephrine caused an activation of uterine motility (+ effect)

an activation followed by a decrease (+ — effect) or no effect at all. Epinephrine provoked an activation (+ effect) when the uterus displayed the pattern as described sub b. When the pattern as described sub c. appeared, the + — effect of epinephrine was observed in most cases. When the uterus was quiescent (pattern a) epinephrine most of the times had no effect. Inhibition was not observed in these rabbits (Table).

Table

Survey of the effects of stress and of epinephrine, expressed in frequency of occurrence of the +, + —, — and 0-effect under different hormonal conditions in ovariectomized does and in untreated rabbits, both intact and ovariectomized

Treatment	Effect of 0,03 mg epinephrine intravenously					Blowing smoke				
	+	+—	—	0	N	+	+—	—	0	N
Oestradiol (500 µg)										
day of treatment and 1st day thereafter	7				7	15			1	16
2 and 3 days after treatment		7			7		7			7
4 and 5 days after treatment	2	6			8	1	5			6
6, 7 and 8 days after treatment	2				2	3				3
Oestradiol and Progesterone										
500 µg oestradiol, 3—5 days later followed by progesterone injection										
on the first day after treatment			11		11			4		4
2 and 3 days after treatment			2[1]	3[2]	5	2			4	6
4, 5 and 6 days after treatment	2				2	6			3	9
Simultaneous treatment with estradiol and progesterone										
1 and 2 days after treatment				4	4	1			9	10
3 and 4 days after treatment	4				4	3				3
Progesterone (12½ mg)										
day of treatment				3	3				4	4
2—7 days after treatment	1			6	7					
intact, untreated	10	6		5	21					
ovariectomized, untreated	2	9	3	4	18	5	3		13	21
Total number of experiments					99					89

[1] 2nd day. — [2] 3rd day.

2. In ovariectomized, untreated animals different patterns of uterine motility were also observed. During the days following ovariectomy uterine activity increased. This effect of ovariectomy on uterine motility was also observed by Fuchs (1972) and by Coutinho and De Mattos (1968). Regular contractions of short duration and of high amplitudes were most commonly observed 2 till 5 days after ovariectomy. In this period epinephrine most of the times caused the + — effect. On the days of ovariectomy and on the first day thereafter uterine activity consisted of long lasting regular contractions with low amplitudes. Epinephrine caused the + effect or had no effect at all in this situation. Three times an inhibitory effect of epinephrine could be observed (see Table). On the first day after ovariectomy stress and epinephrine administration had no effect in the majority of cases.
3. Administration of 500 µg estradiol benzoate to the ovariectomized doe, invariably depressed uterine activity to very low levels one day after the injection. The

duration and the amplitude of the contractions were considerably diminished. However, between the second and the fourth day after treatment a gradual increase in uterine activity occurred in all animals. Sometimes the short contractions occurred in groups (bursts of activity). This increase is in accordance with observations of Coutinho and De Mattos (1968). During the day of estradiol-treatment and one day thereafter epinephrine always provoked the + effect. If a recording session of more than six hours duration started shortly after the administration of estradiol, a decrease of spontaneous activity and an increase in sensitivity to epinephrine and to stress could be demonstrated. Two or three days after estrogen treatment the effect of epinephrine was in all cases an initial activation followed by a period of inhibition (+ — effect). Four and five days after estrogen-treament either a + effect or a + — effect was observed, whereas six, seven and eight days after estrogen treatment only + effects of epinephrine were observed. Stress stimulation resulted in reactions similar to those observed after administration of epinephrine (Table).

4. When the treatment with estradiol benzoate was three or four days later followed by the administration of 12,5 mg progesterone, uterine activity was diminished. The contractions had a low frequency (2 contractions per 2 minutes) and the amplitudes seldom exceeded 50 μV. Duration of the contractions varied from 10 to 20 seconds. The contractions were poorly coordinated. After this treatment, epinephrine always inhibited uterine activity, when administered on the first day after the progesterone injection.

   Twice an inhibition due to epinephrine was observed on the second day after progesterone treatment. However on the third day thereafter epinephrine had no effect, whereas six days after the progesterone injection a + effect of epinephrine was observed. Similar results were obtained after blowing smoke (Table).
5. In animals treated simultaneously wich progesterone and estradiolbenzoate uterine activity was low and irregular. Epinephrine administration on the first and second day after this combined treatment had no effect. Three and four days thereafter, however, epinephrine caused a + effect. An inihibitory effecy of epinephrine was never observed in this group. The effects of stress were similar (Table).
6. Progesterone treatment without priming with estradiol benzoate resulted in a complete inhibition of uterine activity. Epinephrine had no effect up to seven days after the progesterone injection. Only once an activation after epinephrine administration was observed (Table). From the table it is clear that the different effects of epinephrine and stress on uterine motility depend on the type of sexsteroid treatment. Identical effects can be obtained by stressing the does by blowing smoke into the cage. Administration of epinephrine or blowing of smoke always provoked a similar cardiac reaction, i.e. a shortlasting tachycardia followed by a period of bradycardia (Fig. 1a and 1b). In one and the same doe uterine responses to epinephrine may differ on successive days, whereas the heart frequency always displayed the same response. One example of three different uterine responses on three successive days in one doe is illustrated in Fig. 2.

B. Adrenergic blocking agents and the + — effect of epinephrine

During the time of estrogen withdrawal in overiectomized does, epinephrine and stress always provoked an activation, followed by inhibition (+ — effect). When during the period of inhibition (lasting from 8 to 15 minutes) a second dose of epinephrine was administered, the inhibition of uterine activity nevertheless continued, apart from the occurrence of a few isolated spikes (Fig. 3). Even oxytocine,

administered during the inhibition, was not able to activate uterine motility (Fig. 4). Also, stress-stimulation within 10 minutes of a spontaneous burst of activity, was unable to provoke a uterine reaction, although the heart rate reacted in the characteristic way (Fig. 5).

10 minutes after pretreatment of the animal with the alpha-adrenergic blocking agent Dibenyline® (3 mg per kg bodyweight), adrenaline was not able to induce both the initial increase in uterine activity and the subsequent inhibition. It should be mentioned, that a period of at least 10 minutes was necessary in order to establish a complete alpha-adrenergic blockade. Alpha-adrenergic blockade prevented also the occurrence of bradycardia, observed after the administration of epinephrine, as did atropine (0.3 mg/kg bodyweight). When on the contrary the animal was pretreated with the beta-blocking agent Inderal® (propranolol) epinephrine often (13 out of 16 trials) caused a stronger initial increase in uterine activity, followed by a prolonged period of inhibition. The occurrence of a more pronounced activation due to epinephrine after pretreatment with Propranolol is in accordance with observations of Willems and De Schaepdrijver (1966), Cibils et al. (1971) and Carter and Olin (1972).

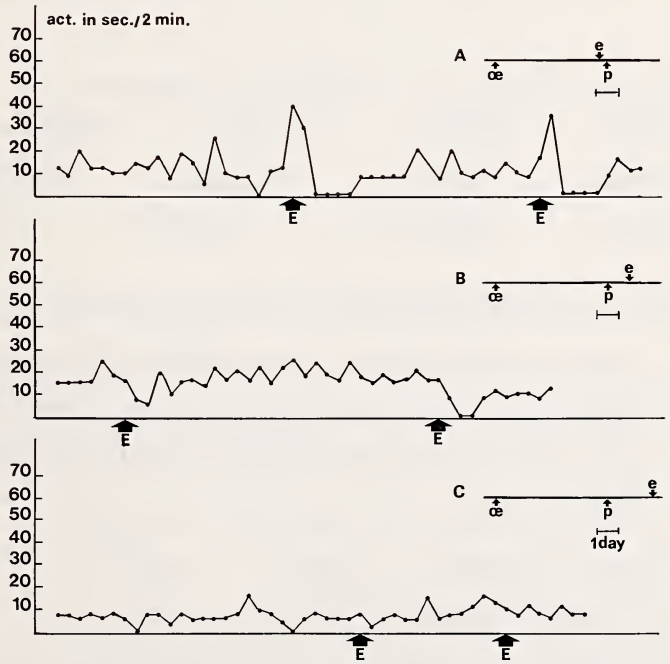


Fig. 2. The relationship between sexsteroid treatment and the kind of effect of epinephrine on uterine motility. Uterine activity is expressed in seconds of activity per 2 minutes. Experiments were carried out on three successive days in the same animal. A. = 3 days after oestrogen treatment (see indication on top of the figure) epinephrine causes the +— effect. B. = One day after progesterone treatment, following on priming with estradiol benzoate epinephrine inhibits uterine activity. C. = On the second day after progesterone treatment epinephrine has no effect on uterine motility. oe = oestrogen treatment; p = progesterone treatment; e = experiment

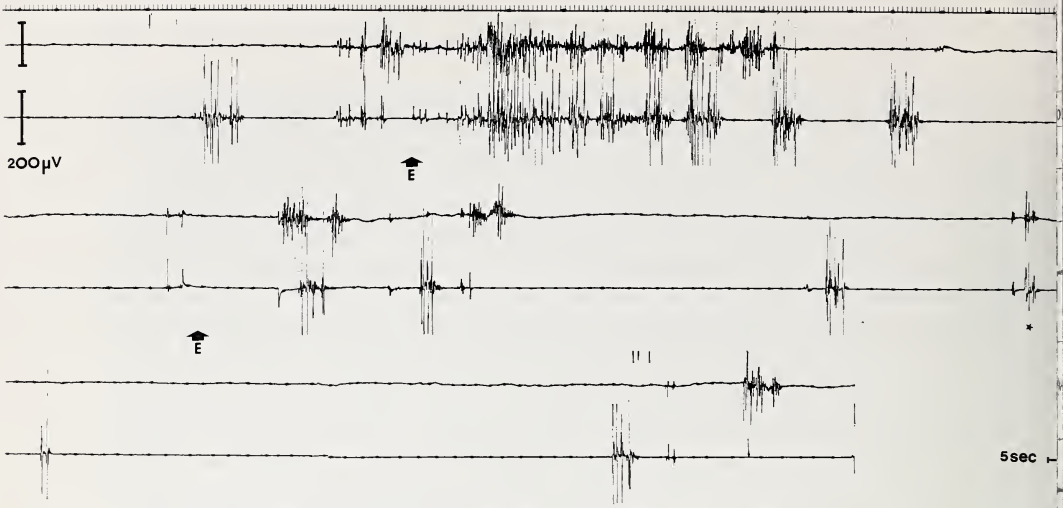


Fig. 3. The effects of 0.03 mg epinephrine (E) intravenously. When epinephrine is administered a strong reaction is observed (+ component of the +— effect). A second administration of epinephrine, immediately after the first one, during the expected — -phase of the +— effect is not able to provoke a reaction as strong as the first gift did

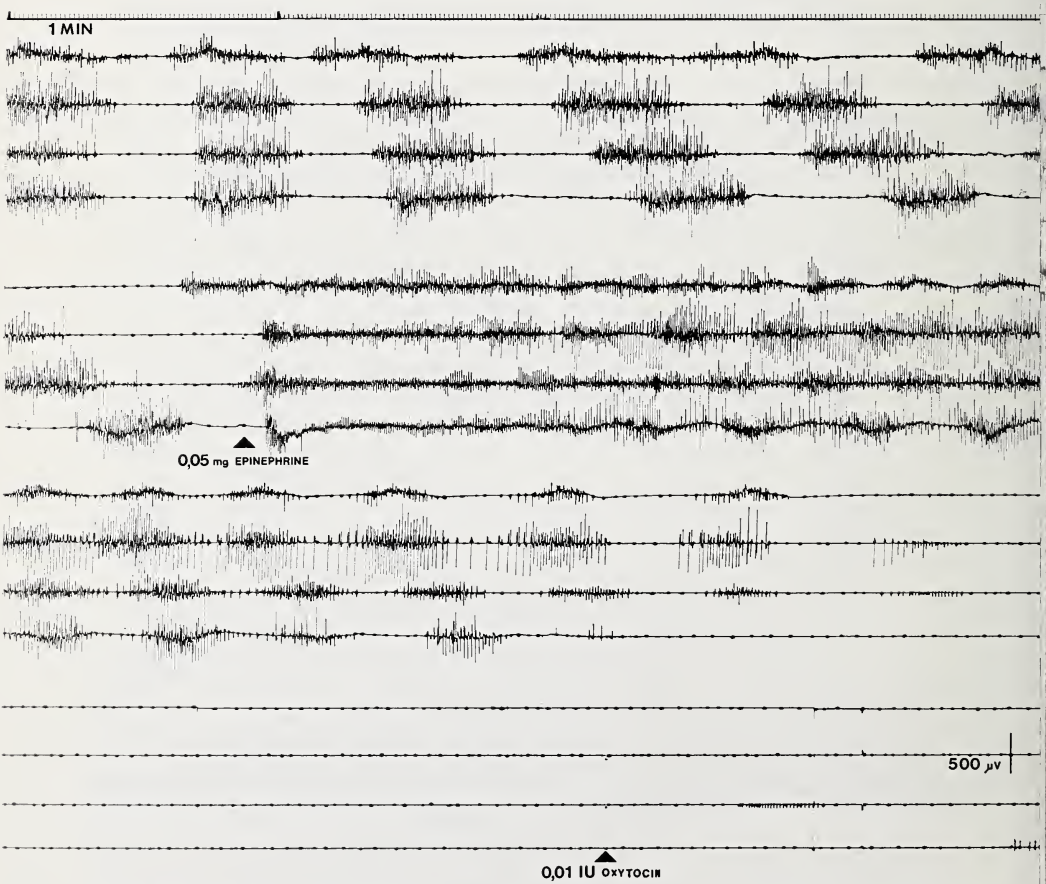


Fig. 4. The effect of 0.01 I.U. oxytocine on uterine motility, administered during the — component of the +— effect of epinephrine in a one day post abortum doe. Oxytocine is not able to provoke a reaction during this inhibitory phase

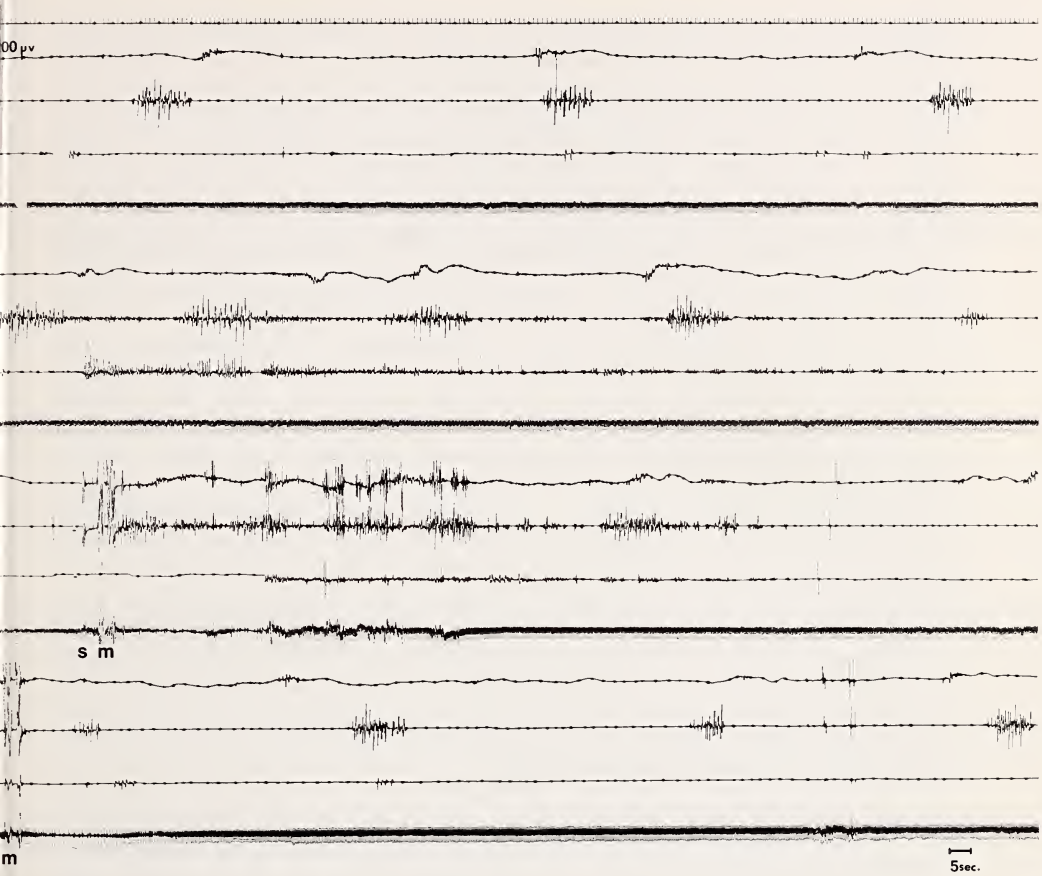
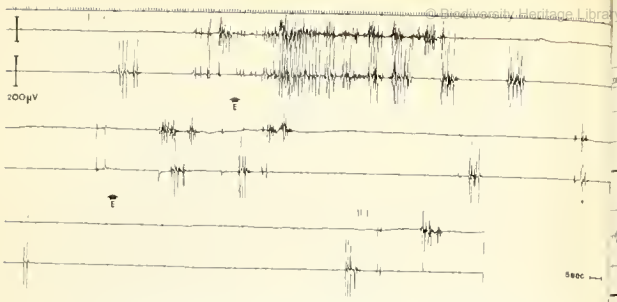


Fig. 5. Uterine activity in a six day post abortum rabbit. Traces a and b give an impression of the normal activity: regular activity, (trace a) sometimes grouped as bursts of activity (trace b); c = The effect of blowing smoke (s) more than 10 minutes after the spontaneous occurrence of a burst of activity is induction of a new burst of activity. The heart rate reacts in the characteristic way (tachycardia, followed by bradycardia); d = The effect of blowing smoke within a period of 2 minutes after the occurrence of a burst of activity. Now the stress stimulus is not able to induce a new burst of activity. The heart rate however, reacts in a similar way as in trace c. m = indications of movements

Discussion

Both stress and epinephrine evoked invariably an identical cardiac reaction, consisting of a short period of tachycardia, followed by a prolonged period of marked bradycardia. The period of bradycardia could both be prevented by administering the alfa-adrenergic blocking agent Dibenyline® or by atropine. Tachycardia is the well-known effect of epinephrine on the myocardium, whereas the subsequent bradycardia is the reactive effect to the vasoconstrictory action of epinephrine. Vasoconstriction induces an increase in systemic bloodpressure, which, via the baroreceptors, stimulates vagal activity, resulting in a decrease in heart rate. It is this vagal activity which is counteracted by atropine. Dibenyline prevents the vasoconstrictory action of epinephrine (Willems and de Schaepdrijver 1966). The reaction of the heart rate to the stress-stimulus proves, that blowing of smoke is indeed



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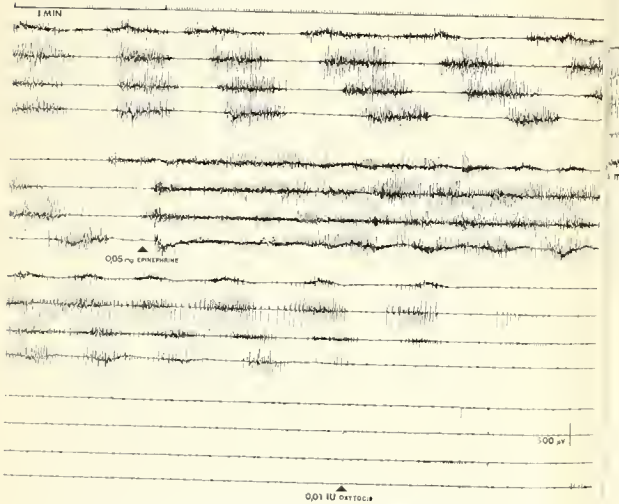

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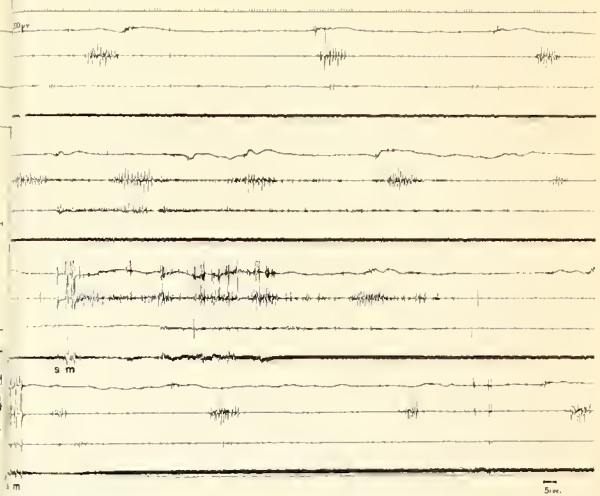

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experienced by the doe as a stressful event, which is suggested by the fact that no difference could be observed between the cardiac reactions to the stress stimulus and to the exogenous administration of epinephrine via an extension of the jugular catheter, which garantees, that the procedure of administering of the drug is not experienced as a stress stimulus. The importance of recording heart rate in this respect is illustrated by fig. 5. Smoke induces a burst of uterine activity and the changes in the heart rate as described above (trace c). However, within a period of 10 minutes after the occurrence of this strong uterine reaction, smoke has no effect on uterine activity, but still influences heart rate. This proves that the lack of uterine reaction (trace d) is not caused by adaptation to the stress stimulus, but should be ascribed to the occurrence of a reactive uterine irresponsiveness.

In contrast to the heart frequency that always showed similar changes in reaction to stress or to epinephrine, the uterus reacted in different ways. The effects of epinephrine and of stress stimulation on the heart rate do not change with changing hormonal conditions, whereas uterine reactions to stress stimulation and to epinephrine are determined by the levels of estrogens and progesterone, as is confirmed by the experiments with sexsteroid treated ovariectomized animals.

Preponderance of the + effect of epinephrine in the unovariectomized does was replaced by the + – effect in ovariectomized does. This suggests that the majority of the unovariectomized animals was estrogen dominated and that the hormonal state of most of the ovariectomized does was that of estrogen withdrawal.

Only in ovariectomized untreated animals a – effect was observed, which suggests a situation of estrogen withdrawal, whereas progesterone is still present in appreciable amounts. Probably this hormonal condition was absent in the unovariectomized animals, which agrees with the assumption that most of them were in natural estrus. Indeed ripe follicles could be seen at ovariectomy. According to Hammond (1925) healthy does are almost all the time in estrus.

During pregnancy the rabbit uterus shows no reaction to stress stimulation or to epinephrine, or reacts by an increase in uterine activity (Bontekoe et al. 1977). In the present experiments, animals treated with progesterone or with combination of estrogen and progesterone reacted, just like pregnant does, to stress or to epinephrine either by an increase in uterine activity, or by no effect at all. During pregnancy the uterus is influenced both by estrogens and progesterone but there exists a progesterone domination. Only towards the end of pregnancy plasma levels of progesterone decline (Challis et al. 1974; Hilliard et al. 1973). Indeed no effect is observed when progesterone domination is more or less absolute, i. e. shortly after the administration of mere progesterone or after the simultaneous administration of both estradiolbenzoate and progesterone. In the group of progesterone treatment after estradiolpriming no effect was observed on the third day after progesterone-administration. Although there can rest only a little progesterone by that time, this may still be exerting a large influence, since it is well known, that estrogens stimulate the production of progesterone receptors in the myometrium (Ramanath Rao and Katz 1977), whereas progesterone itself causes a breakdown of its own receptors (Faber et al. 1972; Milgrom et al. 1972; Fail et al. 1972). This explains, that on the fourth day after progesterone treatment following priming with estradiol an activation due to stress and to epinephrine is most of the times observed.

Inhibition of uterine activity due to stress stimulation and to epinephrine only occurred at delivery and less than 24 hours post partum and post abortum (Bontekoe et al. 1977). In the present experiments inhibition of uterine motility only occurred during estrogen withdrawal, while progesterone influence was still present. This resemblance is well understandable in the light of the findings of Hilliard et al. (1973) who showed that between days 28 and 30 of pregnancy plasma levels of

both progesterone and estradiol drop to very low values. However, Challis et al. (1974) observed, that the concentration of estradiol in the myometrium exceeds that of the plasma by tenfold or more throughout pregnancy, the highest myometrial concentration of estradiol was found on day 30 of pregnancy. Prior to parturition the ratio estradiol in the myometrium and the plasma reaches the highest value, probably caused by an increased uptake by the myometrium. Hence plasma estrogen withdrawal may coincide with myometrial estrogen dominance. The concentration of progesterone in the myometrium however, closely parallels that of the plasma throughout pregnancy. Thus at parturition plasma estradiol withdrawal can be observed, although myometrial values are high. It is impossible to decide whether progesterone treatment, subsequent on priming with estradiol, induces a similar hormonal condition, but it is most likely that the ovariectomized does on the first day after this treatment are indeed comparable with normal labouring and post partum does.

The characteristic reaction of the two and three days post abortum does (+ – effect) (abortion being most of the time expulsion of dead fetuses) to stress and to epinephrine (Bontekoe et al. 1977) is similar to that observed during early estrogen withdrawal in the present experiments. The + effect is observed both longer after an abortion and more than 5 days after estrogen treatment. Estrogen treatment increases the working capacity of the myometrium, resulting in a very good sensitivity to stress stimulation, exogenous epinephrine and oxytocine. The estrogen dominated uterus reacts to stress or to epinephrine with an increase in activity (+ effect). This activation is possible, because no progesterone is present to lessen uterine sensitivity. Estrogen withdrawal results in a decrease of actomyosine concentration, which can be restored by the administration of estrogens (Csapo 1956b). During estrogen withdrawal the effect of both stress and epinephrine is an activation, followed by a period of inhibition, during which the uterus is unable to react to stress, epinephrine and oxytocine. It seems that during the period of estrogen withdrawal the uterus is capable to react, but also needs a period of recovery of about 10 minutes. Indeed, prevention of the initial activation by the alpha-adrenergic blocking agent Dibenyline® prevents the subsequent refractoriness.

This period of rest, after the initial increase in uterine activity could not be prevented by the beta-blocking agent Inderal®, whereas Inderal® was able to block the pure inhibitory effect of epinephrine. This suggests that the – effect of epinephrine is a beta-adrenergic effect, whereas the – component of the + – effect is the recovery phase of an alpha-adrenergic effect.

Bontekoe et al. (1977) observed, that the + – effect is the characteristic effect of stress or epinephrine in two and three days post abortum does. In the more than 24 hours post partum does the + effect was commonly observed. The difference in reactions may become understandable by assuming that in the aborting doe progesterone influence is already vanishing at the moment of expulsion of the dead fetuses, while in the normal post partum rabbits a decline in progesterone level starts prior to parturition (Baldwin and Stabenfeldt 1974), but the complete disappearance occurs after birth. This assumption is supported by the findings of Goto and Csapo (1960), who state that at the end of pregnancy in the rabbit at least a part of the progesterone is of placental origine. In case of fetal death at least the placental progesterone production has ceased, resulting in a decline in progesterone levels, which starts earlier than at normal parturition. In rabbits, progesterone production by the ovaries is a prerequisite for the maintainance of pregnancy. Ovariectomy performed during pregnancy induces an abortion (quoted in Csapo 1956a).

Moreover, the death of fetuses in utero results in luteolysis, hence in a decline in progesterone-production prior to expulsion of the dead fetuses. The feto-placental

unit plays an important role in the maintainance of the corpora lutea graviditatis (Stormshak and Casida 1966).

Estrogen production by the ovaries may still continue for a while. Two or three days post abortum there probably is a situation of mere estrogen withdrawal, explaining the occurrence of the + — effect of stress or of epinephrine.

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Zusammenfassung

Der Einfluß steroider Geschlechtshormone auf die Reaktionen des Uterus auf Adrenalin und Streß beim Laborkaninchen

Die Wirkungen von Streß und Adrenalin auf die Motilität des Myometriums wurden beim Laborkaninchen untersucht. Folgende Versuchsgruppen standen zur Verfügung: a. intakte Tiere, b. ovarectomierte Tiere, c. ovarectomierte Tiere, die entweder mit Oestradiolbenzoat oder mit Progesteron behandelt waren. Auch Kombinationsbehandlungen, wie im Text beschrieben, wurden durchgeführt. Die Art der myometralen Reaktion auf Streß oder auf Adrenalin zeigte sich vom Gleichgewicht zwischen Oestrogenen und Progesteron bestimmt. Unter Oestrogendominanz bewirkten Streß oder Adrenalin eine Zunahme der Uterusmotorik (+ Effekt). Während abklingender Oestrogenbeeinflussung konnte ein + — Effekt beobachtet werden, d. h. nach der Aktivierung folgte eine Hemmung der Kontraktilität. Progesteronbehandlung in der Phase abklingender Oestrogenbeeinflussung führte dazu, daß das Myometrium nur mit einer Hemmung seiner Kontraktionstätigkeit (— Effekt) auf Streß oder Adrenalin reagierte. Unter absoluter Progesterondominanz war der Uterus nicht imstande, mit Motilitätsveränderungen auf Streß oder Adrenalin zu reagieren (0-Effekt).

Im Lichte dieser Befunde werden die Ergebnisse vorheriger Untersuchungen an trächtigen, gebärenden und sich nach der Geburt befindlichen Kaninchen diskutiert.

Die Wirkungen adrenerger α-Blocker (Dibenyline®) und β-Blocker (Inderal®) auf erwähnte Vorgänge werden beschrieben und diskutiert. Dem Auftreten der + — Effektes auf Adrenalinverabreichung wurde durch α-Blocker vorgebeugt. Beide Komponenten traten dann nicht auf. Vorbehandlung mit dem β-Blocker dagegen rief sowohl eine Intensivierung der +Komponente als auch eine Verlängerung der Dauer anschließender Hemmung hervor. Dem reinen — Effekt konnte aber mit Inderal vorgebeugt werden. Die — Komponente des + — Effektes wird daher als grundsätzlich vom — Effekt verschieden gedeutet.

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Studies on Gerbillinae (Rodentia)

II. The karyotype of *Gerbillus campestris*, analysed by G- and C-banding techniques

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Abstract

Studied banding patterns of the chromosomes of *Gerbillus campestris* from South Morocco. Air-dried chromosome preparations were submitted to G- and C-banding techniques. The karyotype consists of 56 chromosomen that can be distinguished on basis of their characteristic G-bands. After application of C-staining method, blocks of centromeric heterochromatin can be observed in each pair of autosomes. Chromosome no. 3 is entirely heterochromatic, but the darker stained centromeric area remains still visible. The X chromosome which seems to be totally heterochromatic can be subdivided into regions with different degrees of staining intensity. The Y chromosome stains heavily throughout its length. — In two pairs of autosomes, structural polymorphism is present.

Comparison of the karyotypes of the two gerbil species *Gerbillus campestris* and *Meriones unguiculatus* revealed a considerable number of chromosome arms with apparently homologous G-banding patterns. With regard to the distribution of heterochromatin, similarities as well as differences can be found.

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