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THE EXTENSIBILITY OF THE CERVIX UTERI OF THE RAT AT DIFFERENT TIMES OF PREGNANCY

BY R. D. HARKNESS AND MARGARET A. NIGHTINGALE
From the Department of Physiology, University College London

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The mechanical properties of the cervix uteri, during pregnancy in the rat, show two distinct changes; first, an increase in the circumference of the collagenous framework, and, second, an increase in its extensibility under prolonged loading (Harkness & Harkness, 1959). In this earlier investigation the time course of the change in extensibility was not studied in detail, only that of the change in circumference. In a subsequent investigation on the effect of hormones on the mechanical properties of the cervix it was found that a mixture of oestradiol, progesterone and relaxin could increase the circumference of the cervix to a size corresponding to the 17th–18th day of pregnancy, but had little effect on its extensibility (Cullen & Harkness, 1960). It therefore became of interest to establish the time course of change of extensibility of the cervix during pregnancy, and to relate it to the change in circumference.

In addition, previous work had shown an abrupt change in the physical properties of the foetal membranes about three days before the end of pregnancy (Harkness & Harkness, 1956) and we thought this might be related to similar change in the birth canal. The present investigation has shown that this is not so. The time course of the change in extensibility of the cervix has proved to be similar to that of the circumference, both showing little alteration until the 12th day, after which they increase progressively until the end of pregnancy.

METHODS

Animals. The rats were albinos of the local strain, weighing 160–200 g at the beginning of pregnancy.

Timing of pregnancy. Females were put with males for 24 hr after a vaginal smear, examined in the morning, showed numerous nucleated squamous cells and no leucocytes.

Physical tests. The methods used for examining the excised cervix have previously been described (Harkness & Harkness, 1959; Cullen & Harkness, 1960). It is sufficient to say here that the cervix, suspended in oxygenated Locke's solution at 37° C, was subjected, for 2–3 hr, to a constant load which tended to separate two parallel stainless-steel rods 0·6 mm diameter, one going through each cervical canal, one rod being fixed, the other movable. The movement of this rod was recorded through a lever on a smoked drum.

The following symbols are used (Cullen & Harkness, 1960; Harkness & Harkness, 1961):
l_0 = inner circumference (mm) of cervix at zero time, obtained by extrapolation (Fig. 1),
K = rate of increase in inner circumference (mm/min) after this rate has become constant so far as could be ascertained (Fig. 1).

The fractional increase in circumference per unit of time (K/l_0) has been used as a measure of the extensibility of the tissue (Harkness & Harkness, 1961).

We have reported previously (Harkness & Harkness, 1956) that the circumference (l) time (t) curve for the non-pregnant cervix and in the early stages of pregnancy can be described initially by the relation $l = a+b \log t$ where a and b are constants. This is incompatible with a linear component (K) in the relationship of circumference to time, but may

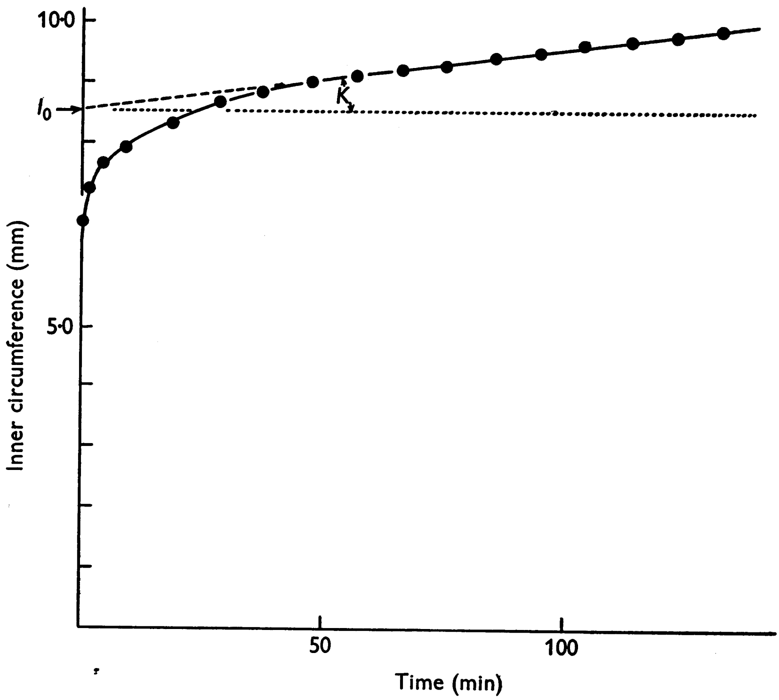

Fig. 1. Example of the effect of a constant load on circumference of cervix. Non-pregnant rat (dioestrus); load 50 g equivalent to 33 g/mm² collagen calculated for length l_0.

still prove a good approximation when this component is small. In some of the cervixes in the present sample this component was demonstrable (Fig. 1). However, in many the rate of change of circumference was so low as to be near the limit of measurement. In those cases linearity was assumed, an approximation justified by the fact that we were principally interested in comparisons between different times of pregnancy, and, in the results, by the magnitude of the difference between the measurements made at these times and later in pregnancy.

Tension per unit cross-sectional area of collagen was calculated from the inner circumference, assuming that the collagen was evenly distributed round the rod as a belt of this length. This is an approximation which underestimates the mean circumference by roughly

5 % at the end of pregnancy (21 days); in the non-pregnant condition and up to the 12th day, when the belt of tissues is thicker relatively to circumference, the difference is about 15 %.

Chemical tests. After the physical tests the tissue was placed in 5 ml. 6 N-HCl, autoclaved for 4 hr at 40 lb./sq.in. (2·8 kg/cm²), and the resulting hydrolysate analysed for hydroxyproline (Neuman & Logan, 1950). The amount of collagen present was calculated from the hydroxyproline content by multiplying by 7·46.

RESULTS

Relation of load to rate of extension. To find the time course of change in extensibility it was necessary to correct the measured rate of extension to a standard condition of load. The relation between load and parameters measured was worked out on cervixes removed on the 21st day of pregnancy and stretched with loads varying from 10 to 100 g.

The results are shown in Table 1. An approximately tenfold increase in load per unit cross-sectional area of collagen gave only a small (30 %) increase in l_0, and about a threefold increase in the rate of extension of the tissue measured by K/l_0. Rate of extension was not linearly related to tension, but approximately to its square root (Fig. 2).

TABLE 1. Effect of load on rate of extension of cervix (21st day of pregnancy)

	1	2	3	4	5
Load (g)	12 ± 2	25 ± 3	33 ± 3	57 ± 11	90 ± 5
Tension (g/mm² collagen for length l_0)	27 ± 4	61 ± 4	86 ± 3	162 ± 20	275 ± 16
Rate of extension (10^3 K/l_0)	6·0 ± 1·0	7·8 ± 1·4	9·8 ± 1·8	13·7 ± 4·4	20·0 ± 2·6
Circumference (l_0; mm)	21·5 ± 1·1	23·6 ± 2·4	26·8 ± 1·4	29·4 ± 2·0	27·3 ± 1·5
Weight of cervix (mg)	194 ± 16	181 ± 2·4	206 ± 13	199 ± 22	190 ± 16
Total collagen (mg)	6·7 ± 0·5	6·6 ± 0·3	7·1 ± 0·3	7·0 ± 0·7	6·3 ± 0·2

There were six rats in each group (cols. 1–5).

l_0 is circumference obtained by extrapolating the linear part of the circumference–time curve to zero time, K is rate of extension (mm/min). The estimate of variation is the standard error of the mean.

Time course of change in extensibility of the cervix in pregnancy. A constant load of 50 g was used and the resultant rate of extension (K/l_0) corrected to 100 g/mm² collagen by using the relation found in the experiments described above. Its applicability to the cervix in early pregnancy and in the non-pregnant condition was not investigated. This would have been difficult to do as extensibility was in most cases very low, and in the non-pregnant animals also very variable. We were mainly interested in comparisons between different times, and the relative changes are unaltered if all the figures are corrected to the average tension used in the non-pregnant samples, no correction being made to the latter.

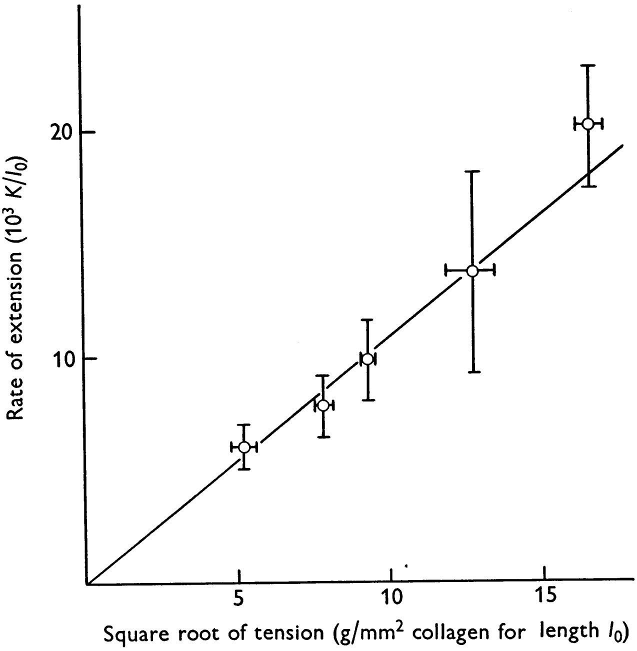

Fig. 2. Relation between rate of extension of cervical tissue and square root of tension. The length of the lines through each point is twice the standard error of the mean.

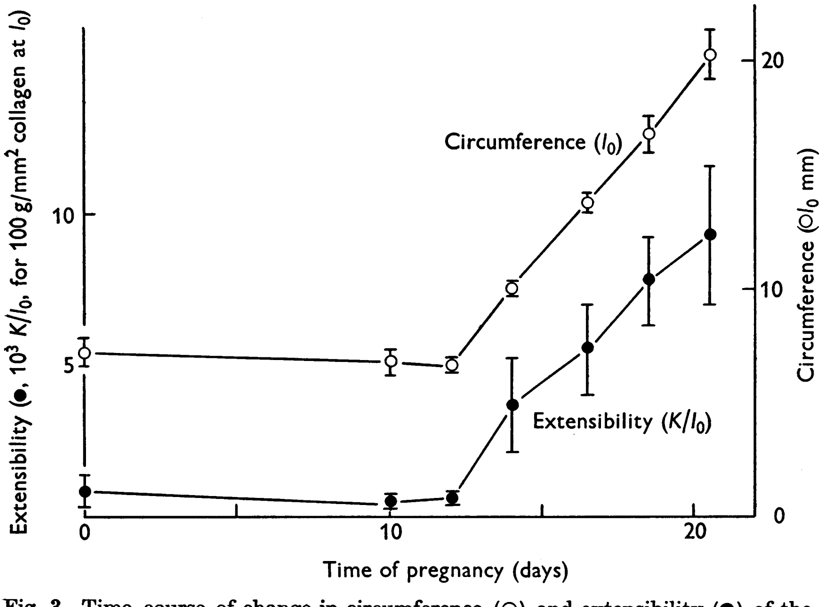

Fig. 3. Time course of change in circumference (○) and extensibility (●) of the cervix during pregnancy. The length of the vertical line through each point is twice the standard error of the mean.

The results are shown in Table 2. The time course of change in extensibility was similar to that of change in l_0, though the proportionate change was greater (Fig. 3). Both properties showed no evidence of alteration until approximately the 12th day, after which they increased progressively until the end of pregnancy.

TABLE 2. Circumference and extensibility of the cervix at different times of pregnancy

	Non-pregnant Dioestrus	Days of pregnancy 10	12	14	16–17	18–19	20–2
1. No. of rats	10	5	5	5	9	10	8
2. Weight of cervix (mg)	68 ± 3	57 ± 4	74 ± 5	117 ± 6	149 ± 16	161 ± 10	192 ± 1
3. Total collagen (mg)	4·9 ± 0·5	4·8 ± 0·5	4·1 ± 0·2	5·4 ± 0·3	6·5 ± 0·5	7·4 ± 0·4	8·8 ± 0
4. Circumference (l_0, mm)	5·4 ± 0·5	5·1 ± 0·3	6·7 ± 0·1	10·0 ± 0·3	13·8 ± 0·4	16·8 ± 0·8	20·4 ± 1
5. Extensibility ($10^3K/l_0$)*	0·8 ± 0·5	0·5 ± 0·1	0·6 ± 0·2	3·7 ± 1·6	5·5 ± 1·5	7·8 ± 1·5	9·3 ± 2
6. Tension at l_0 (g/mm² coll.)	40 ± 3	38 ± 4	58 ± 3	65 ± 2	77 ± 5	80 ± 3	81 ± 2

Symbols as in Table 1. The estimate of variation is the standard error of the mean.
* Extensibility (line 5) is corrected to 100 g/mm² collagen.

DISCUSSION

Comparison with previous investigations. The time course of increase in the circumference of the collagenous framework of the cervix, measured by l_0, is the same as that recorded previously (Harkness & Harkness, 1959). In contrast to the progressive change in the circumference and extensibility of the cervix from the 12th day until the end of pregnancy, weakening of the foetal membranes takes place abruptly between the 18th and 19th days of pregnancy (Harkness & Harkness, 1956). Since all these changes must be regarded as directed towards facilitation of the passage of the foetuses to the exterior at parturition a common controlling mechanism might be expected. In view of the different time course of the latter, however, it looks as though it is, in fact, controlled independently of the change in the cervix.

Relation of change in extensibility of cervix in pregnancy to that produced by hormones. It has previously been found that the circumference of the cervix can be increased up to the value for the 17th–18th day of pregnancy by a combination of oestradiol–17β, progesterone, and relaxin (Cullen & Harkness, 1960). A comparison of these results with the present ones shows that the extensibility was not increased to the comparable level found at this time of pregnancy. In pregnancy extensibility and circumference are related (Fig. 3). If the figures for extensibility of cervixes from hormone-treated animals obtained previously (Cullen & Harkness, 1960; Table 8) are corrected to the same tension at l_0, and compared similarly with circumference, a different relation is found (Fig. 4), the cervixes from hormone-treated animals showing less extensibility for the corresponding size. This discrepancy suggests that change in circumference of the collagenous framework, and increase in extensibility, though following a similar time course in pregnancy, are under separate hormonal control. However, the effects of administration of hormones must be interpreted with caution, since no information is available about quantity in the circulation, and

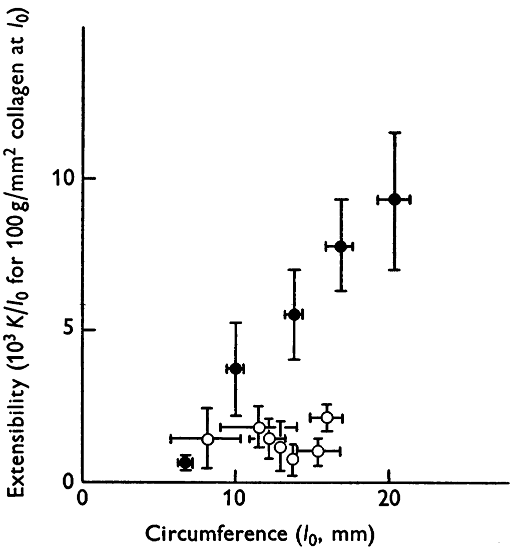

Fig. 4. Relation between circumference and extensibility of the cervix in pregnancy and under the influence of hormones. ● In pregnancy, groups from Table 2, 12–21 days of pregnancy. ○ Spayed rats treated with oestradiol-17 β, progesterone, and relaxin (from Cullen & Harkness, 1960: Table 8). The length of the lines through each point is twice the standard error of the mean.

this may well show wide fluctuation between doses. It is known that both the circumference and extensibility of the cervix may alter rapidly (Harkness & Harkness, 1961). If the rates of response of the two properties to alteration in circulating hormone level were different a discrepancy such as we have found could arise.

SUMMARY

1. Measurements have been made at different times of pregnancy of the rate of extension of the tissues round the cervix uteri of the rat 2–3 hr after addition of a load, when, so far as could be ascertained, this rate had become constant.

2. The time course of change in 'extensibility' measured in this way and corrected to a standard load per unit cross-sectional area of collagen

was found to be similar to that of change in circumference of the collagenous framework of the cervix. Both show little change until approximately the 12th day of pregnancy, and increase progressively thereafter until the end of pregnancy.

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