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# EDEMATOUS CHANGES IN MUCOSAL FOLDS OF THE INTERNAL OS OF THE RABBIT CERVIX

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## Introduction

The cervix plays an important role in maintaining pregnancy, and it is dilated and opened in the period preceding parturition. Numerous data are available about changes in morphological, histochemical, biochemical and physical properties in the connective tissue of the cervix during pregnancy and labor.<sup>2,4,6,7,10</sup> It is less well-known, however, whether the cervix acts to hold embryos in the uterine lumen during the preimplantation stage. Studies in our laboratory<sup>8-10</sup> have demonstrated that the mucosa of rabbit cervix does not change grossly in morphology during early pregnancy and pseudopregnancy, and that a sphincter-like action of the cervical musculature can be excluded, suggesting that the internal os of the cervix can be regarded as the decisive portion for keeping preimplantation embryos in the uterine cavity.

In the present study, therefore, the cervixes from estrous, pregnant and pseudopregnant rabbits were examined histologically, in order to define the changes occurring in the internal os of the cervix during the preimplantation stage.

## Materials and Methods

Thirty-two mature, female Japanese White does were used. Four animals were killed unmated, 20 were mated twice and then given an intravenous (i. v.) injection of 50 IU of human chorionic gonadotrophin (hCG: Gonatropin, Teikoku-Zōki, Japan), and killed at various times from 2 to 15 days *post coitum* (*p. c.*) — four does at 4, 5 and 6 days *p. c.* and two at 2, 7, 9 and 15 days *p. c.*, respectively. The remaining 8 does were given an i. v. injection of 50 IU of hCG and sacrificed 2, 4, 5, 6, 7, 10, 14 and 18

days following hCG injection, respectively.

The cervixes, with a portion of uterine horn attached, were excised immediately after sacrificing, and the extraneous fat was removed. Each of the paired cervixes was pinned on Sealant (Dow-Corning 780) and immediately fixed in Bouin's solution, embedded in paraffin wax and sectioned at 6-8  $\mu$ m. Paraffin sections were stained with hematoxylin and eosin (H. E.) or azan.

### Results

The internal os of the cervix was easily recognized in histological longitudinal sections because the morphology of the cervical epithelium is distinctly different from that of the uterus, not only at estrus as reported previously,<sup>12)</sup> but also following mating and/or hCG injection. In contrast with the progestational alterations of the endometrium, such as fold branching and cell fusion,<sup>8,9)</sup> there were no marked changes in the morphology of the cervical folds. In addition, endometrial epithelial cells had become more basophilic due to their transformation into multinucleated cells. During progestational stages, multinucleated cells and mononucleated cells were found to be mixed together only in the small area of transitional epithelium between the uterine horn and the cervix.

In one of 4 animals examined at estrus, a partially edematous appearance was noted in a small area of the subepithelial stroma of the cervical folds facing the uterine lumen (Fig. 1). In three other animals in estrus and the animals on day 2 of pregnancy or pseudopregnancy, such a phenomenon was not observed (Fig. 2), whereas at 4 days following ovulatory stimulus, mucosal folds of the internal os had become edematous. Thereafter, edema was extensive and reached its maximum 6 days following ovulatory stimulus (Figs. 3 & 4); but on and after the 7th day edema was no longer observed in either pregnant or pseudopregnant does. On the other hand, the external os of the cervix always exhibited an edematous appearance in some degree in all stages examined. In azan-stained preparations, edema in both external and internal os of the cervix was characterized by a marked dispersion of the collagen fibrillar structure and an increase of interfibrillar amorphous ground substance. Such a phenomenon was never observed in the subepithelial stroma of the mid-cervix.

### Discussion

TYLER<sup>15)</sup> has considered that edema and invasion by polymorphs in the

rabbit ectocervix might be triggered by an immunological response to some component of semen other than seminal plasma. In the present study, however, there was always some degree of edema in the external os regardless of the reproductive status, suggesting that edema in this region is caused also by some other factor in addition to semen. In mucosal folds of the internal os of the cervix in postovulatory rabbits, edematous changes were noticed 4 days following ovulatory stimulus, reaching a maximum on day 6. As far as we know, edematous changes in the internal os of the cervix have not been reported yet in the literature. Since this phenomenon was observed with or without the presence of embryos, it is obvious that partial occurrence of edema in the internal os depends on changes in the ovarian hormones. In general, estrogens are known to elicit edema of the reproductive organs. Our previous study<sup>10</sup> demonstrated that the rabbit cervix, as well as the uterus,<sup>10</sup> became wholly edematous with estrogen replacement following ovariectomy. Moreover, appearance of the edema in the internal os of the postovulatory does was coincident with an increase in the output of estrogen by the ovaries.<sup>3,6</sup> These observations suggest that the edematous phenomenon in the internal os is estrogen-dependant. INOUE<sup>6</sup> has demonstrated that water imbibition by the rat cervix during pregnancy may be elicited chiefly by histamine released from the mast cells in this organ, and such a softening of the cervix is caused effectively with estriol treatment.

Since preimplantational embryos lie free in the uterine cavity during 4-6 days after mating,<sup>1,10</sup> edematous changes in the internal os of the cervix might be a factor for preventing transcervical expulsion of blastocysts into the vagina.

### Summary

The cervixes from estrous, early-pregnant and pseudopregnant rabbits were investigated histologically. The internal os of the rabbit cervix was easily recognized in histological longitudinal sections due to the morphological differences between the uterine and the cervical mucosal folds. Subepithelial stroma in the internal os became edematous 4-6 days following ovulatory stimulus, and the most wide-spread edema occurred on day 6. Very limited, partial edema was occasionally found during estrus, also. In the external os of the cervix, there was always some degree of edema regardless of the reproductive status.

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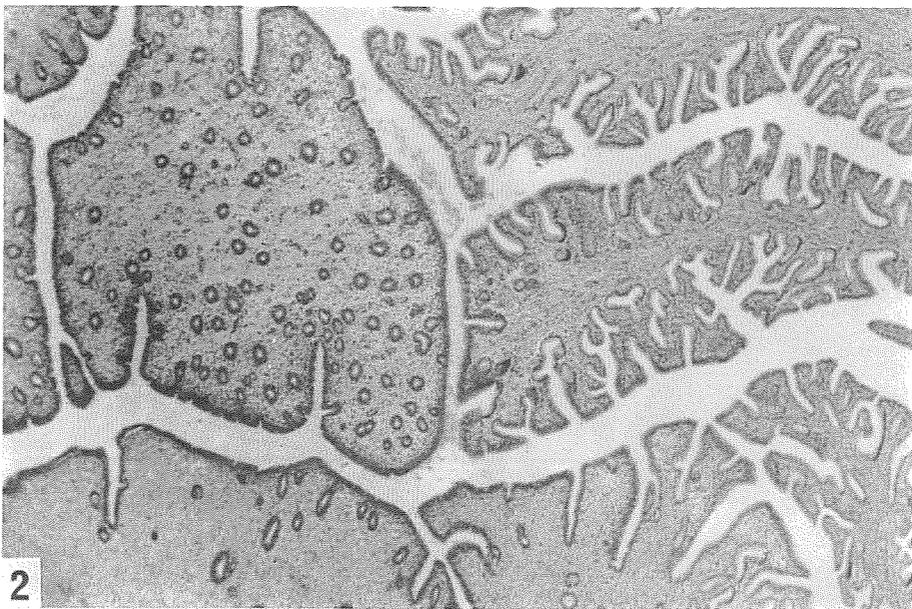
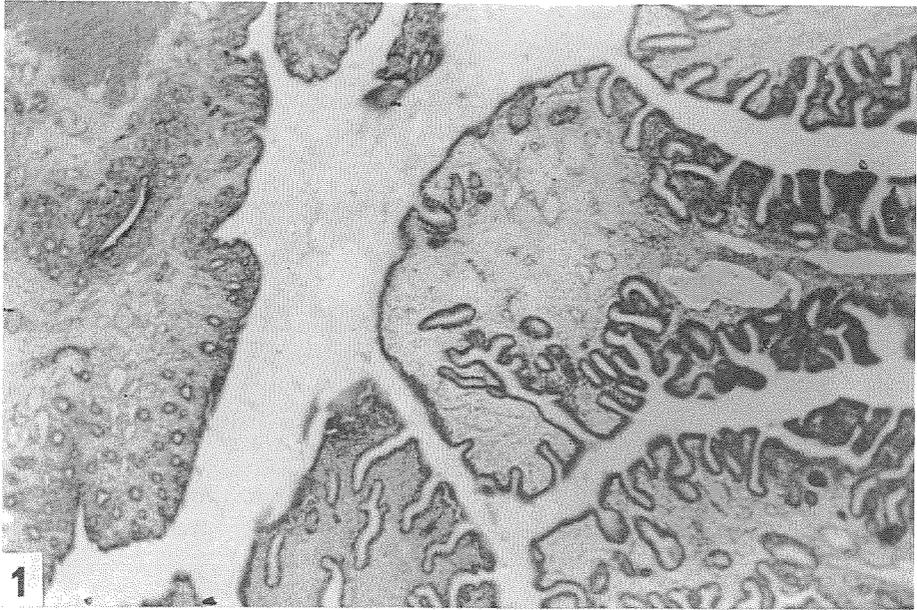
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**PLATE 1**  
**EXPLANATION OF FIGURES**

A portion of the internal os of the cervix from unmated, estrous rabbits.  
The cervical mucosa is on the right side in each figures.

In one of four animals examined (Fig. 1), edematous appearance is seen in the subepithelial stroma of the cervical fold facing the uterine lumen, but not in the remainder (Fig. 2). H. E.  $\times 33$ .



## **PLATE 2**

### **EXPLANATION OF FIGURES**

A portion of the internal os of the cervix from rabbits on the 6th day of pregnancy (Fig. 3) and on the 6th day of pseudopregnancy (Fig. 4). The cervical mucosa is on the right side in each figure. Note the pronounced appearance of edema in the subepithelial stroma of the cervical fold facing the uterine lumen. H. E.  $\times 33$ .

