

AN EXPERIMENTAL MODEL OF "HEALING" OF PSEUDOEROSIONS OF THE CERVIX UTERI

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Experiments on 60 virgin female CC57W mice showed that 27-124 days after the end of systematic and prolonged intravaginal injections of polyurethane changes similar to the "healing" of pseudoerosions of the human cervix uteri are observed in the cervix and vagina. These changes can be associated with the morphological features of focal hyperplasia of estrogen-producing follicular tissue and the conversion of these foci (evidently reversibly) into zones of proliferation morphologically identical with microfolliculomas.

It was shown previously that the intravaginal injection of plastic sponge made of polyurethane or rubber latex into mice induces the formation of gradually progressive endophytic precancerous foci of proliferation of the cervix uteri and vagina. The epithelium of these foci is at first stratified squamous. As a result of further progression of the primary precancerous foci of proliferation changes take place identical with the pseudoerosions of the cervix uteri in women (conversion of this experimental pseudoerosion into cancer has also been observed) [2].

The object of this investigation was to simulate and to make an experimental morphological study of the process of regression of pseudoerosion of the cervix uteri; such an investigation could shed light on the causes and characteristics of the "healing" process and also, possibly, on the treatment of cervical pseudoerosion in women.



Fig. 1. Small primary endophytic foci of proliferation formed in the vagina by stratified squamous epithelium (27 days after end of systematic intravaginal injections of polyurethane, duration of experiment 466 days). Hematoxylin-eosin, 230 \times .

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TABLE 1. Changes in Epithelium of the Genital Tract and Ovaries of Mice after Systematic Prolonged Intravaginal Injections of Plastic (polyurethane) Sponge

Series of experiments	No. of animals	Duration of experiment (in days)	Period of injection of sponge (in days)	Period of follow-up observation (in days)	Pathohistological changes											
					vagina					ovaries						
					No. of cases studied	initial (diffuse)	papillomas	endophytic foci of proliferation	No. of cases studied	hyperplasia (diffuse or focal)	micro-follicles					
								primary	pseudo-erosion							
I	15	279-466 (351)	215-439 (312)	27-64 (47,8)	13	2	10	10	1	11	6	5				
II	12	279-377 (298,3)	155-262 (190,7)	76-124 (108)	12	3	9	7	2	7	7	0				
III	11	265-464 (399)	265-464 (399)	—	11	—	11	7	4	4	4	0				
IV	22	509-534 (521,7)	509-534 (521,7)	—	22	4	18	12	6	6	6	0				

EXPERIMENTAL METHOD

Experiments were carried out on virgin female CC57W mice aged 1.5-2 months. Technical details of the systematic intravaginal injections of fragments of sponge and the preparation and investigation of the pathological material were described previously [1]. In some cases in the present investigation the mice were killed 27-124 days and not 24 h after the end of the period of injection of the polyurethane fragments, as was done previously [1, 2]. Altogether four series of experiments were carried out. The various experimental procedures and the results obtained are summarized in Table 1.

EXPERIMENTAL RESULTS

Histological examination revealed multiple tiny papillomas of the vagina in more than half of the animals studied (in 48 of 58 mice).

In series I and II in 17 of 25 cases the papillomas were combined with endophytic foci of epithelial proliferation described in Table 1 as "primary endophytic foci of proliferation." The changes corresponded to the precancerous foci described previously in the cervix uteri and vagina of mice by the end of the second month after the beginning of systematic intravaginal injections of polyurethane [2]. The stratified squamous epithelium took part in their formation and its cells were mainly similar to basal or parabasal cells (Fig. 1). Only in three cases did the endophytic epithelial islets found under the papillomas have marked bifunctional features in the animals of series I and II. A combination of stratified squamous and prismatic, mucus-forming structures was found in these outgrowths. They spread not only in the underlying connective tissue (like primary foci of proliferation), but also in the muscular tissue and they corresponded to the progressive endophytic epithelial precancerous foci of proliferation described previously (which developed after the first two months of the experiment), regarded as the experimental analogue of cervical pseudoerosion [2].

In series III and IV papillomas were combined in 19 cases with primary and in 10 cases with progressive endophytic foci of epithelial proliferation of the pseudoerosion type (Fig. 2). The ratio between the progressive and primary endophytic focal epithelial changes in the mice of series I and II (taken together) was 3:17, whereas in mice of series III and IV (also taken together) it was much (3 times) higher, namely 10:19.

In five of 25 cases in series I and II and in four of 33 cases in series III and IV only the earliest, diffuse changes, regarded as initial [1], were present in the epithelium.

Evidence of increased proliferation of granulosa-cell elements of the atretic follicles (signs of formation of the corpus luteum were found in only one case) was observed. Individual foci of proliferation of follicular tissue were approximately 1.5-2 times larger than Graafian follicles. In six cases in series I similar proliferative changes were observed, but in five other cases the processes of pathological proliferation of the follicular cells in the ovaries were much more advanced, and nodules of proliferating follicular tissue, morphologically indistinguishable from microfollicles, were found (the tumor nodule occupied one-third or even one-half of the area of the ovary in the section) (Fig. 3).



Fig. 2

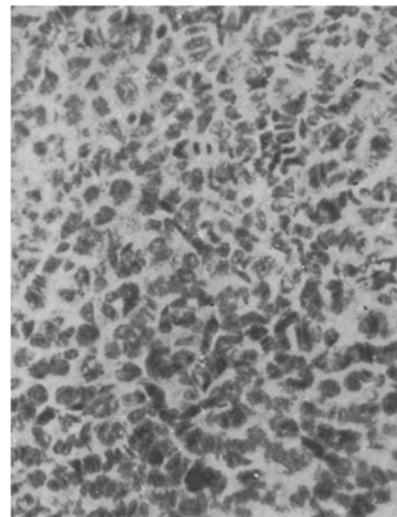


Fig. 3

Fig. 2. Experimental cervical pseudoerosion in a mouse (systematic prolonged injections of polyurethane; 305th day of experiment). Hematoxylin-eosin, 230 \times .

Fig. 3. Area of hyperplastic tumor-like nodule in the mouse ovary: cells vary in size and have a round or polyhedral nucleus, which varies considerably in size; mitosis on the right. Hematoxylin-eosin, 740 \times .

Judging from the results of the investigation, the bipotent epithelium [3, 6] of the endophytic foci of proliferation of the cervix uteri and vagina remains sensitive for a long time to the action of sex hormones. The more intensive change in the differentiation of this initially stratified squamous epithelium toward the formation of mucus-secreting prismatic structures is evidence of a gradual weakening of the effects of estrogens on it [3, 6]. On the other hand, the signs of a change in the differentiation of the endophytic epithelial structures identical to the morphological features of "healing" of pseudoerosion of the human cervix uteri during the first 2 months after the end of intravaginal injections of polyurethane (the possibility of some aplasia of these structures cannot be ruled out) may be linked with the sharp increase in estrogen-producing functions observed in the ovaries.

In the late stages after the ending of polyurethane injections (76-124 days, series II) no tumor nodules could be seen in the mouse ovaries. These last results are in agreement with data in the literature on the absence of any sharp line of demarcation between the early and later stages of tumor proliferation of the granulosa-cell tissues of mouse [5, 6] and human [4] ovaries.

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