PRECANCEROUS CHANGES IN THE EPITHELIUM OF THE CERVIX UTERI AND VAGINA OF MICE AFTER INTRAVAGINAL INSERTION OF FOAM PLASTIC

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UDC 618.146+618.015]-006.6-036.3-02:615.477.88.032.671

Systematic and prolonged (10-20 months) intravaginal insertion of a sponge made from butadiene-carboxylate latex—an artificial rubber polymer, and of a polyurethane sponge leads to the appearance and gradual progression of precancerous changes in the cervix uteri and vaginal.

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It has previously been shown that systematic intravaginal insertion of a pad consisting of a soft, elastic polyurethane foam (foam plastic sponge) into mice leads to the appearance, after about 2 months, of endophytic foci of epithelial proliferation and papillomas of the cervix uteri and vagina [2]. It was subsequently found that the further progression of the pathological changes (either after systematic intravaginal insertion or with the use of a permanent polyurethane pad) extends not to papillomas, but to endophytical outgrowths of epithelium. The new epithelial structures arising in this manner correspond in their morphological properties and their relatively stable character to one of the commonest precancers occurring in the female reproductive organs: pseudoerosion of the cervix uteri [4].

In this connection it is of considerable interest to study the conditions under which the use of a plastic sponge as an intravaginal pad, and also as a container for intravaginal administration of various medicaments would be harmful. It is therefore particularly important to study and compare experimentally the action of sponges made from different plastics on the mucous membrane of the cervix uteri and vagina. An experimental investigation of this type is particularly necessary also because attempts are already being made to use sponges for intravaginal and intrauterine administration of substances in medical practice and to prevent conception [8].

The object of this investigation was to study and compare the effect of prolonged systematic intravaginal insertions of a sponge made from butadiene-carboxylate latex (an artificial rubber polymer), used for various purposes in surgery, and from polyurethane on the mucous membrane of the vagina and cervix uteri in mice.

EXPERIMENTAL METHOD

Experiments were carried out on virgin female mice of line CC57W. The initial age of the animals was 1.5-2 months. The technique of introduction of the rubber and polyurethane foam sponge (systematic insertion twice each week; a piece of sponge weighing about 1 mg was inserted each time), the methods of obtaining and fixing the pathological material and of cutting and staining the histological sections were identical with those used in a previous investigation with polyurethane foam [2]. In the present investigation only cases under observation for long periods (one year or more) and studied histologically were considered.

EXPERIMENTAL RESULTS

The experiments lasted about 10-20 months (Table 1). The initial changes (slight disturbances of maturation of the epithelium lining the cervix uteri and vagina, the appearance of small simple endophytic outgrowths of this layer [1-3]) were the same in both groups (groups 1 and 2). Precancer was found in most

Laboratory of Carcinogenic Agents, Research Institute of Oncology, Ministry of Health of the USSR, Leningrad (Presented by Academician of the AMN SSSR L. M. Shabad). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 67, No. 4, pp. 91-95, April, 1969. Original article submitted January 11, 1968.

TABLE 1. Pathohistological Changes in Epithelium of Cervix Uteri and Vagina of Mice During Prolonged Systematic Insertion of Polyurethane and Rubber Sponge

Sponge	Group	Duration of experiment (in days)	Number of animals	Pathohistological changes			
				initial	precancerous		
					total	with signs of pseudoerosion	with signs of pseudoerosion and possible malignant change (microcancer)
Polyurethane	1st	322-596	23	–	23	19	–
Rubber	2st	314-617	18	1	17	8	3
Total	nd		41	1	40	27	3

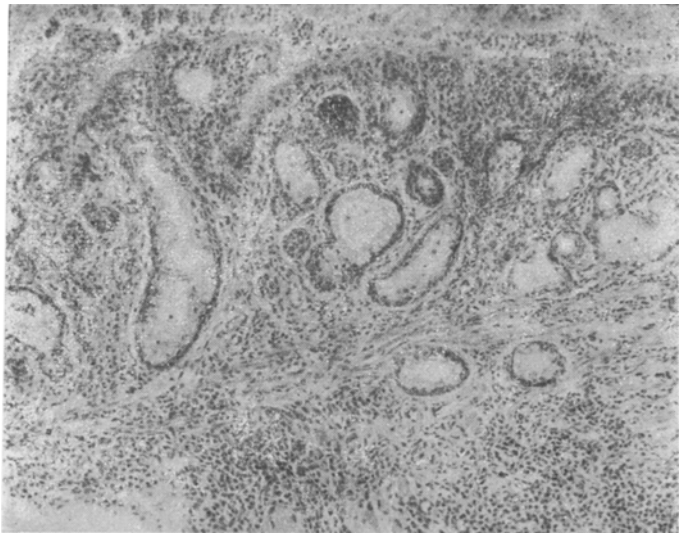

Fig. 1. Area of vagina after systematic prolonged (419th-day of experiment) intravaginal insertion of butadiene-carboxylate latex sponge. Marked invasive growth of epithelium. Gradual "redifferentiation" of epithelium invading subjacent connective tissue and muscle, accompanied by the formation of gland-like structures. Irregular leukocytic infiltration of connective tissue. Hematoxylin-eosin, 80 ×.

animals of both groups– in 40 of 41 cases. The commonest form of precancer consisted of pathological changes corresponding to those previously studied and described [2-5]. They include epithelial outgrowths, branching and anastomosing with each other, invading the underlying connective tissue to various depths, and papillomas as usually observed in animals from 1 to 1.5 months after the beginning of systematic intravaginal administration of a 0.05-0.1% suspension of the powerful carcinogen 9,10-dimethyl-1,2-benzanthracene in ethylene glycol or approximately 2 months after the beginning of experiments with intravaginal administration of polyurethane [2, 3]. In most cases discussed in this paper, however, distinctive signs of further progress of these pathological changes also were observed–phenomena similar

Fig. 2. Area of vagina after systematic prolonged (360th day of experiment) intravaginal insertion of butadiene-carboxylate latex sponge. Gland-like epithelial structures infiltrating vaginal wall of mouse. Slight irregular leukocytic infiltration of connective tissue. Hematoxylin-eosin, 80 ×.

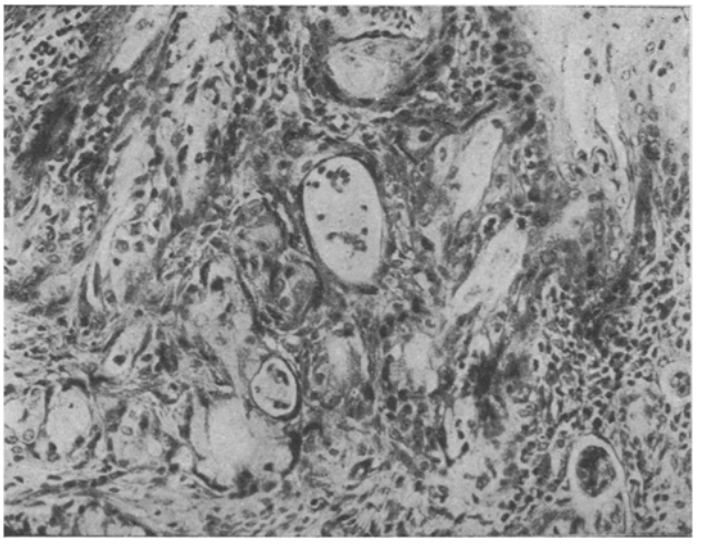

Fig. 3. Part of Fig. 2 under high power. Large, pale epithelial cells in epithelial complexes infiltrating connective tissue (on staining with mucicarmine, mucus is detected in the cytoplasm of these large pale cells). Signs of atypical growth in some epithelial complexes. Small clusters of leukocytes here and there in the connective tissue. Hematoxylin-eosin, 170 ×.

to the condition known as pseudoerosion of the cervix uteri in women. In group 1, for instance, this phenomenon was observed (Table 1) in 19 of 23 cases, and in group 2 in 11 of 18 cases, and in three of these cases signs indicative of possible malignant change (microcancer) were found. In the experiments with polyurethane foam, as also in those with foam rubber, progression of the pathological changes extended only to endophytic foci of epithelial proliferation (evidently no further growth of the papillomas takes place after 2-3 months of the experiment [2]). As a rule, during invasion of islets of epithelium into the subjacent tissues the differentiation of their epithelium changes in direction to one of simple prismatic type,

producing mucus. Throughout the endophytic epithelial complexes, the pattern always remains characteristic of epithelium of the part of the genital tract located distally to the mouse uterus (cervicovaginal epithelium [1, 3]) rather than that of uterine epithelium. In sections stained by the Hotchkiss method, mucopolysaccharides were detected in the mucus present in the cytoplasm of the epithelial cells.

The features described above, together with the frequent presence of a central cavity gave the endophytic epithelial complexes a gland-like structure (Figs. 1-3). Growth of the complex evidently took place through proliferation of undifferentiated cells (similar to the basal cells of the epithelium of the cervix uteri and vagina in mice [1]) located at its periphery (giving the epithelium the appearance of two layers of prismatic cells). In certain cases the nucleus of these cells was dark and apparently elongated in the horizontal direction, so that they resembled the "reserve cells" of the cervical epithelium in women.

In the experiments described above gradual progression of the precancerous changes ultimately concluded with the formation of epithelial foci with signs of malignant change in three cases (microcancer).

The mechanisms of the carcinogenic action of plastics have not yet been settled. It has been shown that adsorption can take place from whole discs of endogenous carcinogenic substances [6]. It has recently been found that pieces of polyurethane and polysilicone in the peritoneal cavity of rats are gradually absorbed, and that phagocytes participate in the transportation of polymers in the body [9, 10]. In the pathogenesis of the epithelial proliferation which was observed, the importance of the mechanical factor associated with irritation of the mucous membrane cannot be ruled out [4, 5, 7].

Under experimental conditions, therefore, prolonged systematic intravaginal insertion of foam rubber and foam polyurethane led to the development and gradual progression of precancerous changes in the cervix uteri and vagina.

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