HISTOPHATHOLOGICAL AND HISTOCHEMICAL CHANGES IN THE CERVIX UTERI UNDER CONTRACEPTIVE PILLS

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Summary

Histopathological and histochemical changes in the cervix in women using the combined contraceptive pills and in adult female rabbits using the combined and mini-pills were investigated. Cytological examination of both vaginal and cervical smears was performed. Glandular hyperplasia was most prominent finding in women using the pills as well as in rabbits. Cytological examination of the smears showed a mid-zonal shift in most of the smears. The PAS reaction and Alcian blue stain were increased in pill users. The alkaline phosphatqse enzyme was increased in the cervical glands in pill users.

INTRODUCTION

Over population is a freat problem in developing countries. The oral methods of contraception contribute effectively with other methods to reduce the birth rate. That cervical changes might occur is not surprising since the cervical epithilium is capable of responding to both estrogen and progesterone components of these drugs(Carmichoel et al 1941, Edmondson et al 1945, Dito et al 1961, Geschickter et al 1962).

Hyperplasia of the cervical glands was reported in pill users (Maqueo et al 1966, Kyriakos et al 1968, Graham et al 1968, Gall et al 1969).

Microglandular hyperplasia was also reported to accompany the use of pills(Soost 1968, Nichols et al 1971).

Most authors agree that there is no causal relationship between cervical carcinogenesis and steroid contraceptives (Diddle et al 1966, Brehm et al 1966, Rock 1966, Laurie et al 1971). On the contrary some investigators confirmed such a relation(Melamed et al 1969, Talbert et al 1969, Stern et al 1970).

The aim of this work is to study the histopathological and histochemical changes in the cervical epithelium under the effect of oral contraceptive pills.

MATERIAL AND METHODS.

One hundred patients using different types of combined contracptive pills (Ovral, Anovarl , Primovlar) together with fifty patients under ovral the same conditions and not receiving any sort of contraceptive medication and serving as control were included in the study.

Biopsy specimens were taken from every patient by Schauberts cervical biopsy forceps and biopsy curette. They were taken from the circumference of the external os at the squamp-columnar junction. They were fixed in 95% alcohol, blocked, sectioned and stained by :

1. Ordinary Haematoxylin and Easin stain.
2. PAS stain (Mc Manus,1946, modified by psarse,1959).
3. Alcian blue stain(Steedman,1950,Lison,1954).
4. The calcium phosphate method for alkaline phosphatase(Gomori,

1952, Lillie,1954).

5. The Feulgen reaction for DNA(Feulgen and Rossenbeck,1941).

Cervical smears were taken from the squamo-columnar junction and vaginal smears from the posterior fornix of the vagina, fixed in equal parts of 95% ethyl alchol and ether and stained according to the standard papanicolaou technique(Papanicolaou,1954.)

The experimental work consisted of 30 female rabbits of the Buscat type. They were divided into three groups. Group I received the combined pills Lyndiol 1. The drug was administered for five days every week.

Group II were given the mini-pills (ethynodiol diacetate 0.25 mg.) every day without interruption while group III served as control. The drugs were administered in a dose equal to the human dose/Kgm. body weight (Paget et al,1964). After one year the animals were killed their cervices were subjected to same histopathological and histochemical examination as the human samples.

RESULTS AND DISCUSSION.

Histopathological examination of the ectocervical epithelium revealed increased vascularity and its penetration by perpendicular vascular channels reaching two thirds of its thickness in 65% of the cases (fig 2) when compared to controls (fig. 1) Basal cell hyperplasia was found increased in 38% of the patients.

A remarkable finding was the presence of vesicles(fig.3) between the layers of squamous epithelium which were observed in 26% of females receiving the pills as compared to 3% in the control group. This coincides with the results reported by Gall et al(1969).

In the present work a single case with mild dyplasia of the squamous epithelium was detected(fig.4). The patient was not a high multipara and showed no evidence of cervical infection and the contraceptive was considered a possible aetiologic factor.

The vascularity of the endocervical stroma was found incresed in 83% of the pill users as compared to 30% in the contro group. This might explain the frequency of contact bleeding in pill users.

Endocervical glandular hyperplasia was the most prominent finding in the patients receiving the pills(fig.5). It was found in 79% of the cases as compared to 22% of the control group. The same results were reported by Maqueo et al (1968). Microglandular hyperplasia (fig.6) occurred more frequently in the pill users (13%) while none of the patients of the control group showed such a change.

The results of the experimental work nearly go hand in hand with those of the human part. The vascularity was increased in 80% of the animals of the first group as compared to 20% in the control group while the group of animals receiving mini-pills

showed no such change . Glandular hyperplasia as in the human patients constituted the most prominent change encountered in the first group of animals receiving the combined pills. It was found in 70% of these animals as compared to00% in the animals of the control group and it was found in 40% of the animals receiving mini-pills.

Histochemical examination showed that the PAS reactio was increased in the endocervical glands in pill users (Fig.7) as compared with the control(Fig.8) group . The reaction was unchanged of diastase digestion due to absence of glycogen.

The Alcian blue reaction was also increased in the females receiving the pills.

It seems therefore that the acid mucopolysacchaides are the ones mostly affected with the use of the contraceptive steroids. These results agree with that of Kellett et al (1969).

In the animal experiments we did not encounter any difference in the PAS reaction Alcian blue stain between those animals receiving the combined and mini-pills and the control group. This may be explained by the fact that the dose of the hormones used a contraceptive is not sufficient to increase the polysaccharide content of the cells and the cervical secretion. A similar opinion was expressed by Hafex (1970).

The concentration of alkaline phosphatase enzyme was increased in the endocervical glands of the females receiving the pills as compared to the control group(Fig.9,10) This may reflect the increase activity and secretion of the cells. The enzyme was unchanged in the

in the ectocervied epithelium of both pill users and control group. No difference was found between the animals receiving pills and the control group.

The intensity of the Feulgen reaction was the same in the pill users and the control group. Also there was no change in the reaction in the three groups of animals included in the study. Knowing that the basic biochemical lesion in a malignant cell is increased in the amount of DNA (Boyd,1961) and Knowing that the Feulgen reaction is specific for DNA (pearse,1960) so it is reasonable to conclude that the amount of DNA in the cells is not increased with the use of the pills and that there is no tendency to malignancy or dysplasia in pill users.

The group of patients the pills showed a shift of the maturation index to the mid-zone. This agrees with the results of Liu al (1967) and Batzelen et al. (1968).

Clumping and folding of the cells occurred more frequently in the pill users which is believed to reflect the relative progestingeffect (Reyniak et al , 1969).

There was no difference in the incidence of monilial infection in the pill users and the control group white trichomonas infection was not found in both groups of study.

In this work no case with dysplasia or other features malignancy was detected in the smears.

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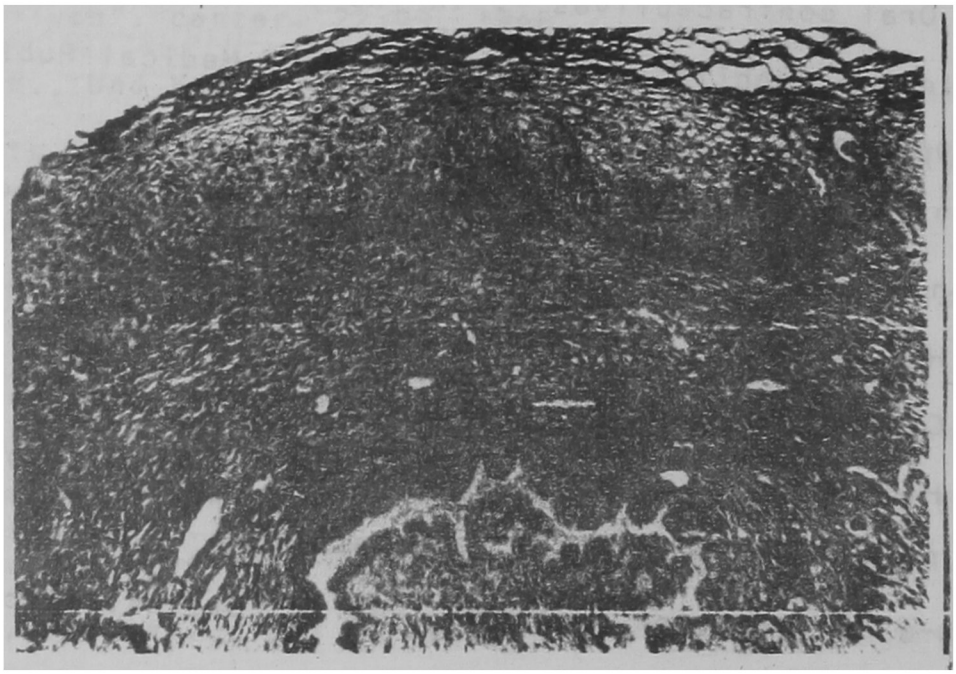

Fig. 1. Normal cervix of a control patient

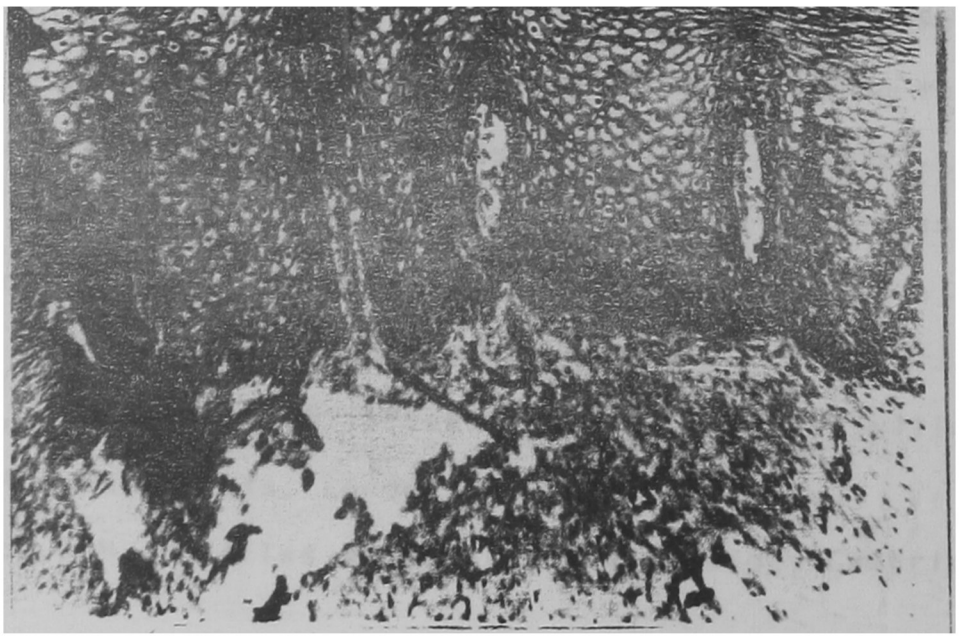

Fig. 2. Increased vascularity of the ectocervical epithelium

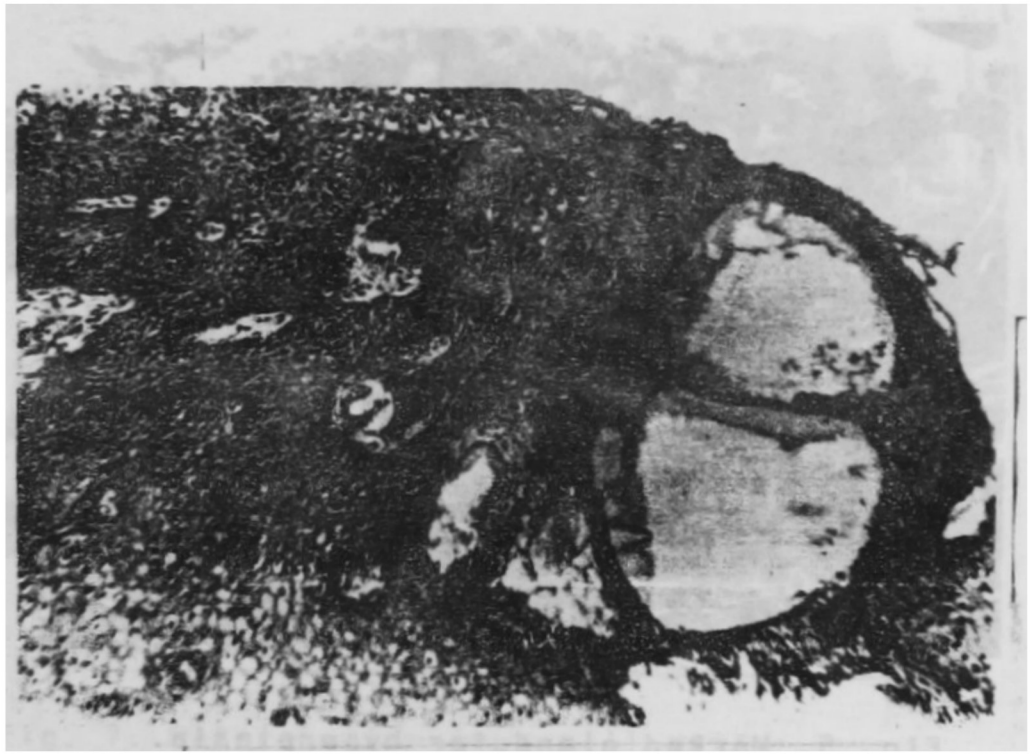

Fig.3. Two large vesicles are seen between the layers of squamous epithelium.

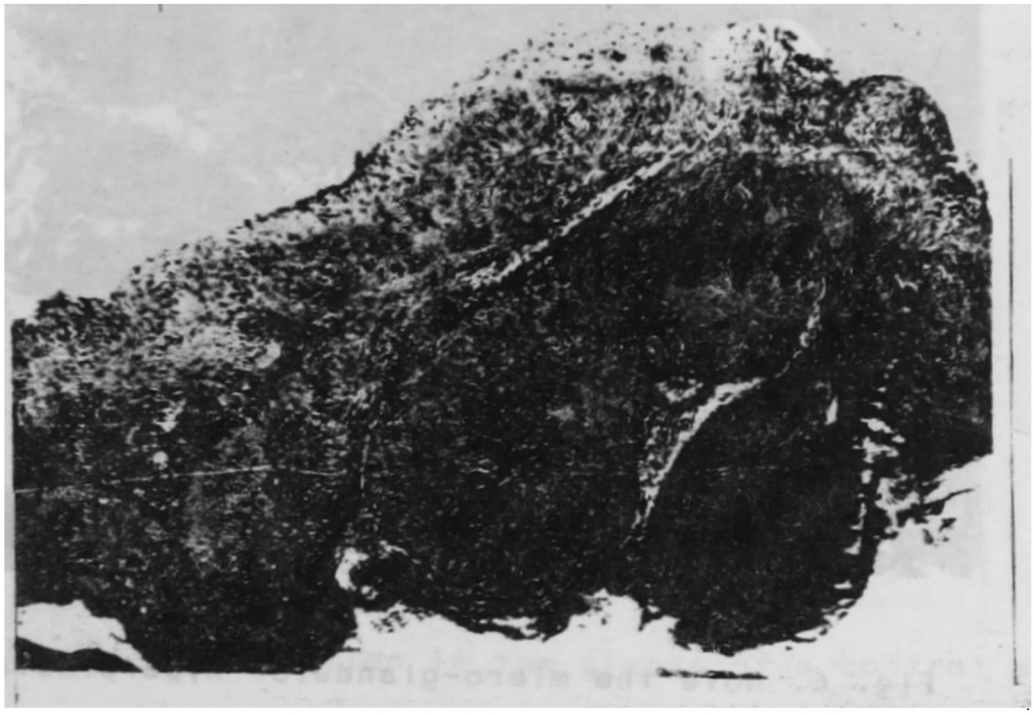

Fig. 4. Dysplasia of the ectocervical epithelium.

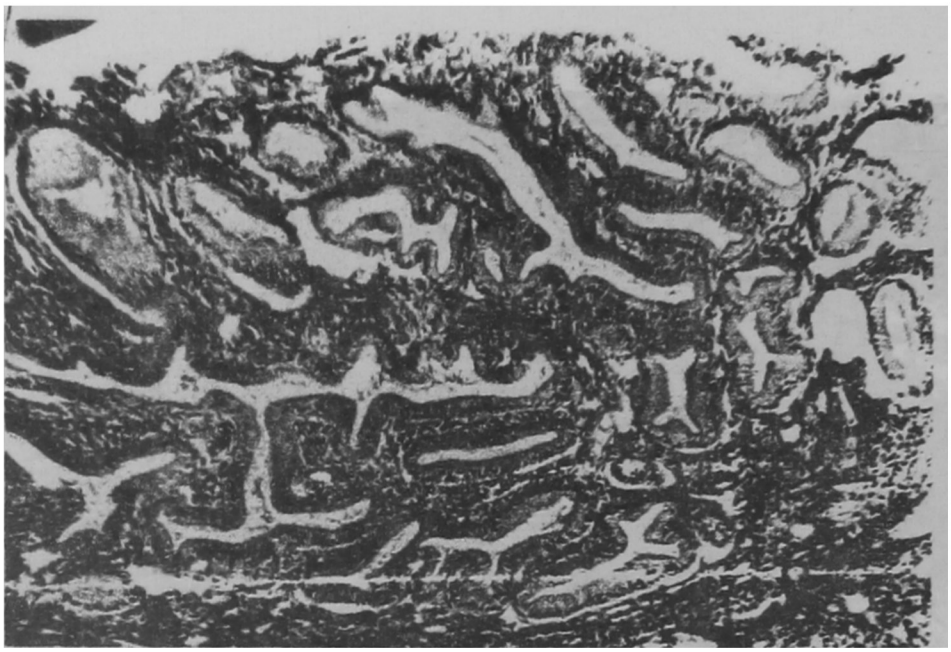

Fig. 5. Marked glandular hyperplasia.

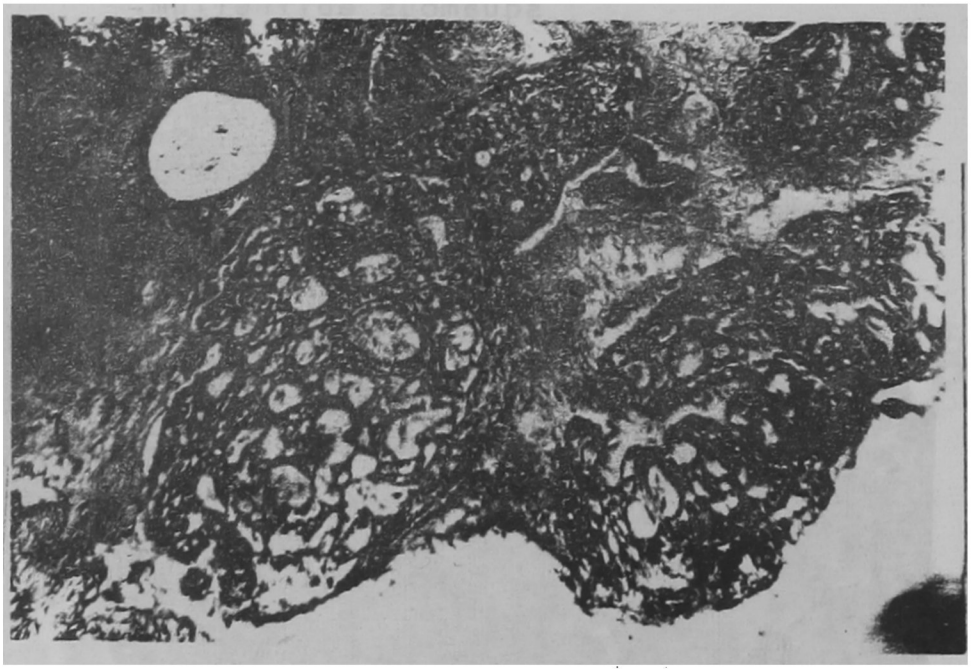

Fig. 6. Note the miero-glandular hyperplasia in a pill-user.

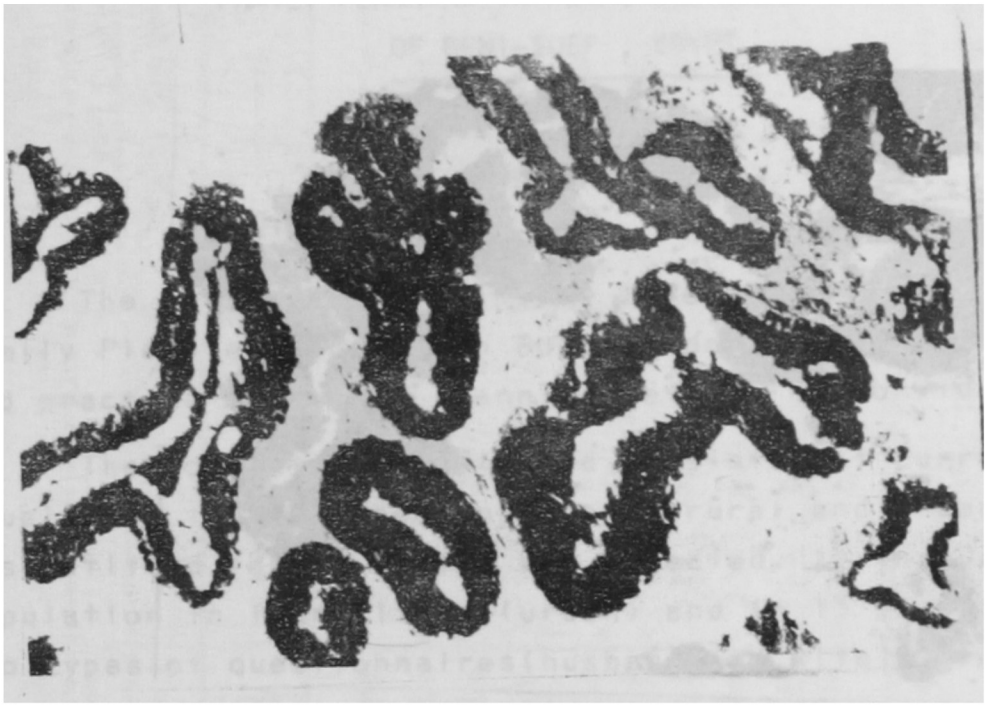

Fig. 7. PAS reaction in a pill user.

Fig. 8. PAD reaction in the glands of a control patient.

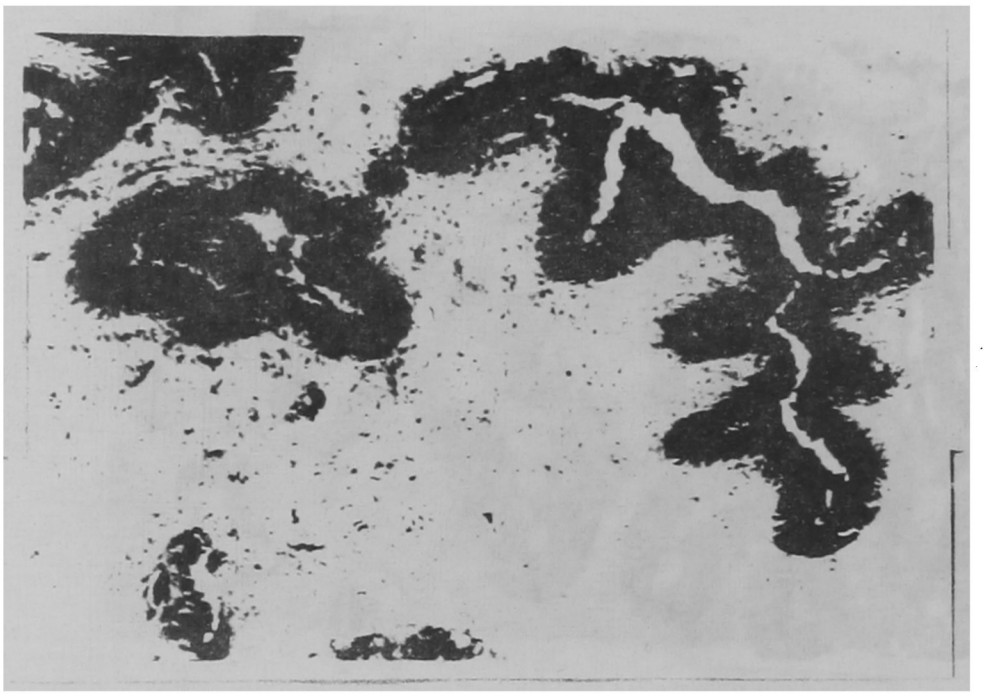

Fig. 9. Alkaline phosphatase reaction in the glands of a pill user.

Fig. 10 Alkaline phosphatase reaction the glands of a control patient.