

# ENDOMETRIAL HISTOLOGY WITH ORAL CONTRACEPTIVES

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Oral 'pills' have definitely made a revolutionary impact as one of the methods of contraception. After long and exhausting trials their efficacy is now well established. Efforts have been directed to study the endometrial changes as to have an insight into the complex target organ response to these hormonal preparations. Most of the oral pills used today are similar in their composition and endometrium reacts to them in the same way.

Present study was undertaken with the view to evaluate the changes produced by combination type contraceptive pills and an attempt has been made to correlate the changes produced with the duration of use of the pills.

## Material and Methods

Forty-one women taking combination type contraceptive pills for fertility control were studied from the family planning clinic of Swarup Rani Nehru Hospital, Allahabad. Twenty women of proved fertility were taken as control.

Detailed clinical history was taken and systemic examination and gynaecological

examination were carried out to know the suitability of the cases. Oral contraceptives used during the present series were—

1. Primovlar E.D. (0.5 mgm norgestrel + 0.05 mgm ethenyl—estradiol).
2. Ovral—28 (0.5 mgm norgestrel + 0.05 mgm ethinyl—estradiol).

The cases taking oral contraceptives were between 19-39 years of age with parity 1-6. Duration of use of pills ranged from 1 month to 48 months.

Endometrial tissue obtained was fixed in buffered neutral formalin, processed and stained by H & E., for histological study. Lillies (1966) modification of Bielschowsky Maresch (1954) silver impregnation technique was used to demonstrate the reticulin fibres of stroma in 13 cases.

## Results

Since the endometrial changes produced by Primovlar E.D. (39 cases) and Ovral-28 (2 cases) were identical they are taken up collectively.

## Endometrial Changes

### Surface Epithelium

Surface epithelium was either low columnar or flat (Fig. 1).

Irregularity of the surface epithelium was a constant feature which showed even deep excrescences or polypoidal appear-

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ances (Fig. 2, 3). The irregularity was more marked with the increase of duration of use of pill.

Multilayer surface epithelium giving an impression of squamous metaplasia was observed in 22 per cent of cases but the cells did not have true squamoid character (Fig. 2, 3).

#### Glands

Endometrial glands showed great variation from specimen to specimen. In general the number and size of the glands was decreased depending upon the duration of use. As the duration of use of pills increased the glandular atrophy was more marked (Fig. 4). Few endometria showed even moderately dilated glands in between atrophic glands (Figs. 5, 6).

Glandular epithelial cells did not show characteristic cyclical changes. Persistently deficient secretory phase was observed and the glands were uncoiled. In some of the specimen glands showed thin, scanty secretions (Figs. 5, 6).

#### Stroma

The stroma was characterised by spotty edema but the degree of edema was variable (Figs. 1, 2, 3, 4). Decidual reaction was present in two specimen of day 20 and day 26 (Fig. 6).

Blood vessels were slightly dilated and prominent. Marked dilatation of some of the veins was seen in few endometria (Fig. 2). With the increased duration of use of these pills the prominence and dilatation of the blood vessels was not observed.

Endometrial granulocytes which are characterised by their bizarre nuclei and cytoplasm containing phloxinophilic granules were present in only two endometria. Lymphocytic infiltration was common.

There was variable development of

reticulin net work. At places reticulin fibres were dense and at places sparse (Figs. 2, 3).

There was disharmony of glandular and stromal development and exact dating was not possible. The ratio of gland to stroma was shifted in favour of stroma, and it was more marked with increasing duration of use.

#### Discussion

In accordance with our findings Seigel and Heimen (1965) observed that the endometrium becomes uneven, eventually growing rough through knobby outgrowths and polypoidal excrescences. Twenty-two per cent of the endometria studied in our series showed multilayers at places with plump oval nuclei. This gave an impression of squamoid metaplasia but the cells did not have squamoid character.

Great variation in the glandular development depending upon the duration of use, was also observed by Dallenbach (1971). Charl's (1964) and Sheffield *et al.*, (1969) stated that there is atrophic endometrium and after prolonged use of the drug the glands may even disappear. In our series only one endometrium showed marked atrophy.

Dallenbach (1971) also described premature appearance of persistently deficient secretory changes in the glands with the result they remain uncoiled. Subnuclear vacuolation was seen on day 7—day 8 of the cycle and the secretions were maximum by day 13 or day 15, after which the glands regressed to resting functional state.

Hyperplastic changes of endometrial glands after prolonged use as described by Dodek and Kotz (1967) were not seen in our series. Probably the dose of estrogen in the compound used was too small to provoke hyperplastic changes.

Characteristic spotty edema and relative increase in stroma has been observed by various workers. Waidle (1968) found variable degree of development of reticulin net work as observed in our series.

Taymor (1961) described premature development of decidual reaction from 15th to 20th day depending upon doses of progestin. We observed decidual reaction in only two endometria of day 20 and day 26 probably the dose of progestin component in the pill used was small.

Intense dilatation of stromal vessels have been also reported by Ober *et al* (1964), Crowson *et al* (1965) and Ober (1966). No account with the increasing duration of use of pill is available. In the present study we did not find dilatation and prominence of blood vessels after 48 months of use.

**Summary**

With combination type of contraceptive pills the proliferative phase was cha-

racteristically shortened with incomplete development of glands and advanced stroma. The glands and stroma developed a state of maturity which failed to depict the true day of the cycle, stroma being more advanced than the glands.

There was an early arrest of both growth and differentiation of glandular epithelium at its incompletely developed stage and this was further hampered with the increased duration of use of these pills.

Lag in the development of endometrial glands to that of stroma and the inadequate, early abortive secretory activity results in an endometrium which is not receptive to the fertilized ovum.

**References**

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See Figs. on Art Paper IV-V