

# HISTOPATHOLOGICAL STUDY OF ENDOMETRIUM IN INFERTILE WOMEN

by

NAJMA ABBASI,\* M.B.B.S.,  
S. P. TYAGI,\*\* M.D. (Path.),  
KUSUM SAXENA,\*\*\* M.S.

and

S. HAMEED,\*\*\*\* M.D., D. Path. (London)

Endometrial biopsy is still considered the most important investigation in cases of infertility as it provides an opportunity to examine the target tissue for oestrogen and progesterone hormones. Besides evaluating the occurrence of ovulation it also furnishes with information of some other pathological lesions which may lead to infertility (Ganguly *et al*, 1972). Recently workers from different parts of our country (Chakravarty, 1972; Mehta, 1972; Jhaveri *et al*, 1972; Shah *et al*, 1972; Panda and Dey, 1972; Saxena and Pathak, 1972) have presented their findings about the endometrial reaction in infertile women during the Sixteenth All India Obstetrics and Gynaecological Congress. However, there was paucity of reports from Uttar Pradesh. The authors took this opportunity to present their observations regarding the study of endometrium in infertile women attending the Department of Obstetrics and Gynaecology,

Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh.

## Material and Method

The present study consisted of 500 cases of infertility in whom the male partners had normal semenogram. Endometrial biopsy was done in the premenstrual period except in seven cases in whom the biopsy was done on the 1st day of the menses. The tissue was preserved in 10% formal saline for 24 hours and the sections were cut at 4 to 5  $\mu$  thickness. Besides routine Haematoxylin and Eosin staining, Periodic Acid Schiff's (P.A.S.) and Ziehl-Neelsen Carbol Fuchsin stainings were done for demonstration of glycogen and acid fast bacilli in the histological sections.

## Observations

Out of 500 cases there were 447 (89.4%) females with primary infertility and 53 (10.6%) with secondary infertility (having only one issue). The age of the cases varied from 16 to 42 years. Maximum number (190, 38.0%) belonged to the age group of 21-25 years. Sixty-four cases (12.8%) were above 30 years of age.

The duration of infertility varied from 2 to 20 years. Forty-eight cases (9.6%)

\*Demonstrator in Pathology.

\*\*Reader in Pathology.

\*\*\*Reader in Obstetrics & Gynaecology.

\*\*\*\*Professor and Head of the Department of Pathology.

From the Departments of Pathology and Obstetrics & Gynaecology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh.

Accepted for publication on 9-1-76.

presented with infertility of a period of more than 11 years. An enquiry of menstrual history revealed regular menses in 394 cases (78.8%) and 98 women (19.6%) were having irregular cycles. There were 3 cases of primary amenorrhoea. The average age of the patients at menarche was 14.37 years.

#### Histopathological Findings

Endometrial biopsy tissue was obtained in 452 cases (90.4%), whereas in the rest 48 (9.6%) the material contained mucinous substance, blood clots or endocervical tissue only. Such cases were excluded from the series for the interpretation of morphological changes in infertility. The endometrial reactions as observed in 452 cases have been summarised in Table I.

#### Proliferative Phase

The proliferative endometrium was observed in 100 cases (22.13%). Out of these, atrophic proliferative endometrium was seen in 3 cases (3.0%), early proliferative endometrium in 4 (4.0%), mid-proliferative in 41 (41.0%) and late proliferative type in 52 (52.0%). In some cases secretions in the glands in the form of subnuclear vacuoles had been observed but these were small, irregular and haphazardly arranged (Fig. 1) in contrast to the regularly arranged subnuclear vacuoles of the early secretory type. Subepithelial collagen deposit in the form of clear homogenous band was seen in 7 cases (7.0%) of proliferative type endometrium.

#### Secretory Phase Endometrium

This was observed in 301 cases

TABLE I  
Type of Endometrium as Seen in 452 Cases

Type of Endometrium	Infertility					
	Primary		Secondary		Total	
	No.	Percentage	No.	Percentage	No.	Percentage
Proliferative	91	22.52	9	18.75	100	22.13
Late secretory	241	66.08	31	70.84	272	66.59
Early secretory	26		3		29	
Irregular ripening	17	4.21	4	8.33	21	4.65
Tuberculous endometritis	17	4.21	1	2.08	18	3.98
Proliferative with cystic dilatation of glands	8	1.98	—	—	8	1.77
Proliferative with adenomatous hyperplasia	2	0.50	—	—	2	0.44
Proliferative with adenomyosis	1	0.25	—	—	1	0.22
Proliferative with squamous metaplasia	1	0.25	—	—	1	0.22
Total	404	100.00	48	100.00	452	100.00
Endometrial tissue not obtained	43	9.42	5	9.43	48	9.60
Total Cases of Infertility	447	89.40	53	10.60	500	100.00

(66.59%). The dating of the endometrium in these cases was done according to Noyes, Hertig and Rock (1950). Early secretory endometrium characterised by subnuclear vacuoles and regularly arranged row of nuclei with homogenous cytoplasm above them was seen in 29 cases (9.63%). In the premenstrual phase much emphasis was given to the morphological changes observed in the stroma as compared to the glandular pattern.

While comparing the morphological picture with last menstrual period (LMP) it was observed that in 183 cases (60.89%) out of 301 dating of the endometrium coincided with LMP. Endometrium was found to be lagging by 3 days in 34 cases (11.21%), 4 days in 20 (6.65%), 5 days in 14 (4.65%), 6 days in 19 (6.31%) and 7 or more than 7 days in 17 (5.65%). On the other hand the endometrial morphological picture was enhanced as compared to LMP by 3 days in 3 (0.99%), 4 days in 4 (1.33%), 5 days in 2 (0.66%) and 7 or more than 7 days in 5 (1.66%).

#### *Irregular Ripening*

This type of endometrium was seen in 21 cases (4.65%), 17 cases (4.21%) in primary infertility group and 4 (8.33%) in secondary infertility group. Histologically in all the cases evidence of ovulation was there as evident by the presence of secretory endometrium, however, unripe proliferative endometrium persisted in some areas intermingled with secretory reaction (Fig. 2).

#### *Tuberculous Endometritis*

In the present study there were 18 cases of tuberculous endometritis out of 452 cases of infertility—incidence being 3.98% (4.21% in cases of primary infertility and 2.08% in secondary infertility group). The age of these patients varied from 18 to 35

years, average being 23.7 years. Hindus and Muslims were equal in proportion.

Tuberculous lesions were characterised by the presence of well formed circumscribed granulomas in 15 cases (83.33%), localised and diffuse tuberculous infiltrate in 2 (11.11%) and diffuse granulomatous exudate in 1 (5.56%). The lesions were mostly confined to the superficial portion of the endometrium. The granulomas were of caseating type in 9 cases (50.0%), non-caseating in 6 (33.33%) and of both types in 3 (16.67%). Endometrial glands were replaced to a great extent by the tuberculous granulation tissue in 12 cases (66.67%), while a normal proportion between glands and stroma was seen in 6 (33.33%). Endometrial reaction was proliferative in 12 cases (66.67%), proliferative with cystic dilatation in (15.56%) and secretory in 5 (27.76%). Acid fast staining was done in all cases but *Mycobacterium tuberculosis* could not be demonstrated in any of the sections.

#### *Abnormal Endometrium*

This group included cystic endometrial hyperplasia, adenomatous hyperplasia, adenomyosis and squamous metaplasia seen in 8 cases (1.77%), 2 cases (0.44%), 1 case (0.22%) and 1 case (0.22%) respectively.

#### *Endometrial Reaction in Relation to Duration of Infertility*

An attempt was made to correlate the endometrial reaction with duration of infertility. The results have been expressed in Table II. On perusal hardly any difference in the morphological picture with duration of infertility was observed.

#### *Endometrial Reaction in Relation to Menstrual Cycle*

The results have been summarised in Table III. It was observed that the abnor-

TABLE II  
Endometrial Reaction in Relation to Duration of Infertility

Duration of fertility (Years)	Total cases	Proliferative phase	Secretory phase	Irregular ripening	Tuberculous endometritis	Cystic hyperplasia	Adenomatous hyperplasia	Squamous metaplasia	Adenomyosis	Tissue insufficient
2-3	129	24 (18.60)	80 (62.02)	2 (1.55)	5 (3.88)	2 (1.55)	—	—	—	16 (12.40)
4-5	125	28 (22.40)	70 (56.00)	8 (6.4)	5 (4.00)	4 (3.20)	1 (0.80)	1 (0.80)	—	8 (6.40)
6-8	121	23 (19.00)	77 (63.64)	5 (4.09)	4 (3.30)	—	—	—	1 (0.82)	11 (9.15)
9-11	77	15 (19.49)	49 (63.64)	3 (3.89)	2 (2.59)	2 (2.59)	1 (1.29)	—	—	5 (6.49)
More than 11	48	10 (20.83)	25 (52.08)	3 (6.25)	2 (4.17)	—	—	—	—	8 (16.67)
Total	500	100	301	21	18	8	2	1	1	48

Figures in parenthesis indicate percentage.

TABLE III  
Endometrial Reaction in Relation to Menstrual Cycle

Menstrual cycle	Total cases	Proliferative phase	Secretory phase	Irregular ripening	Tuberculous endometritis	Cystic hyperplasia	Adenomatous hyperplasia	Squamous metaplasia	Adenomyosis	Tissue insufficient
Primary amenorrhoea	3	1	1	—	—	—	—	—	—	1
Secondary amenorrhoea	5	2	1	—	2	—	—	—	—	—
Regular with normal flow	291	51 (17.54)	208 (71.45)	6 (2.06)	7 (2.41)	—	—	—	—	19 (6.54)
Regular with scanty flow	99	21 (21.21)	60 (60.61)	5 (5.05)	7 (7.07)	1 (1.01)	1 (1.01)	1 (1.01)	—	3 (3.03)
Regular with profuse flow	4	—	—	2	—	2	—	—	—	—
Irregular cycles	98	25 (25.51)	31 (31.63)	8 (8.17)	2 (2.04)	5 (5.10)	1 (1.02)	—	1 (1.02)	25 (25.51)
Total	500	100	301	21	18	8	2	1	1	48

mal type of endometrial reaction was seen more in cases with irregular cycles (7 out of 98 cases) as compared to cases with regular cycles (5 out of 394 cases).

#### Discussion

The endometrial tissue in sufficient amount was not obtained in 9.6% of the cases. Other workers have also reported failure to obtain endometrial tissue in varying percentage of their cases (Ganguly *et al* 1972, 5.0%; Mehta, 1972, 5.14%; Saxena and Pathak, 1972, 10.6%; Shah *et al* 1972, 21%). It was rather difficult to ascertain any particular reason for not obtaining the endometrial tissue in these cases.

Secretory type of endometrium was obtained in 301 cases (66.59%). The incidence of this type of reaction in infertility cases has been found to vary from 41.23% to 93% (Stevenson, 1965; Sillo Seidl, 1967; Panda and Dey, 1972; Saxena and Pathak, 1972; Shah *et al* 1972; Chakravarty, 1972; Mehta, 1972; Jhaveri *et al* 1972; Achari and Patnaik, 1972).

While assessing the glycogen content with the help of P.A.S. staining in 248 cases with secretory type endometrium good amount of secretion was noticed in 138 cases (55.64%), moderate in 80 (32.27%) and poor in 30 (12.09%). Other workers have reported a high incidence of poor secretory activity (Zondek and Stein, 1940; Baveja *et al* 1972; Jhaveri *et al* 1972; 18.4%, 25.1% and 26.8%, respectively). Such glycopenic uterine mucosa may be responsible for improper embedding of the ovum.

Irregular ripening of the endometrium—a finding responsible for infertility and abortions due to impaired endometrial development to receive the fertilized ovum, was seen in 4.65% of the total cases or in 6.52% of cases having ovula-

tory cycle (21 out of 322 cases). Noyes (1956) has also reported irregular ripening in 4 cases out of 100 secretory endometrium (4.0%) though Ganguly *et al* (1972) have observed this reaction in 4 cases out of 420 (0.95%). A mixed histological picture could be seen in early secretory stage where the changes of secretory phase could not develop simultaneously throughout the endometrium or when the fragments of the relatively resistant endometrium from the isthmic region are mixed up during endometrial biopsy.

Evidence of ovulation was seen in 322 cases (71.24%) of infertility (79.17% of secondary infertility cases and 70.29% of primary infertility cases). Similarly, high incidence of ovulatory cycles (56.8%) in secondary infertility cases as compared to that (41.2%) in primary infertility cases has been reported by Ganguly *et al* (1972).

Non-ovulatory cycles are quite common in cases of infertility as have been observed by different workers with variable frequency. Higher incidence as compared to that (22.13%) in the present series has been reported by Mazer *et al* (1937), Ganguly *et al* (1972), Saxena and Pathak (1972), Panda and Dey (1972), Shah *et al* (1972) to the extent of 29.32%, 48.33%, 31.61%, 37.42% and 30.4% respectively. On the contrary, there are reports where the incidence of anovulatory cycles is fairly low in comparison to that in the present series (Rock *et al*, 1939, 9.1%; Sharman, 1944, 6.0%; Felding, 1949, 3.9; Achari and Patnaik, 1972, 7.0%; Jhaveri *et al*, 1972, 13.6% and Mehta, 1972, 15.25%).

Presence of homogenous band of hyaline deposit in the subepithelial zone was observed in 7% cases of anovulatory cycle. Sedlis and Kim (1971) have notic-

ed this change in 34% of samples of anovulatory cycles in primary infertility and 17% of 227 endometrial biopsies. This change has been explained due to the fibroblastic proliferation of the stromal cells and their ability to produce collagen in anovulatory cycle, whereas in the secretory phase the stromal cells are denuded and no sufficient time is left to proliferate.

Tuberculous endometritis was present in 3.98% of the cases. The incidence of the disease in infertility cases has been found to vary from 0.8% (Rewell, 1958) to 10.6% (Botella, 1958). The findings in the present series were in agreement with those of Haines (1958, 4.0%); Francis (1964, 3.0%); Munjal *et al* (1970, 3.6%) and Hafeez *et al* (1973, 3.95%). The incidence of endometrial tuberculosis in primary infertility was high (4.21%) as compared to that in secondary infertility (2.08%)—a finding in accord to that of Rabau and Liquornick (1957) though most of the Indian workers (Malhani and Rajani, 1953; Hafeez and Tandon, 1966; Ganguly *et al*, 1972) have reported higher incidence in secondary infertility.

While relating the endometrial picture with menstrual cycle, tuberculous lesion was found to be present in 7.07% cases with scanty flow as compared to 2.41% cases with regular flow. In cases of irregular cycles the failure to obtain endometrial biopsy was high (25.51%) and also anovulatory cycle was observed in 25.51% cases as compared to 21.21% in cases with regular cycle and scanty flow and 17.54% with regular flow.

Thus, the authors feel that the endometrial biopsy has a great role in cases of infertility as it helps to give the information about the occurrence of ovulation, regular ripening of the endome-

trium and other abnormal endometrial reactions due to hormonal imbalance. This is the only method to label the diagnosis of endometrial tuberculosis in an apparently healthy female.

#### Summary

The endometrial tissue was obtained in 452 cases out of 500 cases of infertility. The various forms of endometrial reaction were observed. The morphological changes in cases of primary infertility and secondary infertility were more or less the same except the incidence of tuberculosis was low (2.08%) in the second group as compared to the first (4.21%) and all the cases of abnormal endometrium belonged to the former group. No difference in the morphological picture with the duration of infertility was observed. The incidence of anovulatory cycle and abnormal endometrium was high in cases with irregular cycle.

#### References

1. Achari, Kamla and Patnaik, Sabita: Proceedings of the XVIth All India Obstetrics & Gynaecological Congress, March 1972, p. 69.
2. Baveja, R., Verma, H. C. and Samant, V.: Proceedings of the XVIth All India Obstetrics & Gynaecological Congress, March 1972, p. 20.
3. Botella, L.: J. Gynec. Prac. 9: 387, 1958.
4. Chakravarty, B. N.: Proceedings of the XVIth All India Obstetrics & Gynaecological Congress, March 1972, p. 194.
5. Felding, S.: Acta Obstet. & Gynec. Scandinav. 28: 78, 1949.
6. Francis, W. J. A.: J. Obst. & Gynec. Brit. Cwlth, 71: 418, 1964.
7. Ganguly, G., Mitra, J. and Chatterjee, J. K.: Proceedings of the XVIth Obstetrics & Gynaecological Congress, March 1972, p. 23.
8. Hafeez, M. A. and Tandon, P. L.: J. Indian Med. Assoc. 46: 610, 1966.
9. Hafeez, M. A., Tandon, P. L. and Munjal, S.: Indian J. Path. & Bact. 16: 54, 1973.

10. Haines, M.: *Lancet*. 1: 436, 1958.
11. Jhaveri, C. L., Shah, R. H., Shah, M. R. and Bhatt, H. K.: Proceedings of the XVIth All India Obstetrics & Gynaecological Congress, March, 1972, p. 255.
12. Malkani, P. K. and Rajani, C. K.: Proceedings Indian Association of Pathologists, IVth Meeting, November 1953.
13. Mazer, C., Israel, L. and Kacher, L.: *Surg. Gynec & Obst.* 65: 30, 1937.
14. Mehta, K.: Proceedings of the XVIth All India Obstetrics & Gynaecological Congress, March 1972, p. 244.
15. Munjal, S., Tandon, P. L. and Hafeez, M. A.: *J. Obst. & Gynec. India.* 20: 106, 1970.
16. Noyes, R. W., Hertig, A. T. and Rock, J.: *Fertil. & Steril.* 1: 3, 1950.
17. Noyes, R. W.: *Obst. & Gynec.* 7: 221, 1956.
18. Panda, S. and Dey, A. K.: Proceedings of the XVIth All India Obstetrics & Gynaecological Congress, March 1972, p. 208.
19. Rabau, E. and Liquornik, I.: *Gynec. Pract.* 7: 20, 1957.
20. Rewell, R. E.: *J. Obst. & Gynec. Brit. Emp.* 65: 28, 1958.
21. Rock, J., Bartlett, M. K., Matson, D. D. and Brookline, A. B.: *Amer. J. Obst. & Gynec.* 37: 3, 1939.
22. Saxena, R. C. and Pathak, R. K.: Proceedings of the XVIth All India Obstetrics & Gynaecological Congress, March 1972, p. 165.
23. Sedlis, A. and Kim, N. G.: *Obst. & Gynec.* 38: 264, 1971.
24. Shah, V. M., Shah, M. V. and Sharma, S.: Proceedings of the XVIth All India Obstetrics & Gynaecological Congress, March 1972, p. 212.
25. Sharman, A.: *J. Obst. & Gynec. Brit. Emp.* 51: 85, 1944.
26. Sillo-Seidl, G.: *Zentralblatt Gynak.* 89: 489, 1967.
27. Stevenson, C. S.: *Amer. J. Obst. & Gynec.* 92: 137, 1965.
28. Zondek, B. and Stein, L.: *Endocrinol.* 27: 395, 1940.

*See Figs. on Art Paper IV*