

CORRELATIVE CLINICAL AND MORPHOLOGICAL FINDINGS IN WOMEN USING IUD

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Introduction

The intrauterine devices act mechanically as a foreign body and produce local tissue alterations of the endometrium. Failure of implantation has been stated to be due to the abrasive effect of the device. The present study has been undertaken to evaluate the local tissue changes with the device and also with its prolonged use.

Material and Methods

One hundred and seventy endometrial specimens were procured from 170 women using Lippes loop. The mode of obtaining the tissue is shown in Table I and the duration of use of the device in Table II. Tissue obtained was fixed in buffered neutral formalin and processed for H & E and tetrachrome staining.

TABLE I
The Mode of Obtaining the Specimens

Sl. No.	Mode of obtaining	Number
1.	Biopsy or curettage	156
2.	Curettage with prolapse repair	7
3.	Hysterectomy specimens	7
		170

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TABLE II
The Duration of Use of IUCD

Group	Duration of use of IUCD	Number of cases
1.	less than 12 m.	36
2.	13-24 m.	37
3.	25-36 m.	46
4.	37-48 m.	33
5.	49-60 m.	15
6.	more than 61 m.	3
Total		170

Observations

The cases collected were between the age of 18-45 years with parity between 9 to 11. The menstrual cycles were normal in 61.2%. In rest of the cases there was either menorrhagia, polymenorrhagia, metrorrhagia or continuous bleeding (Table III). Lactational amenorrhoea was in 1.2%.

Histology

General Considerations

The histological status of the endometrium was assessed using the criteria of Noyes *et al.*, (1950). The endometrial pattern observed in relation to the day of biopsy and the type of menstrual cycle is given in Table IV.

TABLE III
Showing the Pattern of Menstrual Cycles in Cases of IUCD

Duration of use in months	Number of cases	Normal		Menorrhagia		Polymenorrhagia		Metrorrhagia		Continuous bleeding		Lact amenorrhea	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Less than 12	36	25	69.4	6	16.7	4	11.1			1	2.8		
13-24	37	19	51.3	5	13.5	11	29.7	1	2.7			1	2.7
25-36	46	26	56.5	7	15.2	11	23.9	2	4.3				
3-4 37-48	33	24	72.7	4	12.1	3	9			1	3	1	3
4-5 49-60	15	10	66.6	3	20	2	13.3						
More than 61 m	3			1	33.3	2	66.6						
	170	104	61.2	26	15.3	33	19.4	3	1.7	2	1.2	2	1.2

TABLE IV
Shows the Type of the Menstrual Cycles the Day of Biopsy and Endometrial Histology Obtained in 166 cases

Menstrual Pattern	Total No. of cases	Biopsy During cycle		Phases of the Cycle		Cystic hyperplasia	Dysharmolny
		1st half	2nd half	Proliferative	Secretory		
Normal cycle	104	39	65	46	55	1	2
Menorrhagia	26	16	10	14	9	2	1
Polymenorrhagia	33	18	15	23	8		2
Metrorrhagia	3	1	2	2	1		
Continuous Bleeding	2			1	1		
Lact. amenorrhea	2				1	1	
Total	170	74 (43.5%)	92 (54.1%)	86 (50.6%)	75 (44.1%)	4 (2.4%)	5 (2.9%)

The endometria corresponded to the was the endometrial pattern to the day day of biopsy in 59.8. Longer the dura- of obtaining the biopsy (Table V). Mor- tion of use of the device the more near phological development of the endome-

TABLE V
Shows the Histological Development of the Endometria in Relation to Day of Biopsy

Duration of use in months	Number of cases	Dating corresponded today of biopsy		Advanced by more than two days		Retarded by more than 2 days		Cystic hyperplasia		Dysharmomy	
		No.	%	No.	%	No.	%	No.	%	No.	%
Less than 12 m.	36	19	52.8	6	16.7	10	27.8	1	2.7	-	-
13-24	37	23	62.1	4	10.8	6	16.2	2	5.4	2	5.4
25-36	46	27	60.8	7	15.2	10	23.9	1	2.2	1	2.2
37-48	33	20	60.6	10	30.3	3	9.1	-	-	-	-
49-60	15	11	73.3	1	7.1	3	21.4	-	-	-	-
More than 61 m.	3					1	33.2	-	-	2	66.6
	170	100	58.19	28	16.5	33	19.4	4	2.4	5 (2.9%)	

trium was advanced in 16.5% and retarded in 19.4%.

Cystic Hyperplasia (Fig. 1) was in 2.4% and dysharmony of glandular and stromal development was in 2.9%. All this resulted in an endometrium which was histologically altered in 41.1%, irrespective of the duration of use of the device.

Surface epithelium

Under one month of use of the device the surface epithelium was denuded (Fig. 2) at most of the places and instead a layer of red blood cells with few lymphocytes and polymorphs were seen. Over 12 months of use the surface epithelium was intact except at places of contact of the device. The cells showed normal cyclical variation. Basal and perinuclear vacuolation was numerous during the secretory phase. Cells with rod-shaped nuclei were also common. After 24 months of use localized heaping (Fig. 3) of epithelial cells was present.

Glands

The changes in the glands corresponded well to the classical alterations observed according to the histological phase of the cycle (Table 6). Lumen of the glands in some had both polymorphs and lymphocytes (Figs. 4 and 5).

Stroma

Besides the usual histological changes in the stroma according to the phase of the cycle, the use of IUD produced following alterations, irrespective of the dating of the endometrium.

- 1- Marked lymphocytic infiltration. Polymorphs were less, and plasma cells were rare (Figs. 6, 7, 8).
2. Interstitial edema.
3. Increased vascularity.

These changes were consistently present in almost all the slides. The distribution, frequency and degree of edema (Fig. 9) and also number of inflammatory cells present varied with each specimen. The incidence changed with the duration of the device (Table VII).

Presence of lymphocytes and polymorphs was more during the first year of use. Subsequently with increasing duration it diminished. Interstitial edema was more frequently present in specimens of longer duration of use of the device and was unusually marked in the inter loop area.

The number of blood vessels was increased (Fig. 10) and in some specimens they were dilated. This was a notable feature in endometria from women with menorrhagia or polymenorrhea.

TABLE VI
Showing the Histological Dating in Relation to the Day of Biopsy

Day of Biopsy	Total Proliferative phase			Early secretory	Late secretory	Cystic Hyperplasia	Dysharmony
	No.	4-7	8-10				
4-7	14	2	6	2	2		
8-10	31	1	17	8	2		3
11-14	29		9	12	6	1	1
15-21	52	3	3	14	21	11	
22-28	40	1	3	4	5	24	1
Total 166							

TABLE VII
Showing the Changes in the Stroma Due to the Device in Relation to Duration of Use

Duration of the device in months	Total No. of cases	Interstitial edema		Increased lymphocytes		Increased polymorphs		Plasma cells	
		No.	%	No.	%	No.	%	No.	%
Less than 12 m.	36	13	36.1	27	75.0	12	36.1	2	5.6
13-24	37	14	37.8	24	64.9	5	13.5	2	5.4
25-36	46	23	50.0	26	56.9	9	19.5		
37-48	33	19	57.7	11	33.3	2	6.1	1	2.2
49-60	15	6	40.0	2	13.3	2	13.3	1	6.7
61 m & above	3	1	33.3						

Discussion

Histological studies carried out by various other workers have not revealed significant tissue changes (Hall and Stone 1962; Lippes 1962; Sujan Tejuja *et al.*, 1964). The incidence of glandular hyperplasia has been reported as 0.2 to 32% (Menon, 1970; Kunders and Sudersanam, 1970; Shahani and Kothari 1973). In the endometria studied it was seen in 2.4% (4 cases) only. All these cases were of less than 3 years of use. Two had menorrhagia, one lactational amenorrhoea and one normal menstrual cycles.

Discrepancy of glandular and stromal development has been noted by Tamada *et al.*, (1967). They attributed this to endocrine or metabolic disturbance. This lag in synchronous development was also observed in 5 endometria (3%) of present series. Increasing duration of use had no relation with this type of morphological alteration.

The endometrium was advanced in 16.5% and retarded in 19.4% out of the 52 biopsies of the first half of secretory phase; 1 per cent had progressed to the stage of well developed secretory phase. Forty biopsies done between 22-28 days showed proliferative picture in 8 (20%).

These results clearly show "Out of tune" characteristic of the endometrium

which was either advanced (16.5%), retarded (19.4%) or showed cystic hyperplasia (2.4%) or dysharmony of glandular and stromal development (3%).

Similarly Lee *et al.*, (1967) reported that after ovulation the secretory changes are somewhat retarded suggesting a disturbed response of the endometrium to ovarian hormones. Wynn (1967) found that ultrastructural changes provide evidence that the device may be inducing a synchronous and premature cyclic development.

The histological features of leucocytic infiltration, increased vascularity, edema and occasional red cell extravasation is in accordance with the work of Morese *et al.*, (1966) which they attributed to foreign body reaction and presence of the Margulies spiral. The incidence of inflammation or infection associated with IUD has been reported as varying between 10 to 39.8%. Further studies in this direction have shown that the inflammation is rarely associated with actual bacterial infection except immediately after insertion. Mishell *et al.*, (1966) did not find any evidence of either local infection, endometritis or generalized pelvic inflammatory disease.

Summary

One hundred and seventy Endometria

from women using IUD have been studied. Histological status was assessed using the criteria of Noyes (1950) Endometrium was morphologically altered in 42%. The features were inadequate endometrium, secretory hypoplasia, dysharmony or lag of glandular response to that of stroma. The stroma showed lymphocytic infiltration, intercellular edema and increased vascularity.

These alterations have been correlated with the menstrual pattern and duration of use of the device. Local abrasive effect of IUD resulting in disturbed response of the endometrium to ovarian hormones have been postulated to be the cause of such changes.

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See Figs. on Art Paper IV-V-VI