A NEW METHOD OF CYTOLOGIC STUDY OF THE ENDOMETRIUM IN LONG TERM INTRAUTERINE CONTRACEPTION

by

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Intrauterine contraception has enjoyed an ever increasing popularity during the past five years. As a conservative estimate there were about 100,000 IUCD in current use until the end of 1964. During the last two years the total number of users has reached over four million; so far as is known, no other method of contraception has shown such a high acceptability record. This method of conception control entails the continuous presence of the device in the uterine cavity or, by its nature, a foreign body in direct contact with the endometrium. The endometrial response to this foreign body has been investigated grossly, [2-4-6-8] histologically, [2-6-10-12-13-14] bacteriologically, [9-14] cytologically [5-7-8-11] and biochemically.[6] Most workers admit that if there is any endometrial reaction it is only transient and often subtle.

Whatever can be said about these endometrial changes and their consequences, the final answer can only be achieved after continued research of long term users.

The aim of this work is to present a new simple method of obtaining an ample sample of the endometrium for a detailed cytologic study in long term users of this method of birth control. A preliminary result of this method is presented.

THE METHOD

The study was done at the time of removal of the IUCD, one year after use, before deciding to reinsert a new device. Once the loop was removed, it was smeared over two slides. Care was taken so that the small endometrial shreds sticking to the loop were obtained on the slide. Sometimes big shreds of endometrium were found attached to the loop after removal. These were collected for histological study. The smears were immediately fixed in 95 par cent ethyl alcohol and stained using a modified Papanicolaou method. The smears were examined by one and the same cytologist, interpreted and classified according to the Papanicolaou method. The presence of an abnormal number of leucocytes or histiocytes were noted as well as the character of atypia in the endometrial cells. The results were correlated to the day of the menstural cycle, to any abnormal bleeding, to any manifest sign of infection in the genital tract, spotting and to vaginal cytology report.

MATERIAL

Fifty unselected patients attending the Family Planning Clinic of Embaba and using lippes loop for one year were the subjects of this study. They were sent to Manial Cairo University hospital in batches. The lippes loop was removed and endometrial smears were collected and studied as previously described. Any complaint in the form of bleeding, discharge or pain was noted, as well as the result of gynaecological examination. A cervicovaginal smear was taken as well.

RESULT

(Illustrated in Table I)

All the endometrial smears taken by this method demonstrate big numbers of endometrial cells arranged in groups, clusters or sheets (Fig. 1). None of the known methods of obtaining endometrial smears, whether by aspiration of the brush, can obtain such a big number of endometrial groups of cells for a detailed study. Cells derived from the stroma, surface epithelium and glandular epithelium could be identified in these smears. In the fifty patients studied, the endometrial smears obtained by the above mentioned method were classified cytologically for any atypical criteria. None of the smears revealed malig-

TABLE 1

Endometrial & Vaginal Smears

No.	Endometrial smear		Vaginal smear		Remarks		
	Class	Leuco-cytes	Class	Leuco-cytes			
1	I	—	I	—	Spotting		
2	II	—		++	Spotting.	amount++,	erosion
3	II	+	I	—	Spotting		
4	II	+	II	—	—		
5	I	—	II	—	Discharge		
6	I	—	II	—	amount++		
7	II	+	II	+	— ,	erosion	
8	I	—	I	—	— .		
9	I	—		—	Spotting.	erosion	
10	I	—	I	+	Spotting		
11	II	+	I	—	Spotting.	amount++,	erosion
12	I		II	+	amount++,	erosion	
13	—		I	—	Spotting		
14	—		I	—	amount++,	erosion	
15	I		II	+	Spotting+,	erosion	
16	II		I	—	erosion		Discharge
17	II		II	+	—		
18	II		III	+			
19	II		II		—	erosion	Discharge
20	I		I		— ,		
21	II		I		— ,		
22	II		I		—	erosion	
23	II	+	I	+	—		
24	II	—	I	—	amount++,	erosion	
25	II	++	I	—	amount++,	erosion	
26	I	—	II	+	Spotting	erosion	
27	I	—	II	+	Spotting		
28	I	+	I&II	+	Spotting	erosion	Discharge
29	—	—	II	—			
30	III	—	I	—		erosion	Discharge
31	—	—	II	++	—		
32	I	—	I	—	—		
33	—	—	II	+++	amount +		

TABLE 1 (Cont.)

No.	Endometrial smear		Vaginal smear		Remarks	
	Class	Leuco-cytes	Class	Leuco-cytes		
34	I	—	II	II	Spotting—	Trichmonas
35	III	—	II	+	erosion	
36	II	—	I	—	Spotting	
37	III	+++	I	—	Spotting	
38	II	—	II	++	erosion	
39	II	—	I	—	Spotting	erosion
40	I	+	II	+	Spotting	amount++, erosion Discharge
41	I	—	I	—	—	
42	III	—	III&IV	—	Spotting —	Carinoma in Situ
43	I	—	I	+	—	
44	I	—	I	+	amount	Discharge
45	II	++	II	++	—	
46	II		I	+	erosion	
47	II	—	I		—	
48	I		I			
49	II		I		Discharge +, erosion	
50	II		II		—	

nant criteria of IV or V class. Four cases i. e. 8 per cent presented such marked atypical changes to be classified as III. Twenty two cases presented mild benign atypia and were classified II (Fig. 3—4) and twenty four showed normal endometrial cells of class I (Fig. 2). The results of the endometrial smears in the fifty cases studied were correlated with the age, abnormal symptoms of bleeding or discharge and cervical infection. Then the results of the cervicovaginal smears were analysed. One of the four cases classified as class III showed cellular atypia and changes suggestive of squamous metaplasia (Fig. 5). In the fifty cases examined intermenstrual sportting was an occasional symptom in 17. Out of the 4 cases, classified as class III, two cases complained of spotting. The same occurred in eight out of the twenty two class II smears and nine of the twenty four class I smears.

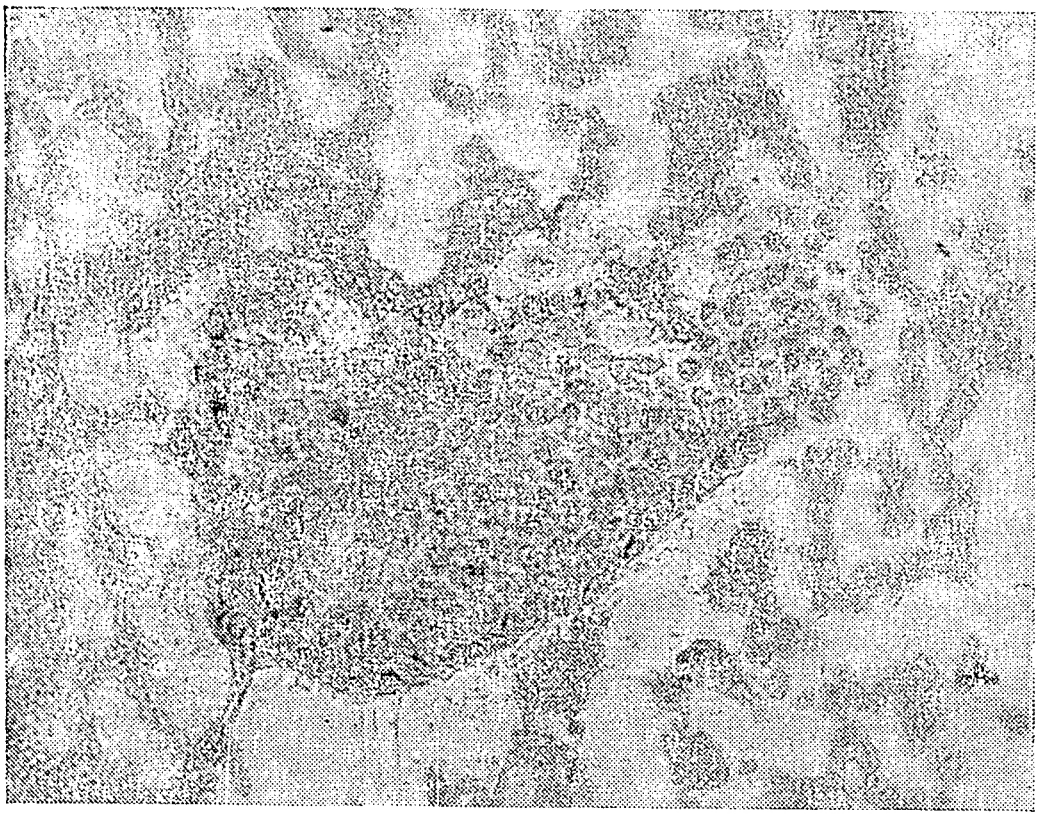

FIG. 1

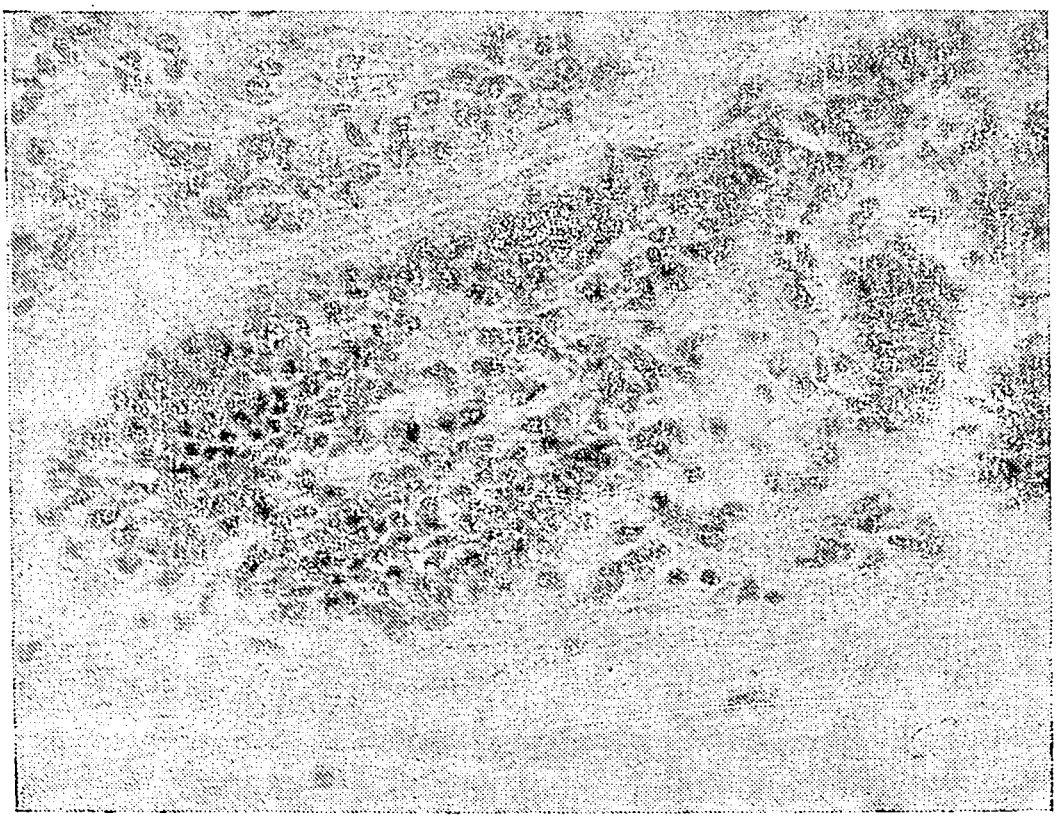

FIG. 2

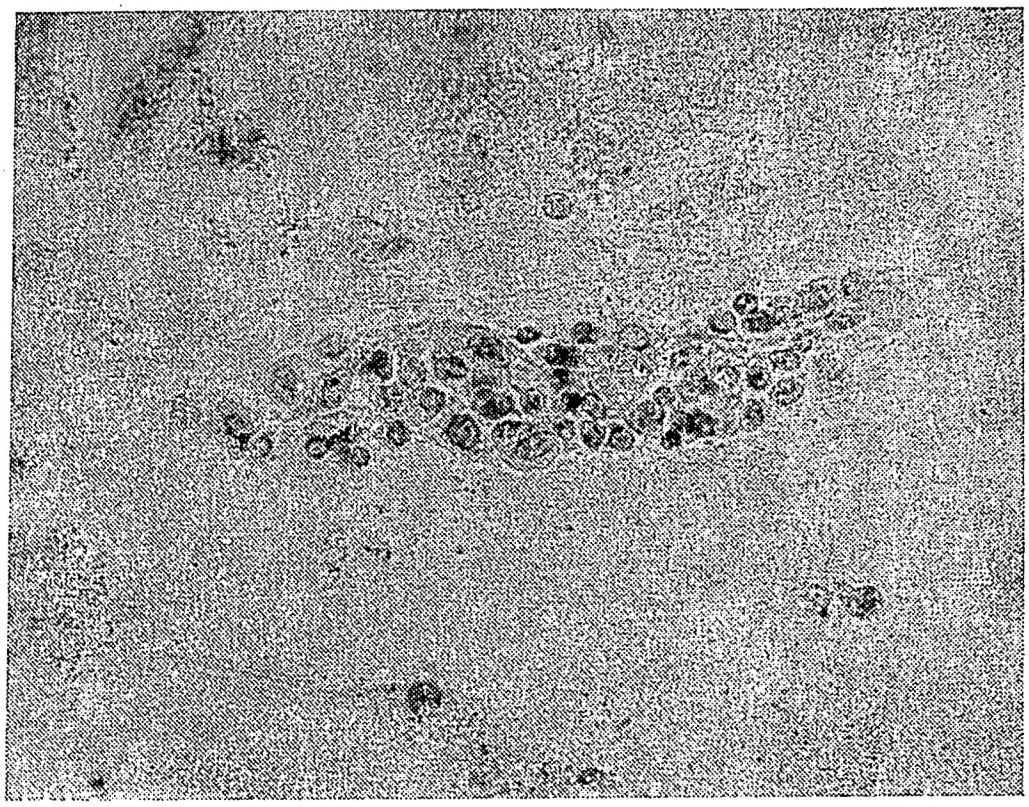

FIG. 3

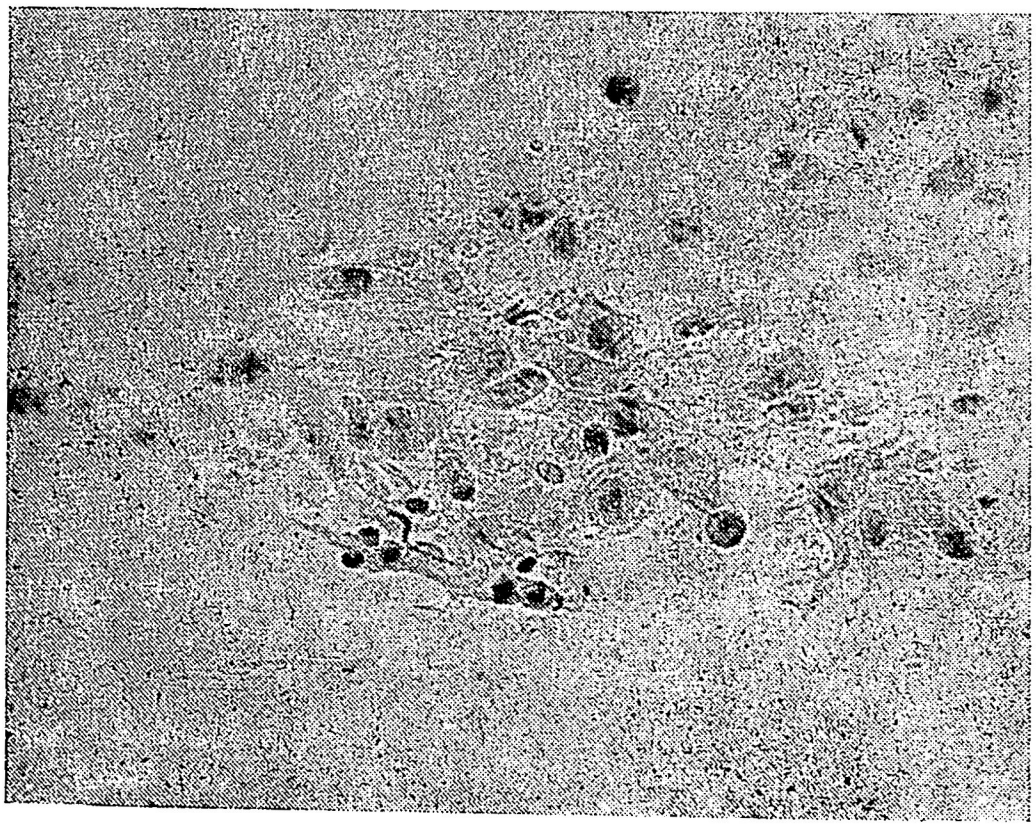

FIG. 4

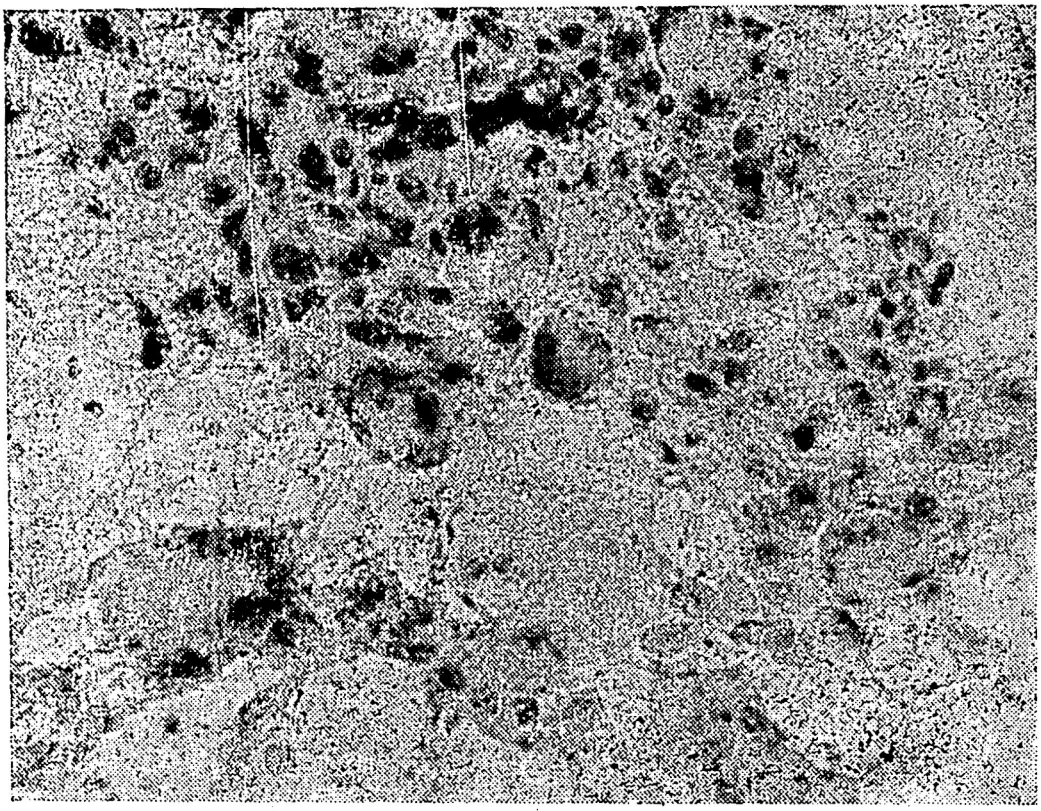

FIG. 5

Nine cases complained of excessive menstrual loss. Five cases of class II endometrual smears out of a total twenty two, and four cases of class I out of the twenty four cases had this symptom.

COMMENT

The world wide interest in intra uterine contraception has only appeared since 1962. Devices of various shapes and material have been tried and the results studied. The short term effect of such devices on the endometrium as examined morphologically, histologically and cytologically have been reported. Moyer and Mishell (1964), studied the endometrial response in association with the placement of the intra uterine device in the uterus in a group of 21 women only a few months after its insertion by endometrial biopsy. In a second group of 8 patients an elective vaginal hysterectomy was performed. Although all the cases studied were short term users, their results indicated that there were changes induced in the form of depression of the endometrial surface at the site of impact by the loop, and focal irregular areas

of recent haemorrhage and congestion. Their histologic studies demonstrate the presence of chronic endometritis, with or without involvement of the myometrium, stromal lymphocytosis and subepithetial leucocytic infiltration. In a similar report by Israel and Davis (1966), 57 hysterectomy specimens were studied after insertion of an intra uterine device, in the form of a ring molded of a chemically inert plastic (ultrathane), for a period from 4-8 months. They found that in all cases the endometrium was thicker and more edematous in the area enclosed by the device, and depressed at the area in direct contact. In many cases spotty focal haemorrhage was observed, and chronic endometritis was present in 13 per cent as compared to 2 per cent in the control group. Wilson (1964) reported similar microscopic endometrial changes in the form of an increased incidence of lymphocytic infiltration of the endometrium. Bonney, *et. al.* (1966) analysed the endometrial changes in a series of vaginal hysterectomy specimens for patients using the device for a period ranging from 4 to 38 weeks. They found that during the proliferative phase, the intra uterine device makes a shallow depression in the endometrium, and there is a moderate amount of mucoid material around the device. On section there is a layer of fibrous reaction under the surface but the glands are not markedly altered. Early in the secretory phase, the endometrium grows between but not beneath the loops of the device, and the histologic maturation seems to be retarded in areas of the surface epithelium under the loop. The subsurface fibrosis becomes more marked and sometimes appears similar to predecidua. The surface epithelium is thinned under the loop, at time to the point of becoming completely eroded away. On day 20—22, the stromal edema is excessive between the loops, and there is often a premature predeciduoid reaction of an abnormally fibrous nature under the loop. Tamada (1964) reported that squamous metaplasia of the endometrium was found in a few cases of patients using the device. Ishihama, *et. al.* (1964) carried out a cytologic and histologic study for patients using the intra uterine contraception method for an average period of 3.1 years and compared the results with control females of the same age. They did not find any material difference in both groups. Israel and Davis (1964) studied endometrial cytology using the brush smear method for 221 patients using the Birnberg bow or the lippes loop No. 2, for a period of 4 months to one year. They concluded that no significant smear changes have been noted to date.

It is important to note here that intra uterine contraception is such a recent development that one must allow for a proper evaluation of reported endometrial changes and their effect in long term users. There are three important points concerning this aspect which should be remembered. First of all, the endometrium is unique in its reaction to any induced change which is shed off with each menstrual period. Secondly, carcinoma of the endometrium very rarely occurs before the menopause, when the device is used. Thirdly, direct irritantion as a possible factor in the etiology of endometrial cancer is most unlikely, and all evidence is in favour of an endocrine or constitutional one. All investigators have failed to find any evidence of glandular hyperplasia or any shift in the secretory activity of the ovary in the presence of the intra uterine device. These facts represent the basis of our present day knowledge concerning endometrial cancer. To exclude prolonged direct irritation of the endometrium as a pre cancrous factor, in the opinion of the authors, must await more further studies for patients using the intra uterine contraception for a long period of time. The reasons for this are the following : (1) Endometrial cancer can be induced in animals by carcinogens. (2) Intra uterine contraception, as far as we know, is the first trial of such a continuous source of irritation to the endometrium, contrary to the cervix which is always subjected in many ways to traumatic factors. (3) There are recorded cases of endometrial carcinoma occurring in the child bearing period of life associated with endometrial bilharziasis. The early development of carcinoma in such a young age, can be explained by the continuous prolonged trauma inflicted by deposition of bilharzia ova in the endometrial tissues.

We can assume that we are still in a stage in which it is difficult to decide with certainty the consequences of the foreign body reactions induced in the endometrium as a result of intra uterine contraception. It is all probable that such changes are only transient and without any serious consequences ; but such a positive opinion is only speculative and awaits future long term studies.

The proposed new method of cytologic study can be utilised to the benefit of such a long term study, as well, in the authors, opinion, to the benefit of such an important method of birth control. Being aware of the endometrial changes induced by the intra uterine device, patients using this method of contraception can be followed up and investigated cytologically every year at he time of removal. The endometrial

shreds or cells sticking to the removed loop represent cytologic specimens derived from practically the whole endometrial surface in contract with the device. Cells representing the surface epithelium, glandular cells, stroma cells and sometimes fibroblasts (Fig. 6) can be shed and studied in the smears. Smears can be classified, and for class I (benign smear) and class II (mild benign atypia), a new I.U.C.D. can be safely fitted. Concerning class III cases, these, in our opinion, should not arouse too much anxiety for the following reasons : (1) The continuous growth of the endometrium and shedding every month gives the endometrial cell the natural property of cellular activity in both the stroma and glandular elements. This fact may make it difficult for a cytologist to give a proper correct interpretation of the smear. (2) The cells sticking to the device represent those elements of the endometrium subjected to the maximum of irritation as they are in direct contant with the device. (3) Degenerative changes of the endometrial cells may give rise to both nuclear and cytoplasmic changes simulating intense atypia. So we follow a scheme in such class III cases to wait for a couple of months and then to do an endometrial biopsy. In all probability the histopathologic report would be normal and the patient can be fitted with a new device.

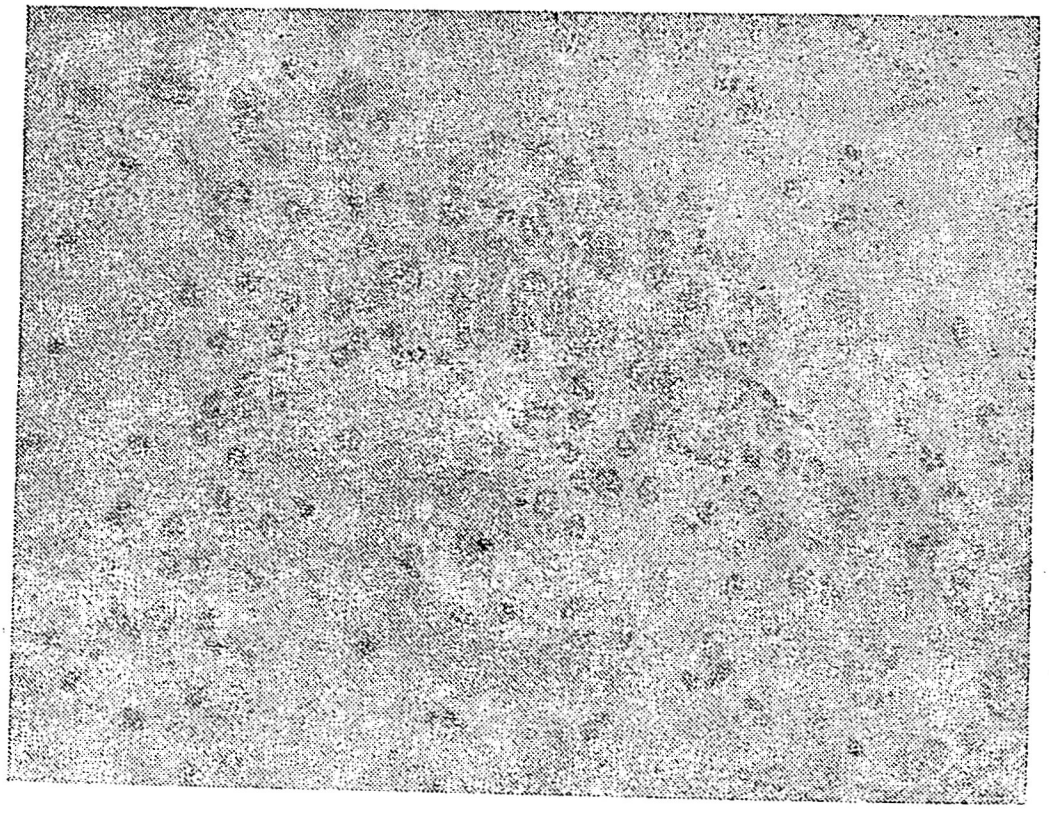

FIG. 6

In our 50 cases examined by such a method, after one year of intra uterine contraception, none showed a class IV or V smear. Four cases were classified as III. One of them had a class IV vaginal smear and was found to be a carcinoma in situ of the cervix. Another case displayed cells in the smear which show tendency to sequamous metaplasia (Fig. 5). Such a change has been reported in the histopathologic study of endometria with intra uterine contraception by Tamada (1964). The authors believe that this squamous metaplasia if present in such smears is a definite contraindication to intra uterine contraception, because in the endometrium they represent a definite type of intense dysplasia. Most of the reported cases of carcinoma of the endometrium in association with Bilharziasis are of the squamous cell metaplasia (Abdine and Shafeek 1955). The results of this study have indicated that bleeding in the form of intermenstural spotting or excessive menstrual loss could not be related to any cellular endometrial change or atypia whether present before or induced by the intra uteraine device.Spotting which was present in 17 cases occurred in the ratio of 2 : 4 in class III, 8 : 22 in class II and 9 :24 in class I endometrial smears. Excessive menstrual loss was a complaint in 9 cases. Only five out of 22 cases who showed class II endometrial smears and 4 out of 24 cases who showed class I smears had had this symptom.

SUMMARY

1. A proposed new simple method of obtaining cytological material from patients using the intrauterine method of contraception is presented.

2. The method can be utilised to study long term users of the I.U.C.D. before a new device is fitted.

3. The importance of finding class III cases is discussed, and its management is described.

4. Squamous metaplasia is considered a contraindication to intrauterine contraception.

5. Abnormal bleeding (spotting and excessive menstrual loss) was not related to any endometrial cellular change.

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