Quantitative study of uterine curettage in the menstrual cycle

B. BISWAS AND J. A. H. FINBOW

From the Department of Pathology, Doncaster Royal Infirmary, Doncaster

SYNOPSIS The histological appearances in 114 endometrial curettings from cases of dysfunctional bleeding have been analysed quantitatively by the method of Dunnill and Whitehead (1972) and Risdon and Keeling (1974).

As applied to this type of specimen, the technique provides indices of both tubular volume and tubular surface to volume ratio.

The histological diagnosis of endometrial hyperplasia is made from the increase in stromal and epithelial elements and the change in the pattern of the glands. These changes, on some occasions, can be difficult to detect.

Quantitative analysis can be used to distinguish minor degrees of abnormal endometrial hyperplasia, in comparing serial endometrial changes in a given patient, and in comparing different menstrual cycles in dysfunctional uterine bleeding.

Endometrial biopsies were collected and put in categories according to the clinical diagnosis. These biopsies were then examined morphometrically to find the volume/glandular surface and glandular/volume ratio. A significant change in these ratios was found.

Endometrial curettage is an essential procedure in the investigation of all forms of disorders of the menstrual cycle.

On light microscopy most forms of menstrual disorders present little difficulty in interpretation but minor degrees of abnormal menstrual cycle can be difficult to assess. This study considers a method of quantitative examination in which minor degrees of abnormal endometrial hyperplasia can be accurately recorded.

Several morphometric methods other than direct linear measurement are available for the measurement of tissue components in histological sections (Dunnill, 1968). All these methods depend on (1) adequate sampling, and (2) random distribution of the structures to be measured.

Materials and Methods

Routine diagnostic endometrial curettings were used. The curettings were fixed in 10 % formol saline, dehydrated, cleared, and embedded in paraffin wax.

Sections were cut at $5\ \mu$ and stained with haematoxylin and eosin.

An eyepiece graticule (Graticules Ltd) containing

a template (according to Weibel (1963)) with 15 lines of equal length connecting the vertices of a regular hexagonal point network was used and gave a constant 150 magnification throughout the study. At this magnification the length (l) of each line cast on the section was 1.4×10^{-2} cm. The section was orientated so that it lay centrally in the vertical axis of the microscopic field, and the most lateral of the lines on the graticule were superimposed on the stroma. The other lines then fell at random. The lines cutting the mucosal surface were cuts (c) and where the ends of the lines fell over the epithelium of the gland counted as hits (h). The number of cuts and of hits were recorded. The slide was moved, with the aid of mechanical stage, until the adjacent field was in view and this was then counted. This procedure was repeated until the biopsy material containing whole glands and stroma had been covered. The non-endometrial elements in the curettage were excluded. The index $c:lh$ was calculated for each biopsy and the mean value was obtained to indicate the significance of the irregular distribution of fragments containing crowded glands within stroma.

It was not possible to calculate the absolute ratio of surface length to volume described by Chalkley *et al* (1949) because of the type of material.

Received for publication 29 April 1975.

The mean number of hits per microscopic field examined was determined and this was proportional to the glandular volume.

Results

The results are set out in figs 1 to 4 and tables I to III.

Statistically significant results were found between group II (premenstrual endometrium) categories, mean $\bar{h}$ 4.01 (SD 1.76), and group III categories (abnormal endometrial hyperplasia), mean $\bar{h}$ 2.66 (SD 1.51) ($t = 2.97$; $P < 0.01$) but no significant difference between the mean $\bar{h}$ value of group III and the other categories.

The mean c:lh ratio for groups III and II was significant ($t = 260$; $P < 0.02$) but there was no significant difference between the mean c:lh ratio for group III and the other categories.

Discussion

Abnormal endometrial hyperplasia can be due to persistent Graafian follicles of the ovary. The changes in the endometrium and the symptoms are

due to low oestrogen levels following abnormal inter-relationship between the ovaries and the pituitary.

The gross histological pattern of abnormal endometrial hyperplasia can be categorized into four groups:

- (1) *Proliferative* Epithelial proliferation, tall elongated glands, and stromal cell proliferation with hyperchromic nuclei and the absence of mitoses
- (2) *Adenomatous* Epithelial proliferation, convoluted tubular glands with back-to-back distribution and stromal cell proliferation with hyperchromic nuclei and the absence of mitoses
- (3) *Cystic* Epithelial proliferation of the surface mucosa, dilated cystic glands, some containing pink amorphous material and stromal cell proliferation without mitoses
- (4) *Mixed* Containing all or two of the groups above.

In the cases of abnormal endometrial hyperplasia examined by us all the above groups were represented. Three of the patients with curettings showing abnormal endometrial hyperplasia had a subsequent hysterectomy and the histology was constant.

This study confirms that abnormal endometrial

Fig 1 A template of 15 lines of equal length arranged according to the specifications of Weibel (1963). They are superimposed on a curettage of an abnormal adenomatous hyperplasia with endometrial carcinoma. 'Hits' are counted where the end points of the lines lie over the mucosal surface; 'cuts' are counted where the lines cross the surface epithelium of the gland. Haematoxylin and eosin $\times 105$.

Fig 2 *Abnormal proliferative endometrial hyperplasia. H and E $\times$ 105.*

Fig 3 *Abnormal cystic endometrial hyperplasia. H and E $\times$ 40.*

Fig 4 Endometrial carcinoma. *H and E* $\times 105$.

Group	Age Range (Years)	Indication for Biopsy	No. of Biopsies	Histological Diagnosis
I	17-42	Dysmenorrhagia, infertility	15	Proliferative
II	15-54	Irregular menstrual period, menorrhagia, infertility	37	Premenstrual
III	16-50	Frequent menorrhagia with prolonged menstrual periods	21	Abnormal endometrial hyperplasia
IV	16-50	Menorrhagia, infertility	18	Secretory
V	49-60	Continuous vaginal bleeding	3	Endometrial carcinoma
VII	35-48	Irregular bleeding	3	Progesterone effect
VIII	22-52	Menorrhagia, infertility	17	Non-secretory

Table I Main clinical and histopathological findings in the patients studied

Group (See table I)	Endometrial Biopsy Specimen							
	Histology	No.	$e:h$ Ratios			h		
			Range	Mean	SD	Range	Mean	SD
I	Proliferative	15	3.92	3.16	1.33	3.48	2.88	1.16
II	Premenstrual	37	4.95	2.88	1.32	8.11	4.01	1.76
III	Abnormal endometrial hyperplasia	21	6.52	3.94	1.79	5.54	2.66	1.51
IV	Secretory	18	8.19	3.08	2.15	11.82	4.34	2.44
V	Endometrial carcinoma	3	2.7	3.60	1.48	2.35	3.52	1.19
VII	Progesterone effect	3	4.12	4.29	2.08	2.05	1.65	1.17
VIII	Non-secretory	17	3.39	2.58	1.03	4.01	2.89	1.08

Table II Results in each set of cases

Differences between the Mean c:lh Ratios for Biopsies in	t	P
Groups II and III	2.60	< 0.02 P > 0.01
Groups III and V	0.31	0.76 > P > 0.75
Groups III and VII	0.32	0.76 > P > 0.74
Groups V and VII	0.52	0.7 > P > 0.6
<i>Differences between the mean h value for biopsies in</i>		
Groups II and III	2.97	< 0.01
Groups III and IV	2.66	0.02 > P > 0.01
Groups III and VIII	0.53	0.6 > P > 0.5

Table III Statistical analysis

hyperplasia is found through the menstrual cycle (Beer, 1970), and that the cystic glandular hyperplastic type (Fraser and Baird, 1972) is found in 2% of cases of polycystic ovarian disease (Goldzieher, 1973). Three biopsies showed endometrial carcinoma, one of which also showed abnormal endometrial hyperplasia, an association found by Southam and Richart (1966). One of these cases occurred in the menarche and was stage I and the other two occurred postmenopausally and were stages II and IV (Gusberg, 1973).

A greater degree of the combination of abnormal adenomatous hyperplasia and cystic hyperplasia was found in curettage taken towards the end of the cycle in cases of dysfunctional bleeding. Wedge resection of the ovaries in three cases, taken at the time of curettage, showed haemorrhagic corpora lutei and multiple follicular cysts.

The utilization of quantitative methods to the examination of endometrial curettage to give the value of the ratio c:lh and h takes about 10 minutes for each section. As the diagnosis of abnormal endometrial hyperplasia is not difficult on the majority of occasions, this procedure to provide accurate

diagnosis in borderline cases would not make a marked increase in workload.

We are grateful to Dr D. N. Shanbhag and his staff, Department of Probability and Statistics, The University, Sheffield, for the statistical analysis, and to Mrs Lyn Boon for secretarial assistance.

References

- Beer, A. E. (1970). Differential diagnosis and clinical analysis of dysfunctional uterine bleeding. *Clin. Obstet. Gynec.*, **13**, 434-450.
- Chalkley, H. W., Cornfield, J., and Park, Helen, (1949). A method for estimating volume-surface ratios. *Science*, **110**, 295-297.
- Dunnill, M. S. (1968). Quantitative methods in histology. In *Recent Advances in Clinical Pathology, Series V*, edited by S. C. Dyke, pp. 401-416. Churchill, London.
- Dunnill, M. S. and Whitehead, R. (1972). A method for the quantitation of small intestinal biopsy specimens. *J. clin. Path.*, **25**, 243-246.
- Fraser, I. S. and Baird, D. T. (1972). Endometrial cystic glandular hyperplasia in adolescent girls. *J. Obstet. Gynaec. Brit. Cwlth.*, **79**, 1009-1015.
- Goldzieher, J. W. (1973). Polycystic ovarian disease. *Clin. Obstet. Gynec.*, **16**, 82-105.
- Gusberg, S. B. (1973). The dysfunctional and the neoplastic: investigative approaches to the problems of endometrial cancer. *Endometrial Cancer: Proceedings of a Symposium* (1971) edited by M. G. Brush, R. W. Taylor, and D. C. Williams, 3-12.
- Risdon, R. A. and Keeling, J. W. (1974) Quantitation of the histological changes found in small intestinal biopsy specimens from children with suspected coeliac disease. *Gut*, **15**, 9-18.
- Southam, A. L. and Richart, R. M. (1966). The prognosis for adolescents with menstrual abnormalities. *Amer. J. Obstet. Gynec.*, **94**, 637-645.
- Weibel, E. R. (1963). Principles and methods for the morphometric study of the lung and other organs. *Lab. Invest.*, **12**, 131-155.