Review article

Terminology in gynaecological cytopathology: report of the Working Party of The British Society for Clinical Cytology

D M D EVANS (CHAIRMAN),* E A HUDSON (SECRETARY),† C L BROWN,††
M M BODDINGTON,¶ H E HUGHES,§ E F D MACKENZIE,** T MARSHALL§

*From *St David's Hospital, Cardiff, †Northwick Park Hospital, Harrow, ††The London Hospital, ¶Royal Berkshire Hospital, Reading, §Glasgow Royal Infirmary. **Southmead General Hospital, Bristol, §Central Pathology Laboratory, Stoke on Trent*

SUMMARY The report defines and recommends terms for use in cervical cytology.

Most cervical smear reports are received by medical practitioners who do not have specialised knowledge of pathology or gynaecology. Therefore it is important that the report is not only scientifically accurate but also easily understood so that the patient receives appropriate management and advice. To promote these aims the British Society for Clinical Cytology set up a working party to make recommendations on the reporting of cervical smears and the terms used. It was suggested that common use of a small but clearly defined vocabulary would improve the communication of results to users of the cytology services and provide an accurate basis for wider reference.

The cytology report

The cytology report on abnormal findings should consist of a concise description of cells in precisely defined and generally accepted cytological terms. This may be followed, if appropriate, by a prediction of the histological condition based on the overall picture and should include a recommendation for the further management of the patient.

When a prediction of histology is included as a supplementary statement to a description of the cytology use of the terminology, cervical intraepithelial neoplasia (CIN) is preferred: it has the advantage of relating the histological report more clearly to the prognosis and management than the artificial separation implied by classification into dysplasia and carcinoma in situ. Caution is advised, however, in the

firm prediction of CIN 3 because the cytologist cannot reliably exclude a microinvasive or invasive lesion. The histological prediction is more accurately recorded on the National Cytology Form, HMR 101/5 (1982), where severe dysplasia or carcinoma in situ (CIN 3), or carcinoma in situ (CIN 3) or? invasive carcinoma are the alternatives provided.

INFLAMMATORY NUCLEAR CHANGES AND DYSKARYOSIS

A continuous range of nuclear abnormalities occurs, from minor changes that are usually associated with inflammatory conditions and which are believed to be essentially benign, through to more striking nuclear abnormalities that correlate with CIN. Cytologists should be encouraged to say precisely what abnormality is present in as many cases as possible, but there will be some in which the abnormality is on the borderline. These abnormalities may be referred to as "borderline nuclear abnormalities." In these circumstances follow up with repeat smears usually allows a more exact cytological diagnosis to be made.

The morphological abnormalities of the nucleus comprise a combination of any number of the following:

- (1) disproportionate nuclear enlargement;
- (2) irregularity in form and outline;
- (3) hyperchromasia;
- (4) irregular chromatin condensation, appearing as stippling, clumps, or strands, and sometimes as condensation beneath the nuclear membrane producing apparent irregularities in thickness of the nuclear membrane;
- (5) abnormalities of the number, size, and form of

Fig 1 Normal superficial and intermediate squamous cells. Both cell types have abundant translucent cytoplasm with angular borders. Nuclei of both intermediate squamous cells have evenly distributed finely granular chromatin, whereas three superficial cells have smaller pyknotic nuclei. (Papanicolaou.) Original magnification $\times 160$, enlarged $\times 5$.

Fig 2 Endocervical cells. These columnar epithelial cells are seen lined up in characteristic palisade pattern and from an alternative aspect in a sheet with nuclei surrounded by narrow rim of cytoplasm. Nuclei appear vesicular apart from one or more prominent nucleoli. (Papanicolaou.) Original magnification $\times 160$, enlarged $\times 5$.

Fig 3 *Normal parabasal squamous cells. These cells usually have rounded outlines with opaque cytoplasm and vesicular nuclei. Chromatin pattern is finely granular but nucleoli may be prominent. (Papanicolaou.) Original magnification $\times 160$, enlarged $\times 5$.*

Fig 4 *Inflammatory changes in parabasal squamous cells. Inflammatory nuclear changes may be particularly pronounced in smears from atrophic cervical squamous epithelium, as shown here. Hyperchromasia is striking and chromatin is coarsely clumped but clumps are evenly distributed. An impression of anisonucleosis is created by coexistence of reactive and degenerative changes in nuclei. (Papanicolaou.) Original magnification $\times 160$, enlarged $\times 5$.*

nucleoli;

(6) multinucleation associated with any of the above.

Figs 1 and 3 show examples of normal squamous cells; fig 2 shows glandular cells.

Inflammation

Inflammation alone causes minor nuclear abnormalities (fig 4). These are usually disproportionate nuclear enlargement with or without hyperchromasia. Wrinkling of the nuclear membrane due to degenerative change may also be associated with inflammation but must be distinguished from the irregularities of form and outline of dyskaryosis. Karyorrhexis and pyknosis must also be distinguished from nuclear abnormalities with malignant potential. There is no need to report simple inflammatory changes.

Dyskaryosis

Dyskaryosis literally means "abnormal nucleus" and is liable to be used in different ways—for example, by some to describe abnormal cells expected to be obtained from CIN 1 or CIN 2, and by others it is only used for severely abnormal cells expected to come from CIN 3.

Dyskaryosis should be used to describe nuclear abnormalities more numerous or more severe than

those associated with inflammation alone. Irregularity of chromatin distribution is the most important change in nuclear morphology. It may be accompanied by irregularity of form and outline, multinucleation, further disproportionate nuclear enlargement, and hyperchromasia. Artefactual cell distortion must be distinguished from dyskaryosis.

The Working Party endorses the recommendation by Spriggs *et al*¹ that "dyskaryosis" and "dyskaryotic" should be used to describe the nuclear abnormalities seen in cells from CIN and it recognises that some cases of invasive carcinoma exfoliate similar cells.

The term dyskaryosis is appropriate when referring to both squamous and endocervical cell abnormalities with the same implication of intraepithelial or invasive carcinoma.

CLASSIFICATION OF DYSKARYOTIC CELLS

Spriggs *et al*¹ recommended a classification that depends on the cytoplasmic characteristics of the dyskaryotic squamous cells. Thus superficial cell, intermediate cell, and parabasal cell dyskaryosis were described. After considerable deliberation this Working Party prefers to emphasise the overriding importance of nuclear abnormalities. This does not exclude cytoplasmic changes from cell assessment,

Fig 5 Mild dyskaryosis. Nuclei are enlarged and hyperchromatic. Clumps and ridges of chromatin are unevenly distributed and there are also folds in some of the nuclear membranes. Three cells are binucleate. Abnormal nuclei occupy less than half area of cytoplasm of most of these cells. Cytoplasm retains translucent quality of normal, superficial, or intermediate squamous cells. (Papanicolaou.) Original magnification $\times 160$, enlarged $\times 5$.

Fig 6 Nuclear abnormalities associated with human papilloma virus infection. These koilocytes show typical central clearing and peripheral condensation of cytoplasm. It is impossible to be certain whether uneven chromatin pattern in larger nucleus is dyskaryotic or degenerate: patient would therefore be followed up. (Papanicolaou.) Original magnification $\times 160$, enlarged $\times 5$.

Fig 7 Moderate dyskaryosis. Disproportionate nuclear enlargement is greater than that in fig 5 and morphological abnormalities of nuclei more severe. Dyskaryosis is classified as moderate in most of the cells but could be called severe in few in which area of nucleus exceeds two thirds of area of cytoplasm of cell. (Papanicolaou.) Original magnification $\times 160$, enlarged $\times 5$.

(a)

(b)

Fig 8 Severe dyskaryosis. (a) Dyskaryotic cells show wide range of nuclear abnormalities, of which uneven chromatin distribution and irregularities of nuclear membranes are most important. Differences in size and shape of cells and their nuclei are striking in this example. Abnormal nuclei occupy more than two thirds of all cytoplasm. (b) Uniformly small size of these severely dyskaryotic cells may cause diagnostic difficulty.

Fig 8 continued opposite

(c)

(d)

Fig 8 continued

Irregular chromatin condensation is predominant abnormal feature of nuclei, although some show degenerative changes. Hyperchromasia is present but is not always a feature in this type of abnormal cell. A few cells in which nucleus occupies less than two thirds could be classified as moderately dyskaryotic. (c) Cluster of severely dyskaryotic cells contrasts with single normal superficial squamous cell and both intermediate squamous cells. Although abnormal cells have irregular chromatin distribution patterns, size and shape is generally fairly uniform. Nuclei are crowded together and this appearance contrasts with orderly pattern of sheet of endocervical cells seen in fig 2. (d) Fragment of epithelium is breaking up in characteristic manner to show severely dyskaryotic cells in clusters of various sizes, single cells, and bare nuclei.

Fig 8 continued overleaf

(e)

(f)

Fig 8 continued

(e) Abnormal nuclear chromatin pattern of these severely dyskaryotic cells distinguishes them from parabasal squamous cells.
(f) These four severely dyskaryotic cells with little cytoplasm show such gross aggregation of chromatin that translucent areas are seen within nuclei. (Papanicolaou.) Original magnification $\times 160$, enlarged $\times 5$.

but when nuclear abnormalities are particularly severe they should outweigh any apparent cytoplasmic maturation. It is recommended that dyskaryotic cells are classified as mild, moderate, or severe according to:

- 1 The diversity of abnormal nuclear characteristics listed above and the degree of morphological abnormality.
- 2 Cytoplasmic characteristics, which include quantity, density, shape, and staining quality.

Mild dyskaryosis

Mildly dyskaryotic cells usually have plentiful, thin, translucent cytoplasm with angular borders, resembling superficial or intermediate squamous cells (fig 5). The nucleus occupies less than half the total area of the cytoplasm. Mild dyskaryosis correlates with cells from the surface of CIN 1. It is doubtful, however, if it can be reliably distinguished from the nuclear abnormalities associated with human papillomavirus infection (fig 6).

Moderate dyskaryosis

Moderately dyskaryotic cells have more disproportionate nuclear enlargement than mildly dyskaryotic cells, so that the nucleus occupies one half to two thirds of the total area of the cytoplasm (fig 7). The nuclear morphology tends to be more abnormal than that seen in mild dyskaryosis. The cytoplasm may resemble that of intermediate, parabasal, or sometimes superficial type squamous cells.

Severe dyskaryosis

Severely dyskaryotic cells typically have a narrow rim of thick dense cytoplasm and they are round, oval, polygonal, or elongated in shape (figs 8a–f). Thus the abnormal nucleus practically fills the cell, or at least two thirds of it. Occasionally, there are severely dyskaryotic cells in which there is plentiful abnormally shaped, often keratinised, cytoplasm accompanied by abnormal nuclear morphology that is more pronounced in degree and diversity than that usually associated with CIN 1 or CIN 2. Their correct interpretation is facilitated by the presence of more characteristic cells showing the changes described above. In those cases the cells should be described as severely dyskaryotic. In severe dyskaryosis the abnormal cells may occur in clumps as well as singly. Severely dyskaryotic cells correlate with cells from the surface of cervical epithelium showing CIN 3 or invasive carcinoma.

Intercellular relation

Evaluation of sheets of epithelial cells in a smear requires slightly different criteria, which may be more difficult to define than the diagnostic characteristics

of single cells (figs 8c and d). Loss of normal regular arrangement (polarity) may distinguish neoplasia from severe inflammation when the nuclear appearances are equivocal. Papillary processes, sheets of metaplastic cells, fragments of CIN 3, and desquamated glands from adenocarcinoma provide examples of the importance of intercellular relation in interpretation (fig 9).

INVASIVE AND MICROINVASIVE CARCINOMA OF THE CERVIX

Invasive carcinoma cannot be diagnosed reliably from a smear. There are cytological features, however, which infer a strong possibility of a more advanced abnormality than that suggested by CIN 3 (fig 10a). It may be useful to refer to these in the cytology report to convey the more urgent need for biopsy. The following characteristics, often several at once, are associated with invasive tumours:

- 1 Variation in size and shape of dyskaryotic cell nuclei beyond that usually associated with CIN 3 and often including unusually small cells of bizarre shape.
- 2 Aggregations of nuclear chromatin, so coarse that translucencies appear.
- 3 Large irregular sometimes multiple nucleoli in dyskaryotic cells.
- 4 Cytoplasmic keratinisation of dyskaryotic cells and the presence of thick anucleate fragments of keratinised cytoplasm.
- 5 Irregularly shaped dyskaryotic squamous cells including fibre cells and tadpole cells as well as other bizarre forms (figs 10b and c).
- 6 Tissue fragments composed of dyskaryotic cells.

The term "malignant diathesis" is sometimes used to describe the necrotic debris, inflammatory exudate, and blood that predominate in smears from ulcerated invasive tumours. These constituents may contribute to an unreliable smear. They are insufficiently specific for diagnosis.

The term "malignant cells" may be read as implying invasive carcinoma. It is preferable to describe the cells as dyskaryotic, and a secondary statement could be added to draw attention to characteristics associated with an invasive tumour. It is a long established custom of reporting at some centres to mention malignant cells before suitable diagnostic and therapeutic measures are undertaken, even for an intraepithelial abnormality. The Working Party feels that this should be discouraged, unless there is firm evidence of invasive tumour.

SMears SHOWING BORDERLINE ABNORMALITIES

The report is made after careful scrutiny of all the

Fig 9 Severe dyskaryosis from endocervical adenocarcinoma. Desquamated gland shows characteristic rosette pattern. (Papanicolaou.) Original magnification $\times 160$, enlarged $\times 5$.

material on the smear and rarely depends on the appearance of one cell. Some cells will be on the borderline between the accepted definitions, but the problem of classification can usually be resolved by the time the whole specimen has been examined. In the relatively few smears that remain equivocal a repeat smear for a mild abnormality or referral for colposcopy and biopsy for more severe abnormalities will be necessary to resolve the problem.

The Working Party has considered the use of the term atypia or another single word for the equivocal smear. It has decided against such a recommendation because the word can be used too often as a substitute for careful observation and definition.

Atypia has been used in a number of senses including that for which this report recommends dyskaryosis. It should be avoided because its previous loose and diverse application makes it unlikely that users will adhere to any definition suggested now. There are smears in which the evidence is such that it is impossible to decide if the cells are the product of inflammation or if they have neoplastic potential. It is suggested that the report should explain briefly the diagnostic dilemma (bordering on mild dyskaryosis). This is more helpful than a word of uncertain meaning.

METAPLASIA

Smears may contain endocervical cells that have some squamous characteristics. These appearances correlate with the surface of immature metaplastic epithelium from the transformation zone of the cervix. Sometimes the squamous features are so pronounced that the cells cannot be distinguished from parabasal squamous cells from immature primary squamous epithelium. Dyskaryosis often occurs in these cells and should be reported and managed accordingly.

CYTOPATHIC CHANGES DUE TO WART VIRUS

The human papillomavirus causes a variety of appearances in smears.² These may mimic some characteristics of well differentiated squamous carcinoma but the severe dyskaryosis of squamous carcinoma will not be present. Wart virus changes accompanied by dyskaryosis should be managed according to the degree of dyskaryosis.³

NUMERICAL CLASSIFICATIONS

The Papanicolaou classification of cytology reports into classes I to V has been discouraged for some time because of the different interpretations which its broad definitions have been given. It is retained in some centres in which there is a clear understanding

(a)

(b)

Fig 10 Severe dyskaryosis from invasive squamous carcinoma. (a) All of these cells are severely dyskaryotic. They appear in various shapes and there are fragments of degenerative cells in the background. (b) Elongated severely dyskaryotic cells are sometimes called fibre cells. These and other bizarre forms are particularly characteristic of invasive carcinoma but may also be seen in smears from CIN 3.

Fig 10 continued overleaf

(c)

Fig 10 continued

(c) This severely dyskeratotic cell has plentiful abnormally shaped keratinised cytoplasm accompanied by severely abnormal nuclear morphology. Elongated tail of cytoplasm has led to description of this bizarre form as a tadpole cell. (Papanicolaou.) Original magnification $\times 160$, enlarged $\times 5$.

between cytopathologist and gynaecologist about its use but it lacks the precision necessary for wider reference. Similarly, attempts to subdivide or redefine the Papanicolaou classification or the introduction of other numerical or alphabetic shorthands will result in varied interpretations.

ENDOMETRIAL CELLS

Endometrial cells can be identified in smears, but the cervical smear is not a reliable test for endometrial abnormalities. The cause of endometrial exfoliation may not be reflected in the morphology of the cells—for example, cells from a well differentiated adenocarcinoma may be barely distinguishable from

endometrial cells exfoliated from a benign lesion or during menstruation.

References

- 1 Spriggs AJ, Butler EB, Evans DMD, Grubb C, Husain OAN, Wachtel GE. Problems of cell nomenclature in cervical cytology smears. *J Clin Pathol* 1978;31:1226–7.
- 2 Butler EB, Stanbridge CM. Condylomatous lesions of the lower female genital tract. *Clin Obstet Gynaecol* 1984;11:171–87.
- 3 Kaufman R, Koss LG, Kurman RJ, *et al.* Statement of caution in the interpretation of papillomavirus-associated lesions of the epithelium of the uterine cervix. *Acta Cytol* 1983;27:107–8.

Requests for reprints to: Dr E A Hudson, Department of Histopathology, Northwick Park Hospital, Harrow, Middlesex HA1 3UJ, England.