CORRESPONDENCE

Current views on CIN

The authors of the recent article on cervical intraepithelial neoplasia have, in the past, made major contributions to gynaecological pathology.[1] It is therefore deeply disappointing to find them clinging to outdated dogma while producing no original evidence in support of their views. They recommend, despite detailed evidence demonstrating gross inconsistencies in the grading of CIN,[2-4] that the current terminology be retained with the addition of a fourth category termed "basal abnormalities of uncertain significance".

The authors emphasise that the lesions which have been collectively termed CIN form a morphological spectrum. However, the lower end of this spectrum extends to encompass gradations of inflammatory atypia and immature squamous metaplasia. Clearly, these morphological findings do not necessarily represent a single—that is neoplastic—disease process. Indeed, it is likely that the minor morphological abnormalities of cervical squamous epithelium which we and others have shown to be associated with the greatest diagnostic inconsistency[2-4] are caused by a variety of different pathological processes. The authors tacitly admit this possibility when they recommend that, in the presence of severe inflammation, ungradable CIN and CIN1 be included in their proposed category of basal abnormalities of uncertain significance.

Morphological classification of disease has two main purposes: to guide treatment and prognosis; and to provide a basis for epidemiological studies and health statistics. Neither of these aims are furthered by creating spuriously accurate subdivisions which are based on non-specific morphological criteria. Where morphological changes are non-specific it may be necessary to adopt a pragmatic classification to guide treatment until more specific diagnostic techniques become available. On the basis of our work on observer variation we have recently suggested a two tier nomenclature for cervical squamous epithelial lesions which would not only improve diagnostic consistency but would also have clear management implications.[2 3] The authors of your leading article reject our suggestion on the insufficient grounds that there is disagreement among different investigators as to the precise location of the divide, and that adoption of such a nomenclature would "encourage the misguided belief that there is a two stage process in the natural history of CIN". Pathologists who are interested in mechanisms of disease are aware that carcinogenesis in the cervix, as elsewhere, is a multistage process which is not necessarily accompanied by stepwise morphological changes. The question of the location of the division point, for the purpose of clinical management, may be settled by a study of risk assessment which is currently in progress.[5] The preliminary analyses from this work support our suggestion that the division point should be located between CIN 1 and 2 (Wilkinson C, personal communication).

At present, one of the major practical problems in gynaecology and surgical pathology is the large number of cervical resection specimens which show no clinically important pathological abnormality. The reported figures vary from 27% of loop diathermy resections carried out for abnormal smears[6] to 64% of cone biopsies performed for mild dyskaryosis.[7] The problems thus largely stem from vigorous treatment of lesions at the lower end of the so-called CIN spectrum. Some may consider that the risk of resecting normal cervices with transient minor morphological abnormalities is outweighed by the benefit from removing, albeit in a minority of patients, the earliest stages of cervical neoplasia. The evidence, however, suggests that cervical resection is not free of morbidity,[8 9] that only a small proportion of patients with mild and moderate dyskaryosis progress to invasive carcinoma[10] (Jenkins MLF, Bradfield JWB, Mackenzie EFD. Abstract presented at the British Society for Clinical Cytology. 1990 29th annual meeting), and that surveillance is an entirely satisfactory way of managing these patients. The psychological impact on the patient of a diagnosis of neoplasia should also be borne in mind.

It is no longer possible for pathologists to hide behind their microscopes and deny all responsibility for the practices of their clinical colleagues. The delusion, perpetuated by some pathologists, that it is possible to detect cervical neoplasia at its earliest stages by the presence of minor morphological changes, the surgical treatment of which can abort progression of the disease, has resulted in overtreatment of a great many women. This cannot be justified on economic, ethical, or scientific grounds. The subject requires rational debate based on critical evaluation of existing evidence, preferably followed by a study which evaluates the applicability of any suggested new nomenclature.

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1 Anderson MC, Brown CL, Buckley CH, *et al.* Current views on cervical intraepithelial neoplasia. *J Clin Pathol* 1991;**44**:969–78.
2 Ismail SM, Colclough AB, Dinnen JS, *et al.* Observer variation in histopathological diagnosis and grading of cervical intraepithelial neoplasia. *Br Med J* 1989;**298**:707–10.
3 Ismail SM, Colclough AB, Dinnen JS, *et al.* Reporting cervical intra-epithelial neoplasia (CIN): intra- and inter-pathologist variation and factors associated with disagreement. *Histopathology* 1990;**16**:371–6.
4 Robertson AJ, Anderson JM, Swanson Beck J, *et al.* Observer variability in histopathological reporting of cervical biopsy specimens. *J Clin Pathol* 1989;**42**:231–8.
5 Wilkinson C, Peters T, Harvey I, Stott NCH. Risk assessment in cervical cytology screening: a new look at an old problem. *Br J Gen Pract* (in press).
6 Luesley DM, Cullimore J, Redman CWE, *et al.* Loop diathermy excision of the cervical transformation zone in patients with abnormal cervical smears. *Br Med J* 1990;**300**:1690–3.
7 Lopes A, Pearson SE, Mor-Yosef S, *et al.* Is it time for reconsideration of the criteria for cone biopsy? *Br J Obstet Gynecol* 1989;**96**:1345–7.
8 Jones JM, Sweetnam PM. The Cardiff cervical cytology study. Morbidity from and effectiveness of cone biopsy of the cervix. In: Anderson MC, ed. *Proceedings of Fourth World Congress.* London: International Federation for Cervical Pathology and Colposcopy, 1982; **99**:102.
9 Ismail SM. Cone biopsy causes cervical endometriosis and tubo-endometrioid metaplasia. *Histopathology* 1991;**18**:107–14.
10 Robertson JH, Woodend BE, Crozier EH, Hutchinson J. Risk of cervical cancer associated with mild dyskaryosis. *Br Med J* 1988;**297**:18–21.

*erb*B2 expression in breast and other human tumours

Having been involved during recent years in the study of *erb*B2 expression in breast and other human tumours,[1 2] we were interested to see the report from Fox and colleagues[3] regarding the apparent absence of *erb*B2 protein overexpression in male breast carcinoma. Shortly after this report was published, a 71 year old man was referred to the Department of Surgery at the Royal Victoria Infirmary with a six week history of a mass beneath the right nipple. The appearances of a fine needle aspirate were consistent with ductal carcinoma, and histological examination of the subsequent mastectomy specimen showed an invasive ductal carcinoma (Bloom's grade 2) (fig 1) with a comedo in situ component. Assessment of *erb*B2 protein expression (performed routinely in all breast carcinomas) using NCL CB11 at a dilution of 1 in 20 and an indirect immunoperoxidase method showed membrane staining throughout the tumour, indicative of overexpression (fig 2). A section of a known *erb*B2 positive breast carcinoma and omission of primary antibody were used as positive and negative controls, respectively.

This observation indicates that *erb*B2 overexpression (and therefore possibly amplification) is a feature of a proportion of male breast carcinomas. Since Fox and colleagues were unable to demonstrate overexpression in any of their 21 cases it

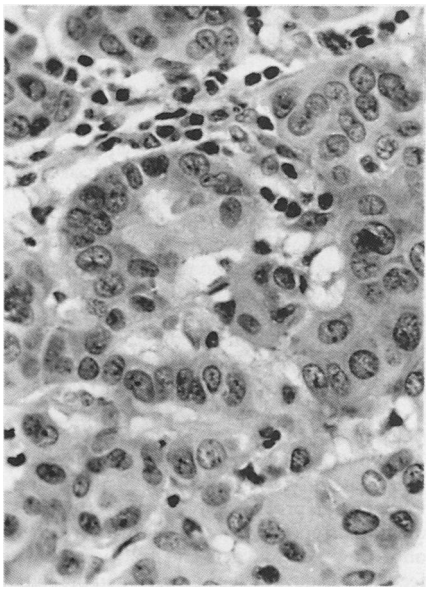

Figure 1 Invasive ductal carcinoma of male breast.

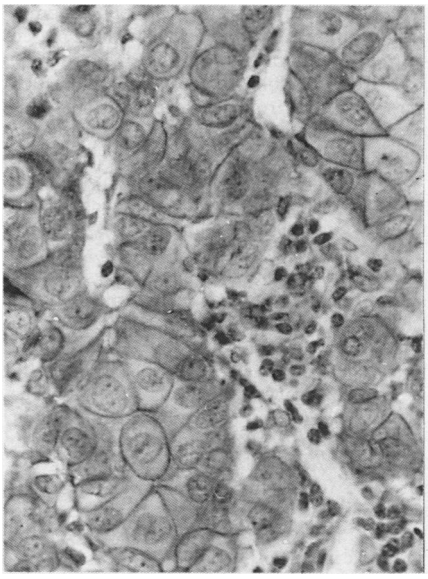

Figure 2 Male breast carcinoma showing membrane staining with NCL-CBII antibody, indicative or erbB2 overexpression.