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Grading of cervical intraepithelial neoplasia

SIR,—The main arguments of the article by Dr Sezgin M Ismail and colleagues[1] are based on two questionable assumptions: the accepted value of grading cervical intraepithelial neoplasia and the policy of treating women with all grades.

The terminology of cervical intraepithelial neoplasia regards the potentially premalignant epithelial disorders of the cervix as a continuous range of disease, and this is a concept that it theoretically irreconcilable with subdivisions. Grading was introduced for classification (the annual cervical cytology return requires data on the number of cases of cervical intraepithelial neoplasia grade III, for example) and for selecting patients for treatment, but it has always been acknowledged that grading is arbitrary and subjective. Secondly, Dr Ismail and colleagues assume that it is current practice to treat women with all grades of cervical intraepithelial neoplasia, citing the report of the ninth study group of the Royal College of Obstetricians and Gynaecologists. This study took place in 1981 and, although its recommendations were authoritative at the time, they do not necessarily apply eight years later. There has been intense discussion recently about the treatment of minor abnormalities, and it is now common practice for women with lesions no worse than cervical intraepithelial neoplasia grade 1 to be followed up rather than treated, although, inevitably, different policies are adopted in different departments.

The lack of agreement by histopathologists is largely owing to the imprecision of the currently available criteria for diagnosis; perhaps if Dr Ismail and colleagues had used slightly modified criteria[2] their results may have been different. It is a mistake to place too much emphasis on the proportion of the thickness of the epithelium showing differentiation and too little emphasis on nuclear abnormalities.[3] Unfortunately, nuclear detail is not shown well with formol saline fixation, and Bouin's fluid is strongly recommended for fixing cervical biopsies. Histopathologists and colposcopists certainly need to be aware of the difficulties in diagnosis, particularly at the bottom of the range, as well as the overlap with benign conditions, but it is my belief that these problems are already widely appreciated.

I agree with Dr Ismail and colleagues that the epithelial abnormalities of the cervix may be divided into only two categories: those that require treatment and those that do not and can be followed up. This pragmatic approach still requires a dividing line to be defined within the range of cervical intraepithelial neoplasia, so the issue cannot be entirely avoided.

It must also be borne in mind that the decision whether to treat a woman with an abnormal result on smear testing depends on several other factors, including the result of the test and the distribution of the lesion, in addition to the result of the colposcopic biopsy. Furthermore, the biopsy specimen does not necessarily always reflect the most severe lesion on the cervix.

The most effective saving of resources will be made by referring women with mildly abnormal smears for colposcopy only if the changes persist. Once a woman has been seen in the colposcopy clinic and a biopsy specimen taken further follow up by colposcopy and cytology may well be as costly as immediate treatment and will certainly be more so if treatment is eventually needed.

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1 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. (18 March.)
2 Anderson MC. Premalignant and malignant disease of the cervix. In: Fox H, ed. *Haines and Taylor: Obstetrical and gynaecological pathology.* Edinburgh: Churchill Livingstone, 1987:255-301.
3 Buckley CH, Butler EB, Fox H. Cervical intraepithelial neoplasia. *J Clin Pathol* 1982;**35**:1-13.

SIR,—The results of Dr Sezgin M Ismail and colleagues[1] are not surprising to clinicians working with premalignant disease of the cervix.

In practice the potential variability in histological diagnosis is taken into account and decisions to treat are based on a combination of test results (cytology, histology, and coloposcopy) and clinical information, such as age, parity, and smear history and a history of any previous cervical surgery, among other criteria. Any further revision in the terminology of grading cervical intraepithelial neoplasia is unlikely to clarify the situation.

Though developing a more accurate method for separating lesions with a malign potential from those without is desirable, no such test exists. The trials required to evaluate such tests are unlikely ever to be performed because of the implication that some women would be allowed to develop invasive cancer. Indeed, the concept of such a test may be flawed. The critical factor that determines whether a cervical intraepithelial neoplasm progresses to invasive disease may well lie not within the lesion but in the environment to which it is exposed.

The most important single factor in deciding whether to treat a woman who seems to have cervical intraepithelial neoplasia is the wish of the woman herself. In all cases she makes the ultimate decision, having been given the facts as we know them. In my experience most women with borderline abnormalities elect to have treatment rather than repeated colposcopic and cytological reviews.

Having read the comments of Dr Ismail and colleagues about histopathological diagnosis, I was surprised to find that their discussion extended to cervical cytology and particularly surprised at their extrapolation from their findings in making recommendations about the cervical cytology programme. In doing this Dr Ismail and colleagues seem to equate minor cytological abnormalities with borderline histological results when many reports in the past few years agree that a substantial proportion of women with minor cytological abnormalities have histological abnormalities that we ignore at our peril.

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1 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. (18 March.)

SIR,—Dr Sezgin M Ismail and colleagues provide further evidence that the present classification for cervical intraepithelial neoplasia is arbitrary and difficult for pathologists to use reproducibly.[1] Several other studies have shown a similar problem with reproducibility,[2,3] and this is supported by our experience. Dr Ismail and colleagues suggest that examining more sections to search for abnormal mitoses and introducing a borderline category might help. We suggest that this is not sufficient to rectify all the difficulties of the classification.

In an unpublished study of the practice of cutting cervical colposcopic biopsy specimens at multiple levels we found that any benefit in improved diagnosis was minimal compared with disagreement in reporting the grade of cancer, which we found in 30% of reports, disagreement occurring over the presence or absence of cervical intraepithelial neoplasia in about 15% of cases. We have also reported appreciable aneuploid DNA levels in lesions judged as being due to simple human papillomavirus infection of the cervix by three skilled cervical pathologists examining sections cut at multiple levels and using atypical mitotic figures as a marker for exclusion from this category.[4] The precise relation of aneuploidy to atypical mitoses and to human papillomavirus type, and the relation between these and prognosis, is unclear. The importance of aneuploidy requires further assessment. It is therefore premature to assume that atypical mitoses provide a safe basis for classification of low grade cervical abnormalities. No evidence is available, and whether a borderline group will improve the reproducibility of diagnosis or help to distinguish progressive from non-progressive lesions remains to be established. The benign behaviour of many of these lesions