Cytological changes preceding cervical cancer

Dr Robertson and colleagues must be con-
gratulated for holding up the "red flag of classification" to the "bulls of gynaecological
cytology". They are correct in pointing out particularly as the frailty of the current
reporting system becomes increasingly evi-
dent.

A basic premise in the currently recom-
mended terminology and management of cervical smears is that the degree of
dyskaryosis correlates with the grade of
cervical intraepithelial neoplasia (CIN). However, published information1 and KC61 indicate that is far from the case. Reasonable correlation occurs between severe dyskaryosis and CIN3, but considerably more variation is observed as the degree of dyskaryosis and CIN diminish. Whether or not dyskaryosis and CIN should correlate is debatable, as the definitions involved are purely arbitrary. However, a principal reason why they do not must be that to create a six month observer variance in the histopathological diagnosis of CIN.14

Health Service guidelines emphasise the important requirement to compare cytology and biopsy results.16 However, the crucial audit is whether cytological findings identify clinically relevant histopathological abnormalities and whether the false positive rate is accordingly kept to a minimum.

Surprisingly, with only one or two excep-
tions,17 there has been little discussion with regard to the possible introduction of the American Bethesda system for reporting cervical smears. Indeed, some cytics believe that the current system is doomed following the timing of the publication, which coincided with the printing of several million new HMR forms. However, although the Bethesda system uses the terminology, low grade squamous intraepithelial lesions, its overall complexity and content is analogous to that of the current British system. Accordingly, unlike Dr Robertson, I share previous authors' views18 that the Bethesda system has little to commend it.

I suspect that many gynaecological cytopathologists already perceive nuclear changes as either low or high grade abnormalities. It is within this spectrum that the introduction of the Bethesda system has been given the green light to proceed. There is now little to stop the system from being implemented. Although the Bethesda system has been implemented in the United States, the United Kingdom is in the final stages of implementing this system. As it will be a few years before the system is fully implemented, we can only hope that it will have a different effect on our systems.

In advocating a low and high grade method of reporting, the Bethesda system is cited by us only as an example. We accept that it is rather too elaborate. However, unlike Dr Slater, we hesitate to include "borderline changes", with wart virus and mild dyskaryosis as a low grade abnor-
mality. Among cytopathologists "border-
line" seems almost to have achieved the status of a diagnostic entity. Our experience is that in practice it merely reflects uncer-
tainty in interpretation of a smear. Reparative changes in the cervix, papillo-
mavirus infection, or atypical cells due to inflammation can all present difficulties. The latter may occasionally be confused with invasive cancer, and a six month repeat smear would be inappropriate. We feel that such reports should describe the diagnostic difficulty, advise on further action, and be summarised as "no diagnosis".

To the lay person the term "borderline" is unsatisfactory. It could be quite frightening for some women, giving the impression of a limbo bordering on (?) the abyss. It is not a diagnostic entity and, like the unicorn which had similar problems of identity, should be allowed to pass into mythology.

Pregnancy in von Willebrand's disease

The guidelines on the investigation and management of haemorrhagic disorders in pregnancy are welcome.1 With reference to the management of von Willebrand disease, we have recently studied 23 pregnancies managed at a single centre,2 and add the following comments.

We believe that there is a tendency towards complacency in the management of pregnant women with von Willebrads disease due to an excessive reliance on improvement in the coagulation deficit. The coagulation parameters improve in many instances, but we also have some exceptions, particularly in those more severely affected with low factor VIII (VIII:C)) before conception. In our series, those patients with low baseline VIII-C values (<15 IU/dl; four cases) had only limited improvement in VIII:C by the third trimester, the maximum attained being 54 IU/dl in the group. Bleeding times shortened significantly in only one of seven cases studied, and similar findings have been noted by others.15 In addition, our observations support the view that type II patients carry a higher risk of primary post-
partum haemorrhage (PPH) compared to types (3/11 type II v 0/12 type I). This seems to be independent of the value of VIII-C in the third trimester, and presum-
ably is explained by a failure of the primary haemostatic defect to improve normally. Importantly, secondary PPH occurred to a similar extent in both groups (2/12 type I and 3/11 type II—22% overall) and may be more dangerous as it often occurs after discharge from hospital.

The guidelines should serve to raise awareness and maintain vigilance in the management of von Willebrads disease in pregnancy. We would add that with reference to secondary PPH, while the administration of prophylactic von Willebrand factor (vWF) containing

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10 Robertson, Woodend, and Elliott comment: We agree with most of Dr Slater's comments, but would never have dared make them. They draw attention to the Emperor's new clothes and suggest rebellion in the ranks. We also have long regarded cervical cytology as a screening procedure, with no pretension to diagnostic precision, apart from its detection of severe dyskaryosis.
products in the puerperum is not necessary, patients should receive careful instructions to report excessive vaginal blood loss, so that measures to increase the vWF:Ag may be instituted without delay.

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Zinc assays in patients with α and β thalassaemia trait

We read with interest the investigations by Tillyer and Tillyer on the interpretation of zinc protoporphyrin (ZPP) assays in patients with alpha and beta thalassaemia trait.1 We have been using ZPP assays (protoporphyrin, Hemolab) as a screen for iron deficiency since July 1991.

The normal range quoted by Tillyer and Tillyer is much wider than we would expect from our own experience, and assume that some of their “normals” with high ZPP values were indeed iron deficient, especially as 25% of subjects were pregnant. Other reasons for an increase in ZPP must also be considered, such as interfering substances and, rarely, lead poisoning. Our 95% confidence range is 30–65, rather than 38–104 μmol/mol haem.

We agree that in β thalassaemia trait the ZPP is wider and merges into those ranges found in iron deficiency. It may indicate some impaired iron utilisation in thalassae mia trait. In 58 consecutive patients with β thalassaemia trait (microcytosis + HbA2 ≥ 3-0%, SD) ZPP (mean ± SD) was 63.7 (19.7) μmol/ml haem. A ZPP of > 120 is likely to indicate iron deficiency in thalassaemia trait and we usually request postponing haemoglobinopathy studies until the patient has received a trial of iron treatment. If the ZPP value is raised out of clinical context, it may be useful to make repeat measurements with washed red cells to remove interfering substances.2

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Haemorrhagic disorders in pregnancy

The guidelines produced by the Haemostasis and Thrombosis Task Force1 mention the management of congenital platelet disorders.2 For those patients who do not require platelet transfusions, single donor platelets are considered a reasonable alternative to plasma to correct bleeding. Using a single donor of ABO compatible but otherwise unmatched leucocyte depleted single donor platelets (Cobe Spectra Blood Processor) containing a platelet content of 2-8 x 10^9/l and a leucocyte content of 0-05 x 10^9/l may be necessary.3

There was little bleeding after birth. We suggest that such depleted platelets are a practical alternative to avoiding single leucocyte undepleted donor or type specific platelets when the aim is to reduce the incidence of platelet antigen specific and HLA alloimmunisation.4 An added advantage is the reduced risk of transmission of cytomegalovirus.5

Although DDAVP has been used without complication during labour, cases of maternal water retention precipitating grand mal seizure (after repeated treatment) have been reported.6

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1 Tillyer ML, Tillyer CR. The “normals” we studied were not clinically iron deficient: the MCV and MCH of this group corresponded exactly to established reference ranges and all had plasma ferritin values well within the accepted normal range.

2 Tillyer ML, Tillyer CR: comment: The “normals” we studied were not clinically iron deficient: the MCV and MCH of this group corresponded exactly to established reference ranges and all had plasma ferritin values well within the accepted normal range.


Pregnancy in von Willebrand's disease.

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