Correspondence

Cytological changes preceding cervical cancer

Dr Robertson and colleagues must be con-
gratulated for holding up the “red flag of classification” to the “bulbs of gynaecological
-cytology” and, high grade, adenocarcinoma
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).1,2
However, published information1,2 and
recommendations for classification make it
likely that this 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 they rate a six month repeat smear and
the histopathological diagnosis of CIN.4

Health Service guidelines emphasise the
important requirement to compare cyto-
logy and biopsy results.5 However, the cru-
ical audit question 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,6 the apparent little discussion with
regard to the possible introduction of the
American Bethesda system for reporting
cervical smears.7 Indeed, some cynics believe that Dr Robertson’s introduction was
doomed following the timing of the publica-
tion, which coincided with the printing of
several million new HMR forms. However, though the Bethesda system uses the terms
dyskaryosis, low grade squamous intraepithelial lesions, its overall complexity and content is analogous to that of the cur-
rent British system. Accordingly, unlike Dr
Robertson, I share previous authors’ views8
that the Bethesda system has little to com-
ment in.

I suspect that many gynaecological cytopathologists already perceive nuclear
changes as either low or high grade abnor-
malities. It is therefore reassuring to see that
Dr Robertson’s scientific conclusion supports this view. With little difficulty, cur-
rent national recommendations for termi-
ology and management of cervical smear
could be amalgamated along the following
lines:

Borderline changes, wart virus, and mild
dyskaryosis could be grouped together as
low grade abnormalities. These would necessitate a six month repeat smear and, if persistent, require referral for colposcopy.

Moderate and severe dyskaryosis could be
grouped together as high grade abnor-
malities, with the necessity for immediate
referral for colposcopy.

Gynaecological cytology has now become
a nationalised industry with a propagated
aura of sophisticated diagnostic accuracy.
This has resulted in unbounded success in the
field of “cytology job and working party
creation schemes”. However, as the diag-
nostic gold standard of CIN has partially
collapsed, it is hard to believe that gynaecol-
ogical cytology will not contribute to this.

Which cytopathologist, with their hands
on their hearts, can deny that accurate distinc-
tion between borderline changes, wart virus,
and mild dyskaryosis is difficult, and even
impossible, time consuming, and a largely
pointless pursuit? These changes are all far
more realistically grouped together as low
grade abnormalities, requiring the same
clinical management. The hours saved by
avoiding such mental contemplation would
be enormous.

We should not lose sight of the fact that
the basic function of gynaecological cytology
is merely to screen for relevant disease that
will require subsequent histopathological
diagnosis and clinical management. It must
be seriously questioned whether the exist-
ance of multiple, closely related, diagnostic
categories is warranted. Furthermore, it is
rumoured that this problem is about to be
compounded by division of the category of
borderline changes. Superficially, credibility
for the existence of the current terminology
seems to be the result of mass of defini-
tions returned annually and the
requirement for these subtle distinctions to
be assessed in quality assurance schemes.

It is also questionable as to whether this
complexity should continue to be the staple of
cytology training schools. My proposition is simple: back to cyto-
logical basics, because it is too late.

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2 Evans DMD, Hudson EA, Brown CL et al.
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report of the Working Party of the British Society

3 Evans DMD, Hudson EA, Brown CL et al.
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cervical cytology: Supplement to terminology
in gynaecological cytopathology. J Clin Pathol
1993;46:96-5.

4 Robertson AJ, Anderson JM, Swanson Beck J,
et al. Observer variability in histopatho-
 logical diagnosis of cervical biopsy specimens.

5 Ismail SM, Colclough AB, Dinnen JS et al.
Observer variation in histopathological
diagnosis and grading of cervical intra-

6 NHS Management Executive, Health Service
Guidelines. HSG (73) 41, National Cervical
Cytological Screening Programme 1993. London: DoH,
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7 Hudson E. Cervical cytology. BMJ 1990;
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8 Robertson AJ, Hussein K, Swanson Beck J,

9 National Cancer Institute Workshop. The
1988 workshop on criteria for reporting cervical/vaginal

Dr Robertson, Woodend, and Elliott comment:
We agree with most of Dr Slater’s com-
ments, but would never have dared multi-
ple. They draw attention to the Emperor’s new clothes and suggest rebel-
lion in the ranks. We also have long
regarded cervical cytology as a screening
procedure with limited diagnostic precision
apart from its detection of severe dyskaryosis.

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, papilloma-
virus 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 frighten-
ing for some women, giving the impression
of a limbic 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’s disease,
we have recently studied 23 pregnancies
managed at a single centre,2 and add the
following comments.

We believe there is a tendency towards
complacency in the management of
pregnant women with von Willebrands
disease due to an excessive reliance on
improvement in the coagulation defect. The
coaagulation parameters improve in many
instances, but as a group of six cases
(exceptions, particularly in those more
everly 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.3,4 In addition, our
observations support the view that type II
patients carry a higher risk of primary post-
partum haemorrhage (3/11 type II vs
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 effector system to improve.

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 Willibrand’s disease in
pregnancy. We would like to comment that
with reference to secondary PPH, while
the administration of prophylactic von
Willebrand factor (vWF) containing
Haemorrhagic disorders in pregnancy

The guidelines produced by the Haemostasis and Thrombosis Task Force mention the management of congenital platelet disorders.1 For those patients who do not require platelet transfusions, single donor platelets or platelet type specific donor platelets are advised. I have recently treated a 16 year old girl with storage pool deficiency, during labour, by using a single donation of ABO compatible but otherwise unmatched leucocyte depleted single donor platelets (Cobe Spectra Blood Processor) containing a platelet content of 2.8 × 10^11 and a leucocyte content of 1.9 × 10^7.

There was little bleeding after giving birth.

I suggest that such depleted platelets are a practical alternative to infusing single leucocyte undepleted donor or type specific platelets when the aim is to reduce the incidence of platelet antigen specific and HLA alloimmunisation. An added advantage is the reduced risk of transmission of cytomegalovirus.

Although DDAVP has been used without complication during labour, cases of maternal water retention precipitating grand mal seizure (after repeated treatment) have been reported.2

Zinc assays in patients with a 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, haemoglobin A, ferritin, HbA2, and HbA) 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 presume 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 thalassaemia trait. In 58 consecutive patients with β thalassaemia trait (microcytosis + HBA, > 3-6%) SD ZPP was 63.7 (19-7) μmol/mol 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 appropriate 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.

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