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Cervical Cyto/Histological Nomenclature

Making Practical Sense of Past and Recent Changes

Before the early 1980s the cytology and histopathology categories of precancerous cervical changes were termed mild, moderate and severe dysplasia (or dyskaryosis) and carcinoma in-situ. Furthermore, a distinctive cytoplasmic clearing in squamous cells was termed koilocytosis, without knowing what exactly caused it.

In the early 1980s electron microscopy determined that koilocytosis was due to HPV infection, later confirmed by the emerging DNA technologies (which also confirmed that cervical cancers contain HPV DNA). So koilocytosis and HPV cytological changes are synonymous. At the same time the histological HPV changes were described as flat condyloma and distinguished from premalignant neoplastic dysplasia.

Also at the same time it was accepted that the distinction between severe dysplasia and carcinoma in-situ didn't exist; the new nomenclature of cervical intraepithelial neoplasia (CIN 1, 2 & 3) was introduced and the label "carcinoma in-situ" dropped.

As the study of evolution of HPV infection and CIN progressed it became obvious that most HPV infections regressed spontaneously (in the immuno-competent – may take up to 2 years), that progression of CIN occurred in stages, that progression to invasive cancer does not happen in every case and, when it does, usually takes several years to do so.

Way back in the 1960s a New Zealand gynaecologist, a certain Mr Green, began a clinical trial (would now be deemed unethical) of following up cases of reported cervical dysplasia, with no ablative treatment whatsoever, to try and prove his theory that reported "dysplasia" had nothing to do with invasive cervical cancer. One needs to remember that in the 1960s the concept of neoplasia as a multi-step/multi-mutation gradual process (pre-malignancy) was a novel and controversial concept. In 1972 he presented his ongoing findings at the histopathology department of the Royal Marsden Hospital in London (I was SHO there that year) – he claimed that most reported dysplasia regressed spontaneously, some reported dysplasia persisted but none progressed to cervical cancer. In the 1960s and 70s the existence and role of HPV was unknown and the observed regression of many "dysplasias" was probably due to regressed HPV changes and not high grade CIN.[1]

The Americans then suggested a simpler CIN grading of low (CIN 1) and high grade (CIN 2/3). This correlated with management recommendations – cytological and histological CIN 1 could safely be followed-up while CIN 2 & 3 needed ablation. Cytological HPV changes (koilocytosis) and histological HPV changes (flat condyloma) could also be safely followed-up, rather than ablated by cone biopsy and risking damaging cervical competence in young women.

More recently the US Bethesda system[2,3] introduced new nomenclature aimed at standardising laboratory reporting but which may create more confusion. What was called "borderline changes" becomes "atypical squamous cells of undetermined significance" (ASCUS). "Borderline" is usually used when the microscopist is unsure whether the slight cellular changes are within normal limits or whether these could represent HPV or CIN 1 changes. What we diagnosed as "HPV changes", or "HPV/?CIN 1" on a smear, Bethesda now recommends "low grade squamous intraepithelial lesion" (LGSIL or LSIL). "CIN 2/3" is Bethesda "high grade squamous intraepithelial lesion" (HGSIL or HSIL). Bethesda does however stick to the old recommendation for follow-up of reported HPV and CIN 1 changes, and for colposcopy and ablation of CIN 2/3 lesions.

Management confusion may accompany "ASCUS" cytology reports, when they are followed immediately by colposcopy and by ablation of some histological "CIN 1" lesions

Distinguishing CIN 1 from reactive/inflammatory/reparative non-neoplastic atypia is very subjective and, therefore, over-investigation and too aggressive treatment in young women is possible. The same could be said for "inflammatory" smears being followed-up by immediate colposcopic biopsy rather than cytology. It is important to keep in mind that invasive cervical cancer doesn't develop overnight but takes several years to do so and one practically always sees it in women (not young girls) who have never (or rarely) had screening cytology.

HPV DNA technology has helped diagnosis particularly when oncogenic (high risk) HPV is present, but ablative therapy can only be justified on a histological report of CIN 2/3 and not on an HPV PCR report. The HPV PCR test has replaced screening cytology in some centres where smear reporting was deemed too slow or diagnostically unreliable – the usual routine here is HPV testing every 5 years and colposcopy if oncogenic HPV is reported.

What about the "inflammatory smear"? Different cytology screening staff have different criteria for diagnosing "non-specific inflammation". Some of them ignore neutrophils in smears and report inflammation only when a non-specific perinuclear vacuolation is present. I do not agree with this interpretation because too many neutrophils may signal a clinically important sexually-transmitted bacterial infection.

Reporting "inflammation" is therefore very subjective. I report it only when there is a significant excess of neutrophils. Relatively small numbers of neutrophils may be regarded as within normal physiological limits (including frequent sexual activity). Judging between relatively small and significant excess of neutrophils is not always easy. It is then entirely up to the clinician's judgement as to whether reported "inflammation" needs any further action.

References can be accessed on **www.thesynapse.net**