Diagnostic Pathology: Open Access

Valente, Diagn Pathol Open 2016, 1:3
DOI: 10.4172/2476-2024.1000e104

Editorial OMICS International

Is There Virtue in CIN? At Last an Answer!

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Received date: December 21, 2016; **Accepted date:** December 22, 2016; **Published date:** December 28, 2016

Citation: Philip T. Valente (2016) Is There Virtue in CIN? At Last an Answer!. Diagn Pathol Open 1: e104.

Editorial

Standardization of diagnostic terminology has become the Holy Grail of anatomic pathology. Reproducibility of diagnosis and uniform treatment guidelines are the desired goals. In cervicovaginal cytopathology it started with the Bethesda System which introduced a two tier system of low grade (HPV, CIN1) and high grade squamous intraepithelial lesion (CIN2, CIN3). This was originally intended to replace the bewildering variations of the Papanicolaou class system of the late 1980's which was resulting in under- and overtreatment of cytological abnormalities.

The Bethesda System and its subsequent modifications have been a great success and have been incorporated into Pap HPV co-testing algorithms developed by the American Society for Colposcopy and Cervical Pathology (ASCCP). The widespread acceptance of the SIL system for Pap tests, a two tier system, led many pathologists to reconsider the use of cervical intraepithelial neoplasia (CIN), a less reproducible three tier system. SIL applied to cervical biopsies would presumably result in more reproducible diagnoses.

These considerations together with our improved understanding of HPV carcinogenesis in the lower anogenital tract led the ASCCP and the College of American Pathologists (CAP) to convene a meeting in San Francisco in March 2012 to consider a revision of diagnostic terminology for HPV related precancer and early invasive neoplasia of the lower anogenital tract and standardize an approach for the use of immunohistochemistry in diagnostic biopsies.

The Lower Anogenital Squamous Terminology Standardization Project for HPV Associated Lesions was established with five working groups to develop draft proposals for terminology changes which would correspond to a concept of a unified epithelial biology of HPV related squamous neoplasia and clarify the optimal use of immunohistochemistry in routine diagnostic practice [1]. Over a two day period these draft recommendations were presented to representatives of thirty-five stakeholder organizations consisting of professional societies and government agencies. I represented the American Society of Cytopathology. After a discussion the representatives present were electronically poled and a minimum of 70% of voting delegates had to agree for the proposal to be accepted.

If not accepted the proposal was reworked and resubmitted by the appropriate working group to achieve a broader consensus.

The debate was often lively and pathologists, clinicians and government representatives expressed their concerns often with a passion one would expect at a political convention working out the party platform.

The most controversial area was diagnostic terminology. Some argued that Pap and biopsy terminology should remain separate reserving SIL for Paps and keeping CIN, VIN, VAIN, etc. for biopsies. Others, mainly pathologists recommended applying the more reproducible two tier SIL system to both to enhance correlation and diagnostic reproducibility. Several clinicians vehemently objected to the abolition of CIN since the three tiered grading of CIN was important to avoid overtreatment of lesions in young women. Pathologists countered that distinguishing CIN grade was less reproducible than using low grade *vs.* high grade SIL. The clinicians were unmoved by this argument. After all, the ASCUS of the Bethesda System has been shown not to be "reproducible" in many studies but it is still useful in conjunction with HPV co-testing. A compromise was reached in that Pap would be diagnosed as low grade or high grade SIL; biopsies would also use the SIL system but with the three tier grading system in parenthesis, e.g. high grade SIL (CIN 2, VIN 2, VAIN 2, etc.).

The other major message of the LAST project was the judicious use of p16 staining, only to distinguish high grade CIN from mimics such as immature squamous metaplasia or atrophy. Its use for histologically obvious CIN 3 or CIN 1 was strongly discouraged.

The CAP-ASCCP sponsored LAST Project meeting was a great example of how professional societies can collaborate to establish the optimal approach to evidence based pathologic diagnosis while considering the clinicians needs for patient management. While many questions were answered by the LAST Project, you can be sure that this is not the LAST word on the subject.

References

1. Darragh TM, Colgan TJ, Cox JT, Heller DS, Henry MR, et al. (2012) The Lower Anogenital Squamous Terminology Standardization Project for HPV Associated Lesions: Background and Consensus Recommendations from the College of American Pathologists and the American Society of Colposcopy and Cervical Pathology. Arch Pathol Lab Med 136: 1266-1297.