Abstracts: Summer 2007

The following abstracts are taken from journals of interest to our readers and are reviewed by Thomas M. Julian (TMJ) and Richard S. Guido (RSG).

Review of Cytologic Slides from the National Women's Hospital, New Zealand, Cohort of Women with Cervical Intraepithelial Neoplasia 3 Diagnosed in 1955–1976

MR McCredie, G Medley, KJ Sharples, RW Jones, J Baranyai, C Paul, DC Skegg

Acta Cytol 2006 Nov–Dec;50(6):632–6

Objective. To review cytologic slides, mostly at least 25 years old, from women attending National Women's Hospital, Auckland, who had been diagnosed histologically with cervical carcinoma in situ in 1955–1976.

Study Design. Smears comprised all those from the 2 years following diagnosis as well as all subsequent smears for women who developed "microinvasive" or invasive lower genital tract cancer. The Victorian Cytology Service performed the review using the Australian Modified Bethesda System.

Results. Nine percent of 4,930 retrieved slides were technically unsatisfactory. Original (Papanicolaou) and review coding were available for 4,477 slides. Using categories of equivalence, smears coded as normal (original, 59.2%; review, 61.4%) or showing possible or definite high grade abnormalities (original, 25.9%; review, 29.6%) were found in similar proportions. The kappa statistic (0.79) indicated a high level of agreement between original and review coding. In comparison with the review, the sensitivity of the original coding in detecting high-grade abnormalities was 0.80, while the ability of the original assessment to categorize smears as not high grade (specificity).

Conclusion. This comprehensive review found nearly all archived cytology slides to be technically satisfactory and the broad diagnostic cytologic categories from earlier periods (apart from benign lesions) to be concordant with those currently used.

Comment: I thought it was reassuring that 30- to 50-year-old cytological material when reviewed today is interpreted similarly. Some things may not change all that much despite our best efforts to find the new and improved ways of doing things. (TMJ)

Efficacy and Cost-Effectiveness of Nationwide Cervical Cancer Screening in Taiwan

SL Koong, AM Yen, TH Chen

J Med Screen 2006 Dec;13(suppl 1):44–7. Links

The annual cervical screening programme using the Papanicolaou (Pap) smear test was launched for women aged 30 years and over from 1995 in Taiwan. This study aimed to evaluate the Taiwanese cervical screening policy and to make recommendations based on the empirical findings from cervical screening data between 1995 and 1998. We used a stochastic process to model the natural history of precancerous lesions and cervical cancer. Based on the estimated results, Monte-Carlo computer simulation was used to evaluate the effectiveness in terms of the reduction in incidence of and mortality from cervical cancer for screening regimes with different screening intervals. Annual Pap smear screening with 100% compliance was estimated to lead to an approximate 80% reduction in deaths from cervical cancer. With 50% compliance, around a 40% reduction was expected. Triennial screening with high compliance was as effective as annual screening with low compliance, and more cost-effective. Based on the observed Taiwan Pap smear–screening programme between 1995 and 1998, with 44.5% women attending at least once, there was an estimated reduction of 16% in deaths from cervical carcinoma. The estimated effectiveness was greater when the period was extended to 2001, in which period 61% of women attended at least once. The screening programme by 2001 was estimated to reduce cervical cancer mortality by 50% (95% confidence interval: 29–65%).

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The incremental cost-effectiveness was estimated as 8174 dollars per additional life-year gained. In conclusion, triennial screening targeting women aged 30–69 is recommended, along with efforts to enhance the compliance rate.

Comment: This study shows what universal cervical cytological screening can accomplish. A cost-effectiveness of $8,000 per life-year is truly phenomenal. It shows that our push should be toward universal screening of appropriate populations as much as it should be to more sensitive smears, high-technology interpretation systems, and vaccine. (TMJ)

EMG Biofeedback Versus Topical Lidocaine Gel: A Randomized Study for the Treatment of Women with Vulvar Vestibulitis

I Danielsson, T Torstensson, G Brodda-Jansen, N Bohm-Starke

Acta Obstet Gynecol Scand 2006;85(11):1360–7

Background. To evaluate the efficacy of electromyographic biofeedback and topical lidocaine treatment for women with vulvar vestibulitis.

Methods. A prospective randomized study where 46 women with vulvar vestibulitis were randomized to receive either electromyographic biofeedback or topical lidocaine treatment for four months. Assessments with vulvar pressure pain thresholds and questionnaires regarding quality of life, psychosocial adjustments, and sexual functioning were made before treatment, after treatment, and at six- and 12-month follow-ups. Nonparametric statistical methods were used to analyze differences in outcomes.

Results. Nine women (9/46) dropped out during the treatment period. Both treatments showed significantly improved values for vestibular pressure pain thresholds, quality of life measurements, and sexual functioning at the 12-month follow-up. No differences were found between the two treatment groups. No severe side effects were reported.

Conclusions. Four months' treatment with electromyographic biofeedback and topical lidocaine gave statistically significant improvements on vestibular pain measurements, sexual functioning, and psychosocial adjustments at the 12-month follow-up. No differences in outcome between the two treatments were observed but a larger sample may be needed to obtain significance. The treatments were well tolerated but the compliance to the electromyographic biofeedback training program was low. A combination of both treatments could potentially benefit many women with vulvar vestibulitis.

Comment: Vulvar pain is a difficult problem to treat. This study showing topical lidocaine to be as effective as biofeedback is certainly disparate with what proponents of biofeedback have published. The problem with this study is that it lacks placebo controls or longitudinal controls to tell us how effective either method is in treating the pain. (TMJ)

Colposcopy at a Crossroads

J Jeronimo, M Schiffman

Am J Obstet Gynecol 2006;195:349–53

New cervical cancer prevention strategies are arising from rapidly improving insight into human papillomavirus (HPV) natural history and cervical carcinogenesis, challenging the conventional roles of cytology and colposcopically directed biopsy as the reference standards of screening and diagnosis, respectively. HPV testing has high sensitivity but mediocre specificity and positive predictive value, making the role of colposcopy for the accurate identification of patients requiring treatment even more important. We believe that deficiencies of the colposcopically guided biopsy must be addressed, in particular, the inaccuracy of biopsy placement leading to low sensitivity for detection of CIN3. This opinion outlines our concerns and summarizes new data, suggesting possible steps that may lead to improvement in colposcopic accuracy.

Comment: This important clinical comment highlights some of the critical questions that challenge clinicians in an era of HPV testing. The authors comment on the limitations of colposcopy and how this impacts our ability to diagnosis high-grade disease. This summary is important for any clinician practicing colposcopy, as it will very likely influence the number and location of biopsies he/she performs. (RSG)

Predicting Absolute Risk of CIN3 During Post-Colposcopic Follow-Up: Results from the ASCUS-LSIL Triage Study (ALTS)

JL Walker, SS Wang, MSD Solomon, for the ASCUS LSIL Triage Study (ALTS) Group

Am J Obstet Gynecol 2006;195:341–8

Objective. At present, clinical management of women referred to colposcopy but found to have <CIN2 remains unclear. Using data from the ASCUS-LSIL Triage Study (ALTS) to inform clinical management, we calculated the absolute risk for developing CIN3 within 2 years of referral to an enrollment colposcopy.

Study Design. Women included in the analyses (1) were initially referred to ALTS with a community cytologic interpretation of atypical squamous cell of undetermined significance (ASCUS) or low-grade squamous intraepithelial lesions (LSIL); (2) had a colposcopic evaluation and biopsy, if indicated, resulting in a diagnosis <CIN2; and, therefore, (3) were followed without treatment. Results from subsequent human papillomavirus (HPV) testing, liquid-based cytology interpretations, and a second colposcopic evaluation at least 6 months after and within 2 years of the first colposcopic evaluation were used to calculate absolute risks for CIN3.

Results. Women with HPV-negative test results were at low risk for CIN3 regardless of other test results. Among HPV-positive women, increasing absolute risks of CIN3 were observed with increasing cytology severity: 7% (normal), 11% (ASCUS and LSIL), and 45% (HSIL). The highest absolute risk for CIN3 (67%) was observed for HPV-positive women with HSIL and a colposcopic impression of high-grade/cancer on the second colposcopy.

Conclusion. In the ALTS population, after the first colposcopic diagnosis of CIN2, clear risk stratification for CIN3 outcomes was obtained among women with a subsequent HPV-positive test. Because absolute risk for histologic CIN3 outcomes was high for women with HPV positive tests, HSIL cytology, and a high-grade impression at second colposcopy, it is worth considering whether this combination of findings might warrant immediate excisional therapy in some circumstances.

Comment: Managing patients with mildly abnormal pap (ASC and LSIL) test can be divided into the initial triage and follow-up. This article tries to address how various tests perform in evaluating subjects in the follow-up phase of clinical care. Once the clinician has ruled out CIN 2 or greater with their initial colposcopic examination, they are left with a variety of tools (HPV testing, cytology, and colposcopy) to follow the patient. The strength of this article lies not only with the data provided regarding the sensitivities of the various diagnostic tools but also the absolute risk of different subsets of women for developing CIN 2 or greater. (RSG)

Subsequent Risk and Presentation of Cervical Intraepithelial Neoplasia (CIN) 3 or Cancer after a Colposcopic Diagnosis of CIN 1 or Less

RG Pretorius, PPF Azizi, RJ Burchette

Am J Obstet Gynecol 2006;195:1260–5

Objective. The purpose of this study was to determine the risk and presentation of cervical intraepithelial neoplasia (CIN) 3 or cancer after colposcopic diagnosis of CIN 1 or less.

Study Design. After colposcopy for an abnormal cytology, women with CIN 1 or less had annual cytology evaluations and high-risk human papillomavirus (HPV) tests (Hybrid Capture II). Colposcopy was repeated if the cytology result was ASC-H, or worse, ASC-US/high-risk HPV test positive, or every 2 years if the cytology was normal/high-risk HPV test positive. Differences in rates of CIN 3 or cancer were compared by log rank Kaplan-Meier survival analysis.

Results. With median follow-up periods of 26.3 months, 47 of 2490 women (1.9%) with CIN 1 or less subsequently had CIN 3 or cancer. Subsequent CIN 3 or cancer was more likely if the high-risk HPV test was initially positive (45/1960 women [2.3%]) compared with negative (2/530 women [0.4%]; $p = .0002$) and if women were older (age ≥30 years, 28/1021 women [2.7%]; age 20–29 years, 17/1017 women [1.7%]; age <20 years, 2/452 women [0.4%]; $p = .045$). When CIN 3 or cancer was diagnosed, 45 of 46 women (97.8%) had positive high-risk HPV test and 42/46 women (91.3%) had an abnormal cervical cytology. The yield of CIN 3 or cancer per colposcopy for women (4/205 women [2.0%]) who had normal cervical cytology/positive high-risk HPV tests was lower than for women (41/541 women [7.6%]) who had abnormal cervical cytology/positive high-risk HPV tests (χ^2 test, 8.3; $p < .005$), and it did not increase with increasing length of follow-up.

Conclusion. Annual cytology and high-risk HPV tests with colposcopy for high-risk HPV test positive/abnormal cytology and at least every 2 years for high-risk HPV test positive/normal cytology are advised after a colposcopic diagnosis of CIN 1 or less.

Comment: This article along with the Walker article (*Am J Obstet Gynecol* 2006;195:341–8) highlight the importance of appropriate follow-up strategies for women with ASC and LSIL. The authors used a large retrospective database to evaluate the strengths HPV testing, cytology, and colposcopy in identifying subsequent CIN 2/3. A number of clinical characteristics, age, persistence of HPV infection, and worsening cytology are identified as predictors of the development of CIN 2 or 3. The authors recommend adding HPV testing to annual cytology in clinical care of this patient population. This suggestion does provide added sensitivity; however, this follow-up strategy has not been fully evaluated in a prospective study with an associated cost analysis. (RSG)