Management of Abnormal Smears

9 October 2010
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Management of Abnormal Smears

• 2001 Consensus Guidelines for the Management of Women with Cervical Cytological Abnormalities (Wright et al JAMA 2002;287:2120-29)

• ACOG Committee Opinion No. 330 (Obstet Gynecol 2006;107:963-8)

• 2006 Consensus Guidelines for the Management of Women with abnormal Cervical Cancer screening tests (Wright et al AJOG 2007;346-55)
1 INTRODUCTION

The Guidelines on the Management of Abnormal Cervical Cytology was revised in 2002 because of the revision of the Bethesda System in 2001 and the introduction of HPV testing in the management of atypical squamous cells. This revision is based on new information being available, including the ASC-US/LSIL Triage Study (ALTS) and the use of HPV testing as an adjunct in cervical cytology. In this guideline, HPV testing refers to testing for high-risk HPV types \(^{(1,2,3)}\).

In this revision, the recommendations for atypical squamous cells (ASC) and low-grade squamous intraepithelial lesion (LSIL) are essentially unchanged, except in special

when it forms part of an organized programme of screening \(^{(4)}\).

2.3 The long latency which normally exists between the emergence of precursor lesions and occurrence of invasive, life threatening disease provides the foundation of the screening program for cervical cancer \(^{(5)}\).

3 TARGET POPULATION AND SCREENING INTERVAL

3.1 The target population encompasses all women from age 25 or the time of commencing sexual activity (whichever is later) until they reach 65 years of age. In view of the rarity of
Welcome to The Hong Kong Society for Colposcopy and Cervical Pathology
Colposcopy Service Provision and Standard

(1) All colposcopy should be performed by colposcopists or trainees under supervision.
(2) Colposcopists must have undergone training in colposcopy recognized by the HKCOG.
(3) The service should record the waiting times for both new patients and treatments.
   - for patients with cytology showing invasive lesion, patient should be offered an appointment to be seen within two weeks.
   - for patients with cytology showing high grade SIL, patient should be offered an appointment to be seen within 6 weeks.
   - for patients with cytology showing ASCUS where high grade lesion cannot be excluded or AGUS favors neoplastic or two consecutive ASCUS/AGUS not otherwise specified or low grade SIL, patient should be seen within 12 weeks.
(4) The service should adhere to local written protocols that should reflect published Guidelines in Hong Kong.
(5) The service should ensure adequate data collection for quality assurance at annual reviews.
ASC-US

- Reflex HPV DNA testing – refer for colposcopy if positive; if negative, repeat smear at 12 months
- Repeat smear at 4-6 months and refer for colposcopy if abnormality persists; return to routine screening after 2 repeat negative
- (Immediate colposcopy – if negative, repeat smear in at 12 months)
- Colposcopy service standard: should be seen within 12 weeks
<table>
<thead>
<tr>
<th>Action</th>
<th>Action</th>
<th>Colposcopy service standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASC-H, LSIL</td>
<td>Refer for colposcopy</td>
<td>Seen within 12 weeks</td>
</tr>
<tr>
<td>HSIL</td>
<td>Refer for colposcopy</td>
<td>Seen within 6 weeks</td>
</tr>
<tr>
<td>Invasive cancer</td>
<td>Biopsy if frank growth; otherwise early referral for colposcopy</td>
<td>Seen within 2 weeks</td>
</tr>
</tbody>
</table>
Abnormal glandular cells

- Can perform endocervical sampling
- Refer for colposcopy
- Colposcopy service standard: seen within 12 weeks
- AGC-endometrial cells – endometrial sampling first
- (AGC-favor neoplasia, AIS – early referral for colposcopy)
Management of Abnormal Smears

• Special circumstances – postmenopausal women, pregnant women, adolescents
• Endometrial cells
Thank you

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面白さがたらないかっただら
全額返金しバスターズ!!
詳しくはhenkin.jp
もし、面白くなければ返金します
公開から4日間限定
11.20(金)-11.23(月・祝)

ケンディ・タランティーノ監督
イングロリオジュス・バスターズ
Management of Abnormal Smears

- Cervical cancer in adolescents: screening, evaluation, and management. ACOG Committee Opinion No. 463(Obstet Gynecol 2010;469-472)
Cervical Cytologic Screening Guidelines from the American College of Obstetricians and Gynecologists, 2009.

<table>
<thead>
<tr>
<th>Age</th>
<th>Recommendation for Cytologic Screening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 21 yr</td>
<td>Avoid screening</td>
</tr>
<tr>
<td>21 to 29 yr</td>
<td>Screen every 2 yr</td>
</tr>
<tr>
<td>30 to 65 or 70 yr</td>
<td>May screen every 3 yr*</td>
</tr>
<tr>
<td>Between 65 and 70 yr</td>
<td>May discontinue screening†</td>
</tr>
</tbody>
</table>

* This recommendation applies only to women with three consecutive negative cytologic tests; exceptions include women with human immunodeficiency virus infection, compromised immunity, a history of cervical intraepithelial neoplasia grade 2 or 3, or exposure to diethylstilbestrol in utero.

† This recommendation applies only to women with three or more consecutive negative cytologic tests and no abnormal tests in the preceding 10 years; exceptions include women with multiple sexual partners.

(Sawaya 2010 NEJM 361:2503-5)
• An adolescent with a history of normal cytologic screening in the past should not be rescreened until age 21 years
• If an adolescent has had a Pap test result of ASC-US or LSIL or CIN I histology in the past, but has had 2 subsequent normal Pap test results, rescreening can be delayed until age 21 years

(ACOG Committee Opinion 463)
Management of Abnormal Smears

• Guidelines
• Endometrial cells
• Smear test specimen adequacy
• Infections in cervical smear
• Calling patient back
• Other issues
## Endometrial cells

<table>
<thead>
<tr>
<th>After menopause</th>
<th>Investigation recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;=40</td>
<td>Interpret the smear result together with the clinical findings to determine the management</td>
</tr>
<tr>
<td>&lt;40</td>
<td>Treat as normal</td>
</tr>
</tbody>
</table>
European guidelines for clinical management of abnormal cervical cytology, Part 2


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Accepted for publication 10 September 2008


European guidelines for clinical management of abnormal cervical cytology, Part 2

The current paper presents the second part of chapter 6 of the second edition of the European Guidelines for Quality Assurance in Cervical Cancer Screening. The first part of the same chapter was published in a previous issue (Cytopathology 2008;19:342–54). This part provides guidance on how to manage and treat women with
Management of cervical smears showing endometrial cells

• Follow up by repeat cervical cytology is not appropriate
• Endometrial cells in keeping with the stage of the cycle – no need for further investigation
• Endometrial cells not in keeping with stage of the cycle – no need for further investigation in young women, but may require assessment in older women

Jordan et al 2008 Cytopathology 19:342-54
• Endometrial cells in women with an IUD – no need for further investigation
• Normal appearing endometrial cells in a postmenopausal woman – always warrant further assessment even if the woman is using oestrogen replacement therapy. The minimum assessment should be a vaginal ultrasound to assess the endometrial thickness
• Atypical endometrial cells or cytological findings suggestive of endometrial adenocarcinoma – ultrasound, hysteroscopy and biopsy or diagnostic curettage

Jordan et al 2008 Cytopathology 19:342-54
Other than during the first half of the menstrual cycle, the presence of spontaneously exfoliated endometrial cells in the Pap smear is abnormal. The preferred cutoff day for abnormal shedding ranges from day 10 to 14, according to different authorities.
ASCCP Patient Management Guidelines: Pap Test Specimen Adequacy and Quality Indicators

Diane D. Davey, MD, Chair,¹ R. Marshall Austin, MD, PhD,² George Birdsong, MD,³ Henry W. Buck, MD,⁴ J. Thomas Cox, MD,⁵ Teresa M. Darragh, MD,⁶ Paul A. Elgert, CT (ASCP),⁷ Vivien Hanson, MD,⁸ Michael R. Henry, MD,⁹ and Jeffrey Waldman, MD¹⁰

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ASCCP Patient Management Guidelines

• Negative but lacking an endocervical/transformation zone component – repeat in 12 months; within 6 month may be beneficial for patients with previous squamous abnormality, previous unexplained glandular abnormality, positive high risk HPV within 12 months, inability to clearly visualise the cervix, immunosuppression, insufficient previous screening

• Negative but partially obscuring blood, inflammation, other partially obscuring factors, or partial air drying – same; also consider early repeat if similar obscuring factor in consecutive test
ASCCP Patient Management Guidelines

• Unsatisfactory – repeat within a short interval of 2-4 months; consider specific treatment if due to obscuring inflammation

• Repeatedly unsatisfactory because of obscuring blood, inflammation or necrosis – colposcopy or biopsies

(Davey 2002 J Lower Gen Tract Dis 195-199)
Diagnostic procedures for the evaluation of abnormal cytology

Repeat cytology

- The cervical epithelium needs time to regenerate after cytology. Repeat cytology should not be performed <3 months after a previous test.

Jordan et al 2008 Cytopathology 19:342-54
This Guidance provides information for clinicians providing women with copper-bearing intrauterine devices as long-term contraception. A key to the grades of recommendations, based on levels of evidence, is given at the end of this document. Details of the methods used by the Clinical Effectiveness Unit (CEU) in developing this Guidance and evidence tables summarising the research basis of the recommendations are available on the Faculty website (www.ffprhc.org.uk). Abbreviations (in alphabetical order) used include: acquired immune deficiency syndrome (AIDS); actinomyces-like organisms (ALOs); automated external defibrillator (AED); blood pressure (BP); British National Formulary (BNF); confidence interval (CI); copper-bearing intrauterine contraceptive device (IUD); emergency contraception (EC); Faculty Aid to Continuing Professional Development Topic (FACT); levonorgestrel-releasing intrauterine system (IUS); human immunodeficiency virus (HIV); Medicines and Healthcare products Regulatory Agency (MHRA); non-steroidal anti-inflammatory drugs (NSAIDs); odds ratio (OR); pelvic inflammatory disease (PID); relative risk (RR); Royal College of Obstetricians and Gynaecologists (RCOG); Scottish Intercollegiate Guidelines Network (SIGN); sexually transmitted infection (STI); termination of pregnancy (TOP); World Health Organization (WHO); WHO Medical Eligibility Criteria (WHOMEC); WHO Selected Practice Recommendations (WHOSPR).

What is intrauterine contraception?
This Guidance provides recommendations and good practice points regarding the use of a copper intrauterine device for long-term contraception, the accepted abbreviation for which is IUD. The use of an IUD as conditions where this Guidance suggests a less restrictive approach compared to WHOMEC.

Women at risk of sexually transmitted infections (STIs)
Actinomycetes-like organisms

- Not diagnostic or predictive of any disease
- Role in infection in IUD users is unclear
- IUD should be removed in a symptomatic woman, with appropriate antibiotic treatment and referral to specialist
- No evidence to support the routine removal of an IUD in an asymptomatic woman

Actinomycetes-like organisms

- Little evidence to support routine follow-up unless symptoms occur
- ‘Asymptomatic IUD users with ALOs detected on a cervical smear should be advised there is no reason to remove the IUD unless signs or symptoms of infection occur (Grade B)

• Symptoms: intermenstrual bleeding, pelvic pain, deep dyspareunia, dysuria
• Signs of pelvic infection and/or pelvic mass not due to another cause
• IUD sent for culture
• Penicillin, tetracycline or erythromycin for a minimum of 2 weeks

Other specific infections

• Candida – treat only if symptomatic
• Trichomonas – treat even if asymptomatic, screen for other STDs
Clinical significance of *Trichomonas vaginalis* detected in Papanicolaou smear: a survey in female Social Hygiene Clinic

Steven KF Loo  馮景勳
William YM Tang  鄧旭明
KK Lo  劉乾剛

**Objectives**
To evaluate the clinical significance of *Trichomonas vaginalis* detected in Papanicolaou (Pap) smears in our local population.

**Design**
Retrospective study.

**Setting**
A sexually transmitted disease clinic in Hong Kong.

**Patients**
All patients having Pap smear, wet mount microscopy, and high vaginal swab culture performed in Tuen Mun Social Hygiene Clinic from April 2005 to December 2006 were recruited.

**Main outcome measures**
Sensitivity, specificity, positive and negative predictive values of the Pap smear for the diagnosis of *Trichomonas vaginalis*.

**Results**
A total of 209 patients had the diagnosis of *Trichomonas vaginalis* in the study period. From among these, the results of 149 patients who had Pap smears, wet mount microscopy, and high vaginal swab culture performed were used in the analysis. Sixty cases were excluded because treatments were initiated before the consultation or because the Pap smear had not been done. Among the *Trichomonas vaginalis* cases with positive Pap smears, 58% (85/146) were symptomatic and 41% (60/146) had concomitant sexually transmitted disease. The respective sensitivity and specificity of the Pap smear in our study were: 98% (128/131; 95% confidence interval, 94-100%) and 96% (440/458; 94-98%). In total, 128 patients were defined as true positives by wet mount microscopy or culture, while 18 were defined as false positives. In our study population,
Other specific infections

- Candida – treat only if symptomatic
- Trichomonas – treat even if asymptomatic, screen for other STDs
- Herpes – screen for other STDs; ?HSV-2-specific antibodies
- Chlamydia, gonococcus – needs confirmation
Calling patient back

- Nature of the abnormality – not diagnostic, need colposcopic assessment
- Not cancer – even for HSIL, the risk of cancer only 1-2%
- Procedure of colposcopy – similar to taking a smear with passage of speculum followed by examination and biopsy; whole procedure lasts 10-15 min
- If need treatment, most likely a local treatment, often as an outpatient and carries little if any risk to potential fertility
- (No urgency – even for untreated CIN III may take years before progression to cancer)
- Good time to advise against smoking
Smoking worsens the prognosis of mild abnormalities in cervical cytology

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Liquid Compared With Conventional Cervical Cytology
A Systematic Review and Meta-analysis

Marc Arbyn, MD, MSc, Christine Bergeron, MD, PhD, Paul Klinkhammer, MD, Pierre Martin-Hirsch, MD, PhD, Albertus G. Siebers, MSc, and Johan Bulten, MD, PhD

OBJECTIVE: To compare test performance characteristics of conventional Pap tests and liquid-based cervical cytology samples.

DATA SOURCES: Eligible studies, published between 1991 and 2007, were retrieved through PubMed/Embase searching and completed by consultation of other sources.

METHODS OF STUDY SELECTION: Studies were selected if a conventional and a liquid-based sample were prepared from the same woman or when one or the other type of sample was taken from a separate but similar cohort. The current systematic review and meta-analysis is restricted to studies where all subjects were submitted to gold standard verification, based on colposcopy and histology of colposcopy-targeted biopsies, allowing computation of absolute and relative test validity for cervical intraepithelial neoplasia grade 2 or worse. Randomized trials were selected as well if all test-positive cases were verified with the same gold standard, allowing computation of the relative sensitivity. Impact of study characteristics on accuracy was assessed by subgroup meta-analyses, meta-regression, and summary receiver operating characteristic curve regression.

TABULATION, INTEGRATION, AND RESULTS: The relative sensitivity, pooled from eight studies, with complete gold standard verification and from one randomized clinical trial, did not differ significantly from unity. Also, the specificity, considering high-grade and low-grade squamous intraepithelial lesions as cutoff, was similar in conventional and liquid cytology. However, a lower pooled specificity was found for liquid-based cytology when presence of atypical squamous cells of undetermined significance was the cutoff (ratio 0.91, 95% confidence interval 0.84–0.98). Differences in study characteristics did not explain interstudy heterogeneity.

CONCLUSION: Liquid-based cervical cytology is neither more sensitive nor more specific for detection of high-grade cervical intraepithelial neoplasia compared with the conventional Pap test.

(Obstet Gynecol 2008;111:167–77)
Evidence-based medicine versus liquid-based cytology

- Facilitate HPV testing – the reasoning that HPV triage of ASC-US unequivocally justifies use of liquid-based cytology is contestable
- Potential benefit of fewer unsatisfactory tests with liquid-based cytology is unlikely to justify its use, especially in light of concurrent false-positive testing
- Laboratory simply stopped reading conventional tests

(Sawaya 2008 Obstet Gynecol 111:2-3)
Comparison of Liquid-Based Cytology With Conventional Cytology for Detection of Cervical Cancer Precursors
A Randomized Controlled Trial

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Johanna M. M. Grefte, MD, PhD
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Judith E. M. Vedder
Angélique Beijers-Broos
Johan Bulten, MD, PhD
Marc Arbyn, MD, MSc, DrTMH

The conventional Papanicolaou (Pap) test is considered suboptimal due to false-negative and false-positive test results. This is caused by the poor quality of sampling and preparation (obscuration by blood or inflammation, bad cell fixation, and inhomogeneous distribution of cells) and by errors in detection and interpretation. Liquid-based cytology was developed as an alternative. For the liquid-based cytology, the cervical cells are collected with a traditional sampling device and rinsed into a vial with preservation solution rather than being smeared on a slide. Because only a representative portion of the sample is used, the residual material in the vial may be used for ancillary testing such as reflex human papillomavirus (HPV) testing.

Context Liquid-based cytology has been developed as an alternative for conventional cervical cytology. Despite numerous studies and systematic reviews, controversy remains about its diagnostic accuracy.

Objective To assess the performance of liquid-based cytology compared with conventional cytology in terms of detection of histologically confirmed cervical intraepithelial neoplasia (CIN).

Design, Setting, and Participants Cluster randomized controlled trial involving 89,784 women aged 30 to 60 years participating in the Dutch cervical screening program at 246 family practices. One hundred twenty-two practices were assigned to use liquid-based cytology and screened 49,222 patients and 124 practices were assigned to use the conventional Papanicolaou (Pap) test and screened 40,562 patients between April 2004 and July 1, 2006. Patients were followed up for 18 months through January 31, 2008.

Intervention Screening for CIN using liquid-based cytology or conventional papanicolaou (Pap) test and the blinded review of all follow-up of screen-positive women (blinded to the type of cytology and the initial result).

Main Outcome Measures Intention-to-treat and per-protocol analysis of the detection rates of and positive predictive values for histologically verified CIN in both cytology systems. Outcomes are presented as crude and adjusted rate ratios (adjustment for age, urbanization, study site, and period).

Results The adjusted detection rate ratios for CIN grade 1+ was 1.01 (95% confidence interval [CI], 0.85-1.19); for CIN grade 2+, 1.00 (95% CI, 0.84-1.20); for CIN grade 3+, 1.05 (95% CI, 0.86-1.29); and for carcinoma, 1.69 (95% CI, 0.96-2.99). The adjusted positive predictive value (PPV) ratios, considered at several cytological cutoffs and for various outcomes of CIN did not differ significantly from unity.

Conclusion This study indicates that liquid-based cytology does not perform better than conventional Pap tests in terms of relative sensitivity and PPV for detection of cervical cancer precursors.

Trial Registration trialregister.nl Identifier: NTR1032
JAMA. 2009;302(16):1757-1764
The revised BSCC terminology for abnormal cervical cytology

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Accepted for publication 16 April 2008


The revised BSCC terminology for abnormal cervical cytology

The BSCC terminology was originally published in 1986 and although highly successful, requires revision. Through a process of professional consensus and literature review this has been undertaken by the BSCC. The revision takes account of recent developments and improvements in understanding of morphology and disease process and is compatible with other terminologies in use elsewhere, whilst still maintaining a focus on practice in the UK cervical screening programmes.
REVISED BSCC TERMINOLOGY

16 June 2008: Although yet to be endorsed by the NHSCSP, the proposed changes to terminology in cervical cytology have been published in this month’s issue of Cytopathology.

Briefly, the recommendations are to

- retain the term dyskaryosis.
- switch to a two-tier system of reporting dyskaryosis, with a single category of high-grade dyskaryosis replacing the existing categories of moderate and severe dyskaryosis.
- replace the existing categories of borderline nuclear change (BNC) with koilocytosis and mild dyskaryosis with a single category of "low-grade dyskaryosis".
- retain the term ?glandular neoplasia.
- rename the category of severe dyskaryosis ?invasive to high-grade dyskaryosis ?invasive.
- subclassify borderline change into three groups:
  o Borderline change, high-grade dyskaryosis not excluded
  o Borderline change in endocervical cells
  o Borderline change, not otherwise specified (NOS)

The proposed system moves closer to the Bethesda system (TBS) and the recently published European Guidelines, allowing easy translation of internationally published papers, but would maintain control and flexibility of the classification.
BSCC members approve merger with NAC

17 September 2010: BSCC Council is pleased to announce that 72% of members who voted in the recent ballot voted in favour of a merger. The result of the ballot was announced at the AGM on Tuesday 14th September. The full result of the ballot is as follows:

Votes cast: 143

Votes in favour: 103

Votes against: 40

A two thirds majority was required to approve the merger. Therefore the ballot of members has approved in principle the merger with NAC.

BSCC council would like to thank all members who took the time to cast their vote in this important ballot.

Next steps
As the BSCC is a registered charity, an extraordinary general meeting is required to satisfy the Charity Commission and to formally dissolve the BSCC before forming a new society. A two thirds majority will be required either from those who attend the meeting or through proxy votes. The date for the EGM has not been agreed yet but members will be notified well in advance of the agreed date. All BSCC members are encouraged to attend the meeting or submit a proxy vote.

A working group will now be established to take forward the formation of a new society.
Persistent HPV Infection and Cervical Cancer Risk: Is the Scientific Rationale for Changing the Screening Paradigm Enough?

Eduardo L. Franco

Correspondence to: Eduardo L. Franco, DrPH, Departments of Oncology and Epidemiology, McGill University, 546 Pine Avenue West, Montreal, QC, Canada H2W1S6 (e-mail: eduardo.franco@mcgill.ca).

Few cancer prevention discoveries have been as unequivocal as the finding that human papillomavirus (HPV) infection is a necessary cause of cervical cancer (1). The fact that HPV nucleic acid is found in nearly every exfoliated cervical cell specimen from women with high-grade cervical intraepithelial neoplasia (CIN) or cervical cancer is the justification for designing molecular-based assays to be used in screening. Yet, the paradigm for secondary prevention of this disease has thus far been difficult to challenge. Pap cytology testing has been the technological mainstay of cervical cancer screening programs for more than 50 years. North American and
Age distribution of human papillomavirus infection and cervical neoplasia reflects caveats of cervical screening policies

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Although a second age-related peak of human papillomavirus (HPV) infection is observed in many populations, it does not seem to have any impact on cervical screening policies. We examined the age-specific prevalence of HPV infection among 2,604 women enrolled for cervical screening and correlated the age at diagnosis of 2,491 cervical intraepithelial neoplasia
Summary

• 2008 revised HKCOG guidelines
• In-phase endometrial cells in women >=40 or endometrial cells in patients with IUD inserted: no further action unless symptomatic
• Consider repeat cervical smear in 12 months if smear negative but lacking an endocervical/transformation zone component
• Repeat after 3 months if smear unsatisfactory
Summary

- Actinomycetes-like organisms: may not need to remove IUD
- Other specific infections: diagnosis reliable for trichomonas and herpes; need confirmation for chlamydia and gonococcus
- Smoking worsens the prognosis of mild abnormalities
- No good evidence that liquid based cytology is better
- BSCC has proposed to revise the terminology for abnormal cervical cytology
Thank you

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