Management of abnormal smears

Basic Colposcopy Workshop
17 Dec 2011
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In Hong Kong, Cervical smears - Target population

- 25 (or later when become sexually active) - 65 years old
- Do smears for > 65 if
  - Not had 3 consecutive normal smears
  - Never had a smear
- 2 annual smears, if normal, every 3 years
## Screening frequency

<table>
<thead>
<tr>
<th>Screening frequency</th>
<th>Reduction in cervical cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2 yearly</td>
<td>93%</td>
</tr>
<tr>
<td>3 yearly</td>
<td>91%</td>
</tr>
<tr>
<td>5 yearly</td>
<td>84%</td>
</tr>
</tbody>
</table>

Recommended: 3 yearly screening after 2 normal annual smears
For smears done for women registered with the government cervical screening programme, DH between 2004-2010:

**Figure 7. General categorization of the test results of cervical cytology among registered women (No. of tests = 800,178)**

- 92% normal
- 7% abnormal
- Unsatisfactory 0.3%
- Endometrial cells in >40 yrs – 0.5%

Footnote: The percentage may not add up to 100.0% due to rounding of decimals.

What abnormalities?

• Cytological Abnoramlities (Bethesda system)
  
  – Squamous cells –
    • ASCUS- atypical squamous cells of undetermined significance
    • LSIL – low grade squamous intraepithelial lesion
    • HSIL- high grade squamous intraepithelial lesion
    • ASC-H atypica glandular cells, cannot exclude HG
  
  – Glandular cells
    • Atypical glandular cells NOS, AGC - FN

• Unsatisfactory smears?

• Others – infection etc
How common are these abnormalities?

Figure 9. Distribution of abnormal cervical cytology tests among registered women (No. of tests = 57 960)

- ASCUS - 64%
- ASC-H - 1.2%
- LSIL - 30.8%
- HSIL - 3.3%
- SCC - 0.02%
- Others - 0.6%
- Adenocarcinoma - 0.1%

Footnote: The percentage may not add up to 100.0% due to rounding of decimals.

Management Rationale 1

- Smears – only a screening tool, needs more diagnostic tests to confirm the pathology
- Pap smears – wide range of sensitivity (eg 47-62% for detecting CIN 2-3)
- Limited by
  - Results dependent on high quality sampling
  - Interpretation of smears – subjective
- Cytological terms LSIL and HSIL correlates with CIN 1 and CIN2&3 respectively but not diagnostic
Management Rationale - 2

• Despite a normal smear or smears with very slight abnormalities – cannot exclude a serious problem entirely

<table>
<thead>
<tr>
<th></th>
<th>% high grade lesion (CIN 2-3)</th>
</tr>
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<tbody>
<tr>
<td>ASCUS</td>
<td>5-17%</td>
</tr>
<tr>
<td>ASC-H</td>
<td>24-94%</td>
</tr>
<tr>
<td>LSIL</td>
<td>15-30%</td>
</tr>
<tr>
<td>HSIL</td>
<td>70-75% (1-2% invasive)</td>
</tr>
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</table>
Needs colposcopically directed biopsy

- Decision of when to refer depends on the likelihood that the patient has a CIN 2/3

<table>
<thead>
<tr>
<th></th>
<th>% CIN 2-3</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCUS</td>
<td>5-17%</td>
<td>Repeat in 6 months or HPV testing</td>
</tr>
<tr>
<td>ASC-H</td>
<td>24-94%</td>
<td>Colposcopy within 12 weeks</td>
</tr>
<tr>
<td>LSIL</td>
<td>15-30%</td>
<td>Colposcopy within 12 weeks</td>
</tr>
<tr>
<td>HSIL</td>
<td>70-75% (1-2% invasive)</td>
<td>Colposcopy within 6 weeks</td>
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</table>
CIN Treatment rationale

• Many low grade lesions return to normal on its own, but some will progress
  – Within 24 months
    • 25-75% regressed to normal
    • Up to 15% progress to CIN 2& 3

• High grade lesions
  – Regression 35%
  – Progression – about 1.6% in 2 year, 12% in 10 years
Management of CIN

CIN 1 - observe

• Smear every 6 months
• 3 yearly smear after 3 consecutive normal results (6, 12, 18 m)

• If LSIL persist, repeat colpo at 12-18 months
• If LSIL for > 2 yrs – for tx

CIN 2-3 - treat!

• LEEP/ LLETZ
• Then..
• Smear every 6 months
• Yearly smear after 3 consecutive normal results (6, 12, 18 m) for 10 years, then 3 yearly
Is HPV test result going to affect how we manage abnormal smear?

• HPV- main cause of cervical cancer
• Those with HR – HPV +, more likely to have high grade lesion or progress to high grade lesions/ Ca
HPV DNA testing – a promising alternative test/complimentary test to pap smear?

- **Possible advantages**
  - More objective
  - More reproducible
  - More sensitive than cytology

- Meta-analysis of 25 studies* – pooled sensitivity of
  - HPV testing (HC 2) – 90%
  - Cytology (ASCUS or worse) – 72.7%

* Koliopoulos G Gynecol Oncol 2007
Different strategies?

- Pap smear alone
- HPV testing alone
- Pap first, then HPV
- HPV first, then Pap
- Both together
<table>
<thead>
<tr>
<th>Screening Approach</th>
<th>Definition of Positivity</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
<th>No. of Tests Needed for Screening</th>
<th>Referrals for Colposcopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pap only</td>
<td>ASCUS or worse</td>
<td>56.4</td>
<td>97.3</td>
<td>8.5</td>
<td>99.8</td>
<td>9,959</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td>LSIL or worse</td>
<td>42.2</td>
<td>99.1</td>
<td>17.5</td>
<td>99.7</td>
<td>9,959</td>
<td>1.0</td>
</tr>
<tr>
<td>HPV only</td>
<td>$\geq 1$ pg HPV DNA/ml</td>
<td>97.4</td>
<td>94.3</td>
<td>7.0</td>
<td>100.0</td>
<td>9,959</td>
<td>6.1</td>
</tr>
<tr>
<td></td>
<td>$\geq 2$ pg HPV DNA/ml</td>
<td>81.1</td>
<td>95.5</td>
<td>9.1</td>
<td>99.9</td>
<td>9,959</td>
<td>4.8</td>
</tr>
<tr>
<td>Pap screening followed by HPV triage</td>
<td>Triage of all results of ASCUS; $\geq 1$ pg HPV DNA/ml</td>
<td>53.8</td>
<td>98.7</td>
<td>14.9</td>
<td>99.8</td>
<td>10,145</td>
<td>1.6</td>
</tr>
<tr>
<td>HPV screening followed by Pap triage</td>
<td>Triage of all with $\geq 1$ pg HPV DNA/ml; Pap threshold of ASCUS or worse</td>
<td>53.8</td>
<td>99.1</td>
<td>21.4</td>
<td>99.8</td>
<td>10,563</td>
<td>1.1</td>
</tr>
<tr>
<td>Pap and HPV cotesting</td>
<td>Pap result of ASCUS or worse, or HPV result of $\geq 1$ pg HPV DNA/ml</td>
<td>100.0</td>
<td>92.5</td>
<td>5.5</td>
<td>100.0</td>
<td>19,918</td>
<td>7.9</td>
</tr>
</tbody>
</table>
HPV testing in HK?

- Triage for low grade smears
- Monitoring of low grade lesions or high grade lesions post treatment
HPV testing in HK?

- ASCUS – 50% high risk HPV
- LSIL – 82-85% high risk HPV

IF ASCUS + HR HPV + – refer colposcopy

IF ASCUS + HR HPV neg -
repeat cytology at 12 months rather than 6 months
Low grade at colposcopy- 15% progress to CIN 2/3

- Smear every 6 months
- 3 yearly smear after 3 consecutive normal results (6,12,18 m)
- If LSIL persist, repeat colpo at 12-18 months
- If LSIL for > 2 yrs – for tx

- Smear after 6 months
- Smear and HPV test at 12 months
- If both negative – repeat at 24 months, if neg- return to normal screening
- If either positive at 12 m – repeat colpo
- If LSIL for > 2 yrs – for tx
High grade lesion (12% CIN 3 progress to Ca over 10 years)

- LEEP
  - Smear every 6 months
  - Yearly smear after 3 consecutive normal results (6,12,18 m) for 10 years, then 3 yearly
  - Smear after 6 months
  - Smear and HPV test at 12 months
  - If both negative – repeat at 24 months, if neg - Yearly smear for 10 years, then 3 yearly
Treatment of high grade CIN

• ablative therapy (no histological assessment)
  – cryotherapy
  – cold coagulation
  – diathermy
  – laser evaporisation

• excision therapy
  – LEEP (LLETZ)
  – cone (knife, laser)

• hysterectomy is rarely indicated
Indications for LLETZ

- high grade CIN
- discrepancy between cytology and colposcopic diagnosis
- suspicious of microinvasion
LLETZ

- well tolerated by patients
- performed under local anaesthesia and vasoconstrictor
- outpatient procedure
- acceptable complication rate of 5%
- allow histological examination of specimen
- cure rate of 98% at the end of one year
Loop and ball electrodes
Dental syringe for LA
LLETZ-intracervical injection
Large loop excision of the transformation zone of the cervix (LLETZ)
Large loop excision of the transformation zone of the cervix (LLETZ)
LLETZ – haemostasis with ball electrode
Large loop excision of the transformation zone of the cervix (LLETZ)
Complications of LLETZ

- intraoperative and postoperative bleeding (1-8%)
- Infection
- cervical stenosis (1%)
- cervical deformity
- cervical incompetence
- Injury to nearly structures
- Preterm delivery/ LBW/ PROM
What abnormalities?

- Cytological Abnormalities
  - Squamous cells –
    - ASCUS - atypical squamous cells of undetermined significance
    - LSIL – low grade squamous intraepithelial lesion
    - HSIL - high grade squamous intraepithelial lesion
  - Glandular cells
- Unsatisfactory smears?
- Others – infection etc
Glandular cells

• Endocervix
• Endometrium

• Need to assess both
  – Endocervix – Endocervical brush, EC currettage
  – Endometrium- Endometrial aspirate
## Glandular lesions

<table>
<thead>
<tr>
<th></th>
<th>% CIN 2-3, AIS, Ca</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGC-NOS</td>
<td>9-41%</td>
<td>Colposcopy, biopsy, ECC and endometrial biopsy</td>
</tr>
<tr>
<td>AGC-favor neoplastic</td>
<td>27-96%</td>
<td></td>
</tr>
<tr>
<td>AIS</td>
<td>48-69% AIS, 38% adenoca</td>
<td></td>
</tr>
</tbody>
</table>
If no significant findings on colpo

- AGC- NOS
  - repeat cytology with cytobrush every 6 months for 2 years
- AGC- FN/ AIS
  - Cone biopsy
Cone biopsy
Cold knife cone
Endometrial cells

• Post- menopausal
  – 12% significant pathology –
  – Needs investigation

• Pre-menopausal
  – > 40 years, asymptomatic and compatible with cycle - observe ( ie do nothing )
  – <40 – observe
  – In women with IUCD – observe

HKCOG guidelines/ Jordan et al 2008 Cytopathology 19:342-54
Compatible with cycle?

Other than during the first half (Day 10-14) of the menstrual cycle, the presence of spontaneously exfoliated endometrial cells in the Pap smear is abnormal.

(Remember to put down LMP in the smear request form!)

DeMay 1996 The art & science of cytopathology Vol 1, p124. ASCP Press
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  – Glandular cells

• Unsatisfactory smears?
• Others – infection etc
Unsatisfactory smears?

- Treat any treatable conditions eg infection first
- Repeat smear (at least 3 months later - the cervical epithelium needs time to regenerate)
- Repeatedly unsatisfactory smears eg due to blood/ inflammation/ necrosis – refer coloscopy
Actinomyces in IUCD users?

• Asymptomatic – no need action
• Symptomatic (IMB, pelvic pain, dyspareunia, signs of pelvic infection)
  – Remove IUCD and send for culture
  – Treat with penicillin/tetracycline/erythromycin for at least 2 weeks

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
Special circumstances

- Young women
- Pregnant women
Young women (< 20)

- Most lesions clear on its own
- ASCUS - can repeat smear 12 m instead of 6
- LSIL – can repeat smear instead of colpo
- CIN2 – can observe with smear every 6 months instead of LEEP (repeat colpo in 1 year), but needs LEEP if persist for 2 years
- CIN 3 – LEEP as usual
Pregnant women

• Don’t do endocervical currettage
• LSIL
  – defer colpo till 6 weeks post delivery
• HSIL
  – colposcopy, biopsy only if suspect Ca
  – Repeat colposcopy in 3rd trimester
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 situations 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
Thank you