Cervical screening and the Nurse: current and future directions

Dr Lara Roeske
A specialist gynecological pathology laboratory
- Cervical cytology 300,000 per annum, predominantly conventional
- Cervical histopathology
- HPV testing

A state based Pap test registry
- Follow up, reminders
- Supports programme monitoring and evaluation
- Provides framework for quality monitoring of laboratories

A national register recording HPV dose information
- Course completion statements
- Reminder functions
- Supports programme monitoring and evaluation
Educational Updates for Health Practitioners

VCS Pathology offers free educational updates to health practitioners in Victoria. These updates cover the National Cervical Screening Program, Pap test technique, HPV Human Papilloma Virus and HPV testing, HPV vaccines and testing for Chlamydia trachomatis.

Updates are presented by our liaison physicians, Dr Stella Hely, Dr Sibbah Bouko and Dr Lara Rosse. These sessions usually take one to two hours but can be tailored to suit your needs.

Day or evening sessions can be arranged for both suburban and country practices, but as VCS is a not-for-profit organisation, and our educational updates are free of charge, we like to plan carefully to ensure optimal attendance.

We offer:
- Distance education - webinar
- Educational meetings via your medicare local
- DI A CPS Learning including:
  - Chlamydia Audit - 10 points (category 11)
  - ALM - 40 points (category 11) women + health
- Conference presentations
- Lectures and practical sessions
- Telephone advice

Topics for discussion:
- Pap tests and the current guidelines
- Pap test techniques
- HPV – understanding the virus
- HPV testing
- HPV vaccines
- Pap testing in the future
- Chlamydia testing

To organise an update please contact Lynnel Ritchie in Customer Liaison, on (03) 9250 0380 or via email: lritch@vcs.org.au

About the speakers

Dr Stella Hely
Dr Stella Hely is a Sexual Health Physician and the Senior Liaison Physician at VCS. Well known in the GP and nursing community, Stella has spoken to hundreds of health practitioners over the past giving support to enable the best management of both the cervical screening program and sexually transmissible infections. Stella is a member of the Hepatitis Working Party of AATGD to the introduction of the HPV vaccine onto the National Immunisation Program in 2007. She has written on these topics for a number of medical journals and is regularly invited to speak at medical meetings.

Dr Sibbah Bouko
Dr Sibbah Bouko, a Sexual Health Physician, joined VCS in 2006 as a Liaison Physician to support VCS’s commitment to providing educational services to GP screen providers.

Sibbah’s strong interest in medical education led her to work in medical and humanities Lotto in a number of charities including迪拉 as part of an HIV prevention program. Having worked with Family Planning Victoria for several years, Sibbah also has particular expertise in the area of contraception and adolescent health.

Dr Lara Rosse
Dr Lara Rosse is a General Practitioner and accredited education activity provider with the RACGP who joined VCS in 2009. Her interests include Preventative health, women’s health and sexual health. She is also actively involved in medical education at all levels including presentation to staff, students and parents in school. As a GP, Lara is committed to providing high-quality medical care to her patients with a focus on the health of women and the importance of screening to prevent cervical cancer for women with disabilities and their general practitioners.

For additional information refer to VCS website: www.vcs.org.au
Worldwide prevalence of cervical cancer

- Cervical cancer is the second most common cancer affecting women worldwide and the third most common cause of cancer death

- Cervical cancer is most prevalent in developing countries of Asia and Africa
WHERE ARE WE NOW IN AUSTRALIA?

Australia has amongst the lowest incidence and mortality in the world following the successful introduction of organised screening 20 years ago.
Figure 12.3: Incidence and mortality rates of cervical cancer in women of all ages, 1982–2006

International comparisons
Incidence of cervical cancer and mortality rate, selected countries, 2002

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence per 100,000 women (ASR)</th>
<th>Mortality per 100,000 women (ASR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Zealand</td>
<td>10.0</td>
<td>3.2</td>
</tr>
<tr>
<td>UK</td>
<td>8.3</td>
<td>3.1</td>
</tr>
<tr>
<td>Sweden</td>
<td>8.2</td>
<td>3.1</td>
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<tr>
<td>USA</td>
<td>7.7</td>
<td>2.3</td>
</tr>
<tr>
<td>Canada</td>
<td>7.7</td>
<td>2.5</td>
</tr>
<tr>
<td>Australia</td>
<td>6.9</td>
<td>1.7</td>
</tr>
<tr>
<td>Finland</td>
<td>4.3</td>
<td>1.8</td>
</tr>
</tbody>
</table>
In Victoria 2009

Rate per 100,000 women (age-standardised to the World Standard Population)

- Incidence: 4.4 in 1982, 0.9 in 2009
- Mortality: 0.9 in 2009
Australia: cervical cancer (2008)

**Incidence:**
600-700 new cases each year

**Mortality:**
200-300 deaths each year

**Victoria (2006):**
160 new cases
37 deaths
In Victoria

Rate per 100,000 women (age-standardised to the World Standard Population)

- Invasive squamous cell carcinoma
- Micro-invasive squamous cell carcinoma
- Other invasive morphology
The cervix: squamo-columnar junction
Cervical Cancer: Histology

- Squamous cell cancer- 66% of all new cases
- Adenocarcinoma-19.8%
- Adenosquamous carcinoma-3.2%
- Mixed, unknown histology -11%
Figure 6.4: Incidence of carcinoma of the cervix (squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma and other carcinoma), women aged 20–69 years, by year, 1982 to 2007

Note: The rates were age-standardised to the Australian population as at 30 June 2001.

Source: AIHW Australian Cancer Database.
The greatest impact of the National Cervical Screening Program is on squamous cell cancer.
The vast majority of cervical cancers occur in under-screened women.

Screening history of Victorian women diagnosed with an invasive cervical cancer for the period 1 January 2003 and 31 December 2005

<table>
<thead>
<tr>
<th>Screening History</th>
<th>Squamous cell carcinoma</th>
<th>Other invasive cervical cancer*</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
<td>Number</td>
</tr>
<tr>
<td><strong>A. Women never screened</strong></td>
<td>51</td>
<td>23%</td>
<td>73</td>
</tr>
<tr>
<td><strong>B. Women with inadequate screening</strong></td>
<td>151</td>
<td>69%</td>
<td>50</td>
</tr>
<tr>
<td><strong>C. Women with some screening history</strong></td>
<td>17</td>
<td>8%</td>
<td>33</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>219</td>
<td>100%</td>
<td>156</td>
</tr>
</tbody>
</table>

* Other cervical cancers include small cell carcinoma, mixed adenosquamous and Adenocarcinoma.

** Requires further review
What do Victorian women know about pap tests and HPV?

In 2007, 1000 Victorian women;
• 85% (majority) aware that pap tests 2 yearly
• Very few indicated when to start and stop
• 9.6% mentioned HPV as a factor in cervical cancer
• 94% aware of HPV vaccine
• 87% knew pap tests still needed after vaccination
Pap Smear reports in Victoria 2012

• 602,357 total registered pap smears
• 80% GPs, 5.6% by nurses (0.8% in 1996)

• 91.4% negative
• 6.4% squamous cell abnormality
• 0.8% high grade
Why it is important to ask every woman? 
94.4% in 2012!
The Pap Test

When to start?

When to stop?
Trouble-shooting

• The pap smear is a screening test with inherent limitations
• False negative rate 15-20%
• Miss about 1 in 10 cancers
• PPV HGL 81.4%
Current status of cervical screening

- National Cervical Screening Program est. 1991
- Current recommendations:
  - Interval: 2 years
  - Age range: 18-20 to 70 years, in sexually active women
  - Screening test: conventional cytology (Pap smear)
  - Management of abnormal smears: 2006 NHMRC Guidelines
Cancer of the cervix

Caused by
Human papillomavirus (HPV)

Prevented by
HPV vaccination and Cervical screening
HPV
Human papillomavirus

- Numerous types ~200
- ~50 types infect genital epithelium
- Species specific
- Site specific
- Multi-focal infection
- Multi-type infection common
Transmission

• genital skin-to-skin or mucosa-to- mucosa contact

• Penetrative sexual intercourse is not a requirement for transmission

• Consistent condom use reduces but does not eliminate transmission
Low-risk HPV Types

- Includes types 6 and 11
- 90-95% of genital warts
- 10-20% LSILs
High-Risk HPV Types

- Mainly types 16 and 18

- **16 & 18 cause:** 70% cervical cancer worldwide and up to 80% in Australia
Natural history of HPV infection of cervix

HPV and cervical cancer

MAJOR STEPS IN CERVICAL CARCINOGENESIS

NORMAL CERVIX

Infection

HPV INFECTED CERVIX

Persistence (1 to 10 years)

CIN-3/ PRE-CANCERS

Invasion

CANCER

Clearance

Regression

MILD CYTOLOGIC ABNORMALITIES


VCS Pathology
HPV Key Concepts

• Sex = HPV infection
• Usually transient and asymptomatic
• LSIL = short term HPV infection
• LSIL can usually be safely monitored*
• Persistent infection for many years with a high risk
  HPV type may result in invasive cancer of the cervix
• Genital HPV infection is very common, cervical cancer is a rare outcome
WHY CONSIDER CHANGE TO SCREENING PROGRAM?

• HPV vaccination
• New testing technologies
  • Liquid based technology
  • Computer assisted image analysis
  • HPV DNA tests
Vaccine impact on screening

- Average risk of invasive cervical cancer in population will decline
- Cost-effectiveness of existing screening programs will decline
- The test performance characteristics of cytology are likely to decline
Trends In High-grade Cervical Abnormalities (Histologically-confirmed) By Age

[Graph showing trends in high-grade cervical abnormalities by age from 2000 to 2011.]

- ≤20
- 21-25
- 26-30
- 30+

Proportion of Women (per 1,000 screened)
WHY CONSIDER HPV SCREENING?

Theoretically better suited to new low prevalence environment
Estimated age-standardised incidence rate per 100,000
Cervix uteri, all ages

HPV vs cytology RCTs

GLOBOCAN 2008 (IARC) - 4.8.2011

Estimated cervical cancer incidence 2008
Longitudinal outcomes: HPV and cytology negative women

WHERE TO FROM HERE?
RESEARCH DIRECTIONS
A JOINT INITIATIVE OF
THE VICTORIAN CYTOLOGY SERVICE
AND THE
UNIVERSITY OF
NSW
### Co-Principal Investigators
- A/Prof Karen Canfell
- A/Prof Marion Saville

### Chief Investigators
- Dr. Phil Castle
- Prof Ruth Salom
- A/Prof Dorota Gertig (VCS)
- Dr. Julia Brotherton (VCS)
- Dr. David Wrede (RWH)
- Dr. Jeffery Tan (RWH)
- Dr. Sally Lord (CTC)
- Dr. Andrew Martin (CTC)
- A/Prof Kirsten Howard (USyd)

### Associate Investigators
- Dr. Stella Heley
- Dr. Lara Roeske
- Gillian Phillips
- Dr. Jane Collins
- Sandy Anderson
- Jessica Darlington-Brown
- Others to be determined

### Key Responsibilities
- Protocol development, review and revision.

### Associate Investigators
- Dr. Stella Heley
- Dr. Lara Roeske
- Gillian Phillips
- Dr. Jane Collins
- Sandy Anderson
- Jessica Darlington-Brown
- Others to be determined

### Key Responsibilities
- Give advice on protocol and operational aspects of trial.

### Data Safety Monitoring Board (Chair: Prof. Michael Quinn)

#### Key Responsibilities
- Regularly review safety data in a blinded manner
- Recommend study termination if pre specified stopping criteria are met
- Make safety or monitoring recommendations as appropriate

### Scientific Advisory Committee (Chair: Prof. Bruce Armstrong)

#### Key Responsibilities
- Advise on study protocol development
- Annual progress meetings (more frequent if required)
- Review pilot and main trial analysis

### Quality Assurance Panel

#### Histopathology

**Chair:** A/Prof. Annabelle Farnsworth

#### Key Responsibilities
- Review histopathology slides in a blinded manner

### NHMRC Clinical Trials centre

#### Key Responsibilities
- Provision of randomisation mechanism
- Contribute to statistical aspects of protocol design

### NHMRC Clinical Trials centre

#### Key Responsibilities
- Laboratory Management
- GP Recruitment
- Participant recruitment
- Implement linkage to VCCR & NVPR

### NHMRC Clinical Trials centre

#### Key Responsibilities
- Lead protocol design
- Data management
- Lead data analysis and write-up
Why another primary HPV RCT?

• Evaluate primary HPV in partially vaccinated population using updated testing technology
• More focus on optimal management of HPV positive women
• Specific evaluation of safety, effectiveness and costs in Australian context
• **Pragmatic trial/demonstration of concept**
Key elements

• Women aged 25-64 years recruited through primary care practices in Victoria
• 6-yearly HPV screening (with safety monitoring)
• Consenting women will have LBC sample taken, with laboratory-based randomization
• Management of follow-up via VCCR
• Active recall for rescreening prior to six years
Staged trial outcomes
Pilot, baseline round, sub-studies, longitudinal follow-up

- Primary effectiveness endpoint based on cumulative detection of confirmed CIN3 in screen-negative women at 6 years in each arm
- Laboratory processing times/volumes and feasibility (from pilot)
- Impact on referral and treatment rates (from pilot/baseline)
- Cost/ referral rates contribute to cost-effectiveness assessment (pilot)
- Safety (3-yearly follow-up)
- Effectiveness (inc cross-sectional sens/spec from pilot/baseline)
- Organisation of screening (compliance with longer intervals)
- Acceptability to women (QoL/utilities sub-studies)
- Acceptability to practitioners (focus groups)
Quiz for Nurses
When is an HPV test Medicare rebateable?
When is an HPV test Medicare rebate-able?

• After biopsy-confirmed HSIL (CIN 2; CIN 3)

• Do first test **12 months** after treatment

• Medicare will pay for 2 tests in a 2 year period

• Keep doing them until you have Pap and HPV tests negative for 2 years in a row
The HPV Test—rationale

• Cervical cancer develops in the presence of persistent HPV infection with high-risk HPV

• A negative HPV test very accurately predicts the absence of high-risk HPV

• Allows large number of low-risk women ($n \approx 250,000$) with treated abnormalities to return to the usual screening interval
Trouble shooting

The unsatisfactory pap smear report....
... may leave you feeling unsatisfactory

About 2.9% of all pap smears
Causes of an Unsatisfactory Pap Report

• Blood or mucus
• Inflammatory cells
• Atrophy
• Cytolysis
• Eversion/ectropion
• Pregnancy/post-partum
• Contamination
• Stenosis
Basic management

Unsatisfactory Pap Reports

• Wait 2-3 months before repeating the pap
• Consider LBC
• Discuss with Liaison Physician VCS 92500300
Pap smears and the Pregnant woman

- Preferable to defer
- Wait till at least 3 months post partum
- Eversion, inflammatory exudate and bleeding all more common
- No definitive treatment of HGL
- Colposcopic assessment only
- Increased anxiety
The missing Endo-cervical Component

• Stay calm
• No need for a repeat smear
• Check pap smear history, appearance of the cervix and symptoms if all ok then...
• Routine pap in 2 years
• Do not push/force brush higher
• Consider vaginal estrogen
• 1/8 women over 60 no EC
• No relationship between lack of EC and death from cervical cancer
Why may this result in an unsatisfactory smear?
Eversion or Ectropion

TRANSFORMATION ZONE
Insufficient Squamous Cells

- Atrophy
- Eversion/ectropion
- Use of wooden spatula
- Large amount of mucus
- Any of the causes of cytolysis
- Too little fixative or too late
The Pap Test

What about sexually active women <18 years?
Why might a woman in a vaccinated cohort develop cancer of the cervix?
What is the best approach prior to performing the pap smear in this situation?
Atrophy and the postmenopausal woman

- Consider routine vaginal estrogenisation
- About 2 weeks of treatment
- No vaginal medication 48 hours prior to pap
- Inform and educate women and GPs
- Ease, comfort and improved quality of smear
- Consider contraindications
How would you manage this clinical finding?
Inflammatory Exudate

- Usually physiological
- Common in pregnancy and post-partum
- Low correlation with the presence of an STI
- If asymptomatic wait and rpt pap in 2-3/12
- If symptomatic, abnormal cervix or significant history then test for Chlamydia
- Thrush a possibility
- BV unlikely cause
- Add LBC
True or False

RACGP preventive guidelines the ‘red book’ recommends **annual Chlamydia testing of all sexually active men and women aged 15-30 in general practice**
Acknowledgements

Dr Stella Heley
Assoc Prof Marion Saville
Assoc Prof Dorota Gertig
Dr Julia Brotherton