Epidemiology of HPV Infection

Dr. Suzanne Cotter
Dr. Lorraine Hickey
Health Protection Surveillance Centre
HSE-HPSC
Genital HPVs- Quick Facts

• Most common sexually transmitted infection
• Usually symptom-free and spontaneously cleared
• Causes genital warts, cervical, penile, anal and other genital cancers
• Cervical cancer is a leading cause cancer-related death in women
• Globally and annually
  – > 500,000 women diagnosed cervical cancer; > 250,000 women die from cervical cancer (80% developing countries)
• Cervical cancer is preventable
Genital warts defined as Condyloma

HPV = Human Papillomavirus; VLP = Virus-like particles
HPV Epidemiology- overview

- Reservoir: Human
- Transmission: Direct contact, usually sexual
- Temporal pattern: None
- Communicability: Presumed to be high
HPV Clinical Features

• Most HPV infections are asymptomatic and result in no clinical disease

• Clinical manifestations of HPV infection include:
  – anogenital warts
  – recurrent respiratory papillomatosis
  – cervical cancer precursors (cervical intraepithelial neoplasia, CIN)
  – Cancer (cervical, anal, vaginal, vulvar, penile, and some head and neck cancer)
Human papillomavirus (HPV)

- DNA viruses
- > 100 different types
- ~ 40 types affect the genital area
- Affect skin and mucous membranes of upper respiratory and anogenital tracts
- Exist in host in active or latent form.

Electron micrograph of human papillomavirus. Courtesy of NCI. 1986
Transmission

- Through vaginal, oral or anal sexual intercourse
- Genital contact with an infected person
- Non-sexual transmission from mother to baby in period immediately before and after birth
Factors Associated with Acquisition of HPV Infection in Women

• Young age (less than 25 years)
• Increasing number of sex partners
• Early age at first sexual intercourse (16 years or younger)
• Male partner has (or has had) multiple sex partners
### Clan survey 2003

Age of sexual onset and number of sexual partners of Irish men and women in lifetime

<table>
<thead>
<tr>
<th>Age at first sexual intercourse</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 14 years</td>
<td>3.4</td>
<td>1.8</td>
<td>2.4</td>
</tr>
<tr>
<td>15-16 years</td>
<td>26.8</td>
<td>21.9</td>
<td>23.8</td>
</tr>
<tr>
<td>17 years or older</td>
<td>69.8</td>
<td>76.3</td>
<td>73.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of sexual partners</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3 people</td>
<td>58.0</td>
<td>71.3</td>
<td>66.1</td>
</tr>
<tr>
<td>4-5 people</td>
<td>14.6</td>
<td>13.7</td>
<td>14.1</td>
</tr>
<tr>
<td>6 or more people</td>
<td>27.4</td>
<td>15.0</td>
<td>19.9</td>
</tr>
</tbody>
</table>

Source: CLAN Survey, 2003
HPV acquisition
HPV Persistence
Taxonomy of papillomaviruses

Cutaneous, mostly asymptomatic

Mucosal, cancer-associated

Genital warts

Hand warts

Foot warts

Source: Vaccines. 5th edition. Courtesy de Villiers et al. 2004
## Classification of risk by HPV type

<table>
<thead>
<tr>
<th>Classification</th>
<th>HPV Types</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk (HR) or carcinogenic</td>
<td>16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66</td>
</tr>
<tr>
<td>Possibly carcinogenic (not proven)</td>
<td>26, 68, 73, 82</td>
</tr>
<tr>
<td>Low-risk (LR)</td>
<td>6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81, 89</td>
</tr>
</tbody>
</table>

Gardasil vaccine includes types 16, 18, 6, 11 (bolded)
<table>
<thead>
<tr>
<th>Type of Cancer</th>
<th>Papillomavirus types involved</th>
<th>Percentage of cases HPV-positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical</td>
<td>16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66</td>
<td>&gt;95</td>
</tr>
<tr>
<td>Vulval: Basaloid</td>
<td>16, 18</td>
<td>&gt;50</td>
</tr>
<tr>
<td>Warty</td>
<td>16, 18</td>
<td>&gt;50</td>
</tr>
<tr>
<td>Keratinising</td>
<td>16</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Penile: Basaloid</td>
<td>16, 18</td>
<td>&gt;50</td>
</tr>
<tr>
<td>Warty</td>
<td>16, 18</td>
<td>&gt;50</td>
</tr>
<tr>
<td>Keratinising</td>
<td>16</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Vaginal</td>
<td>16, 18</td>
<td>&gt;50</td>
</tr>
<tr>
<td>Anal</td>
<td>16, 18</td>
<td>&gt;70</td>
</tr>
<tr>
<td>Oral cavity and tonsils</td>
<td>16, 18, 33</td>
<td>~25</td>
</tr>
<tr>
<td>Nail bed</td>
<td>16</td>
<td>~75</td>
</tr>
</tbody>
</table>
Global burden of HPV related diseases
### HPV distribution by geographical region (%)

<table>
<thead>
<tr>
<th>Region</th>
<th>HPV 16 (%)</th>
<th>HR HPV (other than HPV16) (%)</th>
<th>LR HPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub-Saharan Africa</td>
<td>3.2</td>
<td>14.6</td>
<td>13.6</td>
</tr>
<tr>
<td>Asia</td>
<td>1.7</td>
<td>3.7</td>
<td>4.2</td>
</tr>
<tr>
<td>South America</td>
<td>2.9</td>
<td>6.8</td>
<td>6.0</td>
</tr>
<tr>
<td>Europe</td>
<td>1.5</td>
<td>2.3</td>
<td>1.9</td>
</tr>
</tbody>
</table>

## Global Burden of High Risk (HR) HPV Disease

<table>
<thead>
<tr>
<th>Site</th>
<th>AF (%)</th>
<th>Attributable cancers</th>
<th>% all cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix</td>
<td>100</td>
<td>492,800</td>
<td>4.5</td>
</tr>
<tr>
<td>Penis</td>
<td>40</td>
<td>10,500</td>
<td>0.1</td>
</tr>
<tr>
<td>Vulva, vagina</td>
<td>40</td>
<td>16,000</td>
<td>0.2</td>
</tr>
<tr>
<td>Anus</td>
<td>90</td>
<td>27,400</td>
<td>0.2</td>
</tr>
<tr>
<td>Mouth</td>
<td>3</td>
<td>8,200</td>
<td>0.1</td>
</tr>
<tr>
<td>Oro pharynx</td>
<td>12</td>
<td>6,300</td>
<td>0.1</td>
</tr>
<tr>
<td><strong>All sites</strong></td>
<td></td>
<td><strong>561,200</strong></td>
<td><strong>5.2</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Proportion of Cancers Attributable to HPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical cancer</td>
<td>100%</td>
</tr>
<tr>
<td>Cancer of vagina</td>
<td>91–94%</td>
</tr>
<tr>
<td>Cancer of anus</td>
<td>88–94%</td>
</tr>
<tr>
<td>Cancer of vulva</td>
<td>40%</td>
</tr>
<tr>
<td>Cancer of penis</td>
<td>40%</td>
</tr>
<tr>
<td>Cancer of pharynx</td>
<td>25%</td>
</tr>
<tr>
<td>Cancer of oral cavity</td>
<td>10%</td>
</tr>
</tbody>
</table>

Human Papillomavirus types 6,11,16,18 in 73.8% of Cervical Cancers in Europe

* Squamous cell carcinomas and Adenocarcinomas

N=4737 cases

HPV – Cancer of the Cervix
HPV infection - natural history

- Initial HPV infection
- Persistent infection
- CIN 1
- Up to 5 years
- CIN 2/3
- Decades
- Cervical Cancer
- CLEARED HPV INFECTION

CDC
Development of Cervical Cancer

- **Cervical Intraepithelial Neoplasia (CIN) 1**
  - abnormal cells occupy lower third of epithelium

- **Cervical Intraepithelial Neoplasia (CIN) 2/3**
  - abnormal cells occupy lower two thirds to full thickness of epithelium
Burden of Disease

In Ireland
Cervical cancer in Ireland

- "~72 women deaths from cervical cancer annually" 
  - Mean age at death; 56 years
  - Mean age at diagnosis; 44 years
- "~3,100 women living with cervical cancer" ¹
- "In 2007 there were:"
  - 286 Cervical cancer cases ²
  - 59% of which were under the age of 39
  - 81 Cervical cancer deaths ²

². National Cancer Registry Ireland, 2010: data on file
Ano-genital warts – ’89-’05

Rate / 100,000 population

Year

Source: HPSC, 2005
Anogenital Warts, by gender, 1995-2007, Ireland
Ano – genital warts by age group, (year) Ireland

Source: HPSC 2005
Cervical Neoplasia, Ireland 1994-2001

Source: Irish Cancer Registry
Cervical Cancer, Ireland, 1984-2003

Source: Irish Cancer Registry
Prevalence of High Risk HPV by histology

Kitchener et al
n = 24,510

Murphy et al
n = 187
Cervix uteri
Age-Standardized incidence rate per 100,000

Cervix uteri
Age-Standardized mortality rate per 100,000

Conclusions

• HPV causes substantial morbidity and mortality
• Early prevention and protection is key to cancer control
• Vaccines provide opportunity to prevent disease
• Future developments?
  – New vaccines with extended coverage or usage (males)