Online Learning Module: Epidemiology and Natural History of Cervical Carcinogenesis
Course Objectives

• Describe the epidemiology of cervical cancer
• Identify the causative agent for cervical cancer
• Discuss the process of cervical carcinogenesis
Invasive cervical cancer
Epidemiology of Cervical Cancer

- Worldwide – 2nd most common female cancer
- ~500,000 new cases per year
- ~275,000 deaths per year
- 80% new cancers and deaths occur in women who live in developing nations
- Number one cause of cancer and cancer-related death in sub-Saharan Africa
- 20% deaths occur in sub-Saharan Africa
Epidemiology of Cervical Cancer

• Peaks at 35-45 years of age
• Rates are 5-6X’s higher in HIV-infected women
Global Distribution of Cervical Cancer

• Highest Burdens
  – Sub-Saharan Africa
  – Latin America
  – Caribbean Islands
  – Asia
Global cervical cancer incidence

Age Standardized Incidence Rates (ASR) (All ages)
Global cervical cancer mortality

Age Standardized Mortality Rates (ASR) (All ages)
Cause of Cervical Cancer

Human Papillomavirus (HPV)

- Double stranded DNA virus
- Virus integrates into host cell genome
Risk Factors for HPV Infection

- Sexual intercourse
- Early onset of sexual intercourse especially if near time of first menses
- Multiple sexual partners
- Partner with multiple partners
Natural History of HPV

4 Major Steps of Cervical Carcinogenesis

1. HPV infection via sexual contact
2. Persistence
3. Progression to precancer
4. Progression to invasive cancer

• Backward steps can occur: clearance of HPV; regression of precancer to normal (uncommon)
Infection with HPV

Persistent infection over 2-5yrs progresses to precancer

Precancer progresses to invasive cancer
Histopathology
Human Papillomavirus (HPV)

- Reaches the basal layer of the epithelium through small tears in cervical skin
- Over 100 different types - 30 types infect genital tract (types 16/18 most common)
- Types classified as “high-risk” and “low-risk”
- Each HPV type acts as independent infection
Human Papillomavirus (HPV)

<table>
<thead>
<tr>
<th>High-risk types (oncogenic or cancer-associated)</th>
<th>Low-risk types (non-oncogenic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 82</td>
<td>6, 11, 40, 42, 43, 44, 54, 61, 72, 73, 81</td>
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</table>

- HPV types 16 and 18 cause 70% of cervical cancers and 50% of high grade cervical precancer (CIN3).
Human Papillomavirus (HPV)

- Most genital HPV infections are transient and asymptomatic
- Most HPV infections (70-80%) are cleared by the immune system within ~18 months and are not associated with any tissue abnormalities
- HPV infections that persist are linked to precancer
Risk Factors for HPV Persistence and Progression to Cervical Cancer

- Never or rarely being screened for cervical cancer
- Immunosuppression
- Smoking
- Long term oral contraceptive use
- Co-infection (chlamydia)
- High parity
- Nutritional deficiencies
Cervix
Columnar epithelium
Metaplastic epithelium
Squamocolumnar junction
Squamocolumnar junction

New squamocolumnar junction
Epithelia and junctions

- Squamous epithelium
- Transformation zone containing metaplastic epithelium
- Columnar epithelium
- Old squamocolumnar junction
- New squamocolumnar Junction
Ectocervix – Squamous Epithelium

Endocervix – Columnar Epithelium
HPV infection
Histologic changes seen in cervical dysplasia
Precancer
Precancer
Microinvasive cancer
Microinvasive cancer
Invasive cancer
Natural History of HPV

HPV Infection → Low-grade CIN (CIN 1) (60%) 
Low-grade CIN (CIN 1) → High-grade CIN (CIN 2/3) (20-30%) 
High-grade CIN (CIN 2/3) → Invasive cancer (~20%)
Natural History of HPV

- Preinvasive cancer (Cervical intraepithelial neoplasia – CIN)
- Microinvasive cancer
- Invasive cancer

Epithelium
Underlying tissue
Invasive (malignant) cells invade neighboring tissues, enter blood vessels, and spread to different sites.

Precancer cells grow only locally and cannot spread by invasion or metastasis.

Time
Progression Rates to Precancer

- Time from HPV infection to precancer: 2-5 years
- Average age of diagnosis of precancer: 25-35 years
- Risk of persistent HPV 16 infection progressing to precancer: 40% over 3-5 years
Progression Rates to Cancer

- Time it takes for HPV infection to progress to precancer is shorter than the time it takes for precancer to progress to cancer
- CIN 3 has a 20-30% risk of progressing to cancer over 5-10 years
- Peak age of invasive cervical cancer: 35-55 years
1. Cervical cancer is the most common cause of cancer-related deaths among women in Zambia and the sub-Saharan African region.
   (a) True
   (b) False

2. The vast majority of cervical cancers are caused by genital tract infection with the human papillomavirus (HPV).
   (a) True
   (b) False
3. HPV infection may resolve without treatment.
   (a) True
   (b) False

4. The HPV virus is most commonly transmitted:
   (a) Sexually
   (b) By drinking contaminated water
   (c) By an insect vector
   (d) All of the above
Congratulations!

You passed this evaluation with a score of

Please click on the CERTIFICATE button below to print your certificate. Be sure to print & sign your name before submitting the certificate to your supervisor.