Natural history and Epidemiology of Cervical Cancer and HPV

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Agenda

• What is human papillomavirus (HPV)?
• What is the sequence of events between HPV infection and cervical cancer?
• What are the other risk factors for cervical cancer (besides high-risk HPV infection)?
• What is the burden of HPV and cervical cancer?
• Secondary prevention of cervical cancer through screening
WHAT IS HUMAN PAPILLOMAVIRUS?
Human papillomaviruses

Sequence of events

HPV INFECTION → CERVICAL CANCER
Simple model of the natural history of HPV and cervical cancer
UNPACKING THE TRANSITIONS
HPVs are EASILY transmitted through skin-to-skin contacts.

HPVs enter the basal epithelial cells through microscopic tears in the skin.

HPVs infect the basal cells, and when they are triggered to divide to repair the micro-wound, the viral life cycle is activated.
HPV transmission occurs rapidly after initiating sexual activity.

Genital HPV equally common in men and women


Condoms only partially protect against infection

[Graph showing the rate of HPV infection per 100 patient-years at risk for different frequencies of condom use by partner:]

- <5%: 89.3
- 5-49%: 159.9
- 50-99%: 62.3
- 100%: 37.8

Rapid control of infection to undetectable levels is the rule

- Clearance reflects loss of detectable HPV DNA from genital tract
- This happens through immune control of HPV and/or eradication of infection
- Note that absence of HPV detection does not imply absence of infection – HPV can become latent

HPV deep in tissue when latent

- Animal studies show latent infection in basal cells of the epithelium
- These cells are not sampled during routine screening, but the infections are sporadically detected when sampling the entire cervical tissue

Persistent HR-HPV detection is strong risk factor for progression

- Infections which are not controlled below limits of detection within 2-3 years are at high risk of progression to pre-cancer
What is precancer?

Cervical intraepithelial neoplasia (CIN) or squamous intraepithelial lesion (SIL) = terminology to define precancer based on Pap smear or biopsy interpretation

- **CIN1 or LSIL** = productive HPV infection with high probability of regression to normal
- **CIN2/3 or HSIL** = likely precancer with lower risk of regression → TARGET of SCREENING
Modifiable risk factors for progression of HPV infection to cancer

- Long duration oral contraceptive use (> 5 years)
  - High parity (> 5 full-term births)
  - Tobacco smoke
Almost all sexually active people have the HPV infection at some point.

The process of how HPV infection causes cancer:

- **Infection**
  - 90% clear

- **Persistence**
  - 4-5 years
  - 43% regress

- **Progression**
  - 9-15 years
  - 38% regress

- **Invasion**
  - CIN 3
  - Cancer

*The best way to avoid cervical cancer? Have your smear!!*

[https://www.kenttherapyclinic.co.uk/blog/hpv-virus-cervical-cancer-an-easy-to-understand-guide](https://www.kenttherapyclinic.co.uk/blog/hpv-virus-cervical-cancer-an-easy-to-understand-guide)
HOW MANY PEOPLE GET HPV VS. CERVICAL CANCER?
Who is at risk for HPV?

PRACTICALLY EVERYONE!
Global burden of HPV-associated cancers

Numbers of US Cancers Caused by HPV


https://prescancerpanel.cancer.gov/report/hpvupdate
Global vs. US burden of HPV-associated cancers – why the difference?

SCREENING!!
Secondary Cervical Cancer Prevention:
Early detection and treatment → SCREENING

• Screening programs identify HPV infection or cellular abnormalities associated with precancer
• Diagnosis by colposcopy+biopsy and histopathologic interpretation to identify women with precancer
• Treat precancer by ablation or excision (usually outpatient procedure) to prevent progression to cervical cancer
• Type and frequency of screening varies by age
• Choice of screening test in women aged 30-65 left to provider/patient
Example screening management algorithm

Different absolute risk of progression to precancer (CIN3+) based on HPV type
HPV 16/18 are not the most common types, they are the most common types that cause cancer
Woman-level natural history

- Women participating in screening are accumulating their own personal HPV natural history

- How to counsel? How to reduce risk?
1st HPV positive test result

How did I get HPV?
How long have I had HPV?

HPV negative

Should I get the vaccine?
Can I get re-infected?

Is my infection gone-gone' or will it come back like herpes?

2nd HPV positive test result

My last test was negative - I have not had a new partner - is my partner cheating?

Am I at higher risk now for cancer?

What can I do to prevent this infection from recurring or make it go away?

CUMULATIVE HPV SCREENING HISTORY
Recent Sexual Exposures - New Partner

- New acquisition
- Re-infection
- Deposition (from recent sex act)

HPV Negative Test → HPV Positive Test
Prevention strategies

Vaccination

Susceptible

IMMUNE

Recent Sexual Exposures - New Partner
- New acquisition
- Re-infection
- Deposition (from recent sex act)

HPV Negative Test

HPV Positive Test

Clearance HPV uninfected

HPV Negative Test

Persistent Detection HPV infected

HPV Positive Test

Latent Controlled Infection (below limits of detection) HPV infected

HPV Negative Test

Neoplasia/Cancer

Loss of Immune Control

Routine screening
THANK YOU!