HPV DISEASES
Diagnosis, management, therapy

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Training Course in Sexual and Reproductive Health Research
Geneva 2010
EPIDEMIOLOGY

- Frequency in sexually-active general population: 3-25%
- Frequency among 20-35 yrs population: 40-60%
- Mean clearance time: 8 – 24 months
- Frequency of multiple infections: 3-25%
AGE SPECIFIC PREVALENCE

- HPV (any type)
- HR-HPV
- LR-HPV

Age groups:
- <26
- 26-30
- 31-35
- 36-40
- 41-45
- 46-50
- 51-55
- >55
HPV DISEASE

Natural history

- Latent stage
- Subclinical stage
- Clinical stage
Epithelial ‘trauma’

HPV entry into basal germinal layer of epithelium

Expression of viral early proteins

Cellular proliferation

Capsid proteins produced in superficial layers of epithelium
HPV DISEASE

Diagnosis

LATENT STAGE

Identified by virus contact but without clinical or instrumental evidence of clinical lesions

MOLECULAR BIOLOGY
HPV
IS A POOR NATURAL IMMUNOGEN

✓ Non-lytic virus
   Little release of antigens to the immune system
   No local cytokine release to invoke a response

✓ No systemic phase
   Little professional antigen presentation
HPV DISEASE
Diagnosis

SUBCLINICAL STAGE
Identified by virus contact and with instrumental-only evidence of early genital lesions

COLPOSCOPY – HISTOLOGY – MOLECULAR BIOLOGY
5% Acetic acid application effect
HPV DISEASE

Diagnosis

CLINICAL STAGE

Identified by virus contact and clinical evidence of genital lesions

INSPECTION – COLPOSCOPY – HISTOLOGY
MOLECULAR BIOLOGY
Management

LATENT STAGE

Identified by virus contact but without clinical or instrumental evidence of clinical lesions

THIS SHOULD NOT BE CONSIDERED AS REAL DISEASE BUT "HIGHER RISK" EXPOSURE

BACK TO SCREENING PROGRAMS
Management

SUBCLINICAL STAGE

Identified by virus contact and with instrumental-only evidence of early genital lesions

Titolo diagramma
Management

CLINICAL STAGE

Identified by virus contact and clinical evidence of genital lesions

- COLPOSCOPY
- HISTOLOGY

- LOW-GRADE LESION
  - FOLLOW UP vs. TREATMENT

- HIGH-GRADE LESION
  - TREATMENT
HPV DISEASE

Natural history

✓ early regression
✓ persistence
✓ fluctuation
✓ late regression
✓ progression
✓ recurrence
EFFICACY OF TREATMENT

- Cure rate
- Recurrence rate
- Patient’s compliance
- Costs/benefits ratio
THERAPY CONCEPTS

✓ Lesions removal
✓ HPV persistence
✓ High recurrence rate
✓ Need for multiple treatments
Problem approach

Treatment by anatomical site

- vulva and perineum
- vagina
- cervix

Treatment by type of lesion

- subclinical lesion
- warty lesion
- preneoplastic lesion
Treatment options

Medical options

Podofillin
Podofilotoxin
Tricloroacetic acid
5-fluorouracil
Imiquimod 5%
Treatment options

Surgical options

Cold knife surgery
Criotherapy
Diatermy surgery
LEEP - LLETZ
Radiofrequency surgery
CO₂ Laser
# Efficacy of Medical Choice

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% Immediate cure rate</th>
<th>% after 3 mth cure rate</th>
<th>Recurrence rate</th>
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<tbody>
<tr>
<td>Podofillin</td>
<td>35-75</td>
<td>25-75</td>
<td>10-70</td>
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<tr>
<td>Podofillotossin</td>
<td>45-90</td>
<td>35-75</td>
<td>10-90</td>
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<tr>
<td>Tricloroacetic acid</td>
<td>50-80</td>
<td>70</td>
<td>35</td>
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<tr>
<td>5-FU</td>
<td>10-70</td>
<td>40</td>
<td>35</td>
</tr>
<tr>
<td>Imiquimod</td>
<td>70</td>
<td>70</td>
<td>10</td>
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# EFFICACY OF SURGICAL CHOICE

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<tbody>
<tr>
<td>Cold knife surgery</td>
<td>90-95</td>
<td>35</td>
<td>0-30</td>
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<tr>
<td>Criotherapy</td>
<td>65-90</td>
<td>65-95</td>
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<tr>
<td>DTC</td>
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<tr>
<td>LEEP</td>
<td>30-90</td>
<td>-</td>
<td>15-50</td>
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<tr>
<td>CO₂ Laser</td>
<td>90-95</td>
<td>70</td>
<td>20-30</td>
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THERAPY CONCEPTS

BY ANATOMICAL SITE AND TYPE OF LESION

VULVA and PERINEUM

- SUBCLINICAL LESION
  - WAIT & SEE
- WARTY LESION
  - MEDICAL THERAPY vs. SURGICAL THERAPY
- PRENEOPLASTIC LESION
  - SURGICAL THERAPY
THERAPY CONCEPTS

BY ANATOMICAL SITE AND TYPE OF LESION

VAGINA

- SUBCLINICAL LESION
  - WAIT & SEE

- WARTY LESION
  - SURGICAL THERAPY

- PRENEOPLASTIC LESION
  - SURGICAL THERAPY
THERAPY CONCEPTS

BY ANATOMICAL SITE AND TYPE OF LESION

- CERVIX
  - SUBCLINICAL LESION
    - WAIT & SEE
  - WARTY LESION
    - SURGICAL THERAPY
  - PRENEOPLASTIC LESION
    - SURGICAL THERAPY
Cervical Cancer

- Estimated incidence and mortality in the United States (2007)¹

  - 11,150 new cases
  - 3,670 deaths
  - 1:168 Lifetime risk

Cervical cancer

- International estimates
  - Approximately 570,000 cases expected worldwide each year
  - 275,000 deaths
  - Number one cancer killer of women worldwide
Cervical cancer is a sexually transmitted disease.
HPV DNA is present in virtually all cases of cervical cancer and precursors.
Some strains of HPV have a predilection to the genital tract and transmission is usually through sexual contact (16, 18 High Risk).
Little understanding of why small subset of women are affected by HPV.
HPV may be latent for many years before inducing cervical neoplasia.
Pap Smear

With the advent of the Pap smear, the incidence of cervical cancer has dramatically declined
Cervical cancer
but ...

- Single Pap false negative rate is 20%.
- The latency period from dysplasia to cancer of the cervix is variable.
- 50% of women with cervical cancer have never had a Pap smear.
- 25% of cases and 41% of deaths occur in women 65 years of age or older
Cell Type

- Squamous Cell Carcinoma  80-85%
- AdenoCarcinoma  15%
- Adenosquamous
- Others
Cervical cancer Risk Factors

- Early age of intercourse
- Number of sexual partners
- Smoking
- Lower socioeconomic status
- High-risk male partner
- Other sexually transmitted diseases
- Up to 70% of the U.S. population is infected with HPV
Prevention

- Educate all providers, men and women regarding HPV and the link to cervical cancer.
- Adolescents are an especially high-risk group due to behavior and cervical biology.
- Delay onset of sexual intercourse.
- Condoms may help prevent sexually transmitted disease.
Screening Guidelines for the Early Detection of Cervical Cancer, American Cancer Society 2003

✓ Screening should begin approximately three years after a woman begins having vaginal intercourse, but no later than 21 years of age.
✓ Screening should be done every year with regular Pap tests or every two years using liquid-based tests.
✓ At or after age 30, women who have had three normal test results in a row may get screened every 2-3 years. However, doctors may suggest a woman get screened more if she has certain risk factors, such as HIV infection or a weakened immune system.
✓ Women 70 and older who have had three or more consecutive Pap tests in the last ten years may choose to stop cervical cancer screening.
✓ Screening after a total hysterectomy (with removal of the cervix) is not necessary unless the surgery was done as a treatment for cervical cancer.

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thank you