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HPV DISEASES
Diagnosis, management, therapy

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Training Course in Sexual and Reproductive Health Research
Geneva, February 2009

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%

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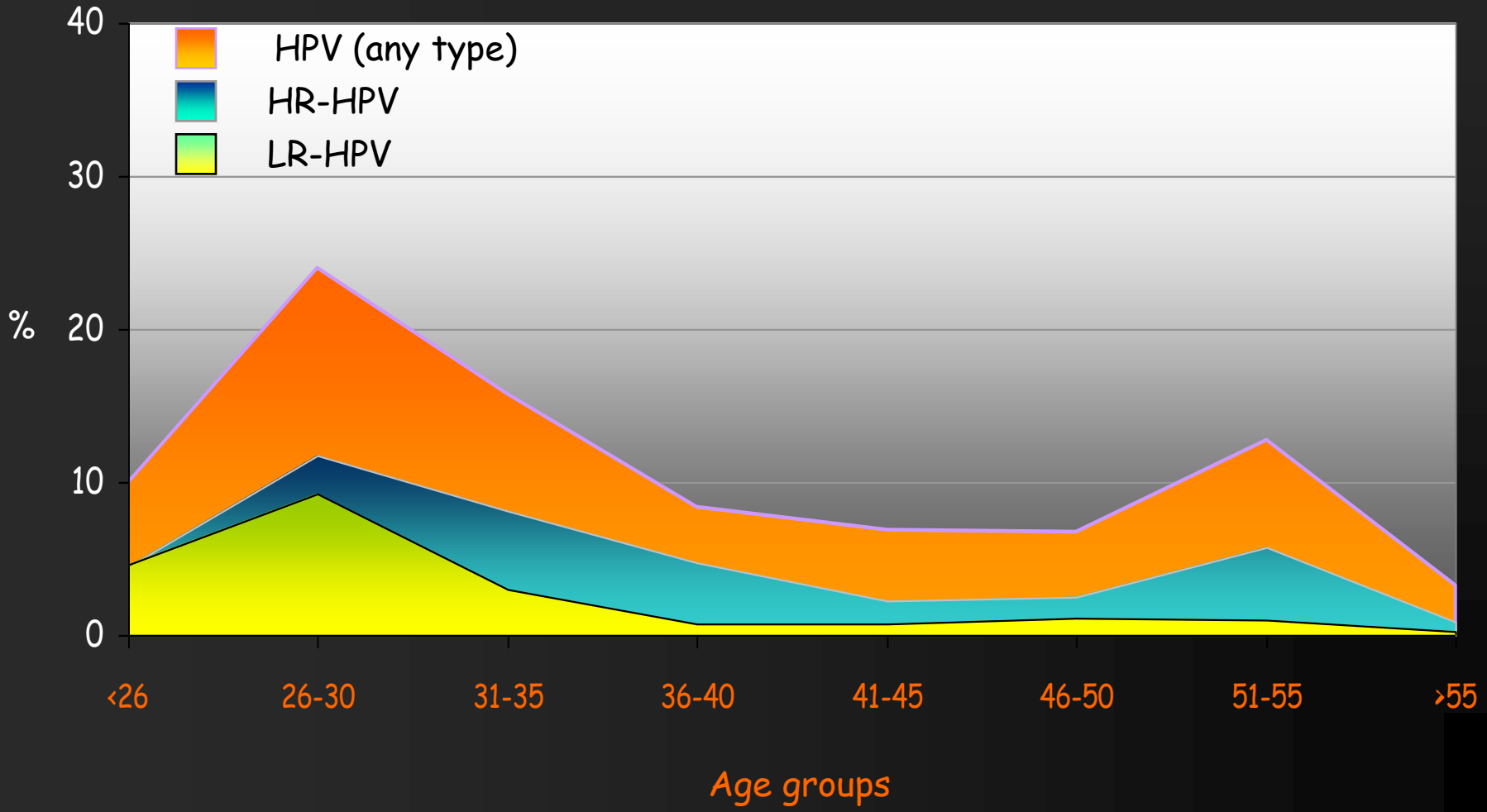
AGE SPECIFIC PREVALENCE



HPV DISEASE

Natural history

- ✓ Latent stage
- ✓ Sublinical stage
- ✓ Clinical stage

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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 of 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

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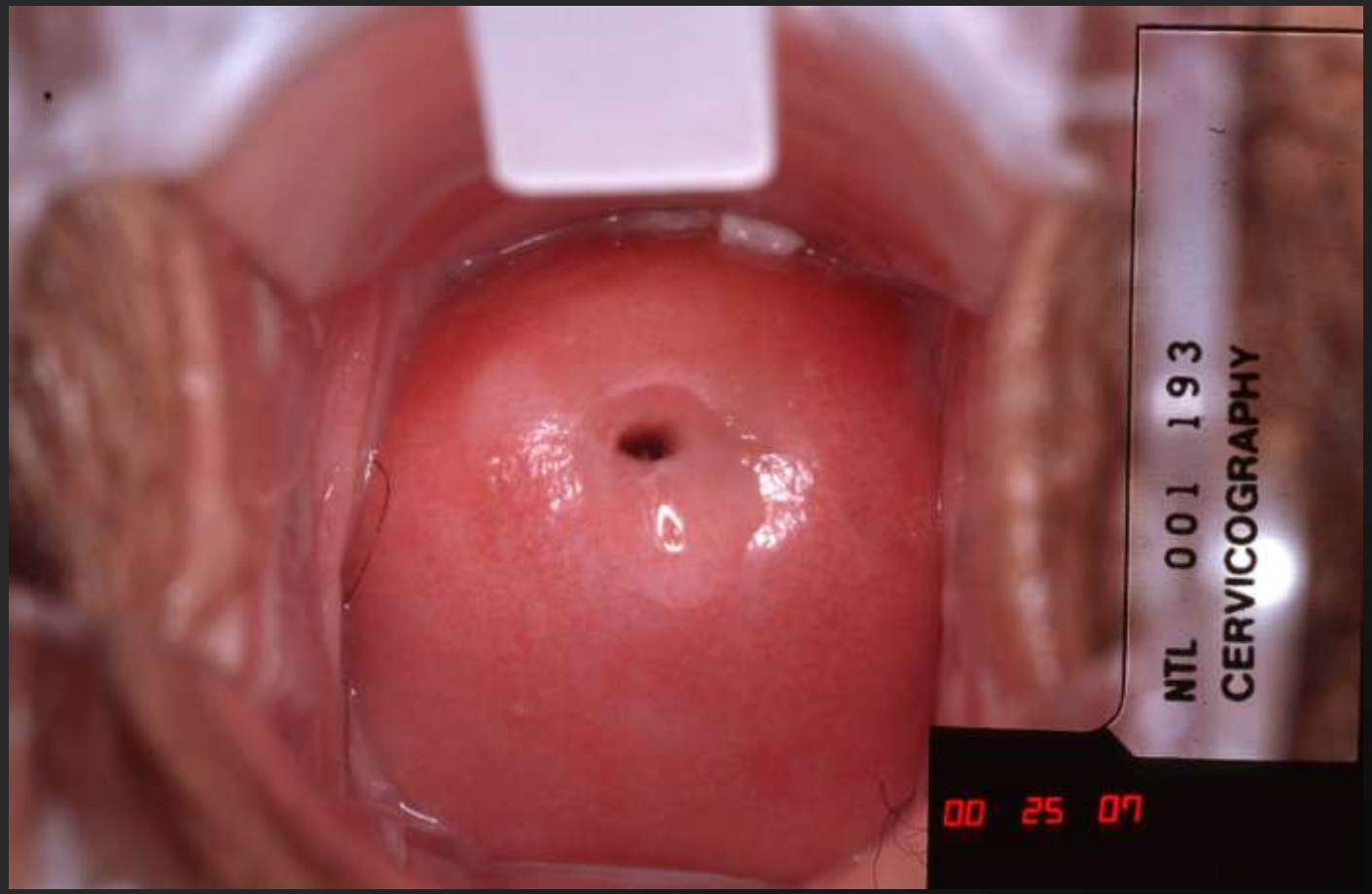

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HPV DISEASE

Diagnosis

SUBCLINICAL STAGE

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

COLPOSCOPY – HISTOLOGY – MOLECULAR BIOLOGY

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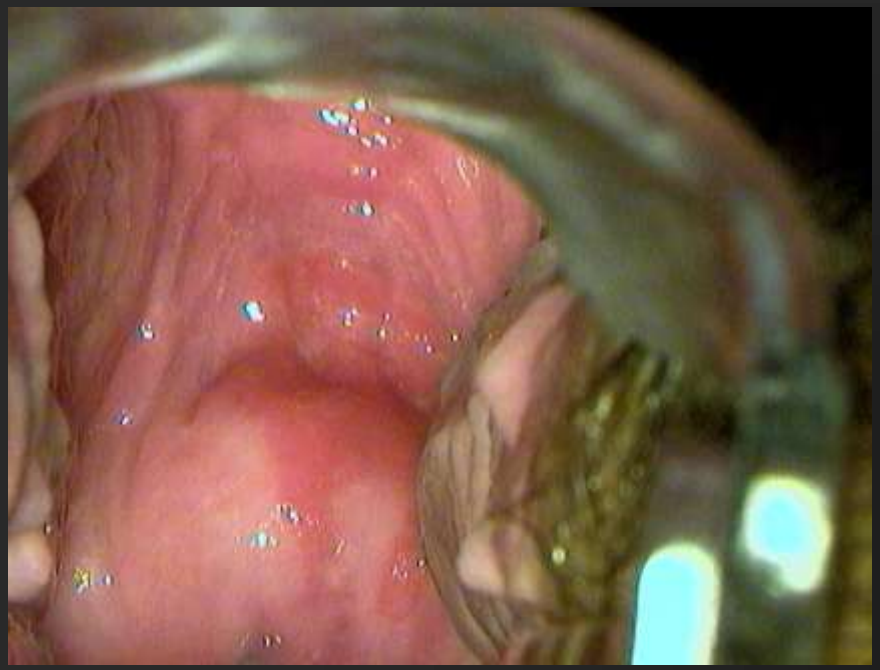

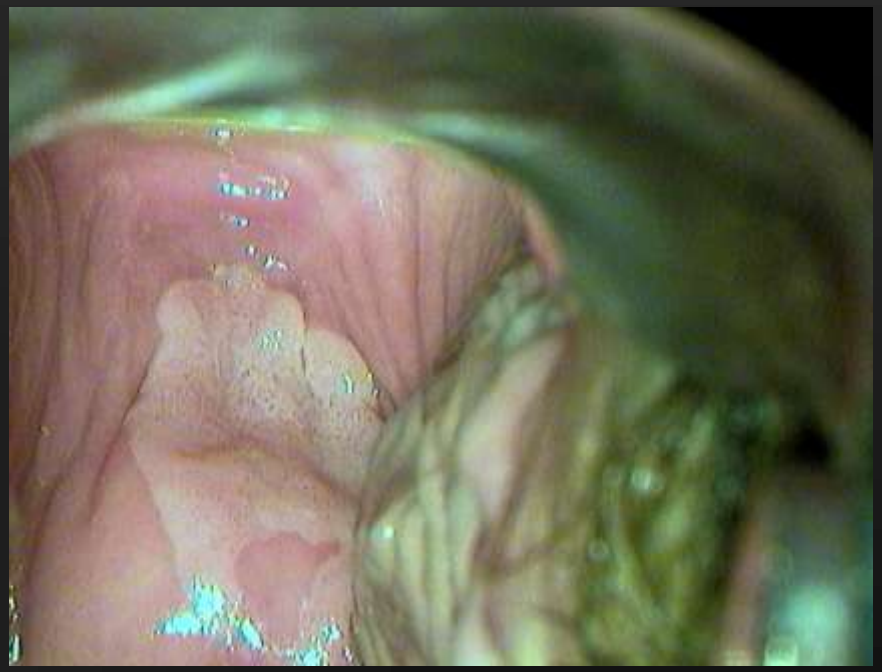

5% Acetic acid application effect

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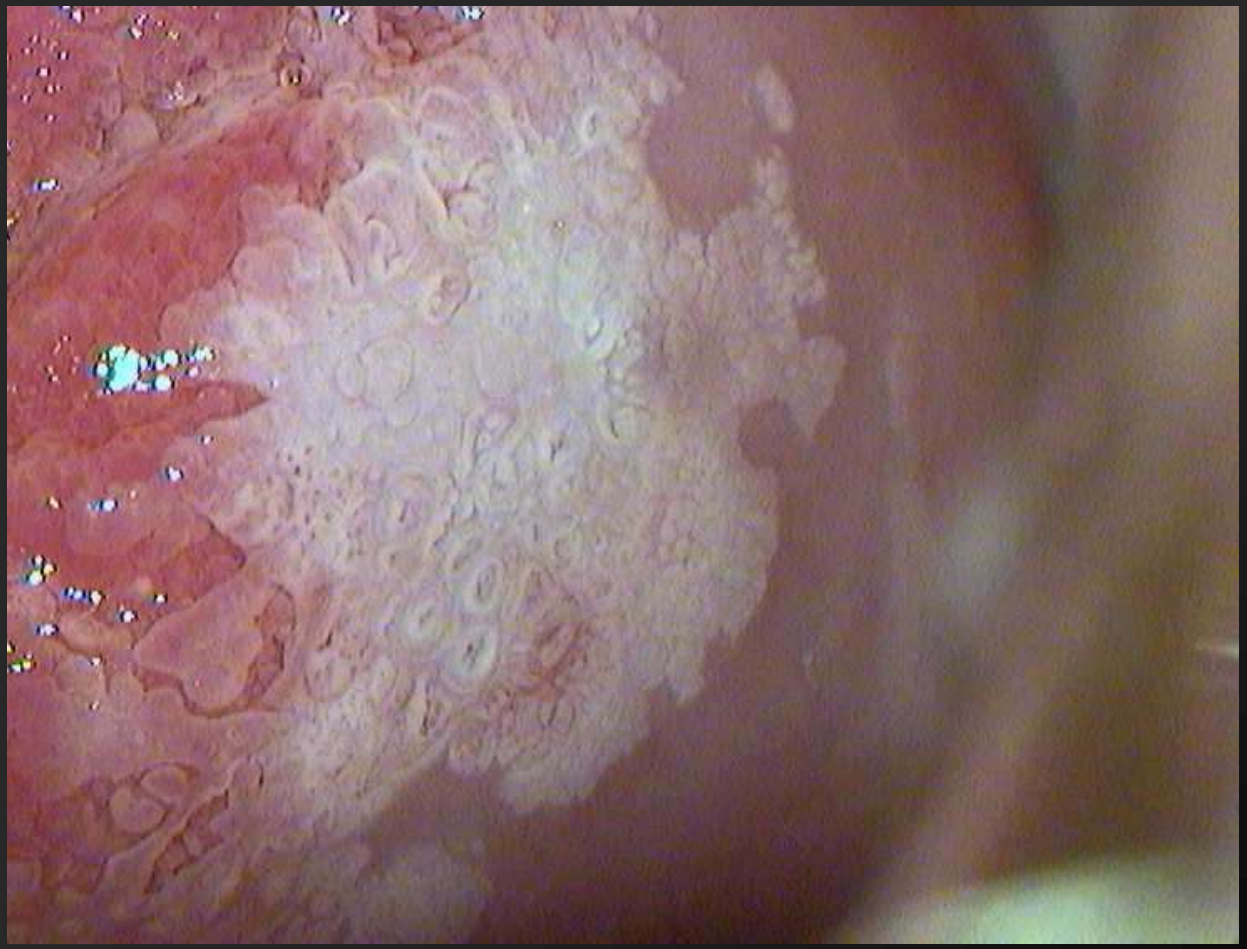

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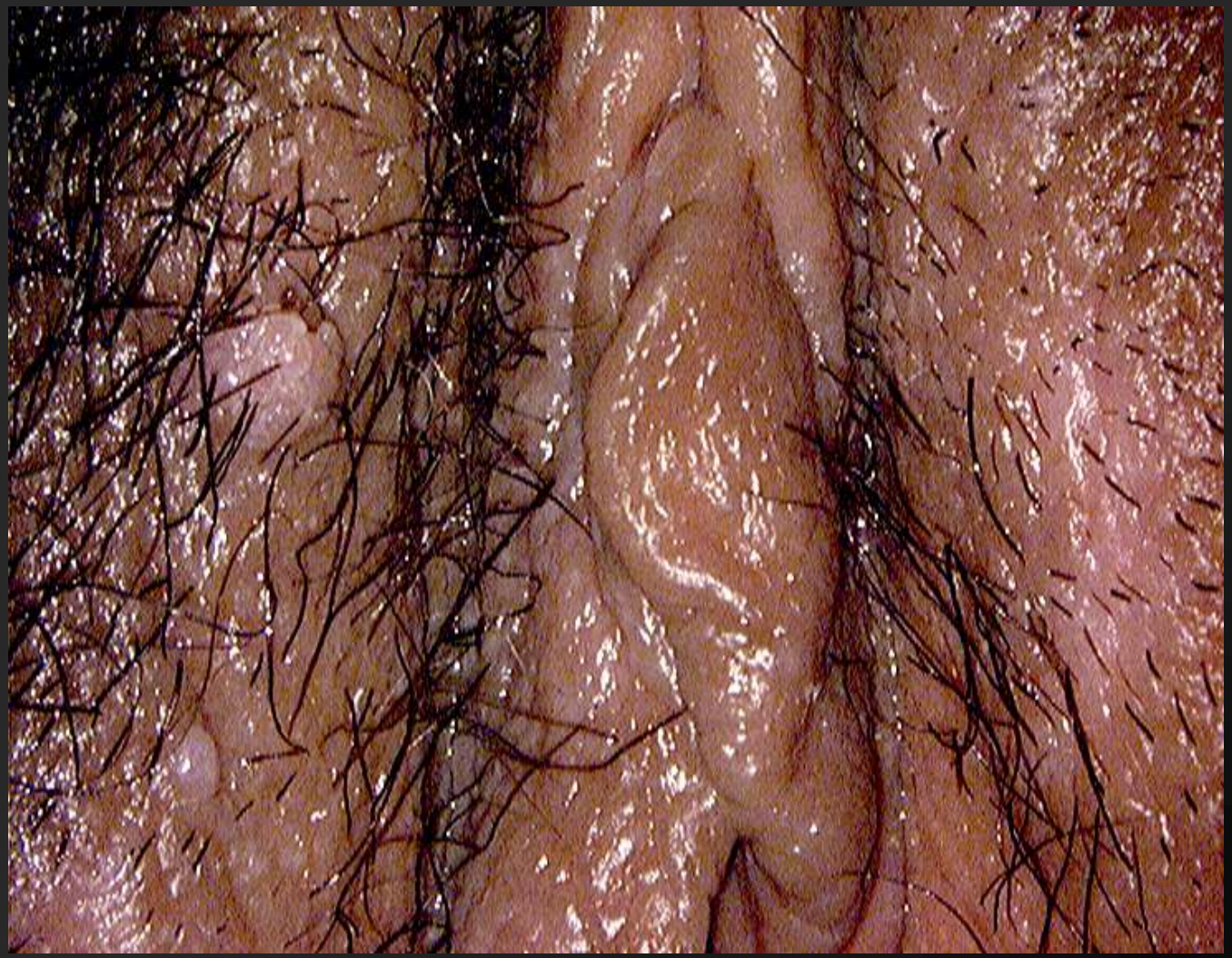
HPV DISEASE

Diagnosis

CLINICAL STAGE

Identified by virus contact and clinical evidence of genital lesions

INSPECTION – COLPOSCOPY – HISTOLOGY MOLECULAR BIOLOGY



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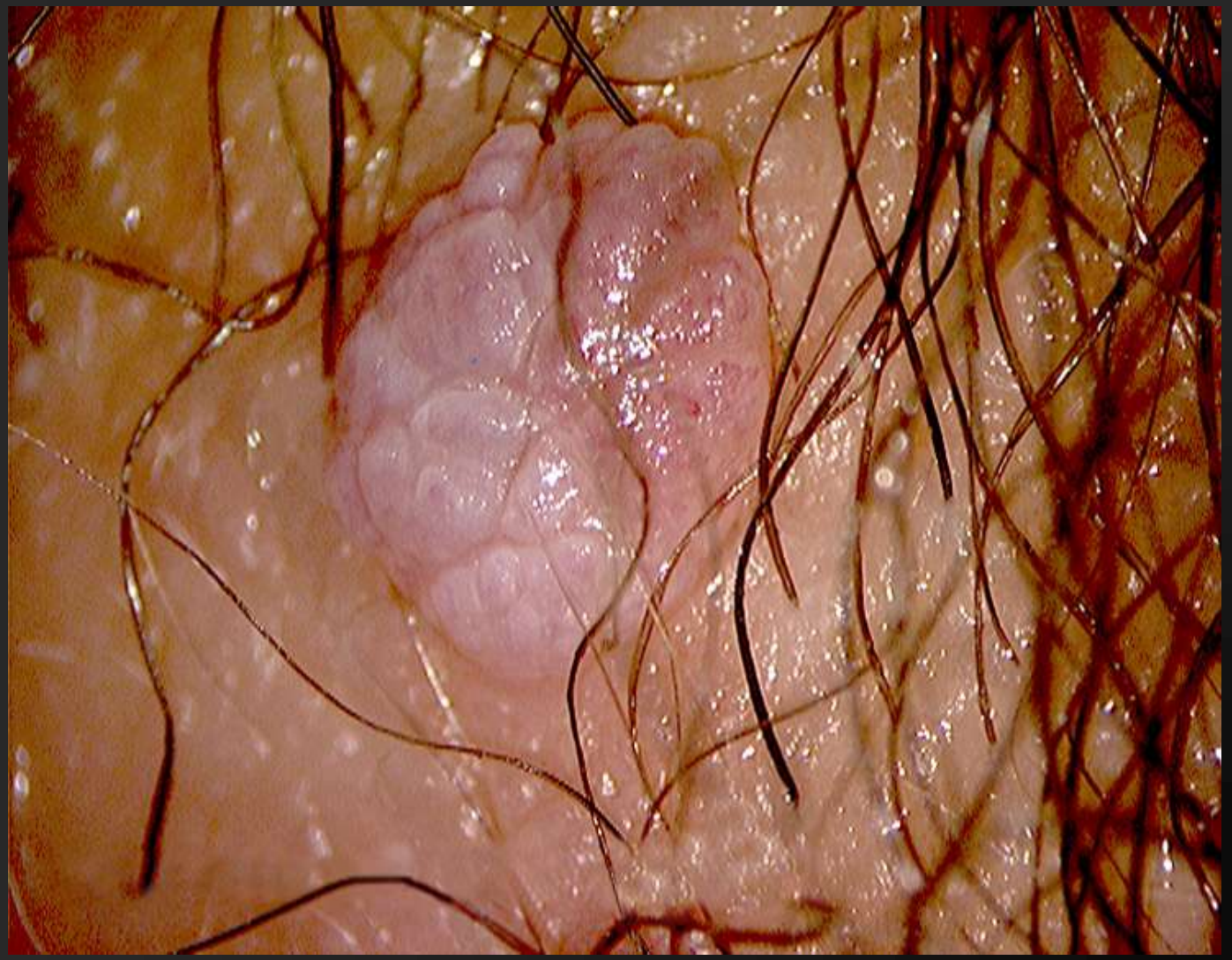

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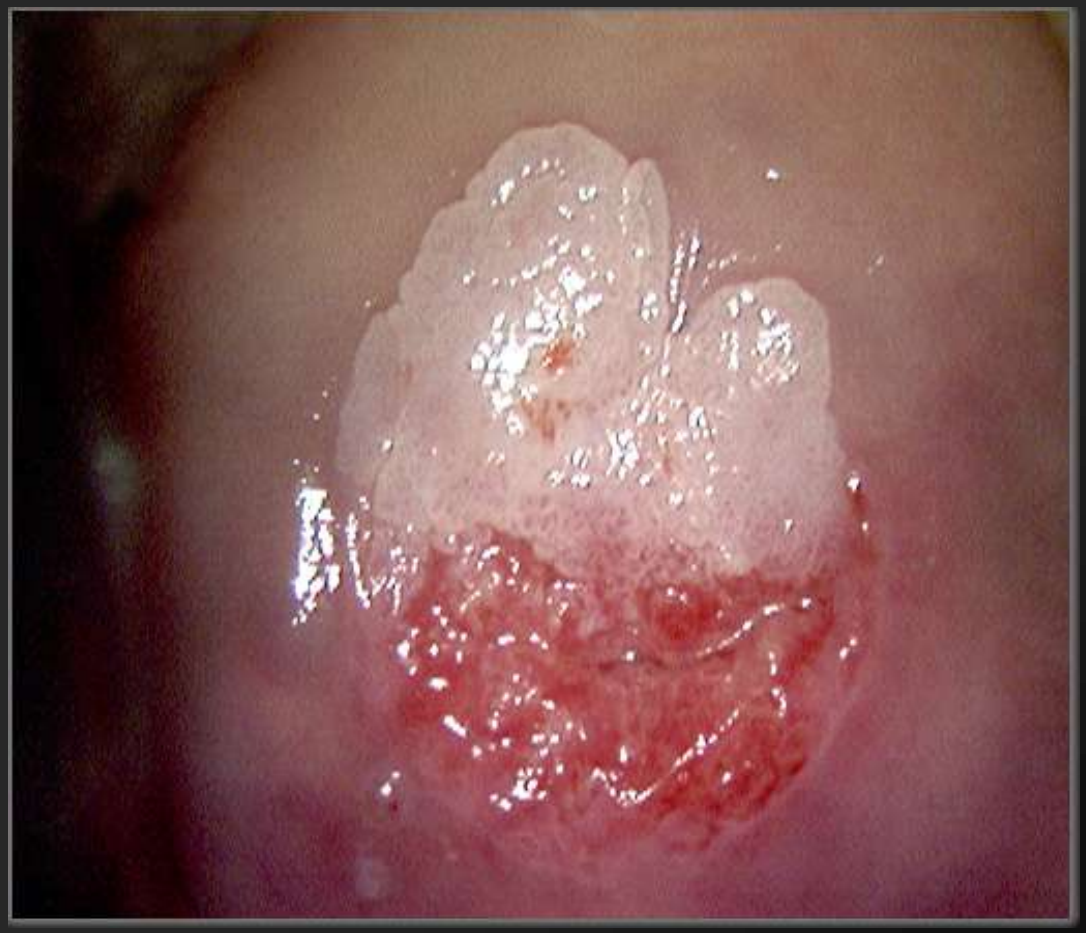

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Management

LATENT STAGE

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

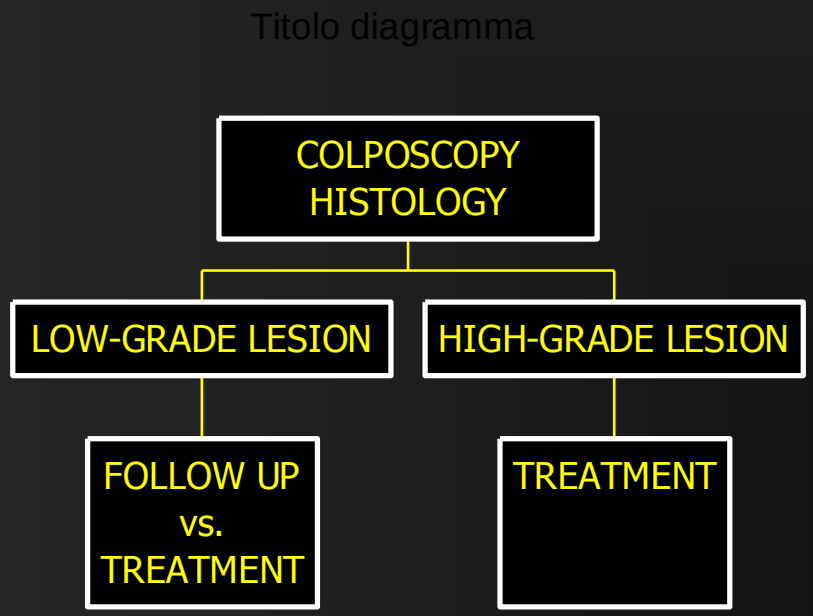
THIS SHOULD NOT BE CONSIDERED AS REAL DISEASE BUT "HIGHER RISK" EXPOSURE

BACK TO SCREENING PROGRAMS

Management

SUBCLINICAL STAGE

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

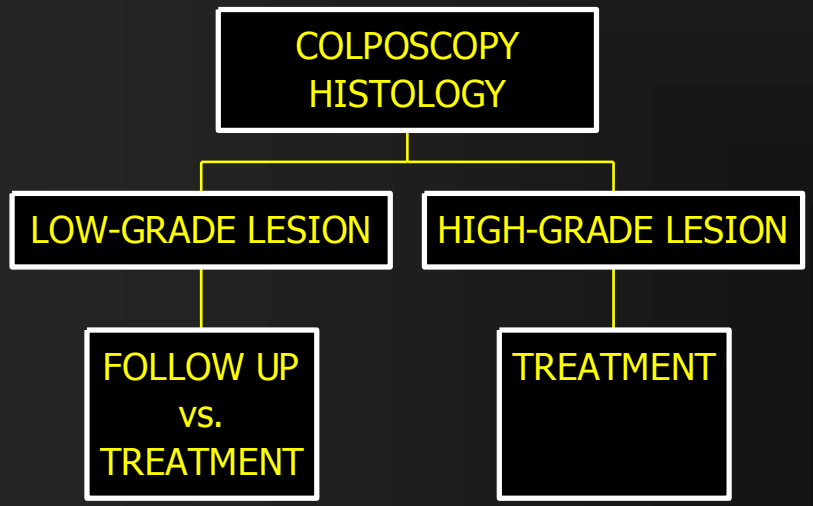


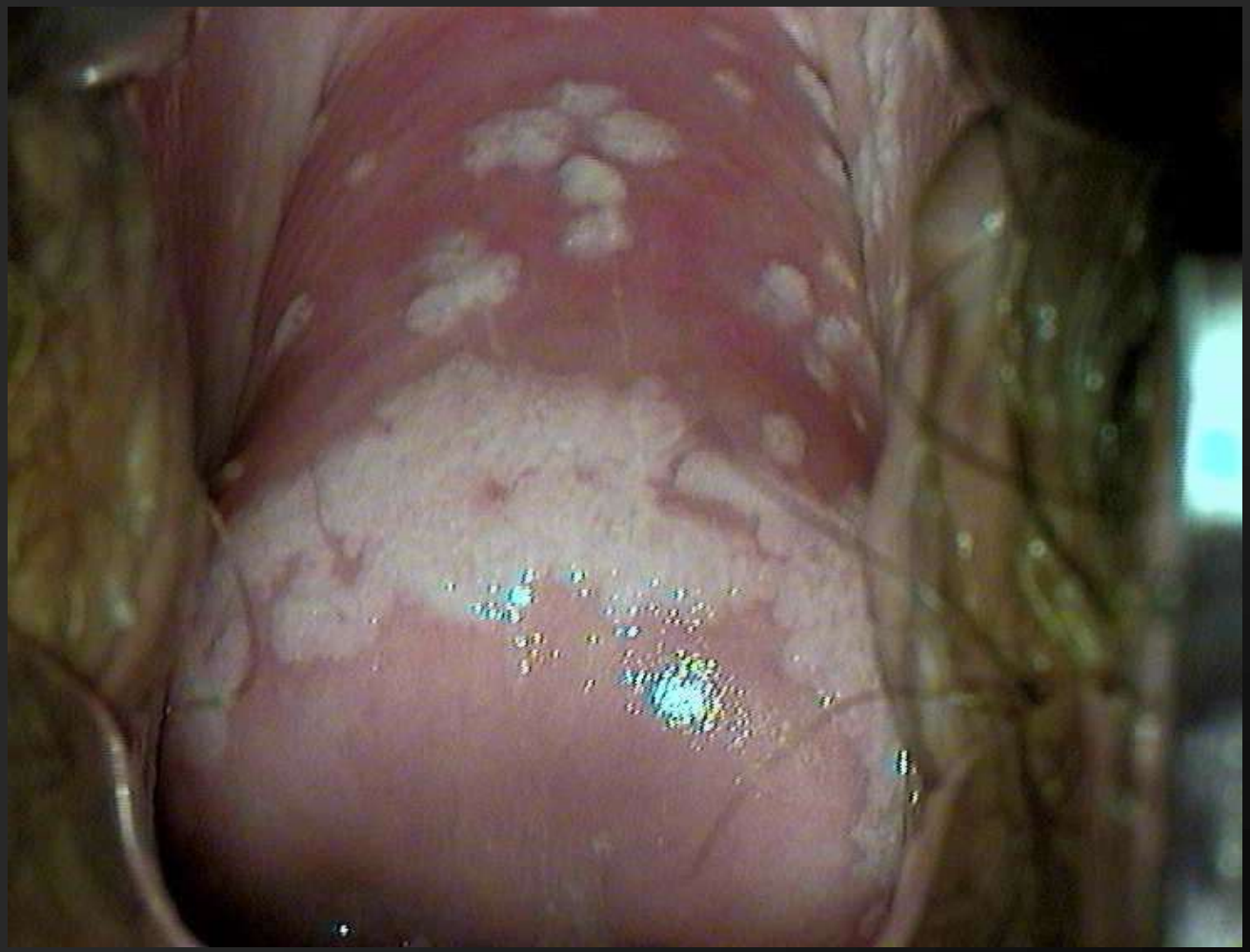
Management

CLINICAL STAGE

Identified by virus contact and clinical evidence of genital lesions

Titolo diagramma





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

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Treatment options

Medical options

- Podofillin
- Podofillotossin
- Tricloroacetic acid
- 5-fluorouracil
- Imiquimod 5%

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Treatment options

Surgical options

- Cold knife surgery
- Criotherapy
- Diatermy surgery
- LEEP - LLETZ
- Radiofrequency surgery
- CO_2 Laser

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EFFICACY OF MEDICAL CHOICE

Treatment	% Immediate cure rate	% after 3 mth cure rate	Recurrence rate
Podofillin	35-75	25-75	IO-7O
Podofillotossin	45-9O	35-75	IO-9O
Tricloroacetic acid	5O-8O	7O	35
5-FU	IO-7O	4O	35
Imiquimod	7O	7O	IO

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EFFICACY OF SURGICAL CHOICE

Treatment	% Immediate cure rate	% after 3 mth cure rate	Recurrence rate
Cold knife surgery	90-95	35	0-30
Criotherapy	65-90	65-95	0-40
DTC	95	80-90	25
LEEP	30-90	-	15-50
CO_2 Laser	90-95	70	20-30

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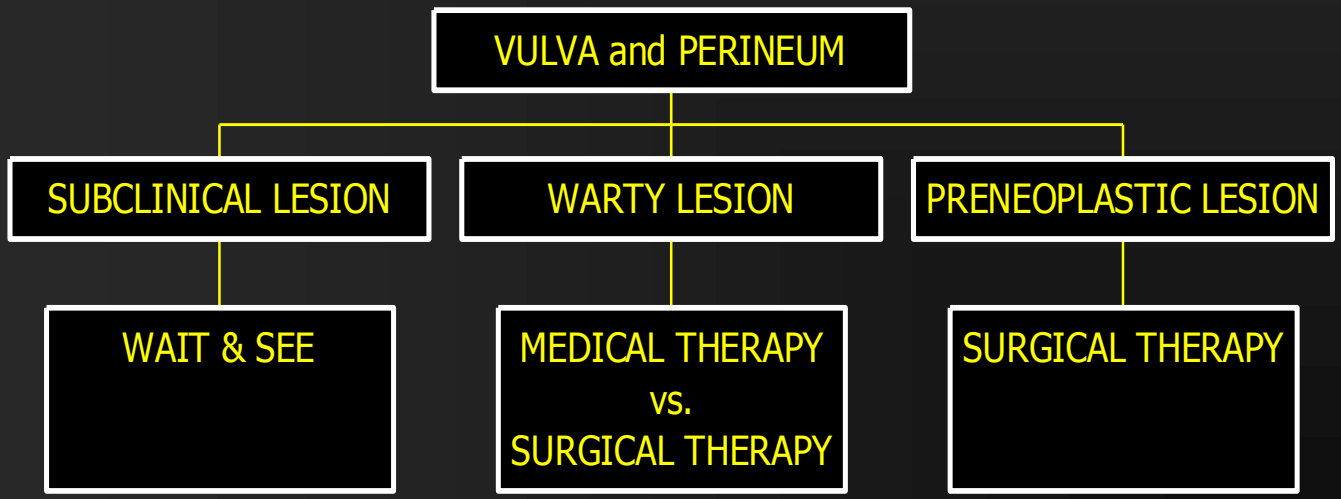
THERAPY CONCEPTS

BY ANATOMICAL SITE AND TYPE OF LESION



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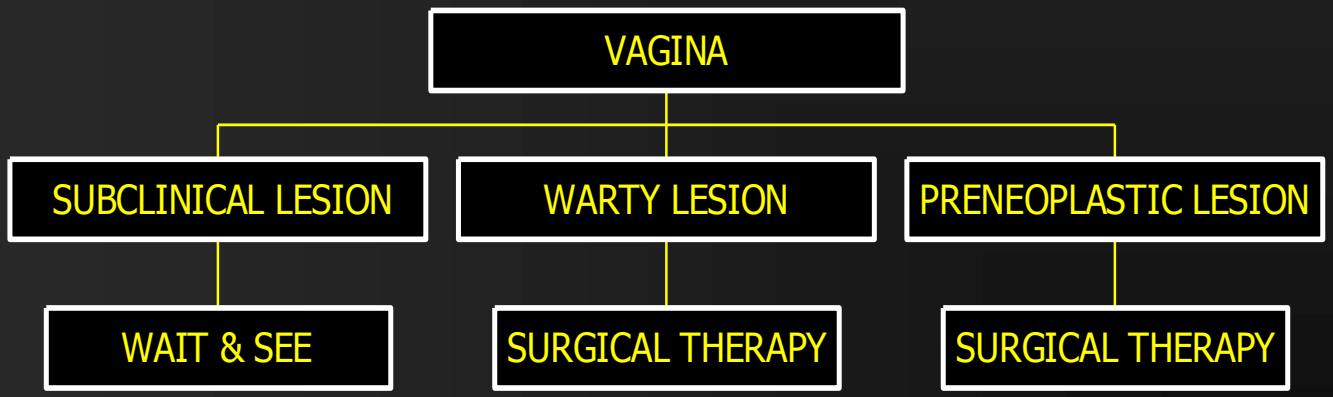

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THERAPY CONCEPTS

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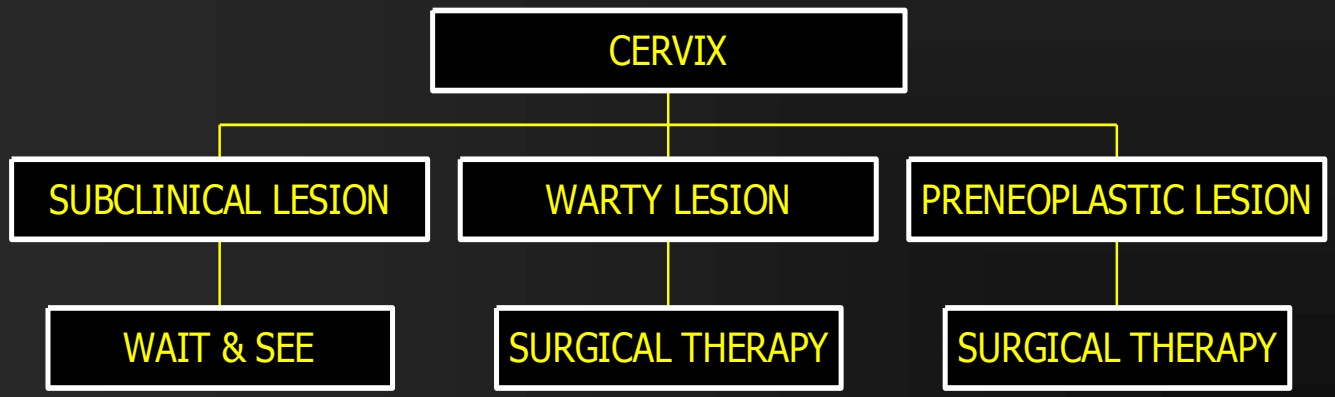
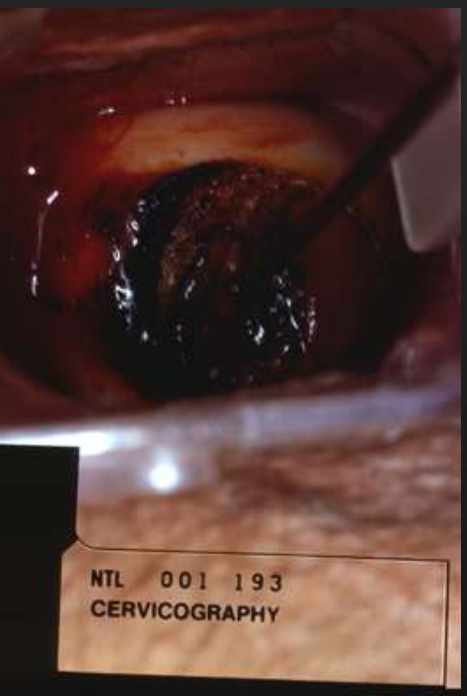
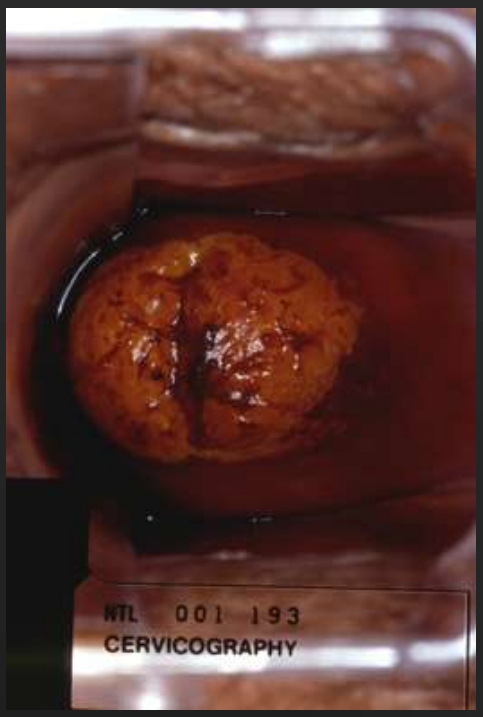



NTL 001 193
CERVICOGRAPHY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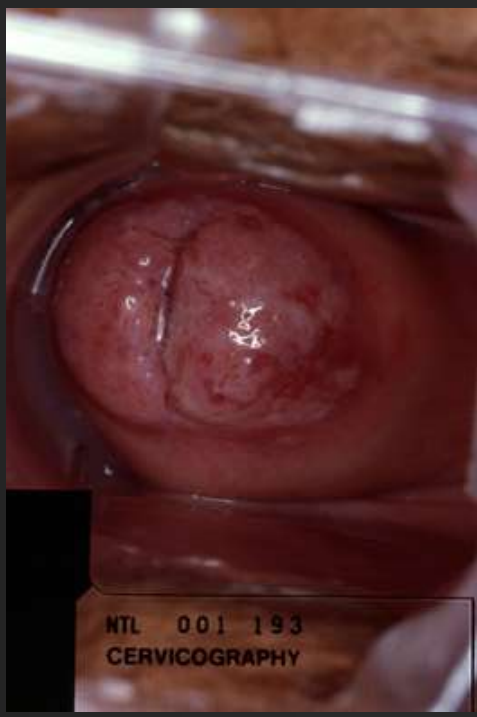
CERVICOGRAPHY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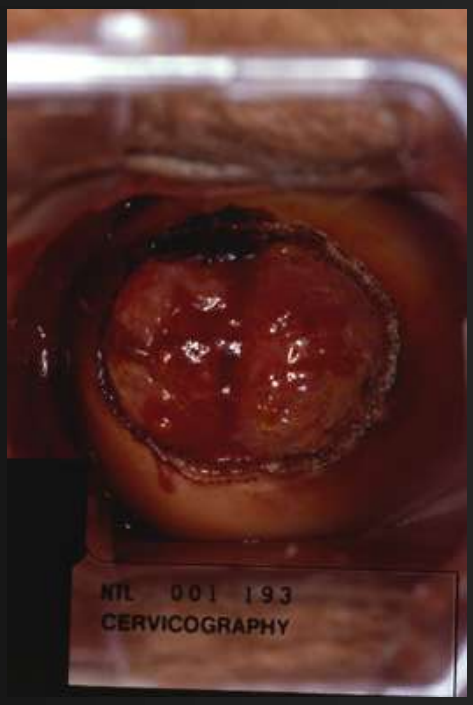
CERVICOGRAPHY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CERVICOGRAPHY

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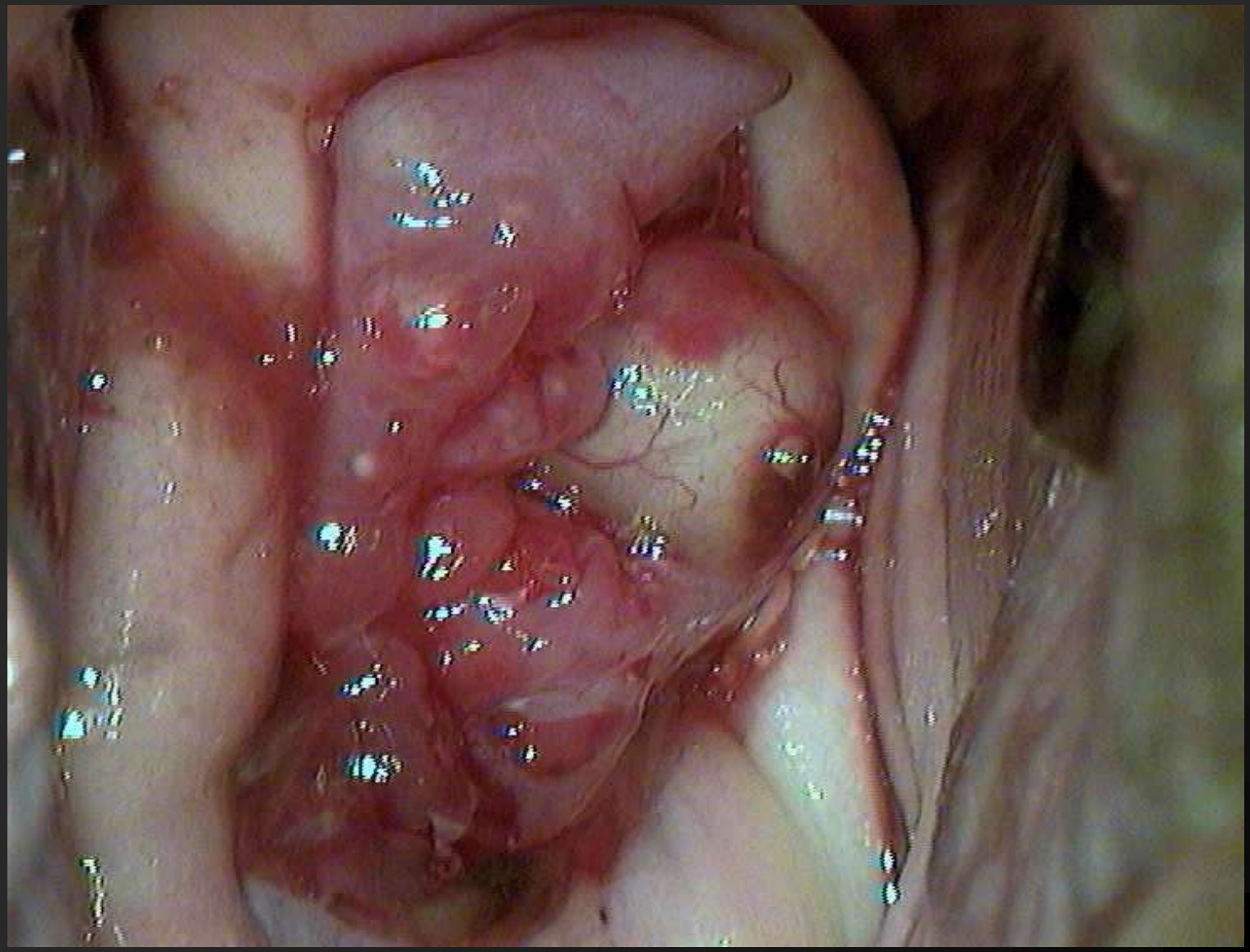

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Cervical Cancer

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

  11,150 new cases

  3,670 deaths

  1:168 Lifetime risk

1. American Cancer Society. *Cancer Facts & Figures.* 2007. Atlanta, GA; 2007

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Cervical cancer

- International estimates
  - Approximately 570,000 cases expected worldwide each year
  - 275,000 deaths
  - Number one cancer killer of women worldwide

Cervical CA Etiology

- ✓ 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

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Cervical cancer

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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

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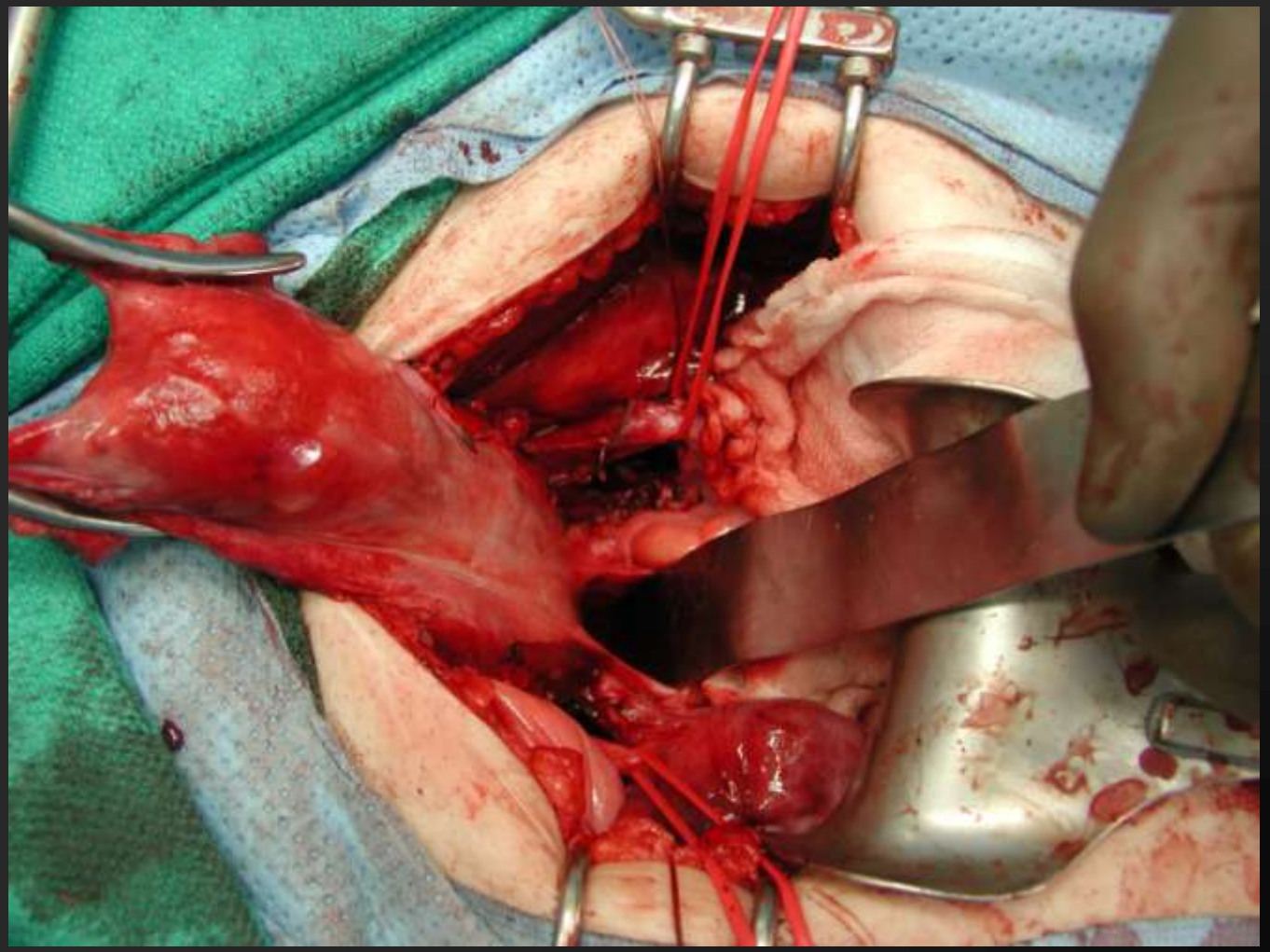

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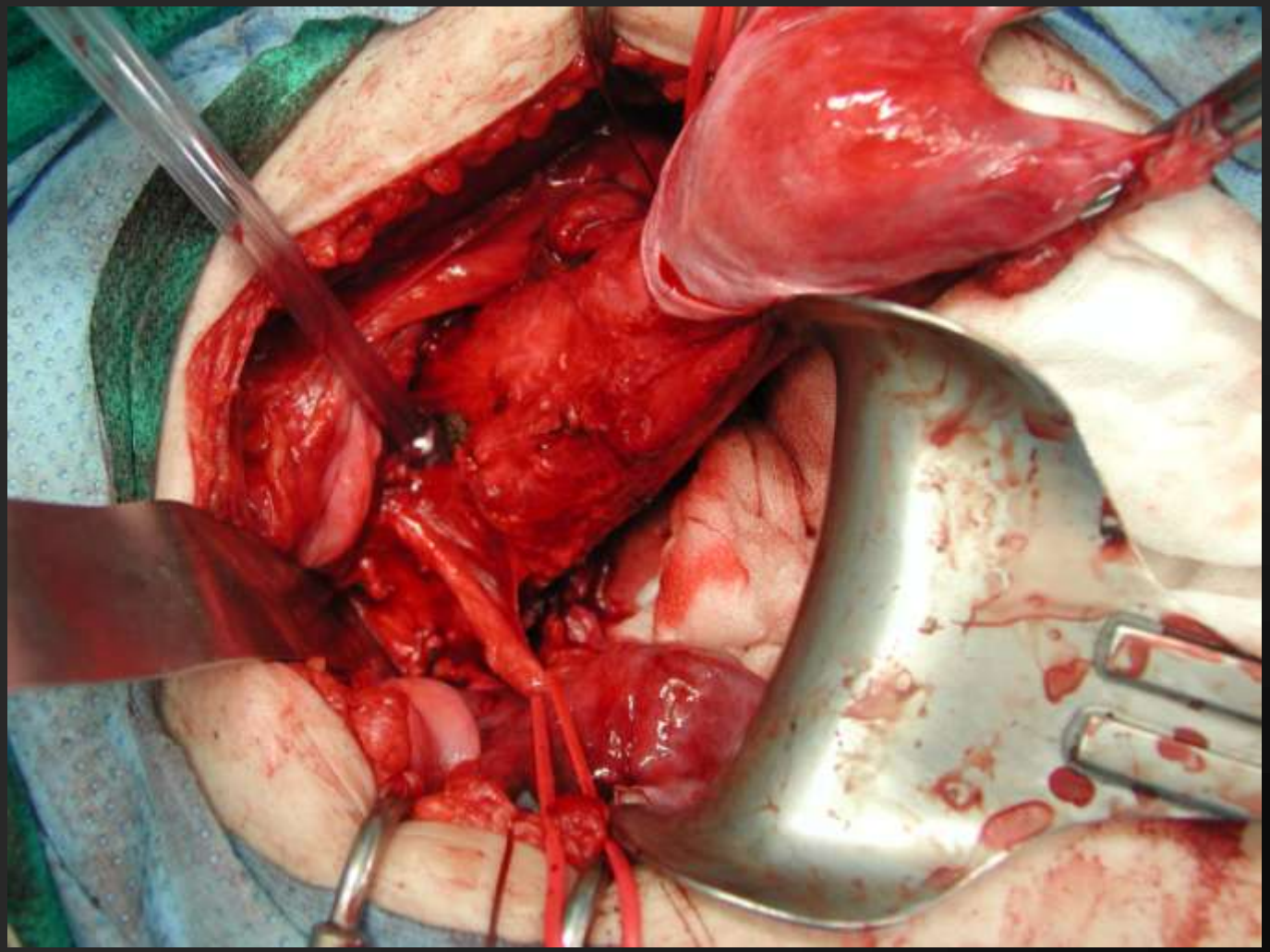

Prevention

- ✓ 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.

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Screening Guidelines for the Early Detection of Cervical Cancer, American Cancer Society 2003

- ✓ Screening should begin approximately three years after a women 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.

American Cancer Society. *Cancer Facts & Figures.* 2004. Atlanta, GA; 2005

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thank you

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