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 ♀ 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
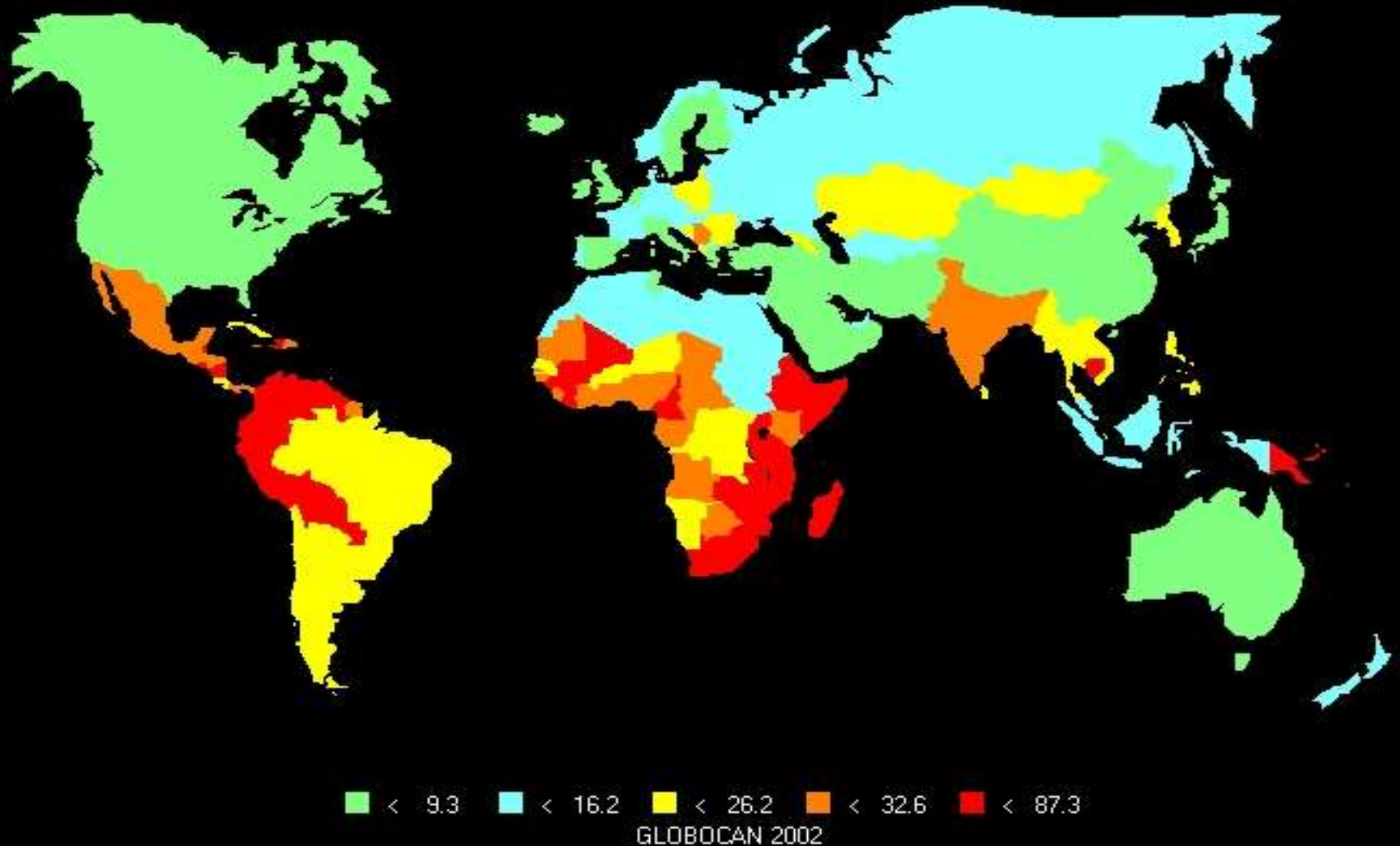- 20% deaths occur in sub-Saharan Africa

Epidemiology of Cervical Cancer

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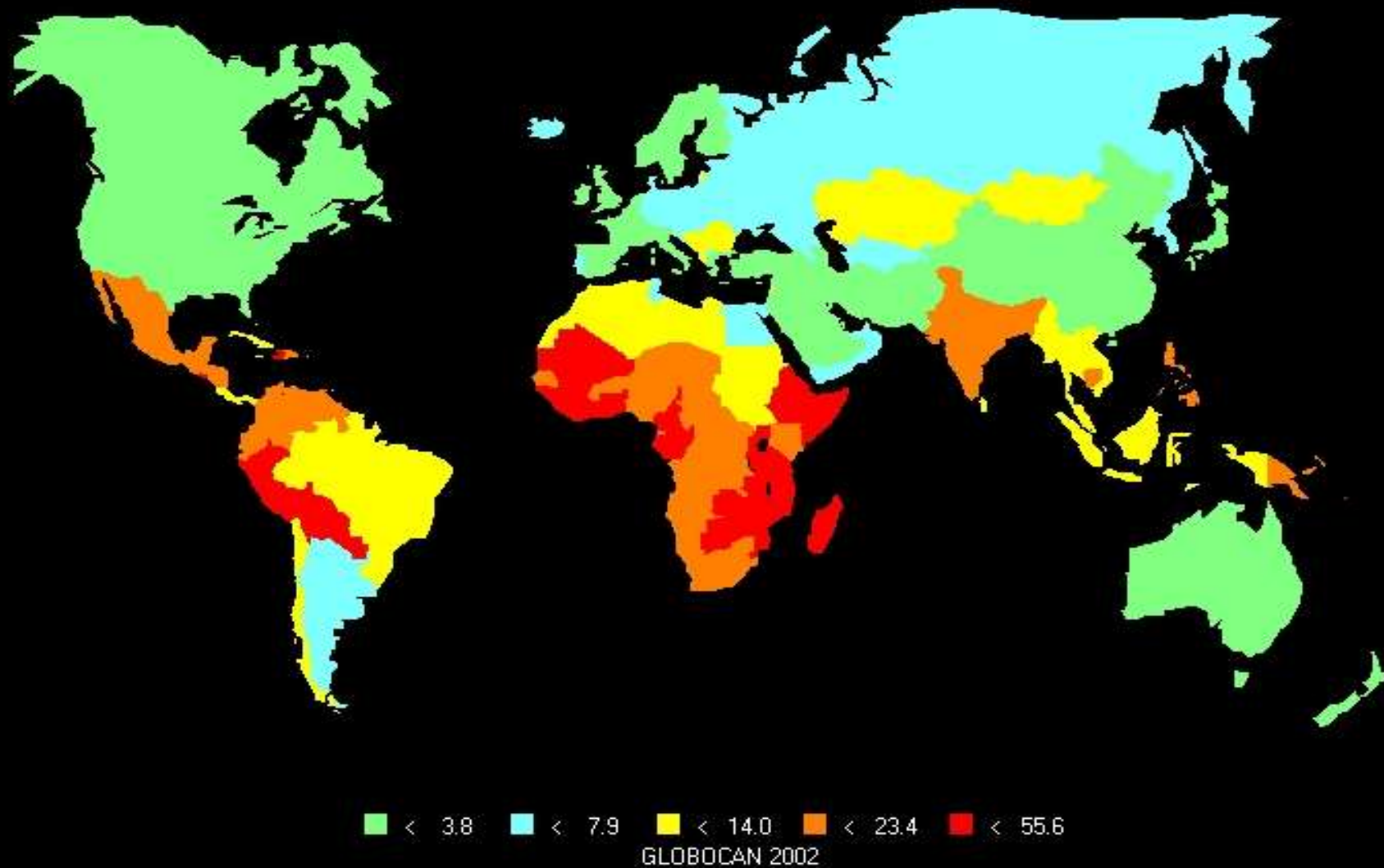
Global Distribution of Cervical Cancer

- Highest Burdens
  - Sub-Saharan Africa
  - Latin America
  - Caribbean Islands
  - Asia

Global cervical cancer incidence

| | < 9.3 | | < 16.2 | | < 26.2 | | < 32.6 | | < 87.3 |

GLOBOCAN 2002

Age Standardized Incidence Rates (ASR) (All ages)

Global cervical cancer mortality
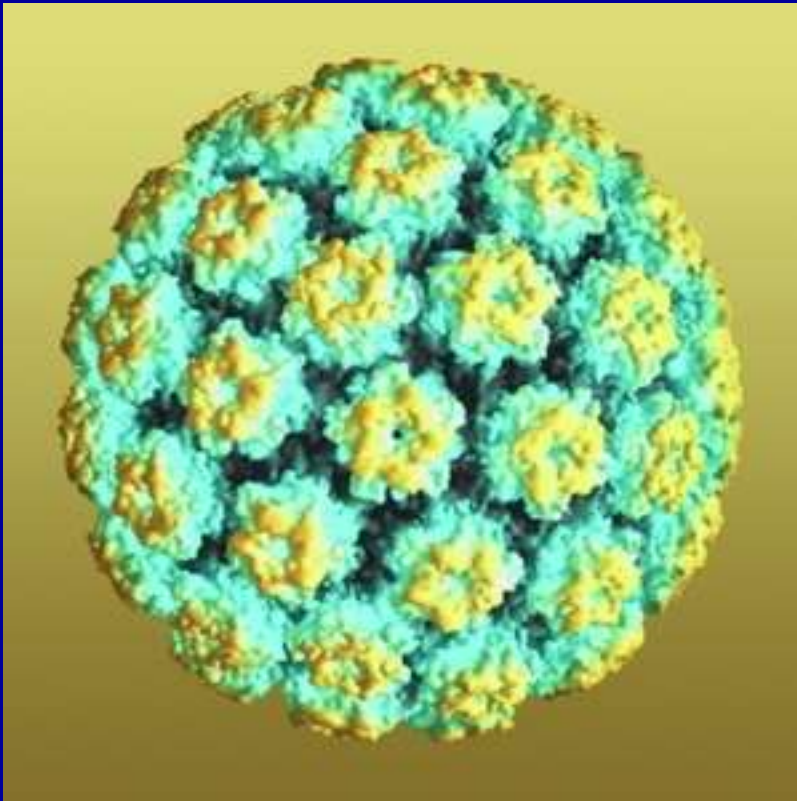

| ◼ < 3.8 | ◼ < 7.9 | ◼ < 14.0 | ◼ < 23.4 | ◼ < 55.6 |

GLOBOCAN 2002

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

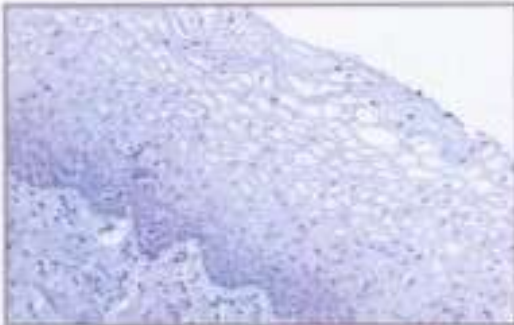Persistent infection over 2-5yrs progresses to precancer
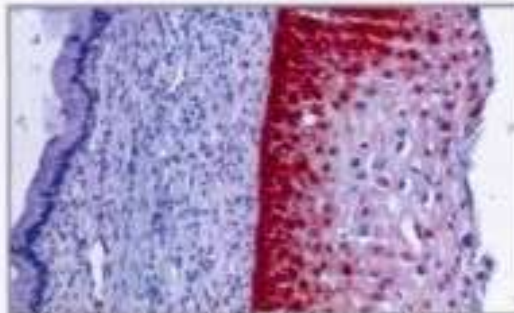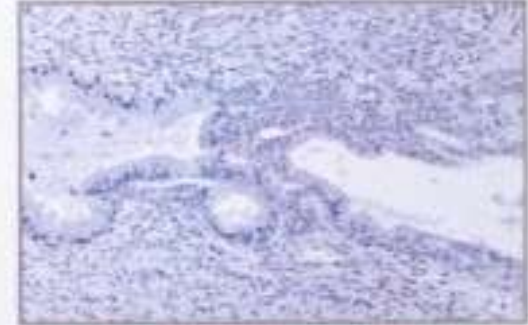
Precancer progresses to invasive cancer

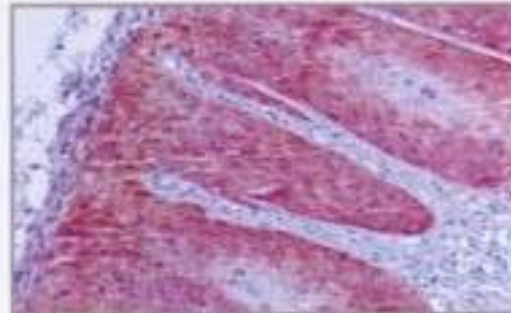# Histopathology

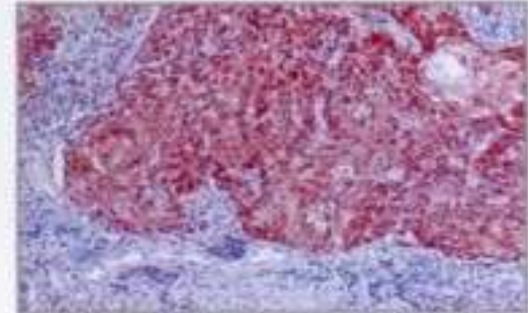Normal proliferation — Inflammation — Metaplasia — Dysplasia (CIN 1,2) — Dysplasia (CIN 3) — Invasive carcinoma

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)

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

- 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

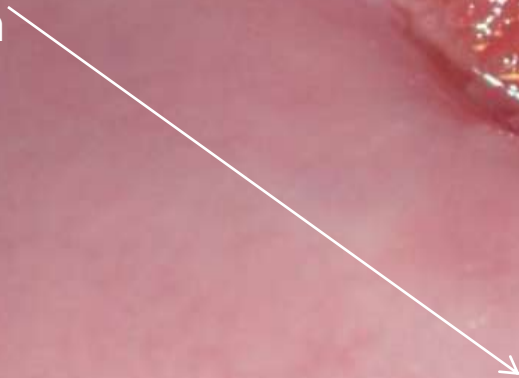# Risk Factors for HPV Persistence and Progression to Cervical Cancer

- **Never or rarely being screened for cervical cancer**
- Immunosuppression
- Smoking
- Long term oral contraceptive use
- Co-infection (chlamydia)
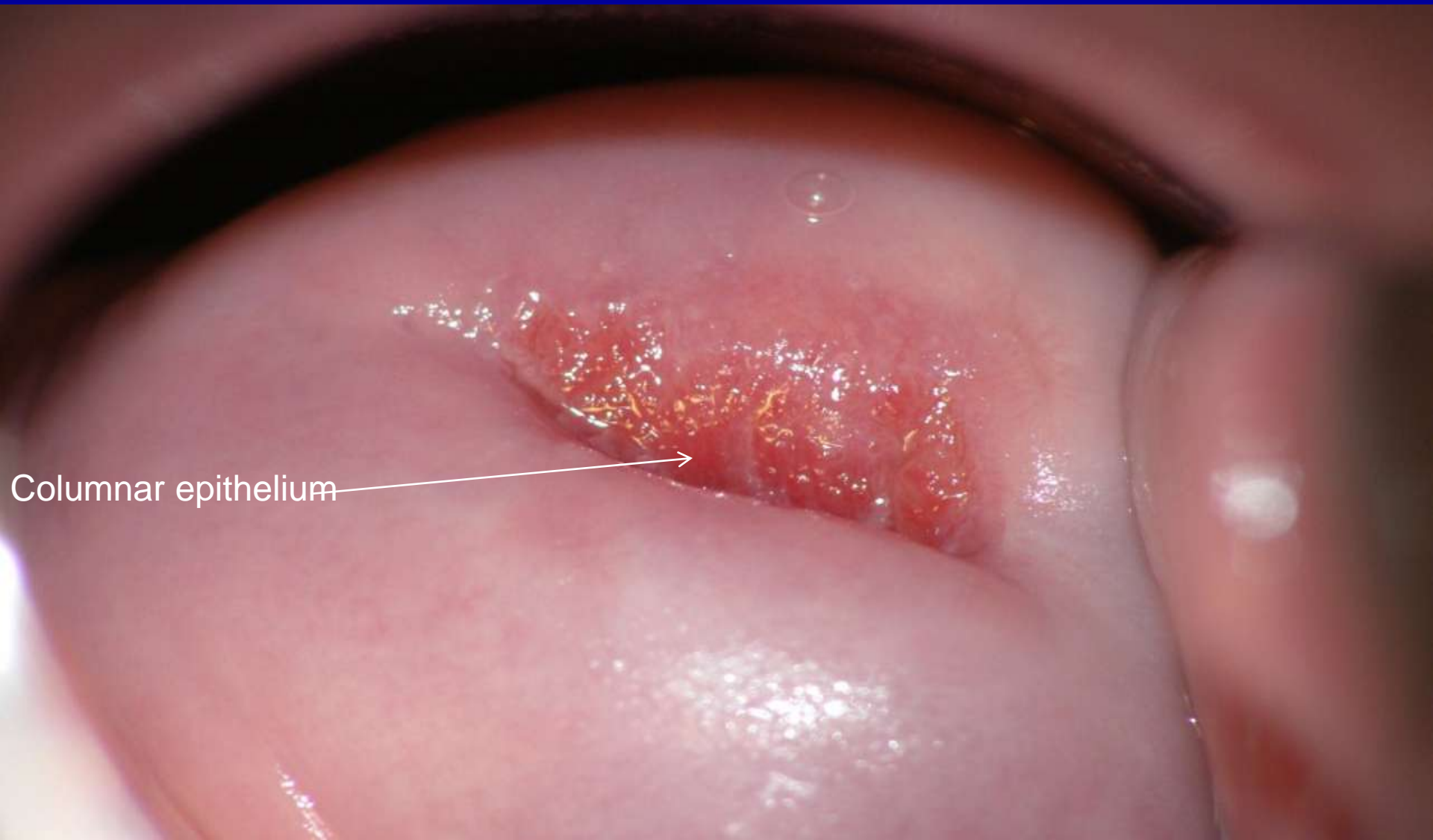- High parity
- Nutritional deficiencies

Cervix

Squamous epithelium

Squamous
epithelium

Columnar epithelium

Columnar epithelium

Metaplastic epithelium
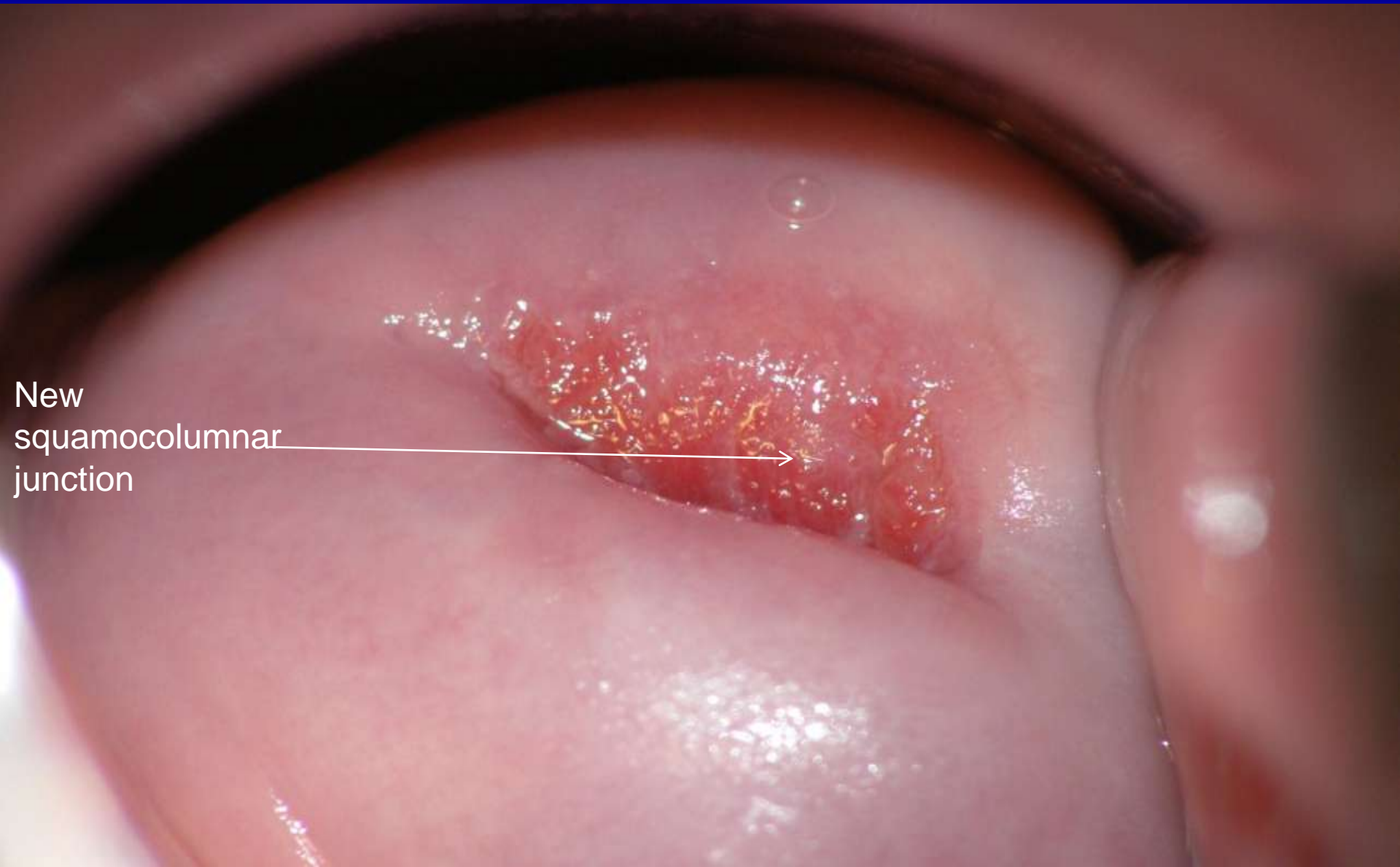

Metaplastic
epithelium

Cervix

Squamocolumnar junction
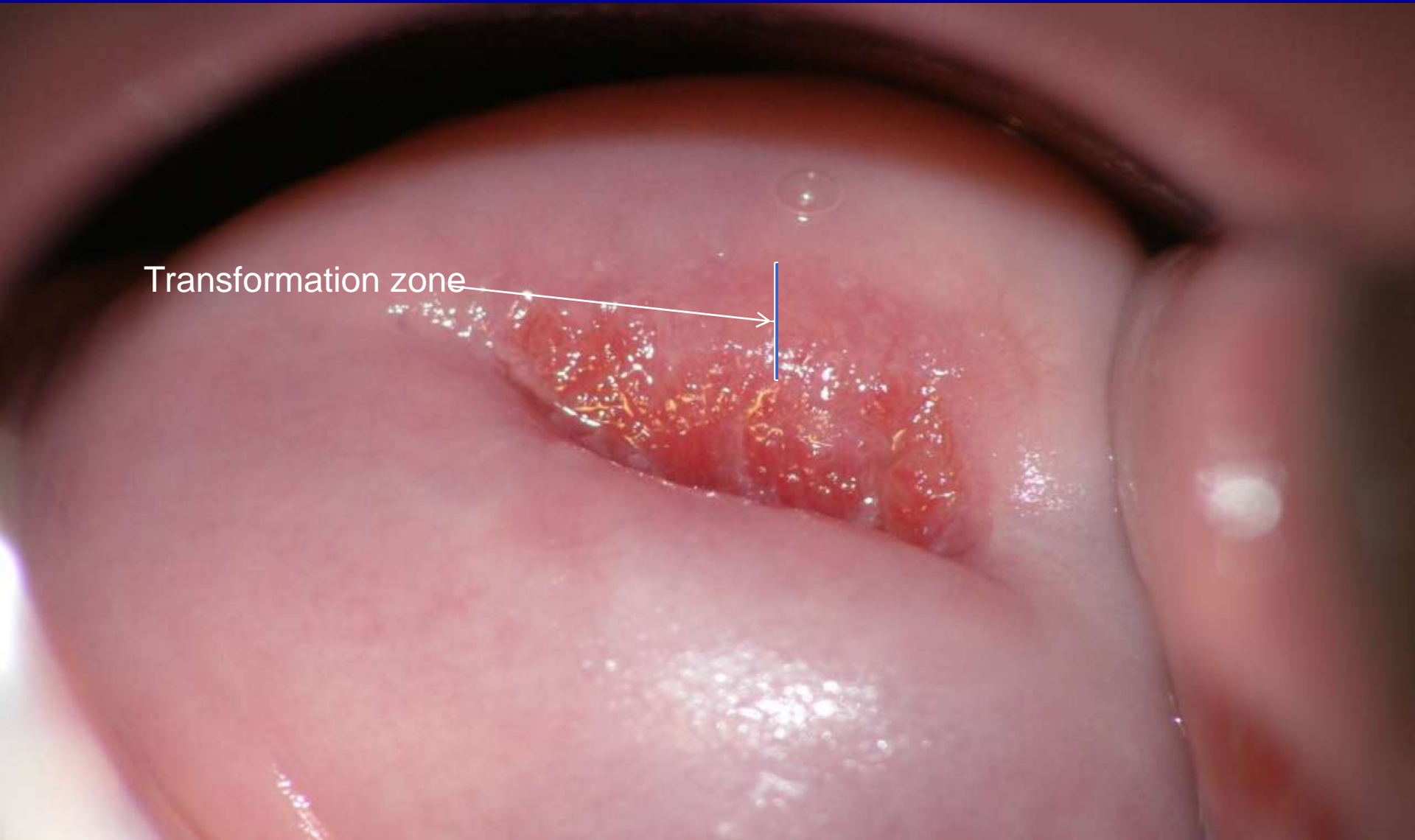
Old squamocolumnar junction
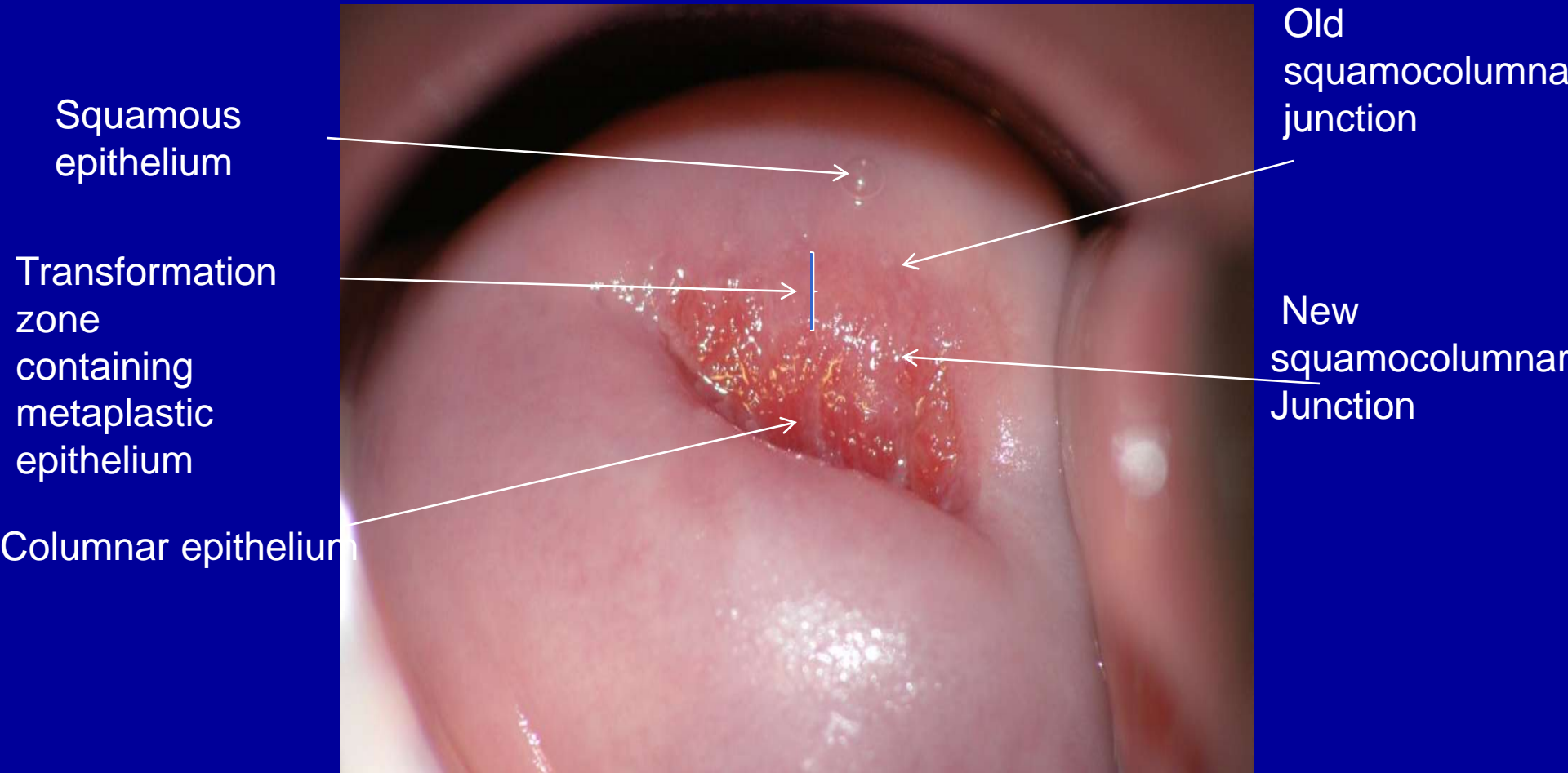
Squamocolumnar junction

New
squamocolumnar
junction

Transformation zone

Transformation zone

Epithelia and junctions

Squamous epithelium

Transformation zone containing metaplastic epithelium

Columnar epithelium

Old squamocolumnar junction

New squamocolumnar Junction
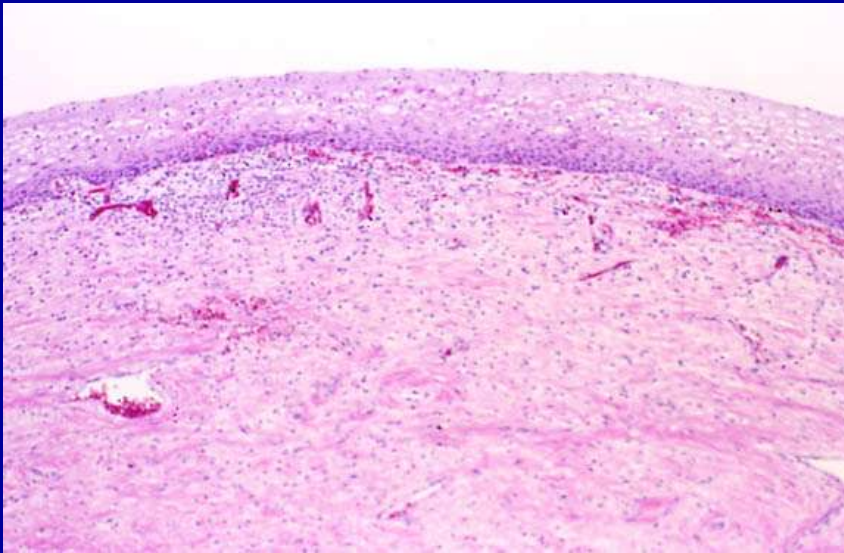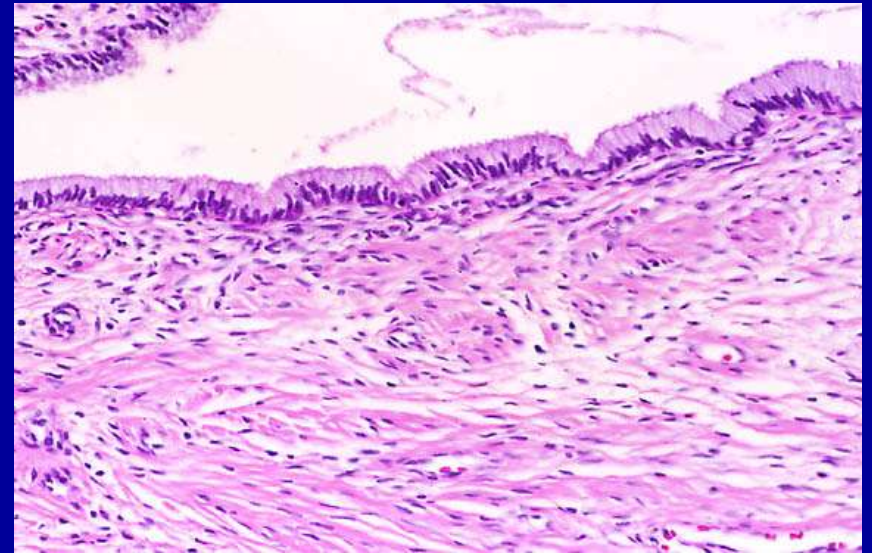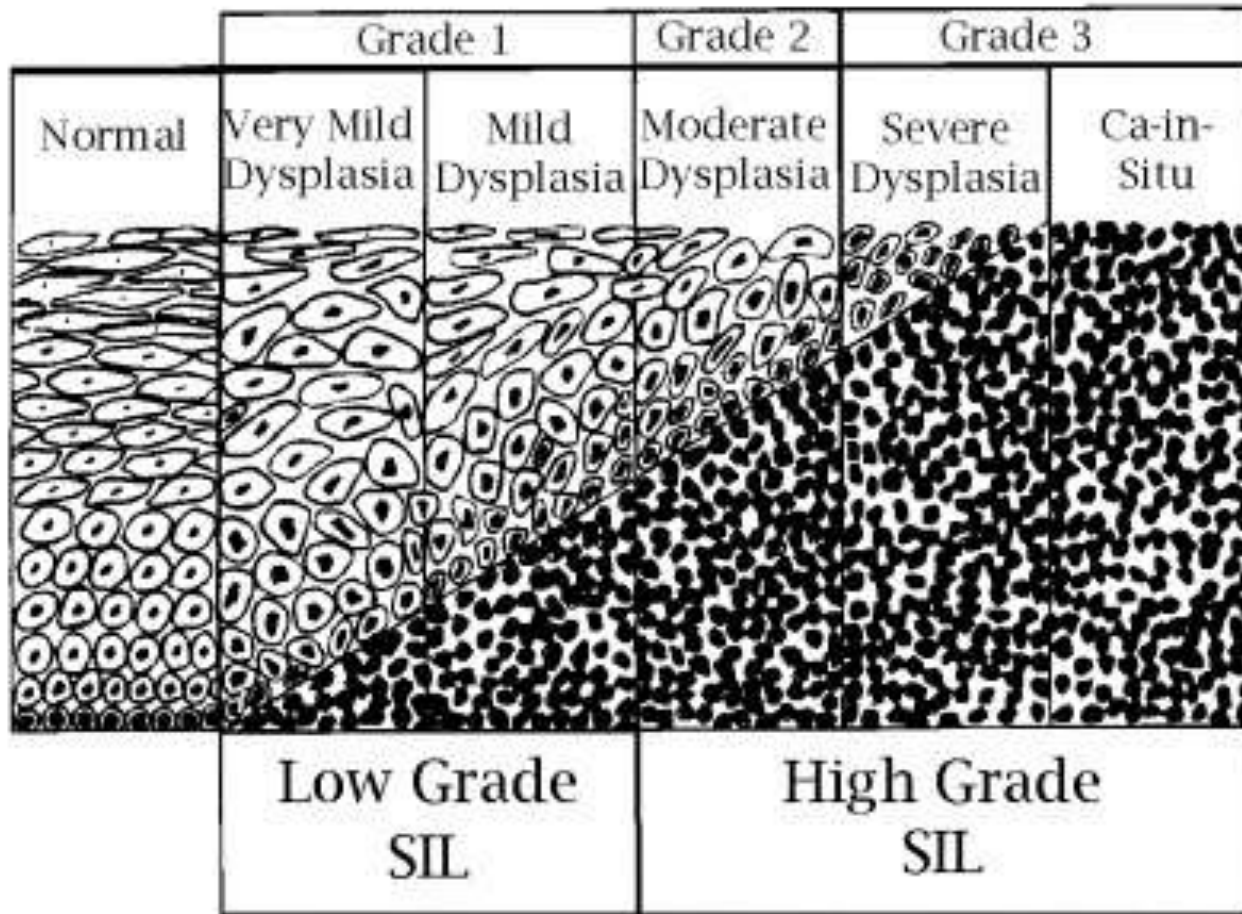
Ectocervix – Squamous Epithelium

Endocervix – Columnar Epithelium

HPV infection

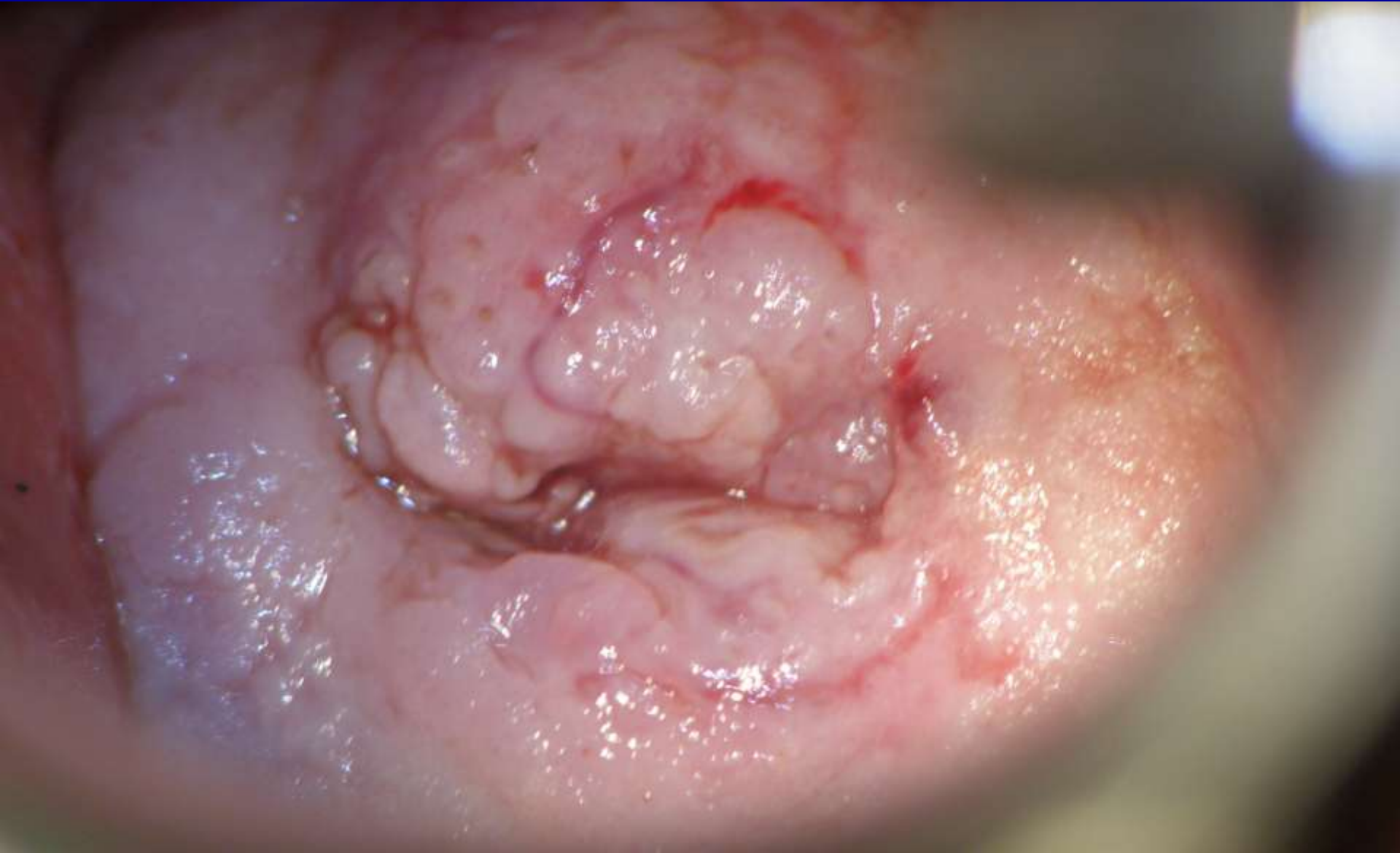# Histologic changes seen in cervical dysplasia
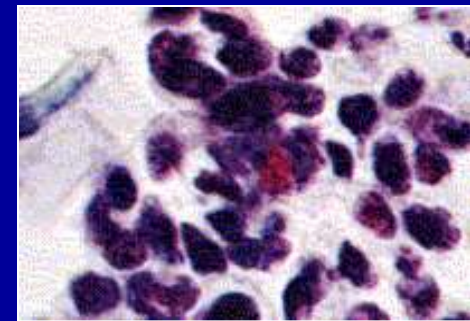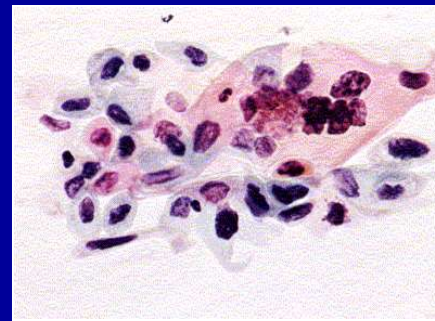
Precancer

Precancer

Microinvasive cancer

Microinvasive cancer

Invasive cancer

Natural History of HPV

HPV Infection → Low-grade CIN (CIN 1) → High-grade CIN (CIN 2/3) → Invasive cancer

60%

20%

20-30%

~20%
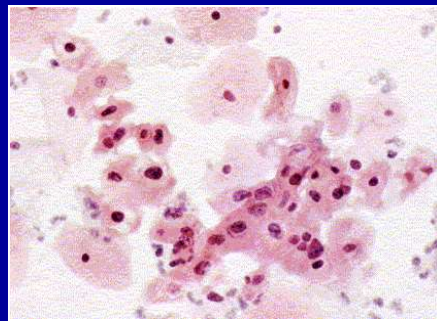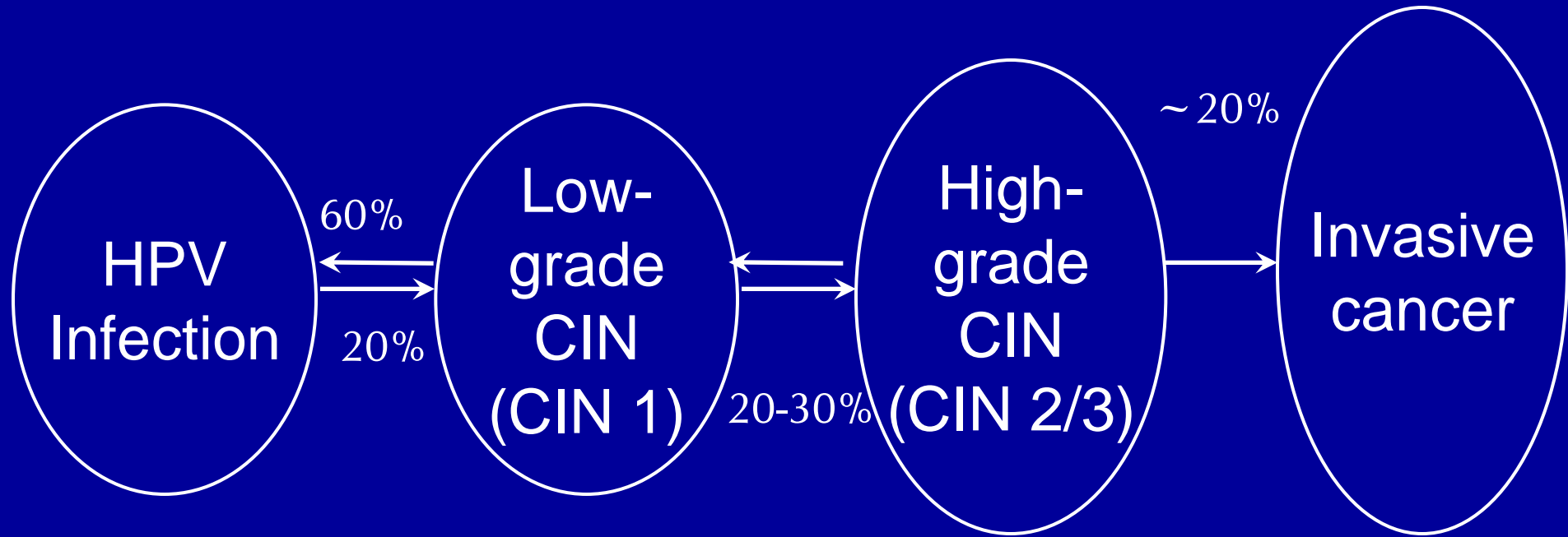
Natural History of HPV

Preinvasive cancer (Cervical intraepithelial neoplasia –CIN)

Epithelium

Underlying tissue

Microinvasive cancer

Invasive cancer

Artwork by Jeanne Kelly. © 2004.

Natural History of HPV

Invasive (malignant) cells invade neighboring tissues, enter blood vessels, and spread to different sites
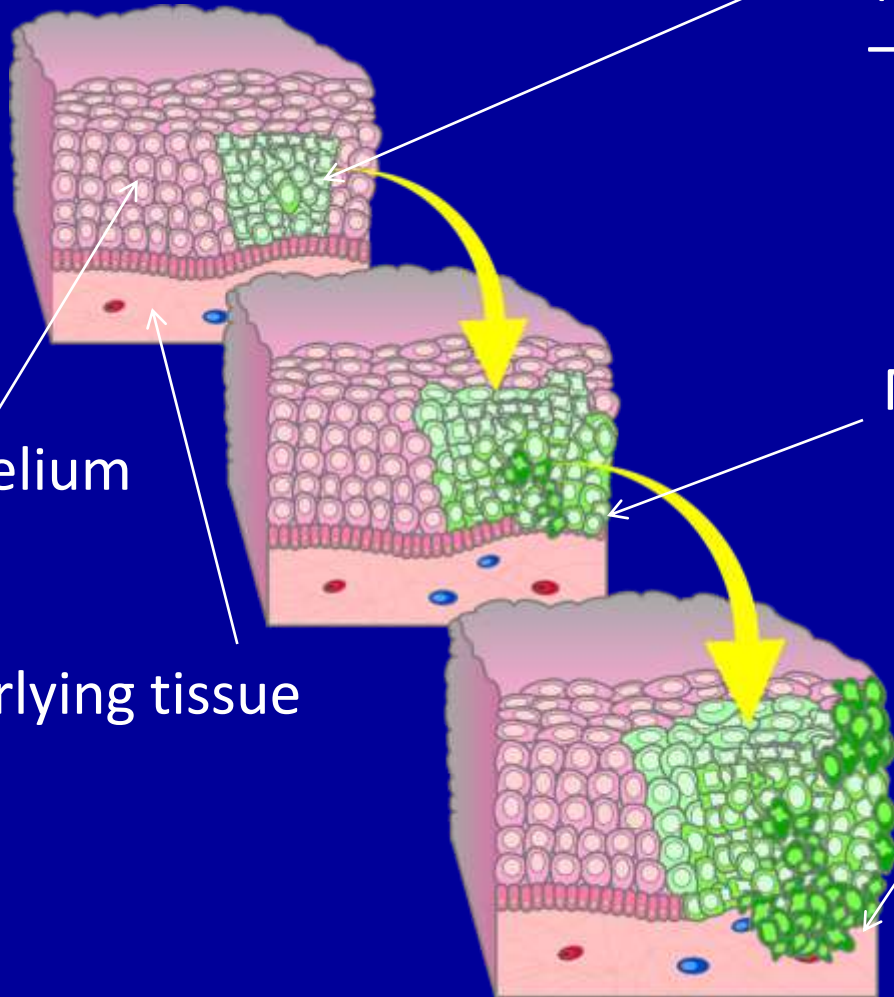
Precancer cells grow only locally and cannot spread by invasion or metastasis.
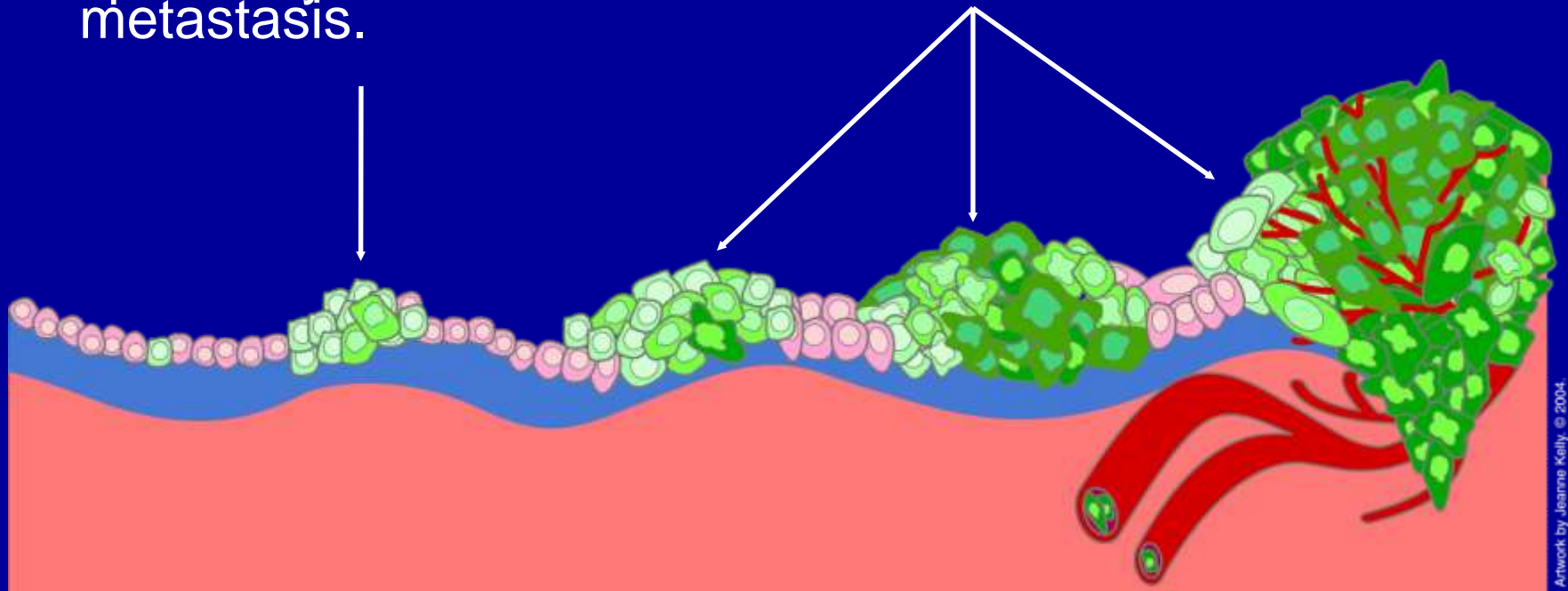
Time

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 prfecancer: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

Evaluation – Page 1 of 2

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

Evaluation – Page 2 of 2

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

Evaluation Score

- 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.

CERTIFICATE