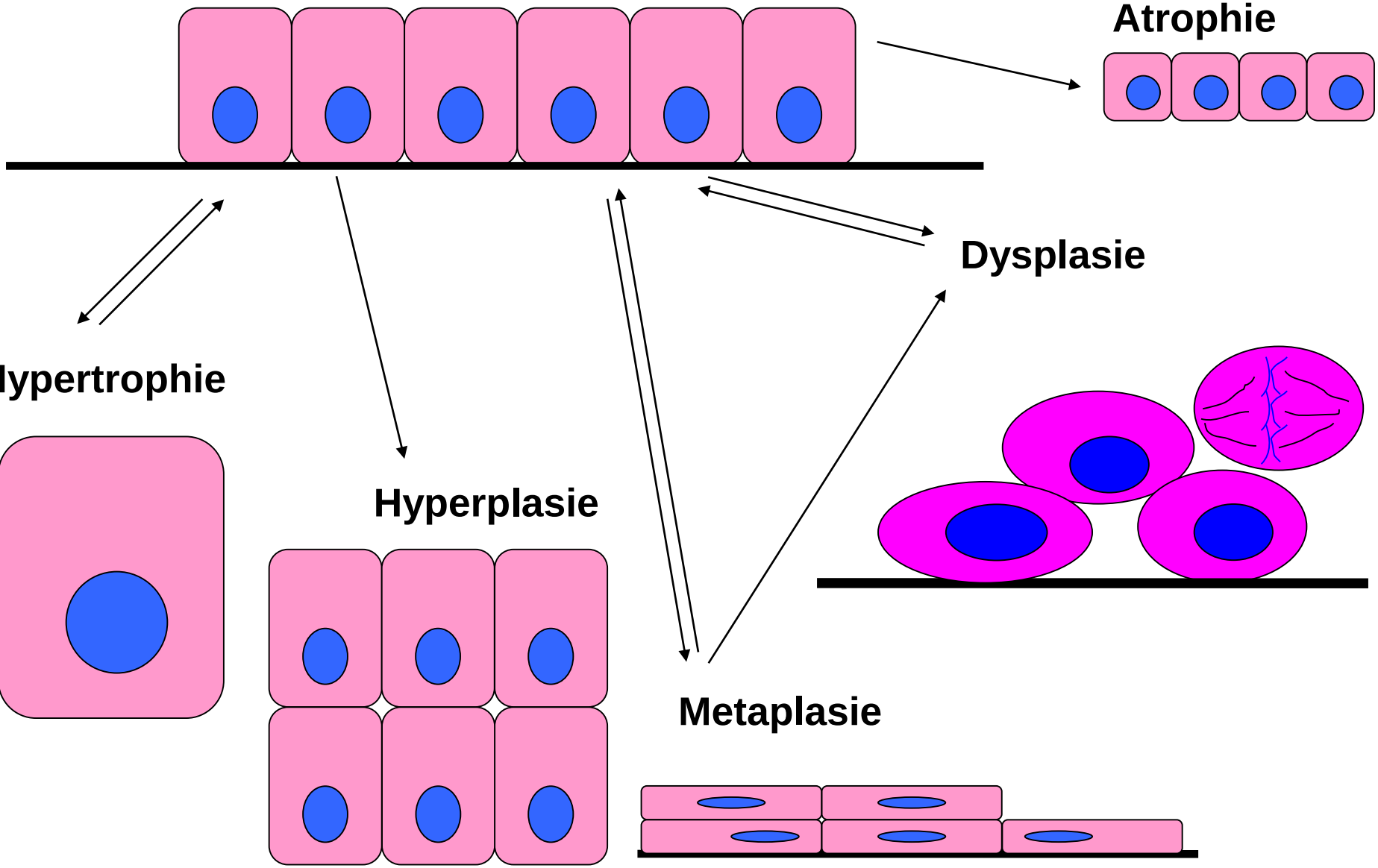
6. Praktikum

Allgemeine Tumorlehre I.

Metaplasie, Zervikale Tumorentwicklung

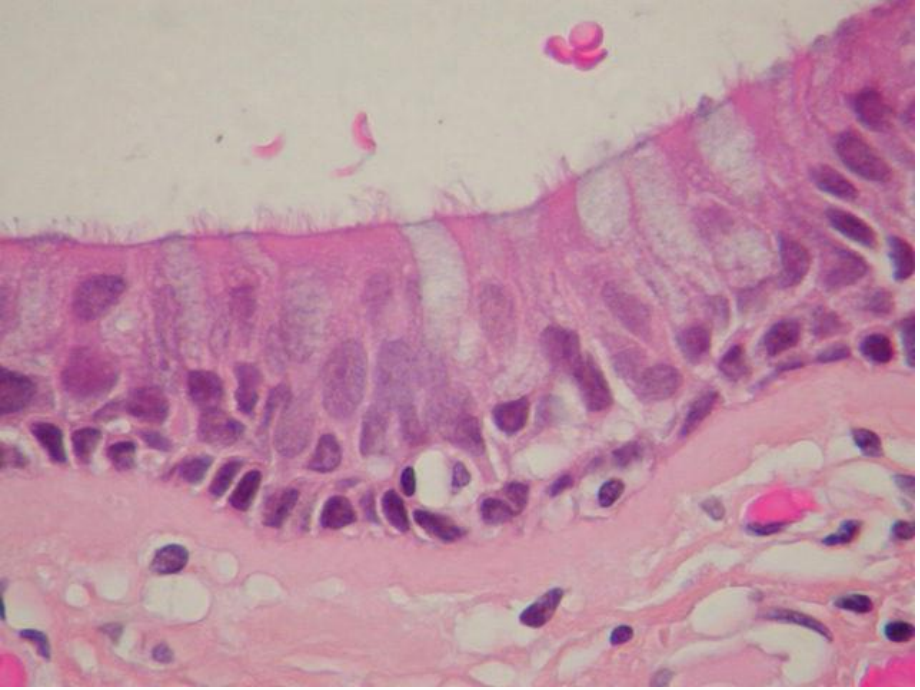
II. Institut für Pathologie
Semmelweis Universität

Adaptation (Grundbegriffe)

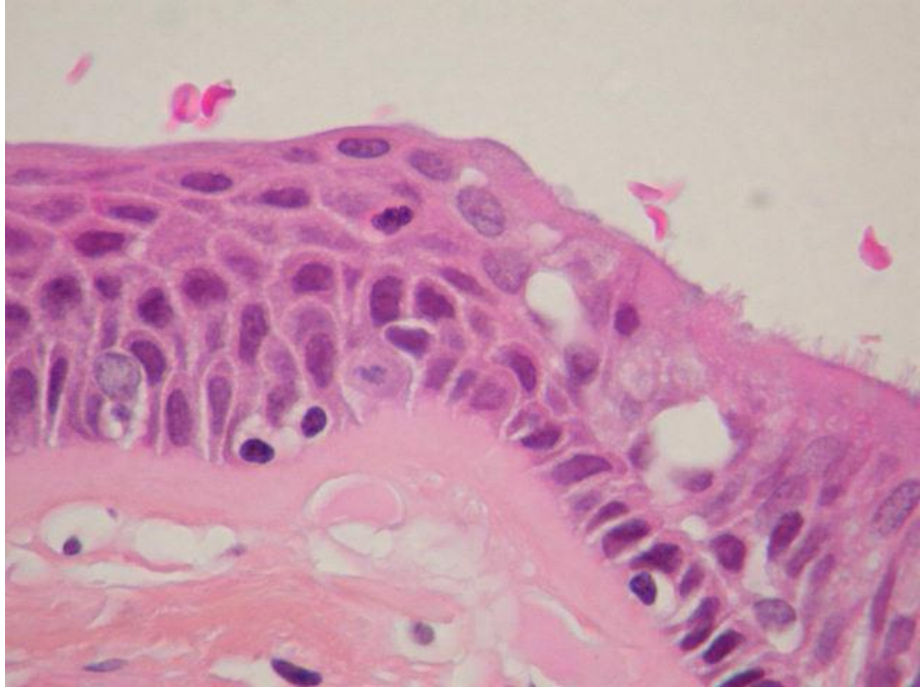


Metaplasie

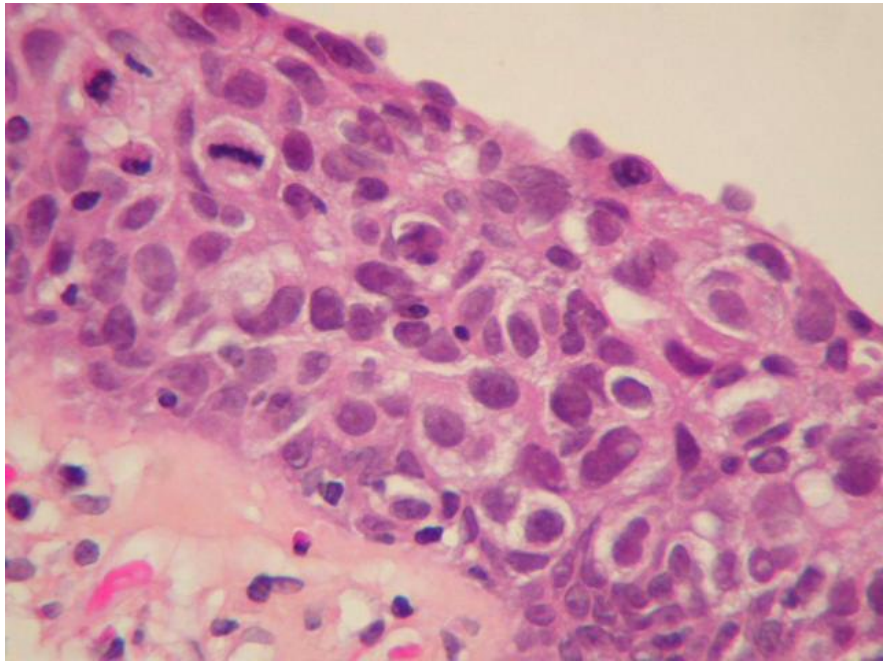
- Umwandlung einer Zellart in eine andere
  z.B. Zylinderepithel → Plattenepithel
- Reversibel!
- Ursache: chronische Irritation, Überbelastung
- Fakultative Präkanzerose



normal Bronchus Flimmerepithel

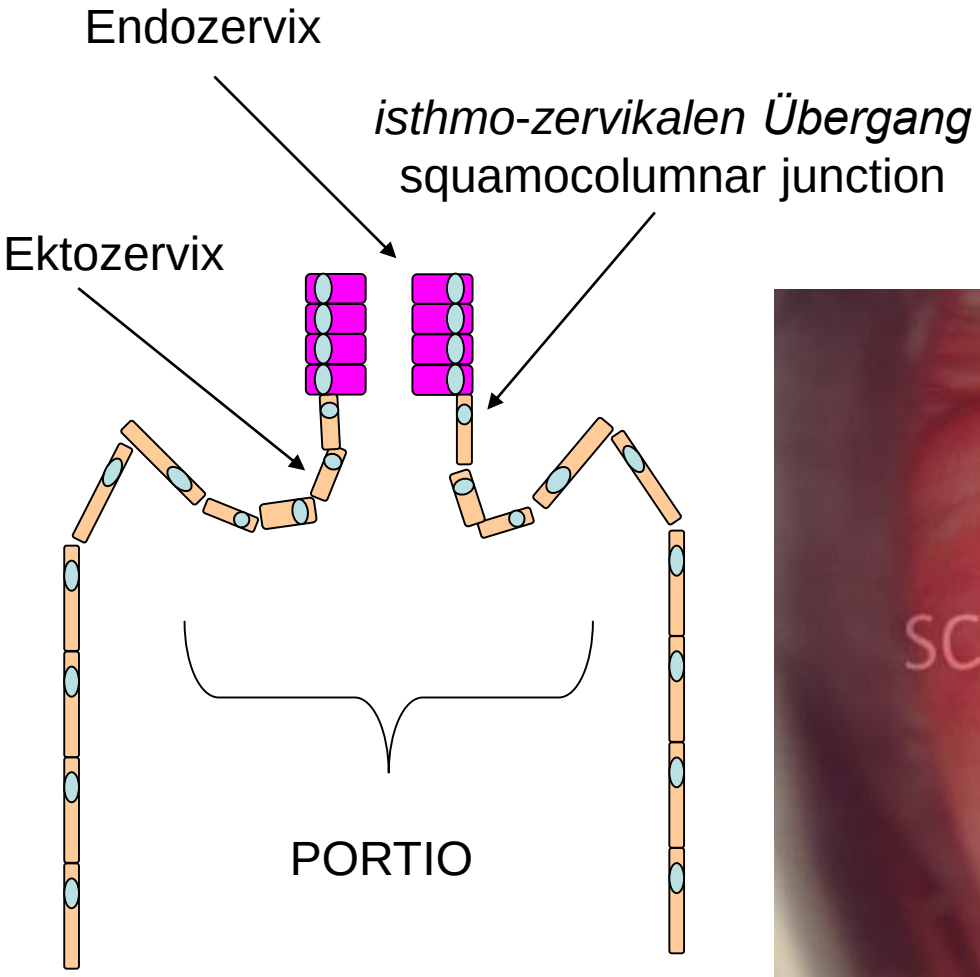


Plattenepithel-Metaplasie

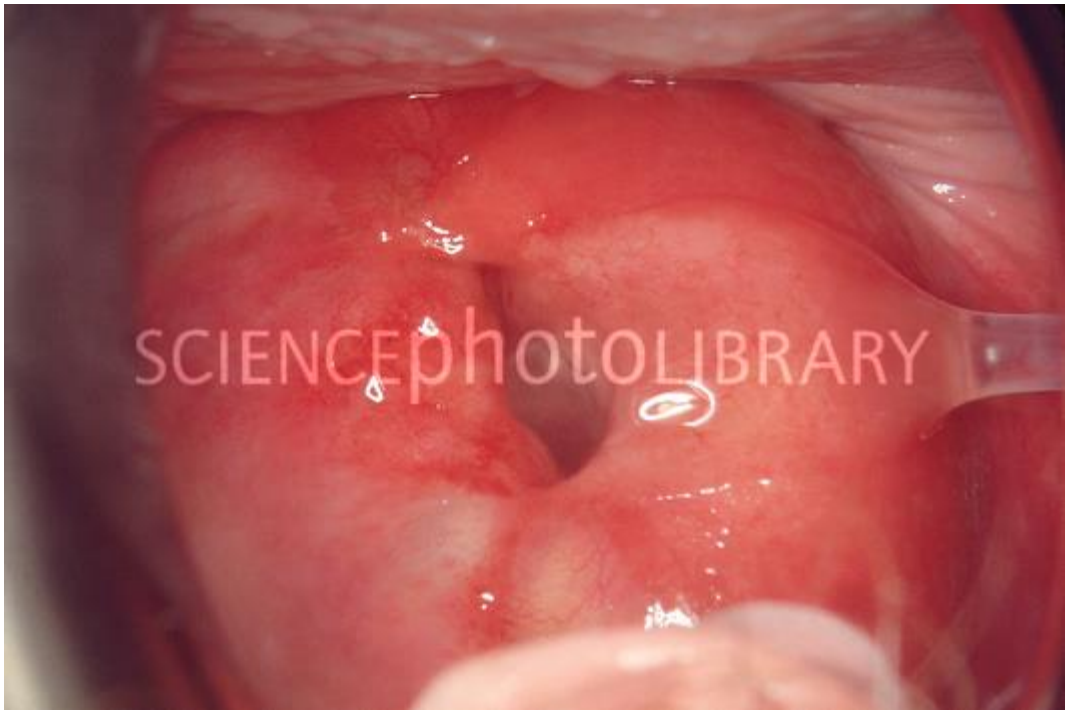


carcinoma in situ

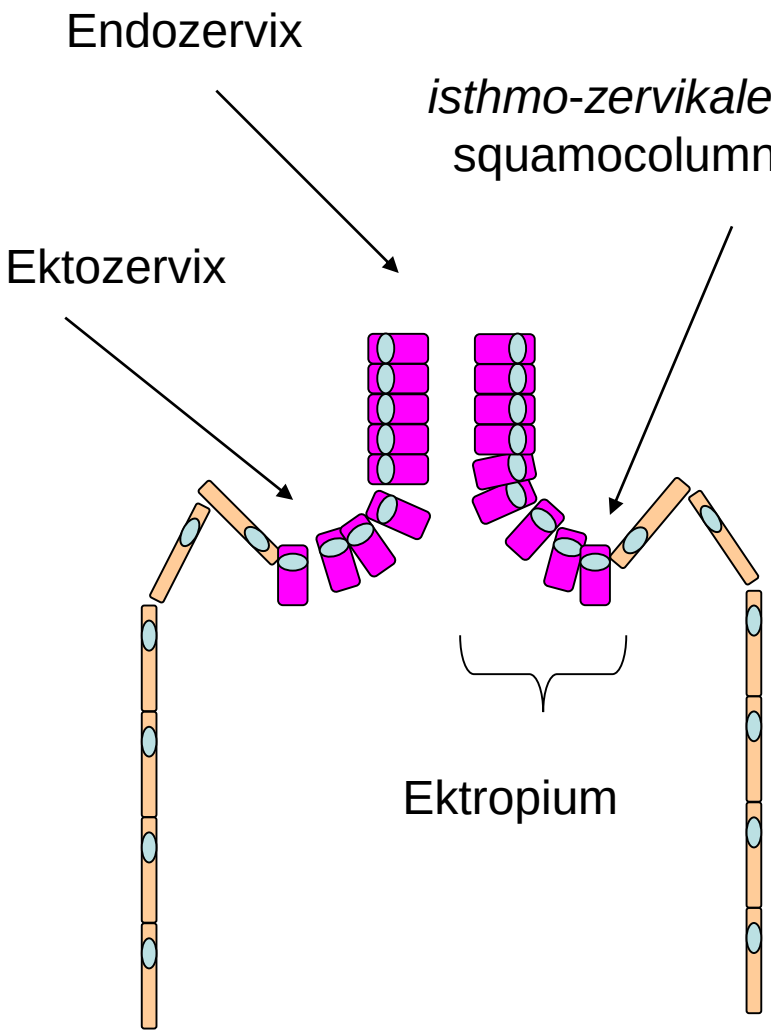
Normale Zervix



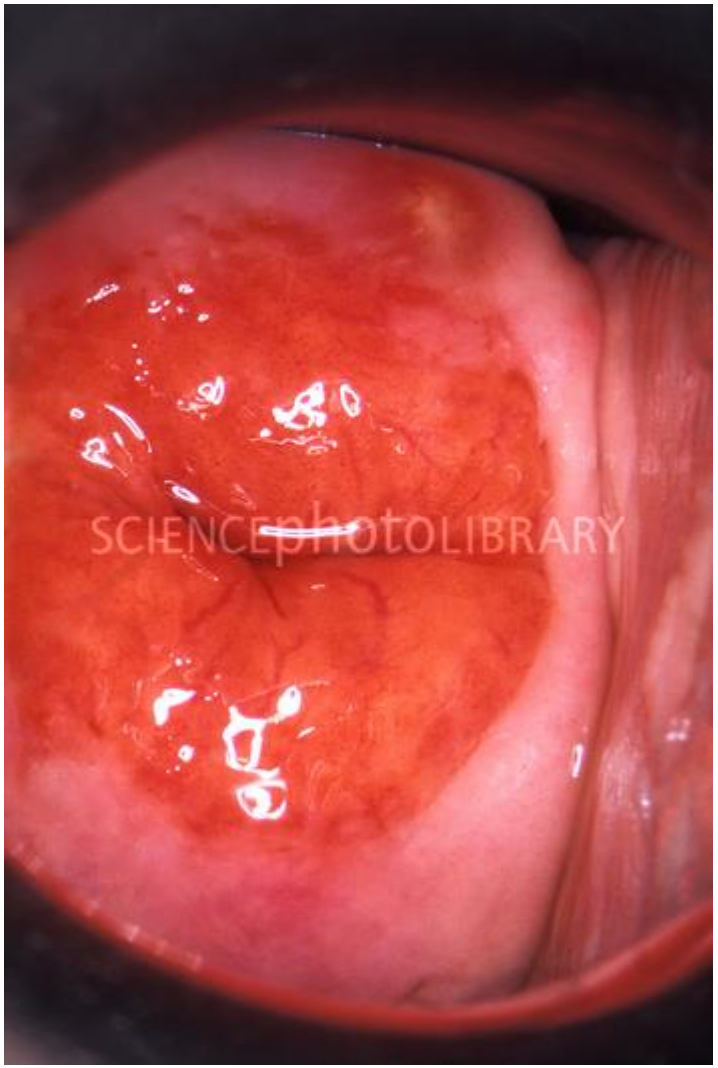
Geburt / Präpubertät



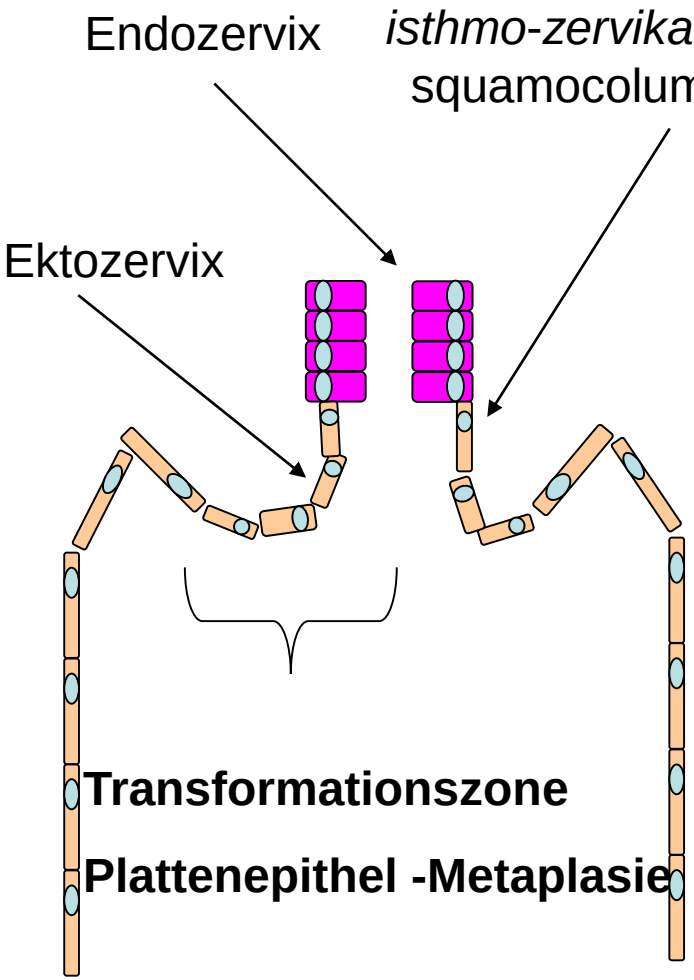
Ektropium



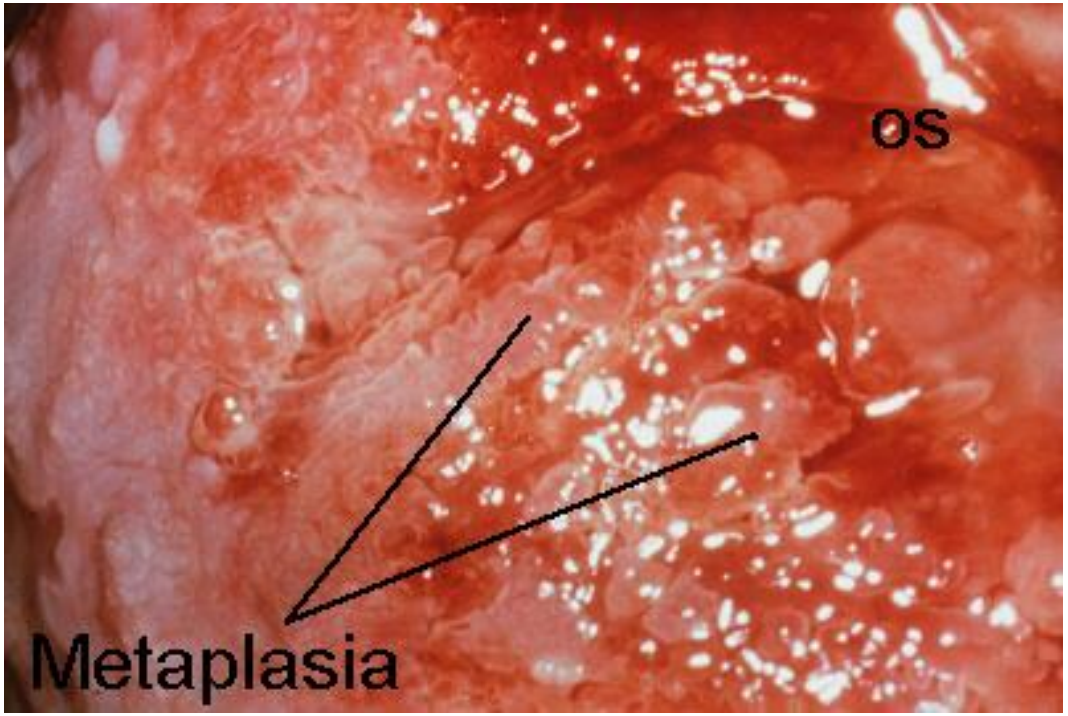
Pubertät



Zervikale Plattenepithel-Metaplasie

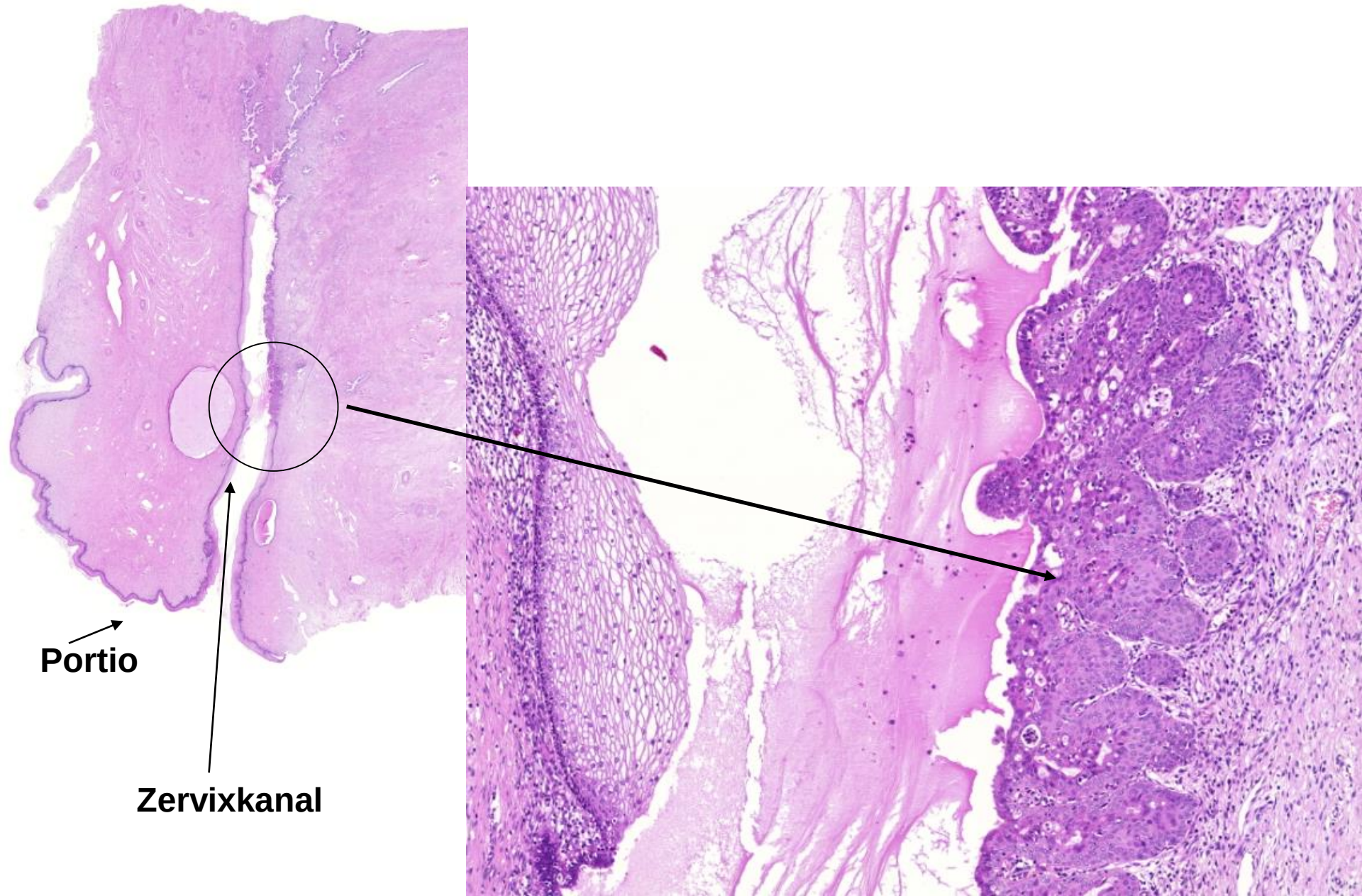


Erwachsene



https://www1.cgmh.org.tw/intr/intr5/c6700/OBGYN/f/Colposcopy/colpoat.html

Zervikale Plattenepithel- Metaplasie



Humanes Papillomvirus (HPV)

- epitheliotrop DNA-Virus
- spezies-, gewebs- und ortsspezifisch
- **Geringrisiko-HPV-Typen**: 1, 2, 4, 7, 6, 11
  - Papillom, Verruca vulgaris (Hautwarze), Condyloma acuminatum (Feigwarze), LSIL

EPISOMAL

- **Hochrisiko-HPV-Typen** : 16, 18, 31, 58
  - LSIL, HSIL, invasives Karzinom

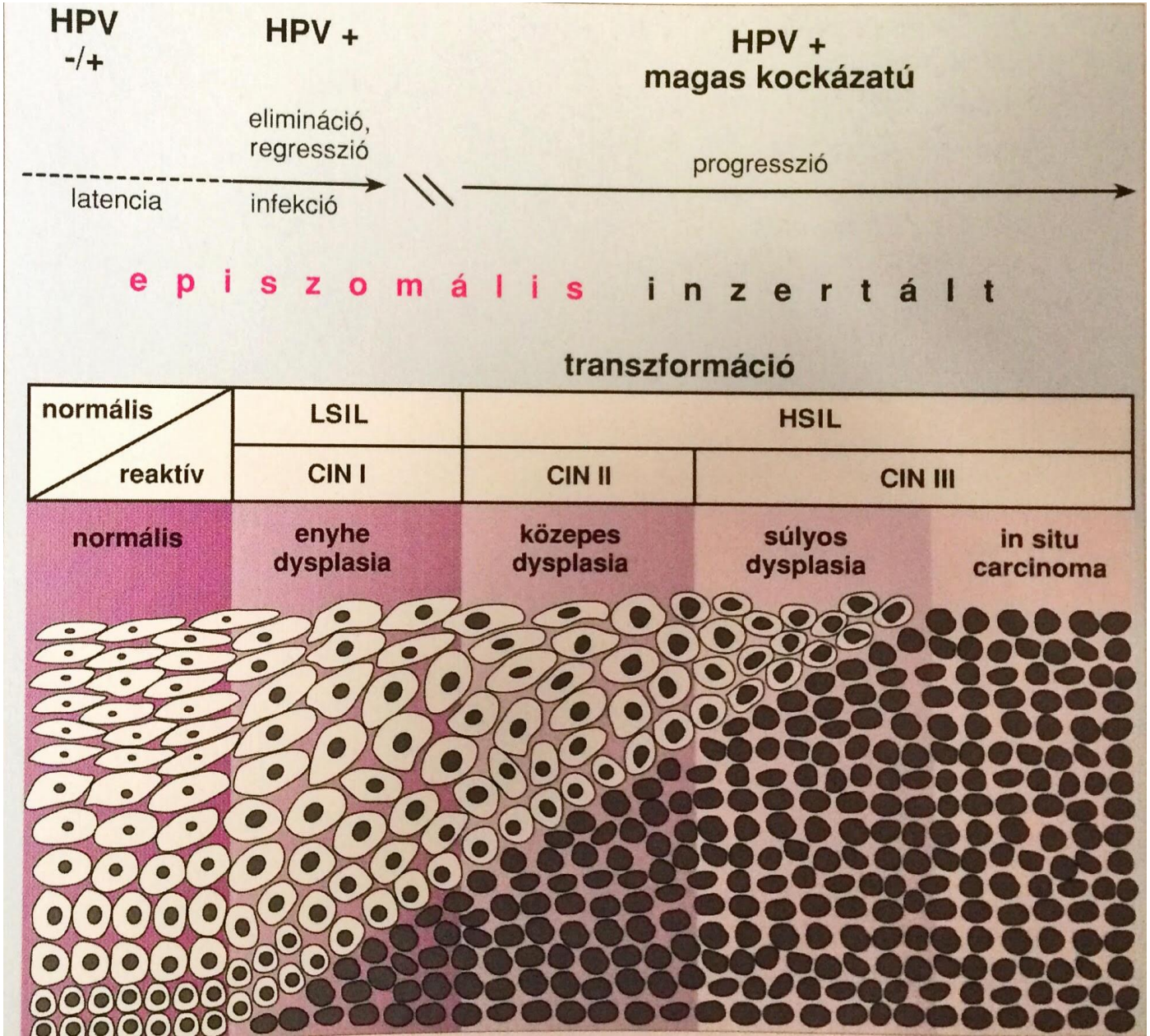
INTEGRIERT SICH INS GENOM

HPV-Infektion in der Zervix

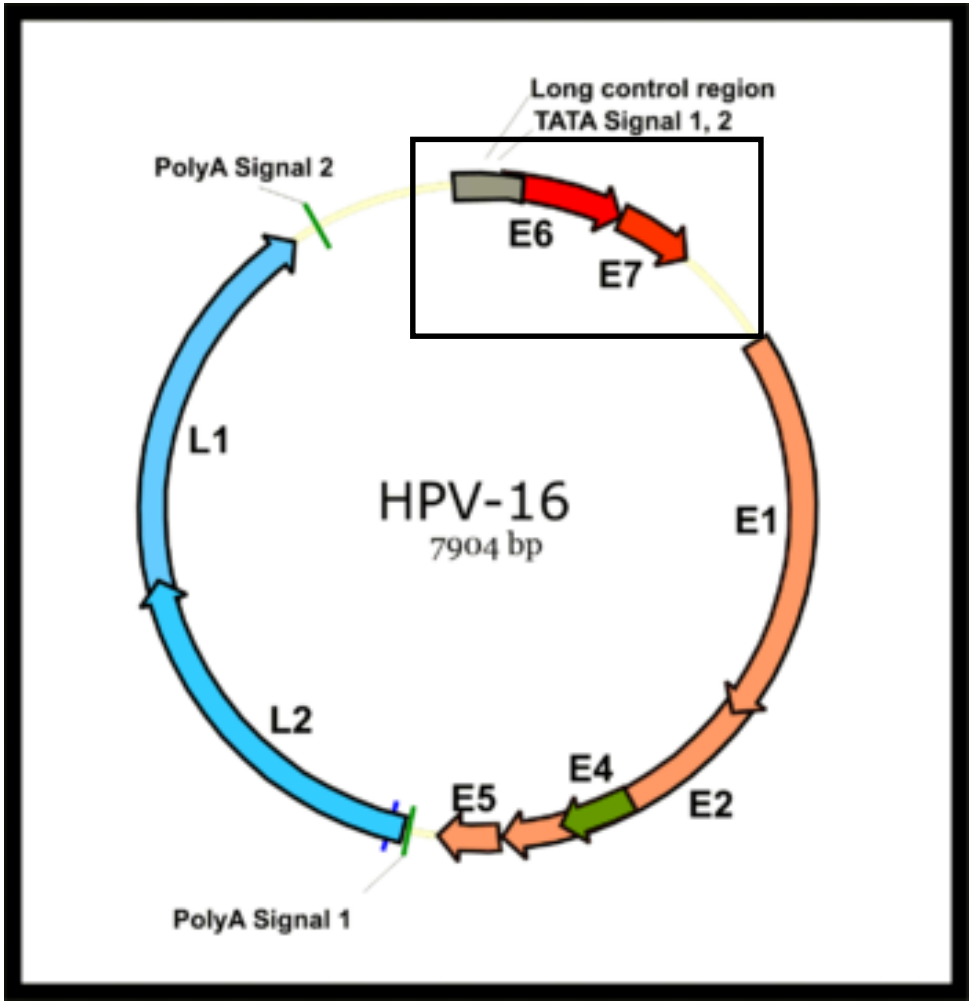
- das HPV-Virus wird durch Geschlechtsverkehr übertragen
  STD!
- 50% aller HPV Infektionen werden innerhalb von 8 - 13 Monaten von dem Immunsystem aus dem Körper entfernt,
  90% aller Infektionen heilen in 2 Jahren
- Die primäre HPV Infektion erfolgt in den Basalzellen der normalen Schleimhaut oder die unreife Zellen einer Plattenepithelmetaplasie. Die Viren verbleiben in den befallenen Zellen während die Basalzellen zu Superfizialzellen ausdifferenzieren. Die Viruspartikelfreissetzung erfolgt nur in den oberen, ausdifferenzierten Zellschichten des Epithels
- Characteristische Zell: KOILOZYT koilos = leer (gr.)

Zervikale Präkanzerose und Stadien des HPV-Infektion

Kopper-Schaff: Patológia

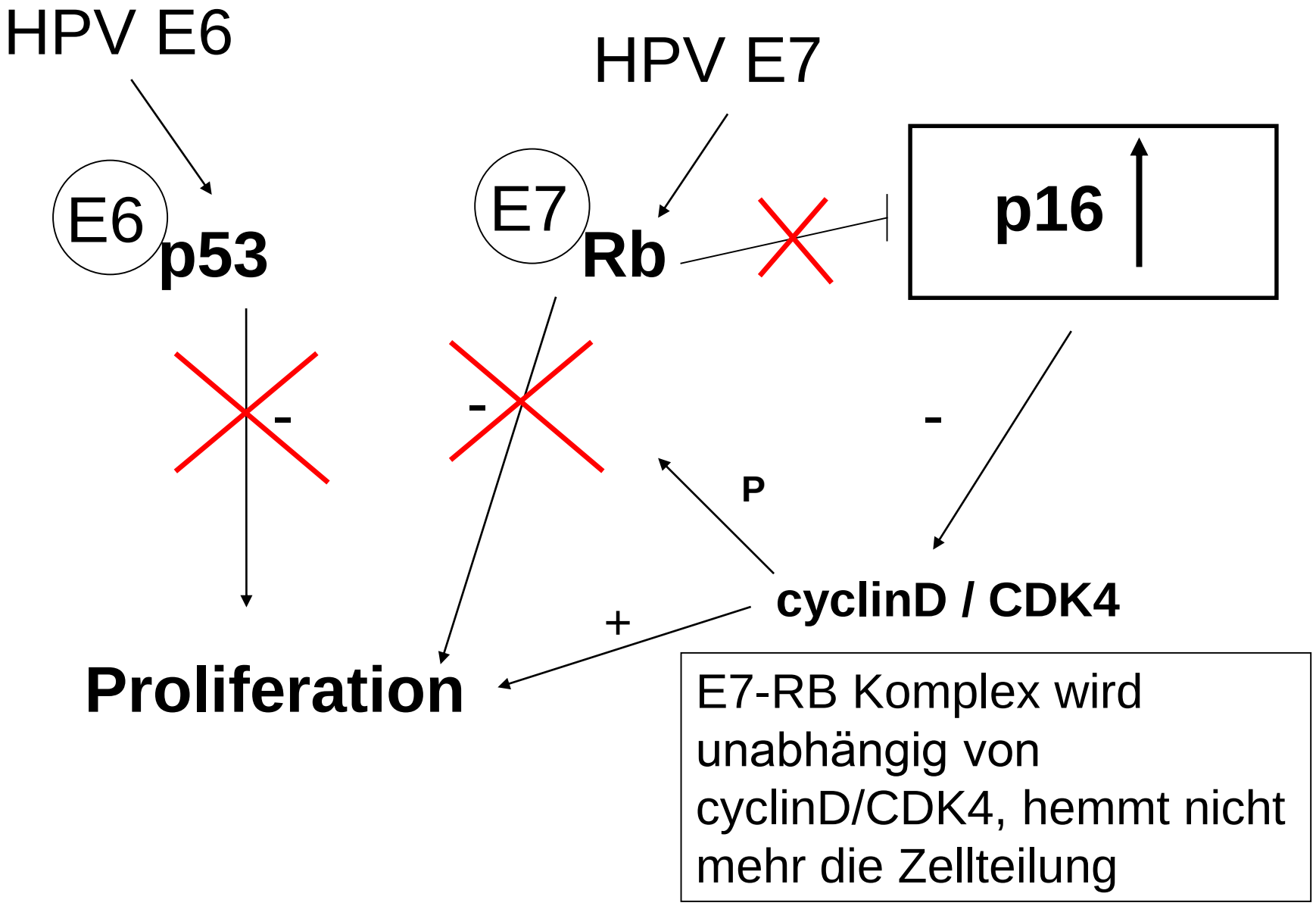


Struktur des HPV Genoms



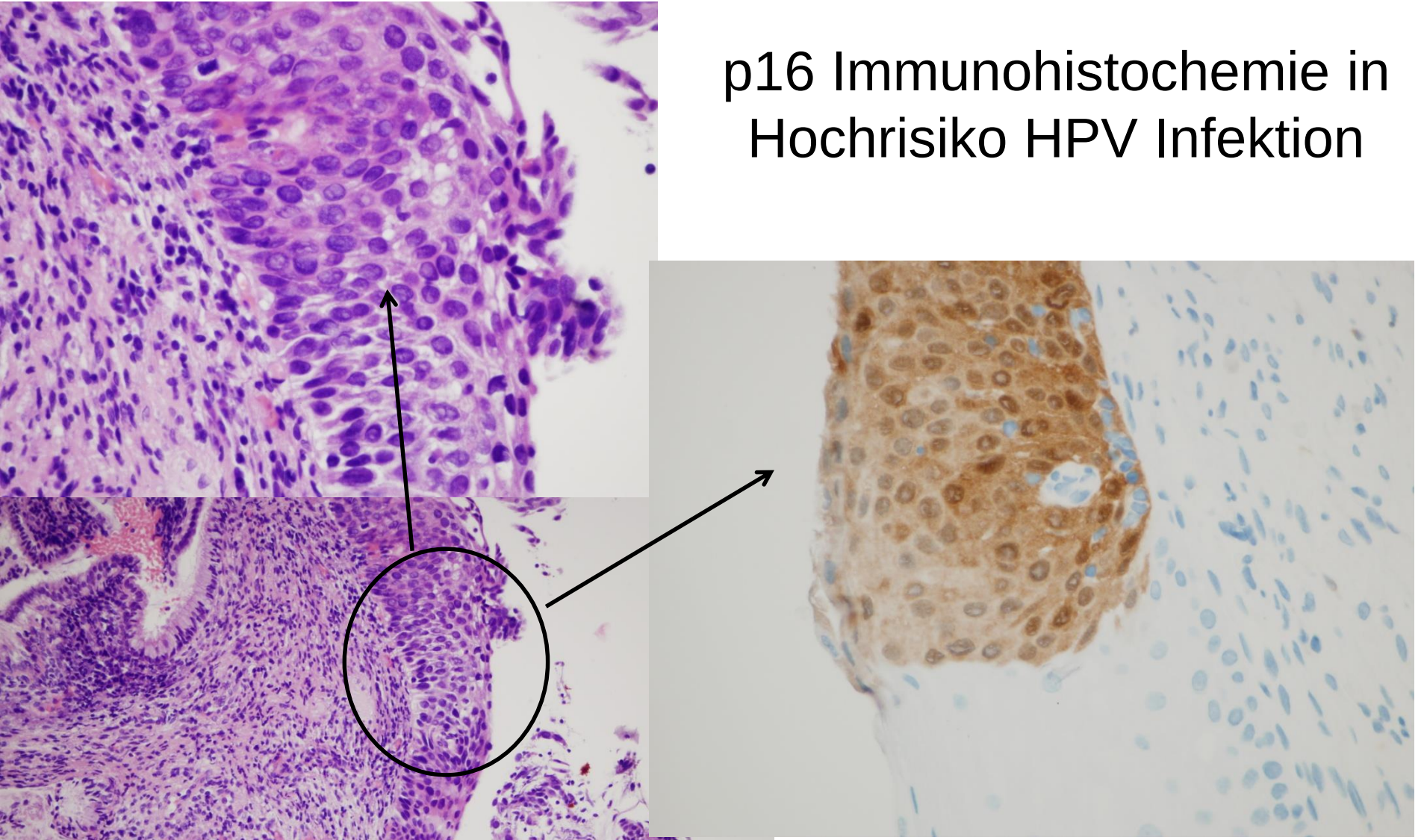
https://upload.wikimedia.org/wikipedia/commons/thumb/e/e7/HPV-16_genome_organization.png/350px-HPV-16_genome_organization.png

Hochrisiko HPV - p16



E7-RB Komplex wird unabhängig von cyclinD/CDK4, hemmt nicht mehr die Zellteilung

p16 Immunohistochemie in Hochrisiko HPV Infektion



DYSPLASIE

= Fehlbildung

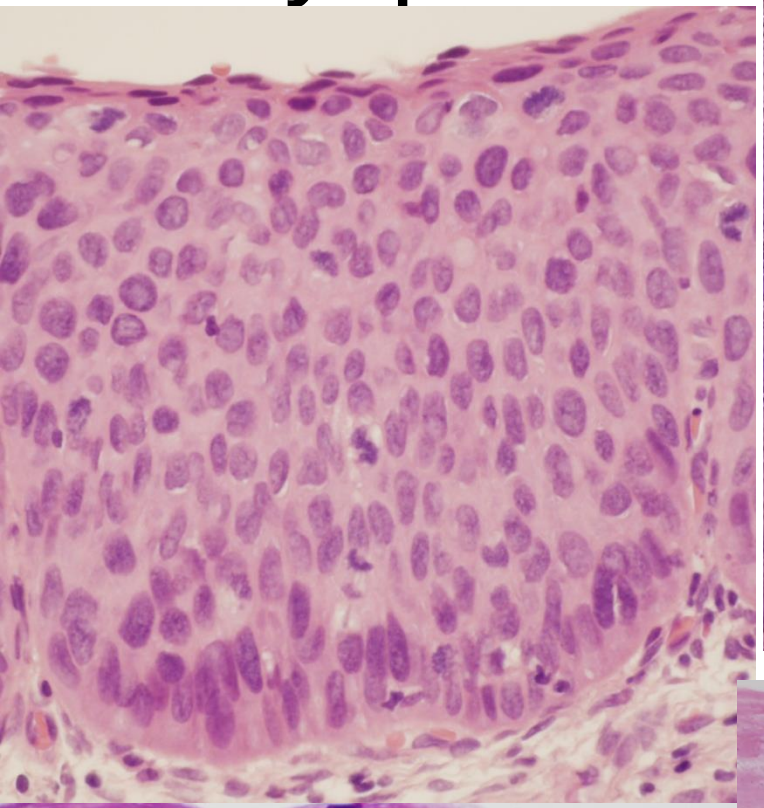
Atypische Zellproliferation und/oder Zelldifferentiation der Epithelzellen

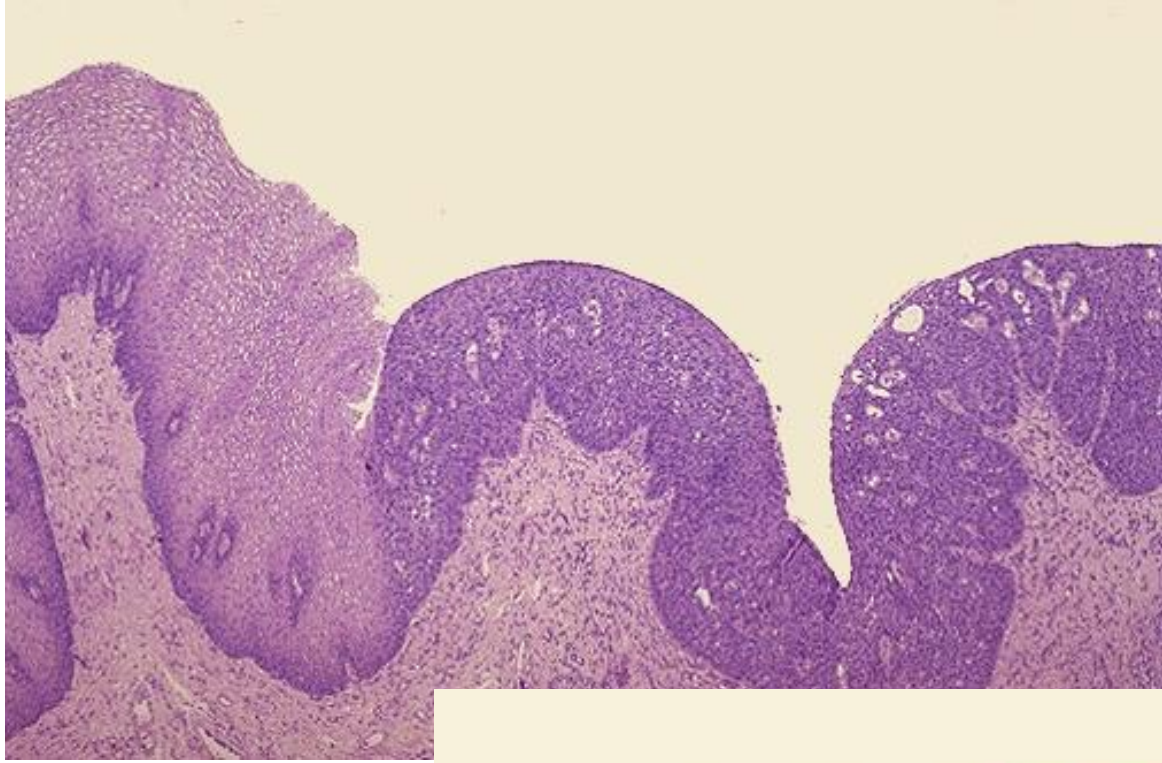
Vorstufe eines malignen Tumors

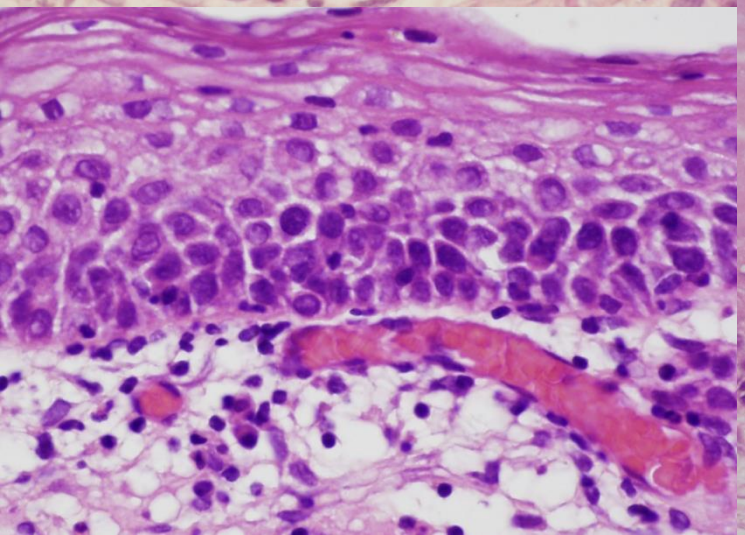
Morphologie

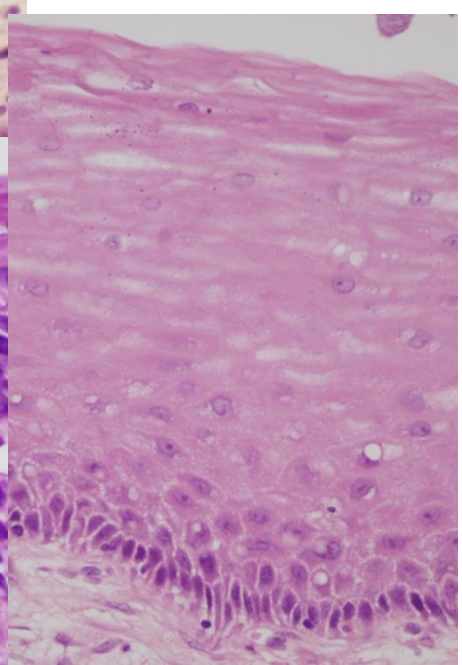
- Normales Epithelstruktur/schichten wird zerstört
- Variabilität von Zellgröße und Zellform (**Polymorphie**)
- Unterschiedliche Anfärbbarkeit und Größe der Zellkerne (**Polychromasie**, **Anisonukleose**)
- Auftreten **unreifener** Zellen statt normale Zellen
- Zellkern/Zytoplasma relation ↑
- Vergrößerung von **Nucleolen**
- Erhöhte **Mitoserate** und **atypische** Mitose
- Mitose nicht nur in Basalschicht

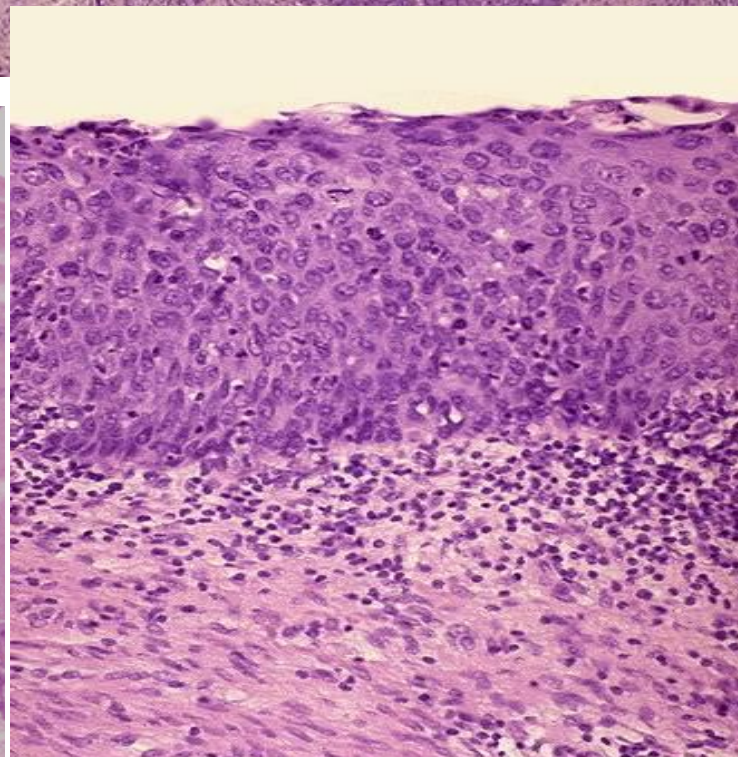
Dysplasie



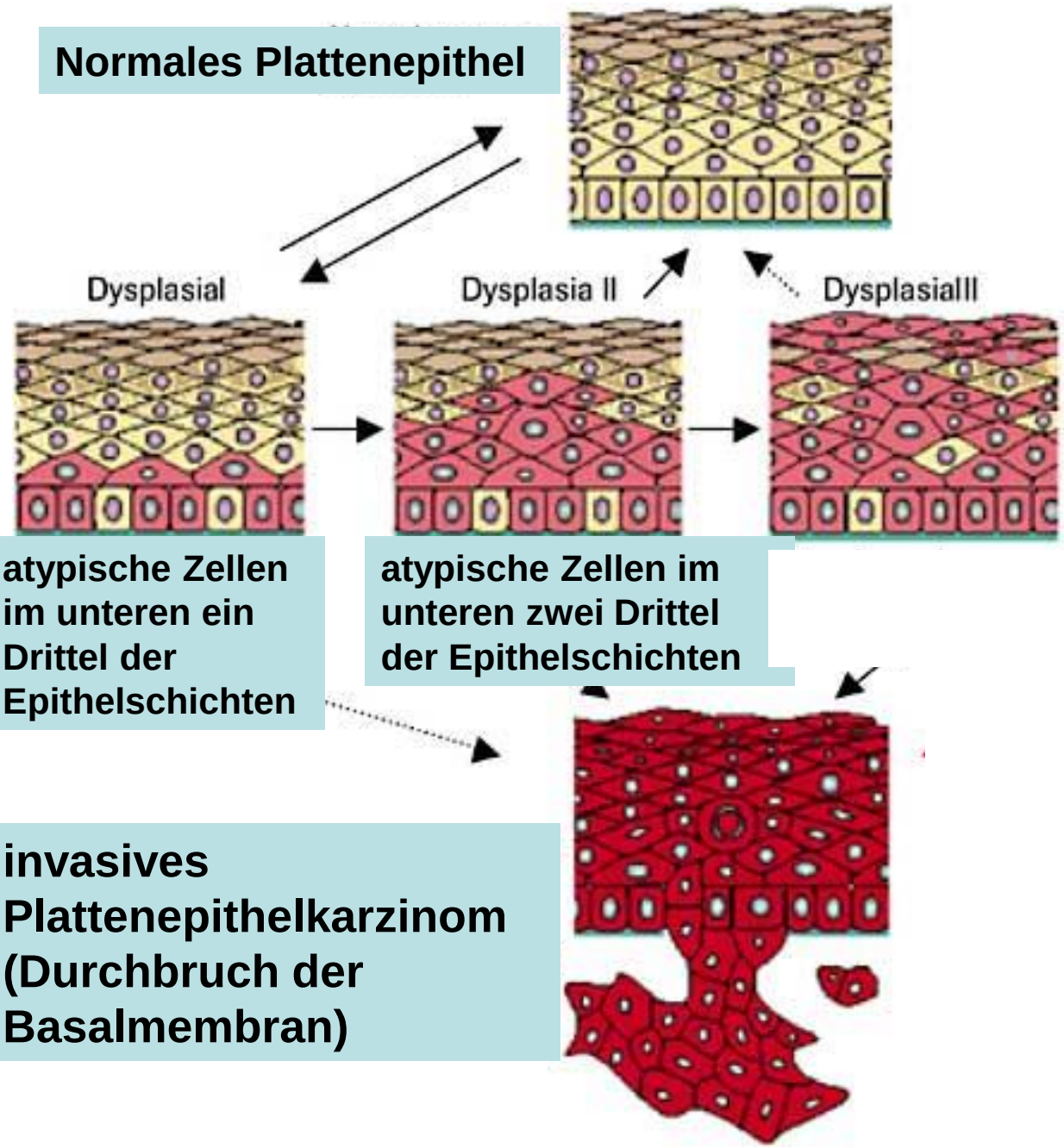








Normales Plattenepithel



atypische Zellen sind in allen Schichten des Epithels vorhanden = carcinoma in situ

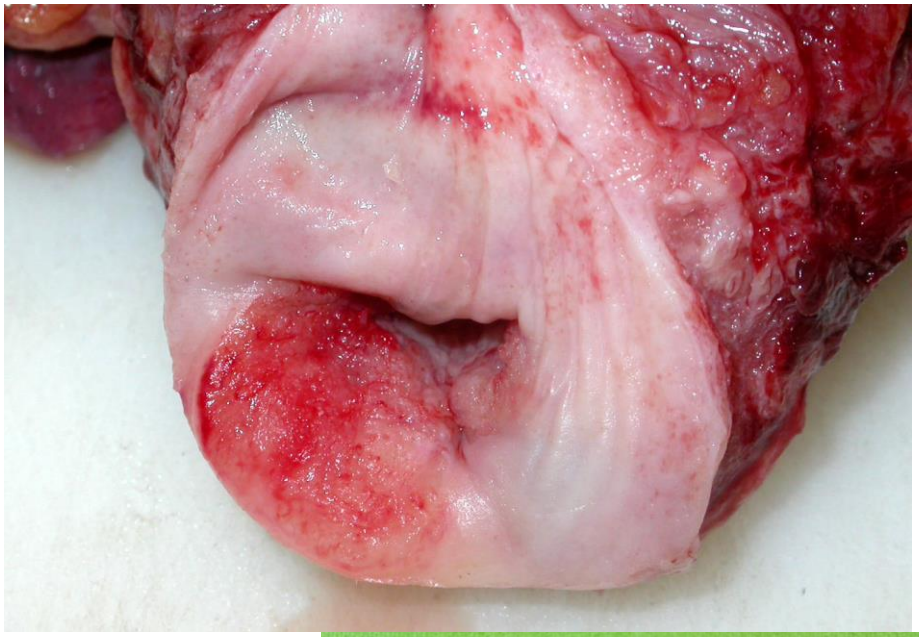
atypische Zellen im unteren ein Drittel der Epithelschichten

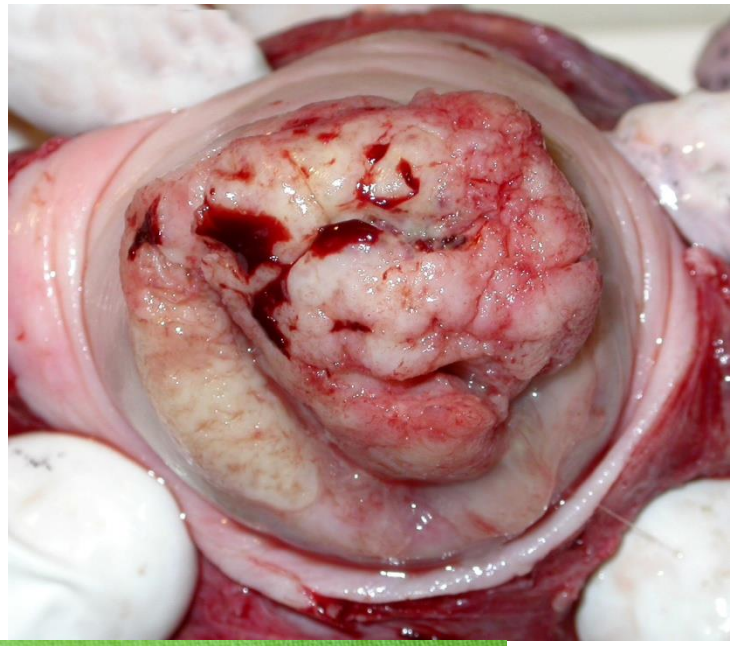
atypische Zellen im unteren zwei Drittel der Epithelschichten

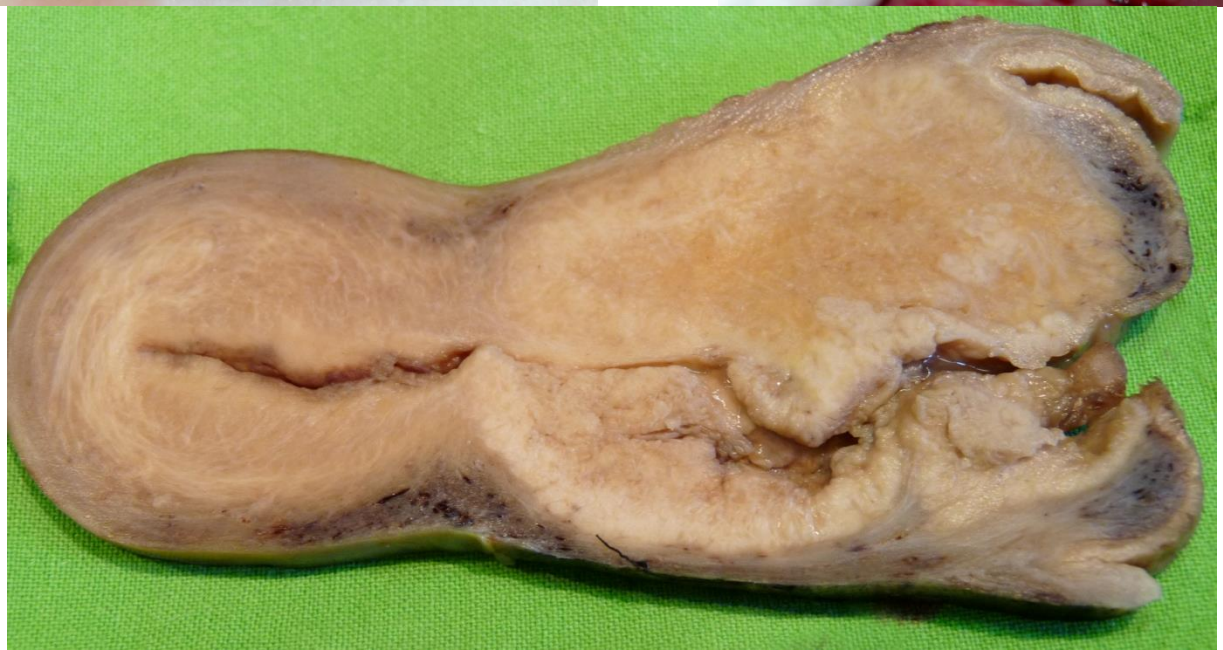
invasives Plattenepithelkarzinom (Durchbruch der Basalmembran)

http://sphweb.bumc.bu.edu/otlt/mph-modules/ph/ph709_cancer/PH709_Cancer5.html

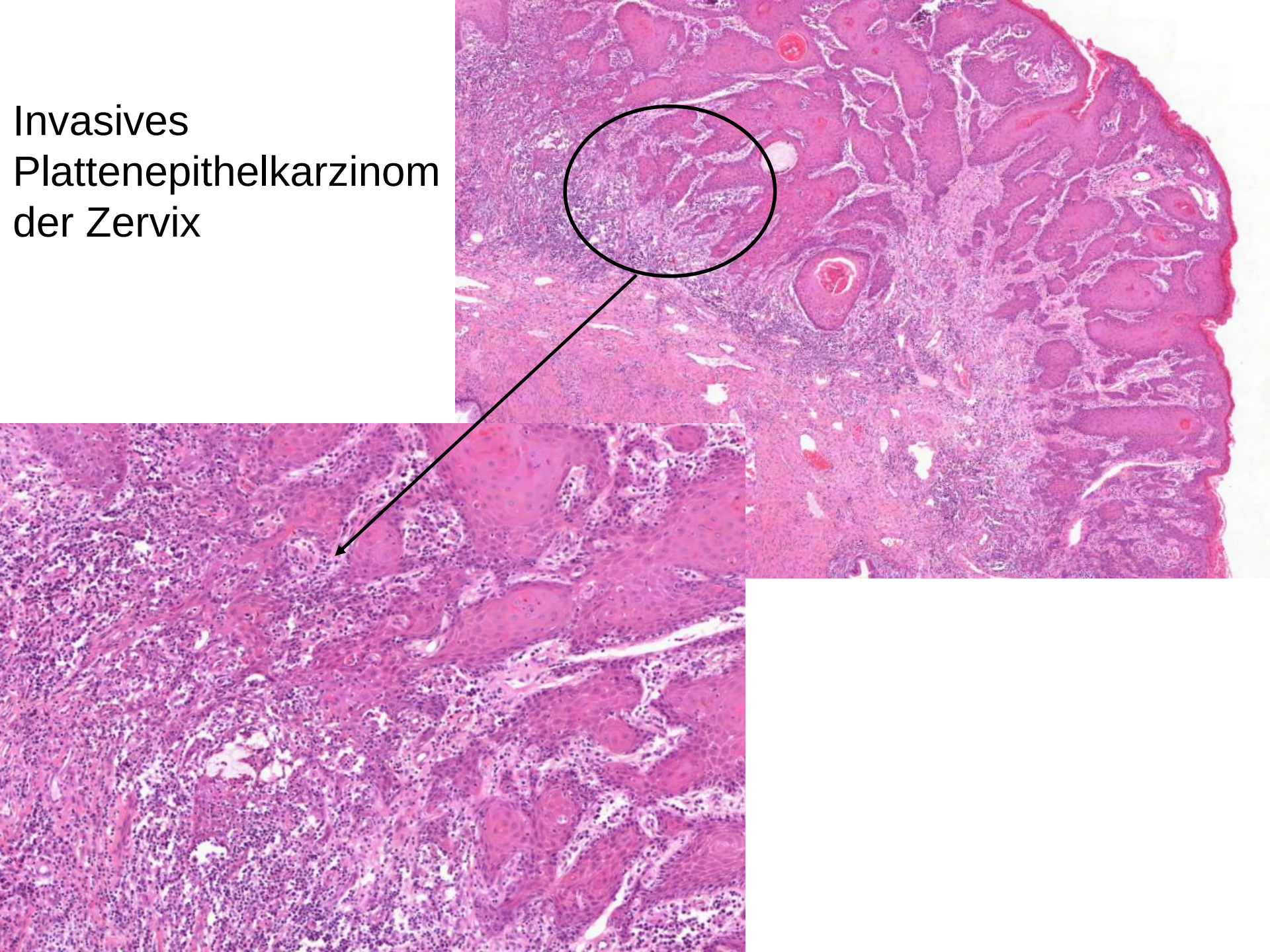
Invasives Zervixkarzinom



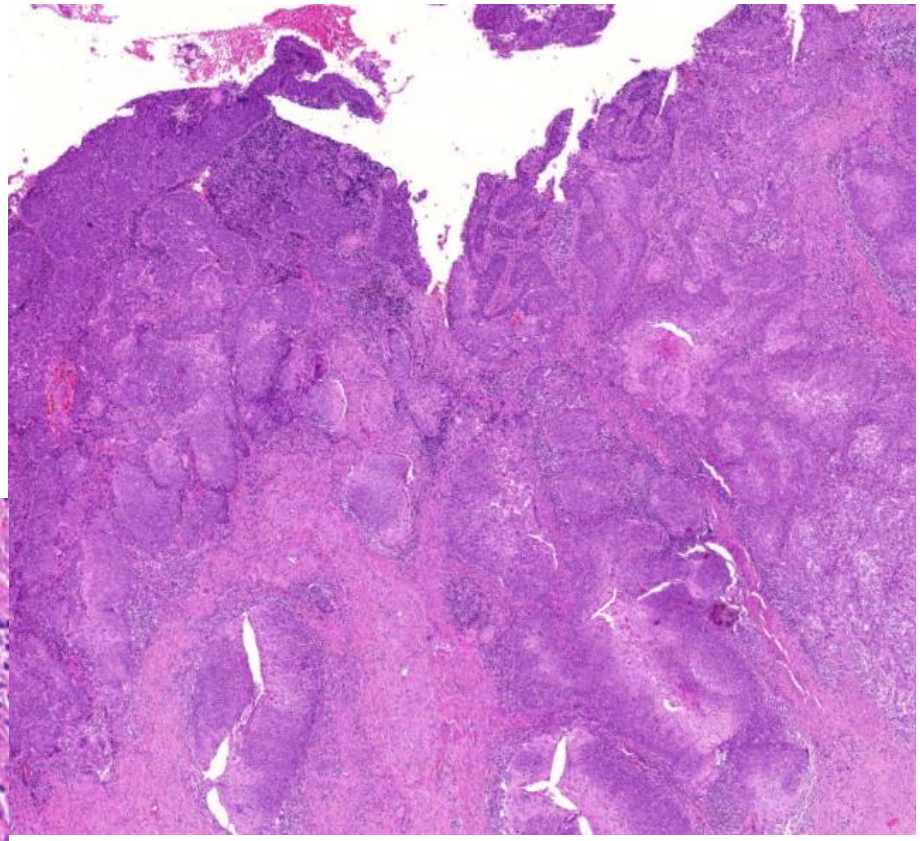


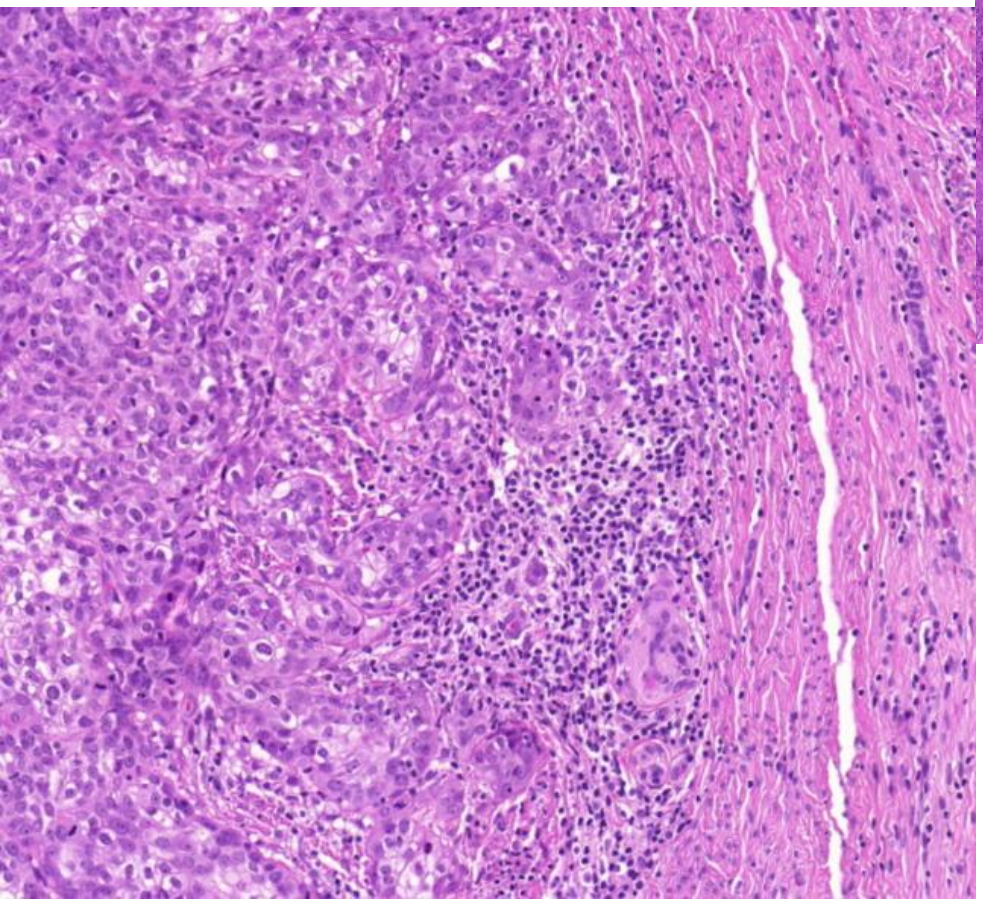


Invasives Plattenepithelkarzinom der Zervix



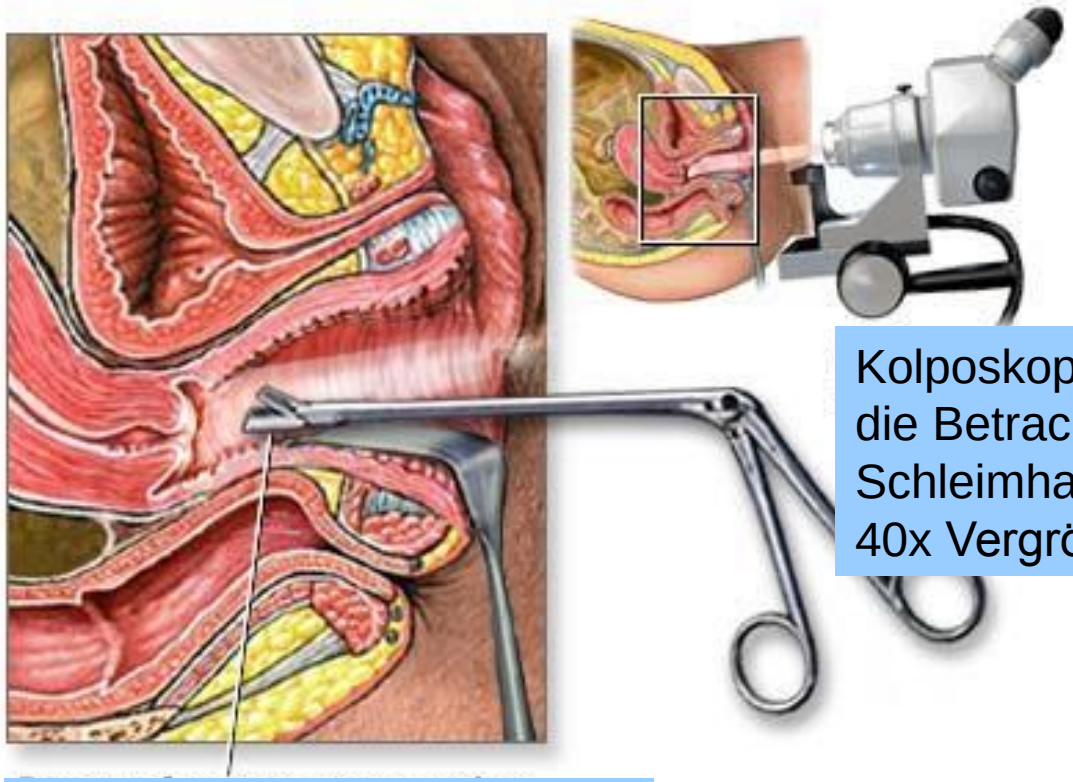
Invasives Plattenepithelkarzinom der Zervix





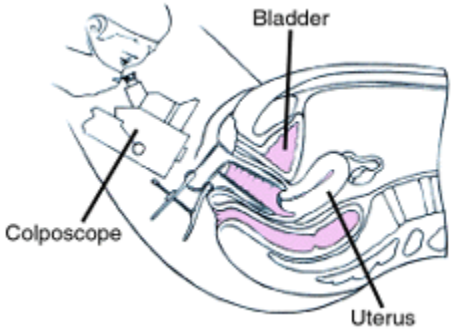
Untersuchungsmethoden

- Exfoliativ-Zytologie
- Kolposkopie (Essigprobe, Schiller-Jodprobe)
- Konisation - Histologie
- HPV-Typisierung (PCR)

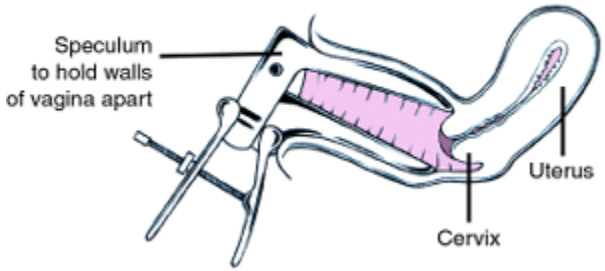


Kolposkop – ermöglicht die Betrachtung des Schleimhautreliefs mit 6x-40x Vergrößerung

Biopsie / Abstrich kann entnommen werden



Kolposkopie



Münchner Nomenklatur - 1975

Qualität des Abstrichs (ausreichend??)

Mikroorganismen

Klassifikation zytologischer Bild

I. Normal

II. Entzündliche Veränderungen

IIID. Zellen einer Dysplasie leichten bis mäßigen Grades

IVa. Zellen einer schweren Dysplasie/Cc.in situ (HPV)

IVb. Schweren Dysplasie/invasiv nicht auszuschließen

V. Zellen eines malignen Tumors

III. Unklarer Befund

Empfehlung

Bethesda System

I. Qualität des Abstrichs

II. Die Bewertung des Abstrichs

III. Ausführliche Diagnose

1. Infektion
2. Reaktive und reparative Zeichnungen
3. Epithel - Veränderungen
4. Nicht-epitheliale Tumor

IV. Vorschlag

**Based on: (Bethesda atlas (*Solomon D., Nayar R. (editors). The Bethesda System for Reporting Cervical Cytology, Second Edition. New York: Springer-Verlag, 2004.*

* ***General Points***

1. The system was developed in 1988 for reporting cervical/vaginal cytology, to provide uniform guidelines for reporting and reviewing gynaecologic Papaniculou smears.
2. It was subsequently modified in 1991 and 2001.
3. Most effective cancer prevention test available till date. It has become the index to which all other cancer screening tests are compared.
4. Yearly screening is estimated to reduce a woman's risk of getting carcinoma by 93%.
5. One of the numerous advances made in cervical cytology in the last decade has been introduction of liquid based cytology. This has improved sensitivity of the technique, reduced the number of specimen with obscuring blood and inflammation and increased LSIL:ASC ratio. Also HPV testing can be directly performed on LBC specimen.

****The Bethesda system 2001 classification (reporting format)***

1.Specimen type	1. Satisfactory for evaluation *describe presence or absence of transformation zone component (*not required in 2001 system) 2.Unsatisfactory for evaluation a. Specimen rejected b. Specimen not processed c. Specimen processed but unsatisfactory
2.General Categorization	1. NILM 2. Epithelial cell abnormality 3. Others
3.Interpretation/result	1. Negative for intraepithelial lesion/malignancy Organisms 1.T. Vaginalis 2.Fungal organisms suggestive of candida spp. 3.Shift in bacterial flora s/o bacterial vaginosis 4.Bacterial morphology consistent with actinomyces 5.cellular changes c/w H. simplex Other non neoplastic findings 1.Reactive cellular changes 2.Atrophy 3.Glandular status post hysterectomy Other findings Endometrial cells in women more than 40 years of age 2. Epithelial cell abnormalities Squamous cells - Atypical squamous cells (ASC-US, ASC-H) - LSIL - HSIL - Invasive squamous cell carcinoma Glandular cells - Atypical endocervical cells 1.Endocervical cells NOS 2.Endocervical cells favor neoplasia - Atypical endometrial cells 1.Endometrial cells NOS - Atypical glandular cells 1.glandular cells NOS 2.Glandular cells favor neoplasia - Adenocarcinoma in situ - Adenocarcinoma 3. Other malignant neoplasms (specify)
4. Suggestions	(if any)

Epithelveränderungen

LSIL

Low grade squamous cell intraepithelial lesion

CIN I, HPV Infektion

HSIL

High grade squamous cell intraepithelial lesion

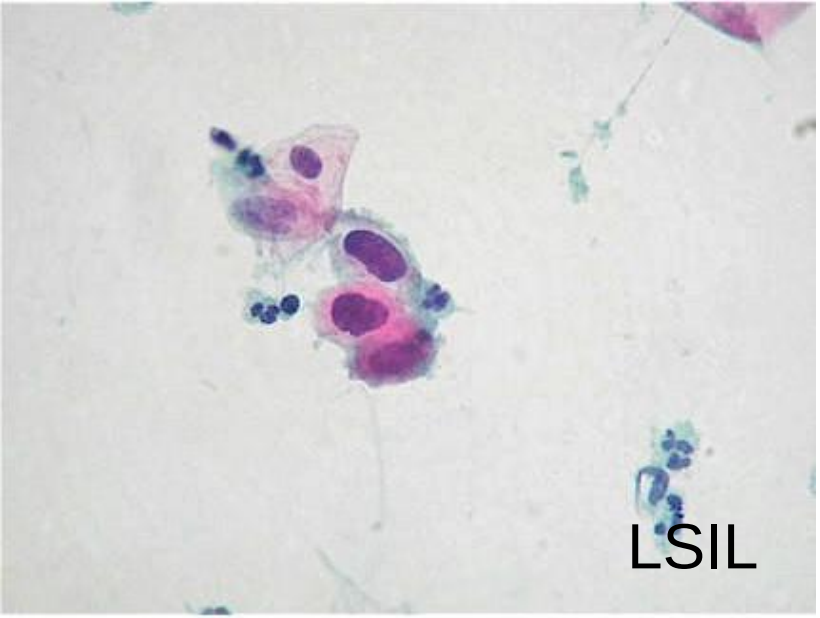
CIN II, CIN III, Cc. In situ

ASCUS

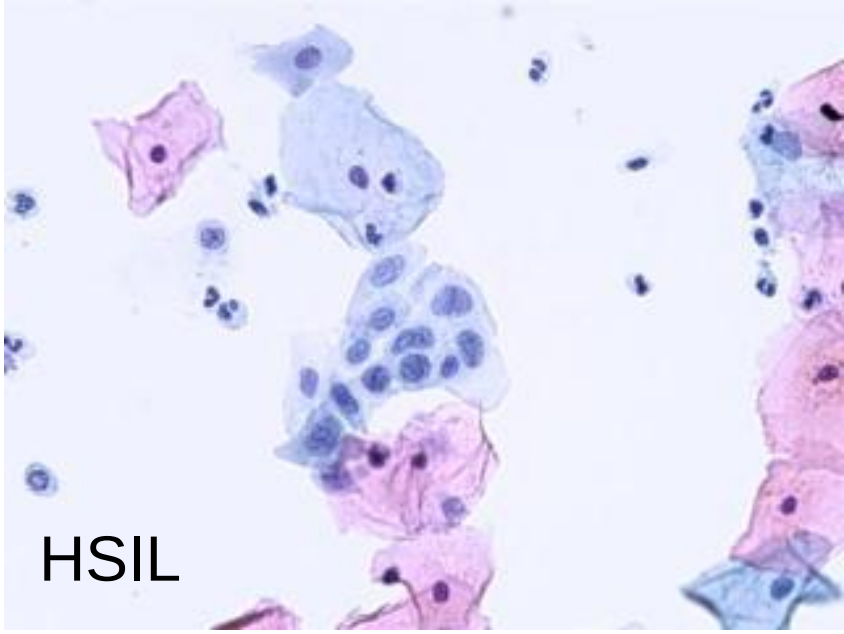
Atypical squamous cell of undeterminated significance

AGUS

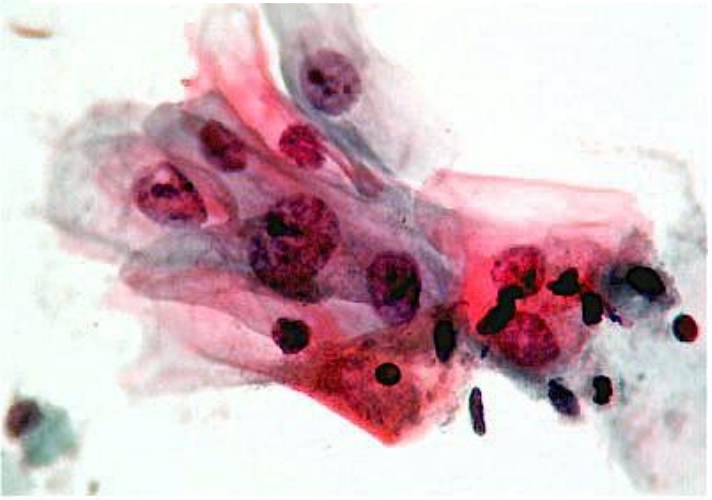
Atypical glandular cell of undeterminated significance



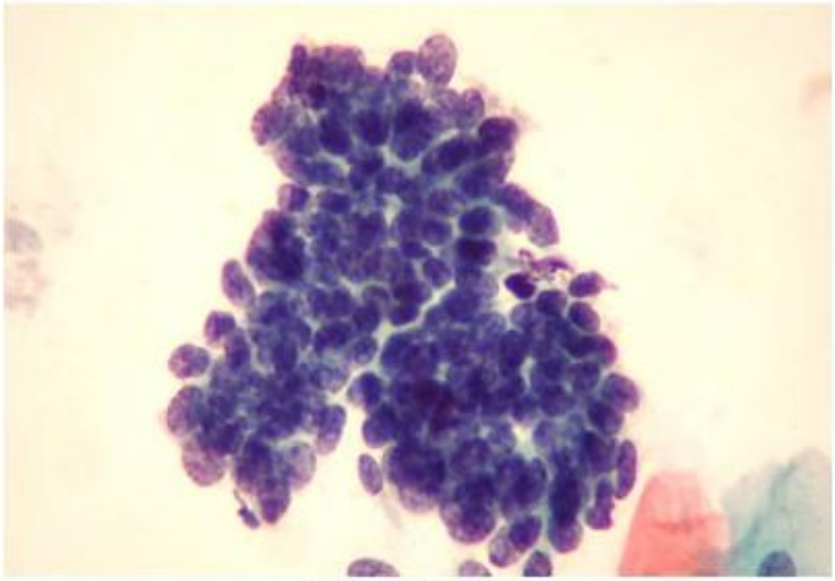
LSIL



HSIL



ASCUS



ADENOCARCINOMA