

General Principles of Cervical preinvasive Disease

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- No conflict of interest

What's the difference between colposcopy and Pap smear taking

SCREENING

- Cytology or HPV test
- Screening test
- Tells whether you are high or low risk of getting pre-cancer/cancer in future



DIAGNOSIS

- Colposcopy
- Biopsy
- Tells you where on the cervix the pre-cancer is and confirm by cervical biopsy



TREATMENT

- Treat pre-cancer on cervix
- Up to 99% cure rate
- Simple and effective



Women go for screening and screening result is abnormal

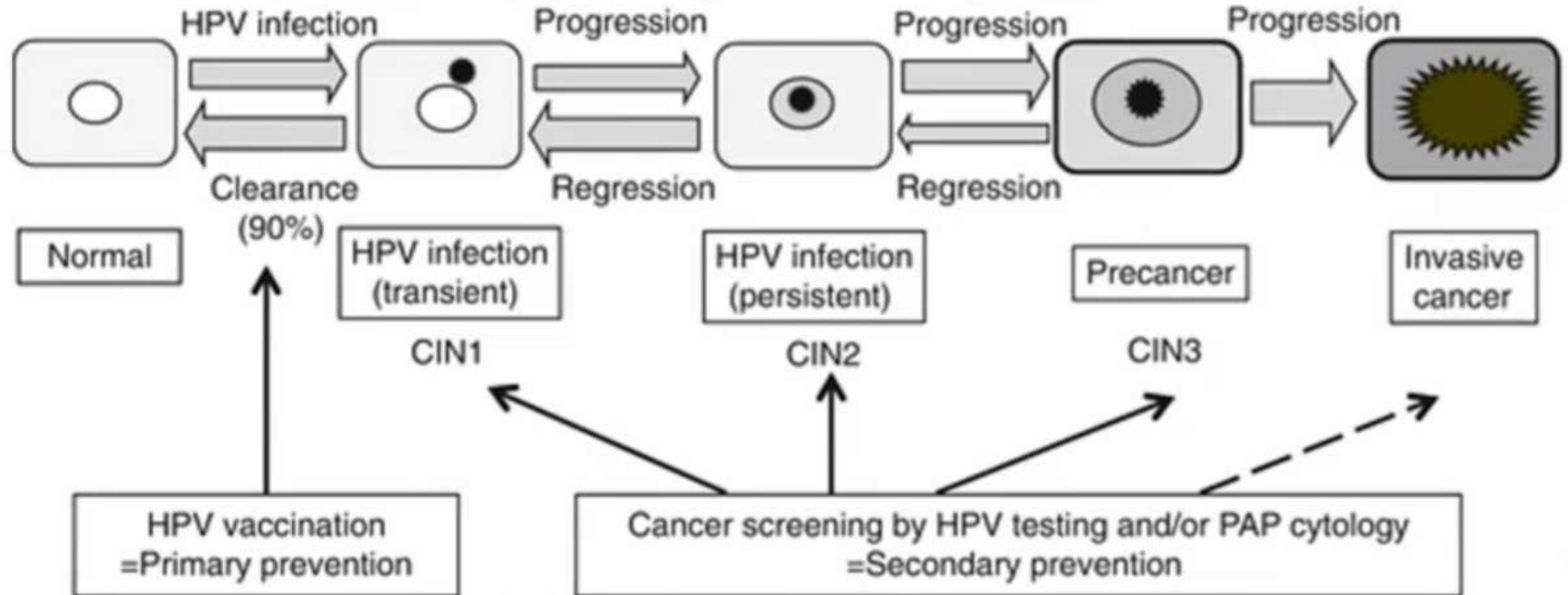
Womens' journey towards cervical cancer prevention

Future cervical cancer prevented.

- Cervical Intraepithelial neoplasia (CIN) since 1968

- Dysplasia  Cancer

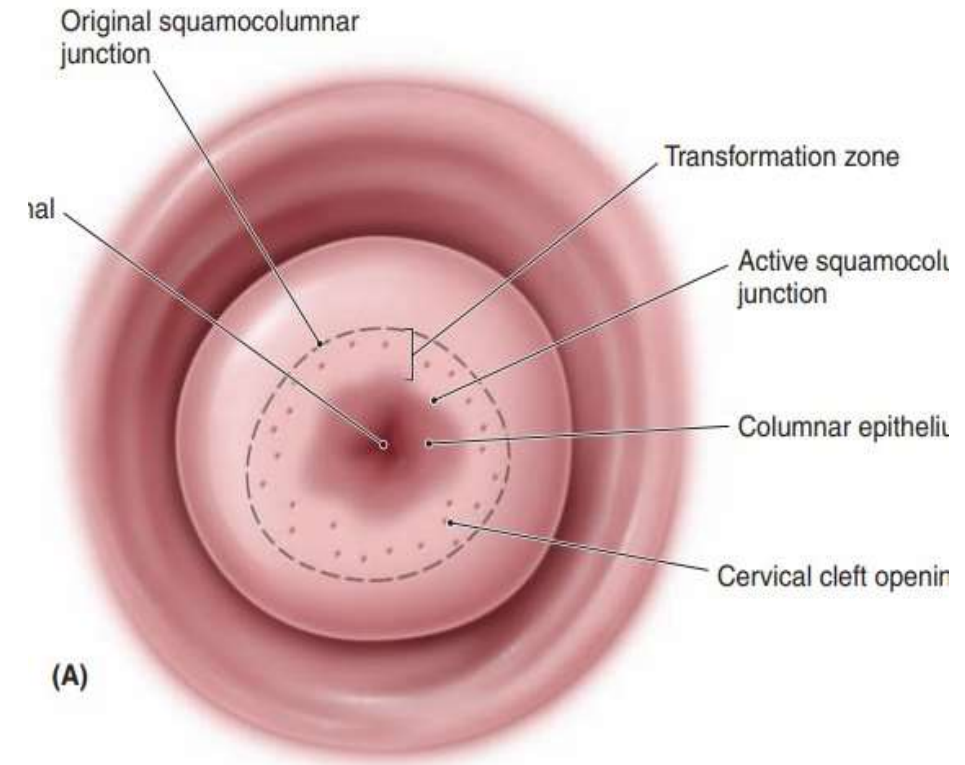
Cervical cancer prevention strategies




Ino K. (2017) Prevention of Cervical Cancer: Era of HPV Testing and Vaccination. In: Konishi I. (eds) Precision Medicine in Gynecology and Obstetrics. Comprehensive Gynecology and Obstetrics. Springer, Singapore

Cervical intraepithelial neoplasia

- A premalignant condition of the uterine cervix.
- The ectocervix (surface of the cervix that is visualized on vaginal speculum examination) is covered in squamous epithelium,
- The endocervix, including the cervical canal, is covered with glandular epithelium.
- CIN refers to squamous abnormalities.
- Glandular cervical neoplasia includes adenocarcinoma in situ and adenocarcinoma.

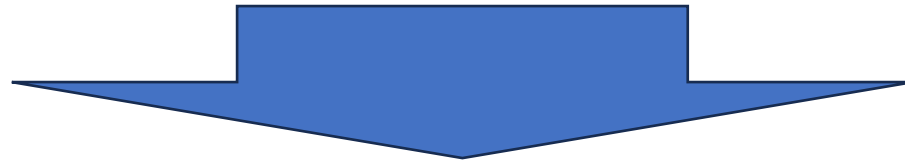


CIN Diagnosis

- Cellular Immaturity
- Cellular Disorganization
- Nuclear Atypia
-  Mitosis

Metaplasia

- Estrogen -> Glycogen in vaginal epithelium
- Lactobacilli -> PH vaginal ↓



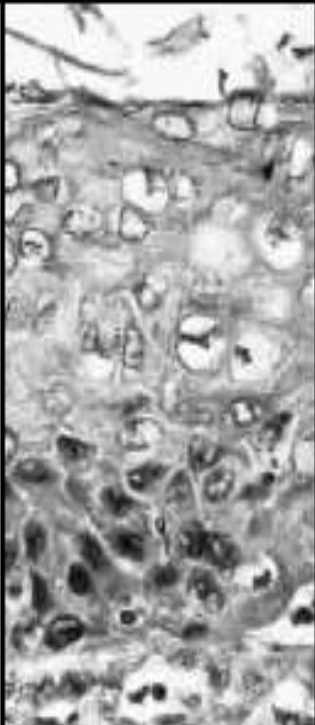
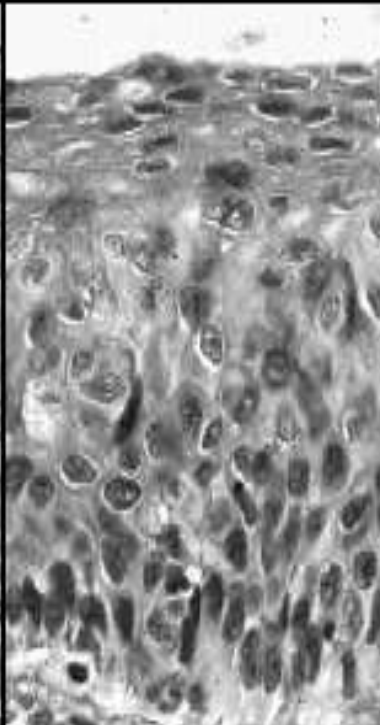
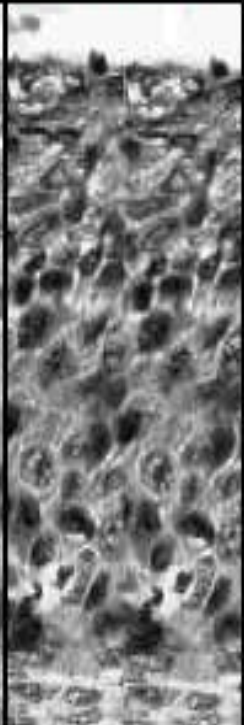

Sub columnar reserve cell -> **Metaplasia**

Columnar -> Squamous

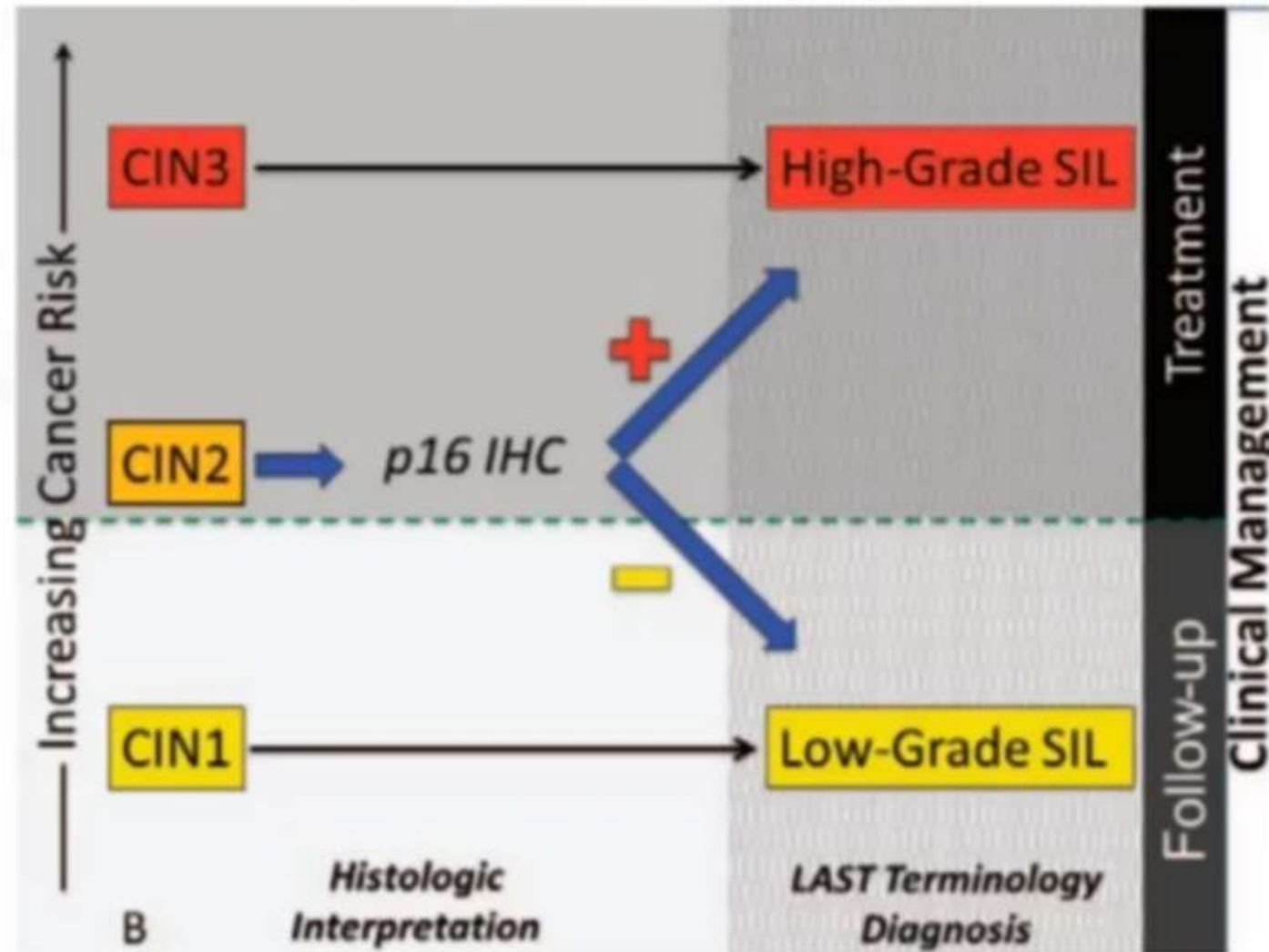
CIN 1

- ❑ a low-grade lesion
- ❑ mildly atypical cellular changes in the lower third of the epithelium

- ❑ Human papillomavirus (HPV) cytopathic effect (koilocytotic atypia) is often present
- ❑ 4 percent CIN 1
- ❑ 5 percent for CIN 2,3

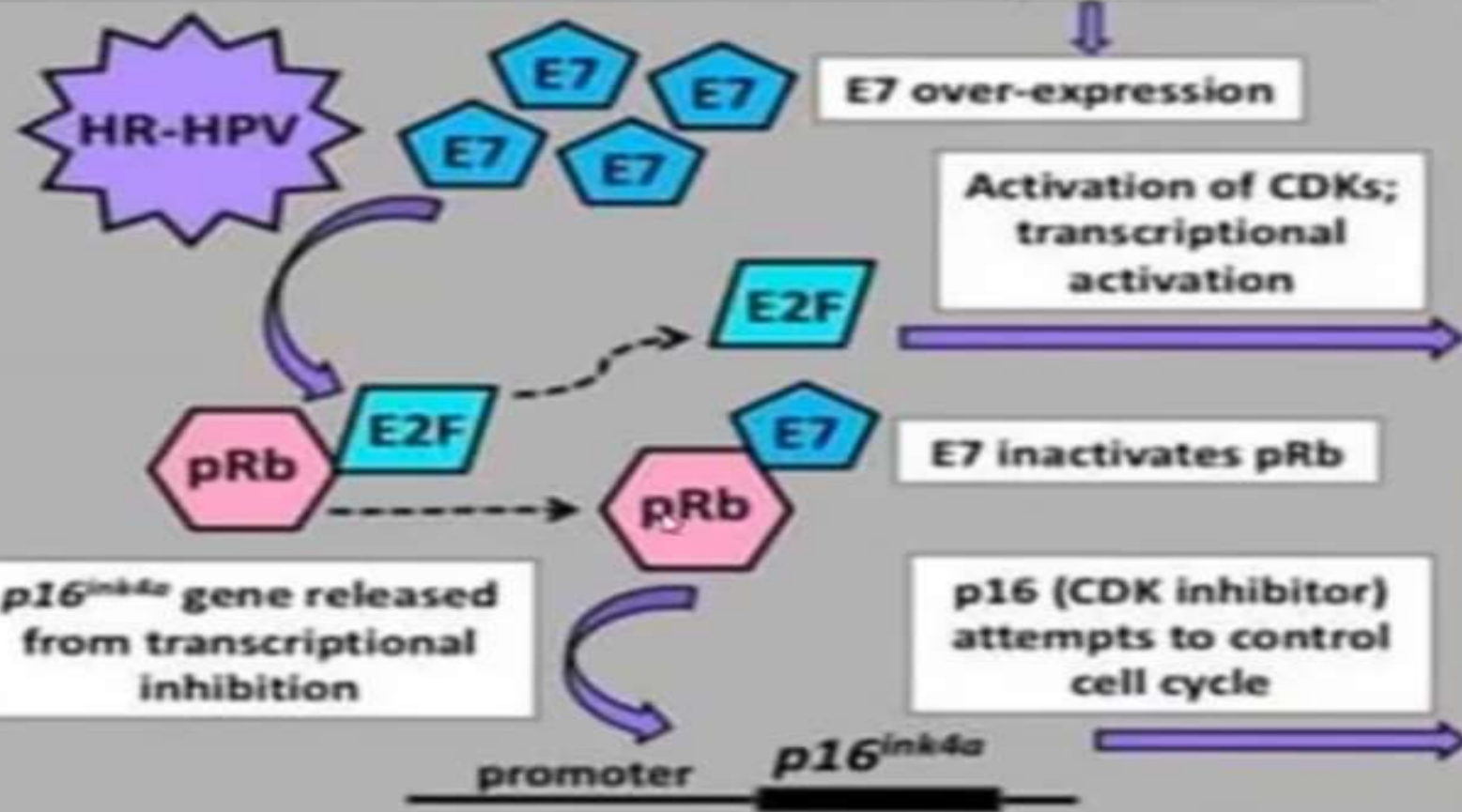
LAST System ^[1]	Cytology	LSIL	HSIL		
	Histology	LSIL	p16 staining should be performed*	HSIL	
Bethesda Classification System ^[2]	Cytology	LSIL	HSIL		
	Histology	CIN 1	CIN 2	CIN 3	
Previous terminology		Mild dysplasia	Moderate dysplasia	Severe dysplasia	Carcinoma in-situ
Histologic images					

**Lower Anogenital Squamous Terminology (“LAST”) Consensus:
2-tiered terminology, “Bethesda-like”:
P16-normal CIN2 favor LSIL; P16-abnormal CIN2 favor HSIL**



High-risk HPV-mediated Disruption of Cellular Mechanisms via Deregulated HPV Oncoprotein Expression Results in p16 Over-expression and Proliferation

Productive infection → Transforming infection*



*also involves E6 over-expression and p53 inactivation



Cell cycle progression (↑ proliferation)

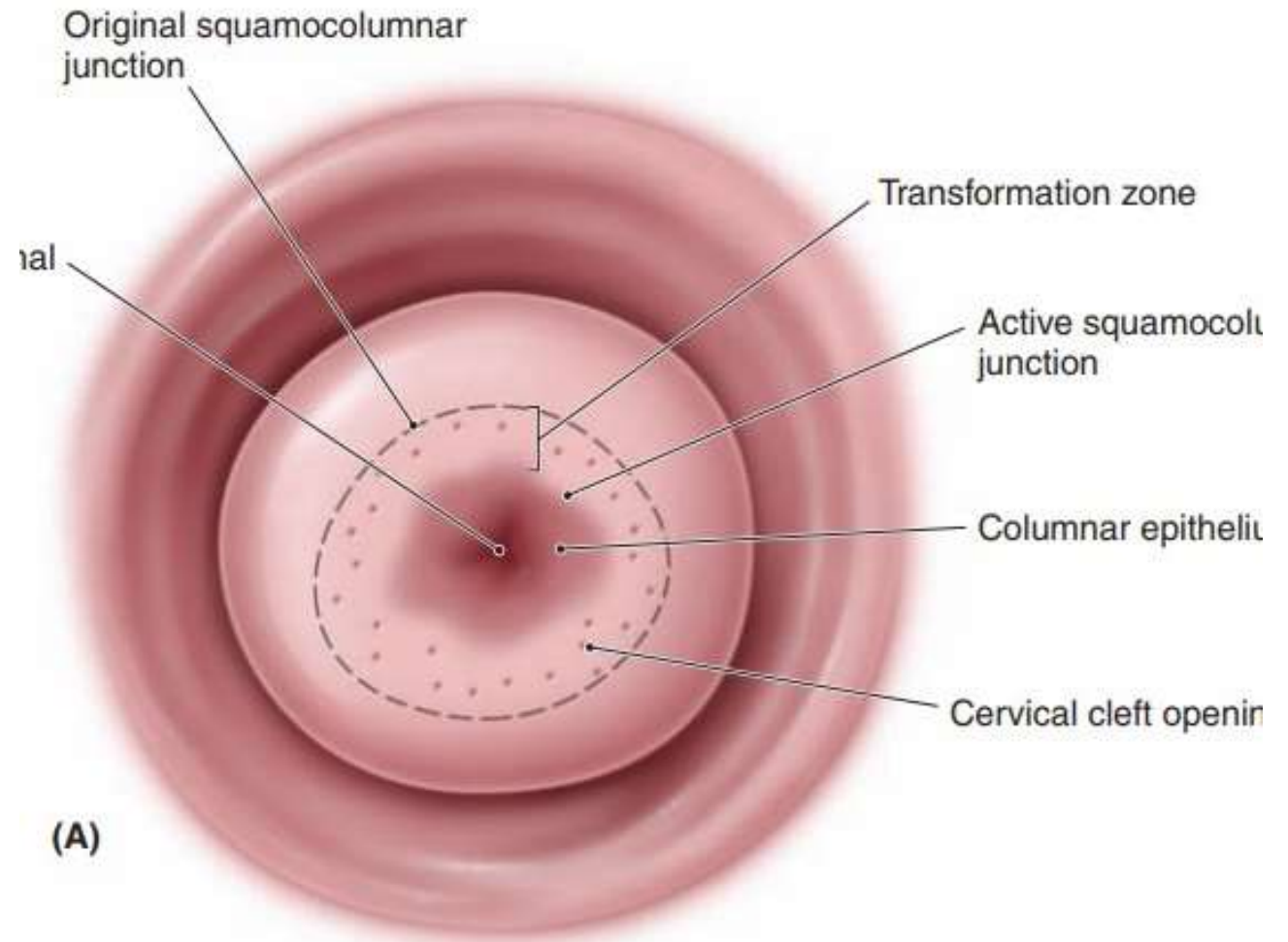


p16 over-expression

CIN

Anterior Lip
Sharp border
Transitional zone

*Metaplasia
&
HPV infection*



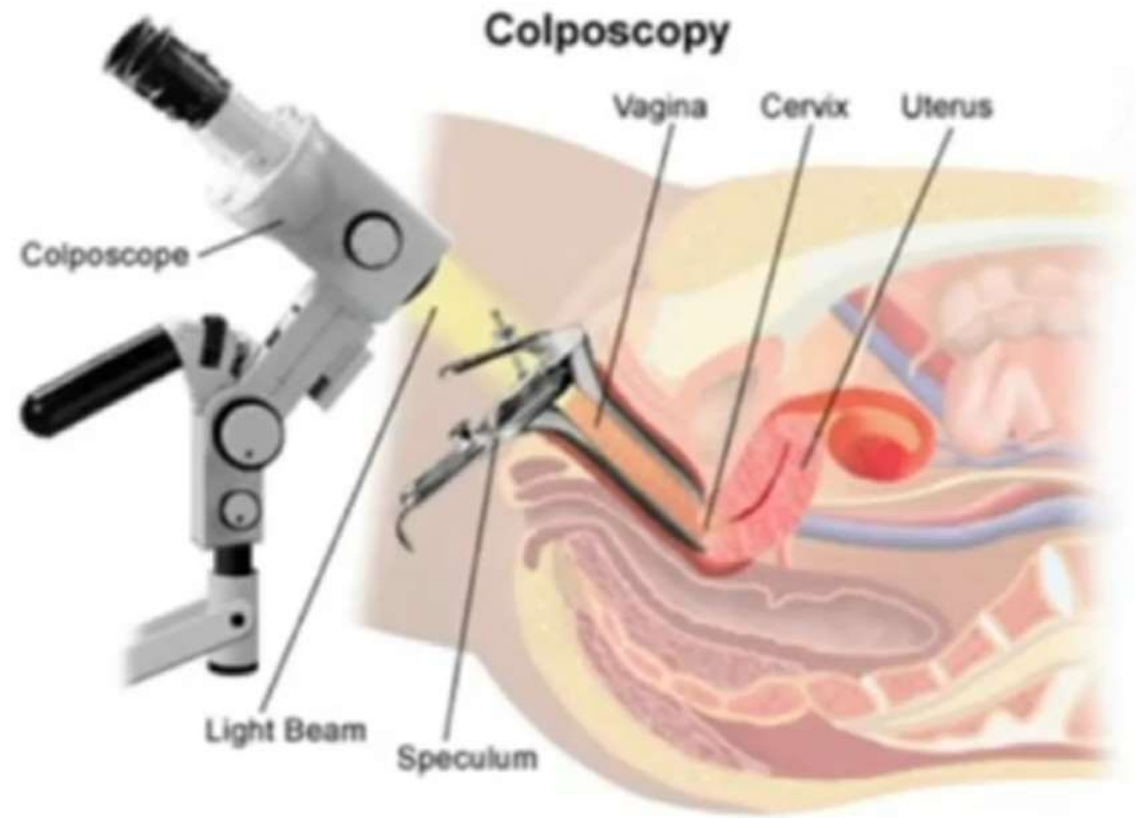
Risk for progression to cancer

- AGE
 - <25 years have a lower risk of developing cervical cancer
- CIN grade
- HPV and cytology results preceding the diagnosis of CIN

Why do we do colposcopy?

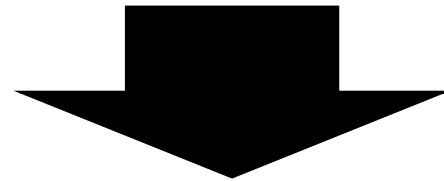
- Determines the presence of pre invasive disease
- Evaluates the extent of disease
- Confirms presence of preinvasive disease
- Effective treatment of pre-cancerous lesions
- Save women from future cervical cancer

Detect and treat **DISEASE**
NOT
HPV infection



LSIL

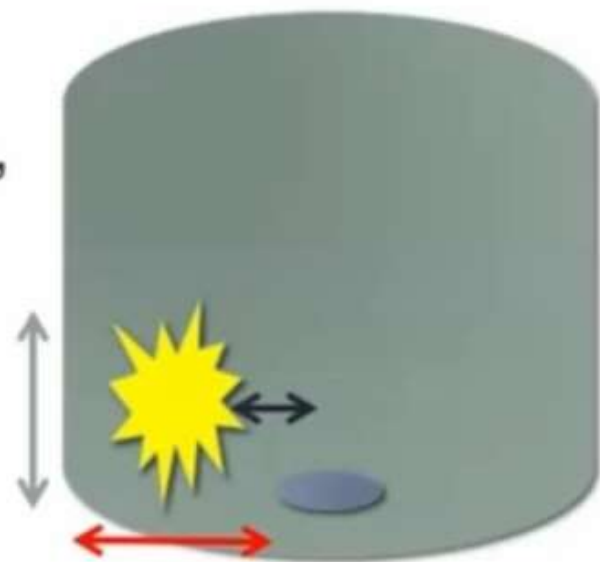
- 75% CIN 1
- 25% CIN 2,3
- 82% HPV+



Colposcopy

Aim of treatment

- Removing/destroying enough tissue to adequately destroy CIN down to the crypts
- Effective treatment down to at least 7-10mm is needed to destroy CIN 3
- Extend of lesion: Proximal and distal edge of lesion from cervical canal
- Ablation: Whole Transformation Zone, whole lesion(s)
- Excision: Negative margins



The cervix is attached to a woman



Women's emotions



Your Environment

Privacy



Your technique



Your manners



Your language

Understand the patient

UNDERSTAND

PATIENTS \geq 25 YO WITH CIN1

- Preceded by LSIL or less — Patients with CIN 1 preceded by
 - ❖ low-grade squamous intraepithelial lesion (LSIL),
 - ❖ atypical squamous cells of undetermined significance (ASC-US)
 - ❖ NILM but positive for human papillomavirus (HPV) are

Low risk for the development of cervical cancer

- In a cohort study in which over 100,000 patients had colposcopy biopsies demonstrating CIN 1 and were followed for a decade, the risk of developing CIN 3+ when preceding cytology was LSIL or less was:
- For LSIL, HPV-positive – One- and five-year risks were 0.7 and 2.3 percent
- For ASC-US, HPV-positive – One- and five-year risks were 0.5 and 2.6 percent The following algorithm provides an example as to how these patients are managed (algorithm 1).
- For NILM, HPV-positive – One- and five-year risks were 0.7 and 2.8 percent
- In all three of these examples, given the low risk of developing CIN 3+

one-year follow-up with HPV-based testing is recommended

Initial screening:

- HPV-positive ASC-US
- Immediate CIN 3+ risk = 4.5%
- Management: Colposcopy



Colposcopy visit:

- Colposcopic biopsy result is <CIN 2
- 5-year CIN 3+ risk is 2.9%
- Management: 1-year follow-up



First follow-up surveillance:

- HPV-positive ASC-US
- Immediate CIN 3+ risk = 3.1%
- Management: 1-year follow-up



Second follow-up surveillance:

- HPV-negative NILM
- 5-year CIN 3+ risk = NA
- Management: 3-year follow-up

Second follow-up surveillance:

- HPV-positive ASC-US
- Risk = NA
- Management: Colposcopy

ASC-H or HSIL — CIN 1

- an increased risk for subsequent high-grade disease
- Concern that an underlying high-grade lesion has been missed by colposcopy and biopsy

- In the study on 100,000 patients had colposcopic biopsies demonstrating CIN 1 and were followed for a decade, the risk of developing CIN 3+ when preceding cytology was ASC-H or HSIL was
- For ASC-H – One- and five-year risks were 1.4 and 5.6 percent
- For HSIL – One- and five-year risks were 3.9 and 6.5 percent

Managed more aggressively

Preceded by HSIL cytology

- An immediate diagnostic excisional procedure or
- Observation (HPV testing and colposcopy at one year)
 - Entire squamocolumnar junction (SCJ) and lesion are visible on colposcopy
 - The endocervical curettage (ECC) is less than CIN 2

Observation

- Colposcopy and HPV-based testing are performed at one year; if negative, then repeat HPV testing is recommended in one year.
- -If HPV testing continues to be negative, then repeat HPV testing is recommended in three years
- -If any test is abnormal during observation, repeat colposcopy is recommended, and management is based on the biopsy result.
- -If HSIL cytology is found at the one- or two-year visit, then a diagnostic excisional procedure is recommended.

Observation:

- Colposcopy & cytology <25 years
- Colposcopy & HPV-based testing ≥25 years at 1 year*

OR

Diagnostic excisional procedure ↑

OR

Review of cytologic, histologic, and colposcopic findings

All tests negative

Abnormal test results

Cytologic HSIL at 1 year

Age-specific retesting in 1 year^Δ

Manage per 2019 ASCCP Guidelines

Continued observation for age <25 years only

Manage per ASCCP Guideline for revised diagnosis

All tests negative

ASC-H/HSIL cytology at 2 years

HPV-based testing in 3 years

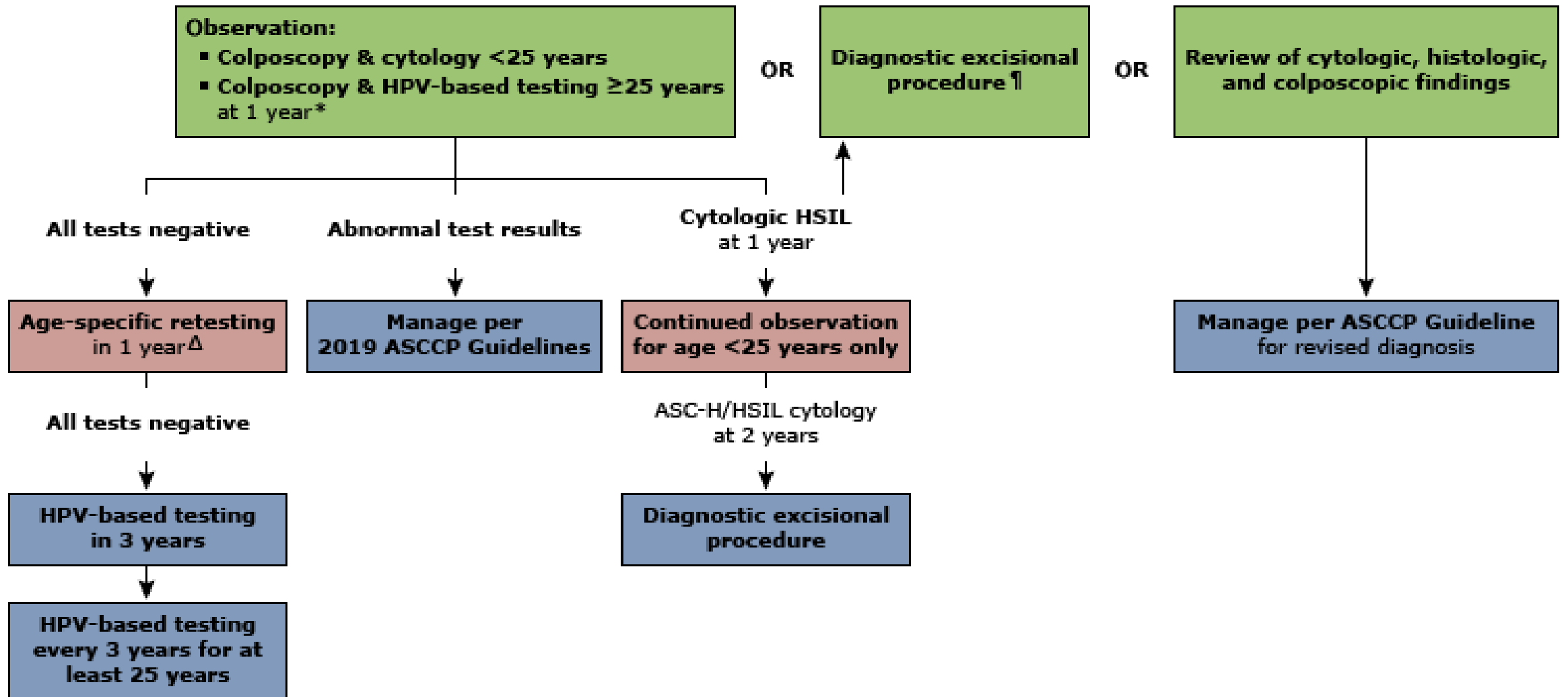
Diagnostic excisional procedure

HPV-based testing every 3 years for at least 25 years

preceded by ASC-H cytology

- Observation is recommended provided the entire SCJ and lesion are visible on colposcopy and an ECC, if collected, is negative. A diagnostic excisional procedure is not recommended.
- -HPV-based testing is performed at one year; if negative, then repeat HPV testing is recommended in one year.
- -If HPV testing continues to be negative, then repeat HPV testing is recommended in three years,(long-term surveillance)
- -If any test is abnormal during observation, repeat colposcopy is recommended, and management is based on the biopsy result.
- -If HSIL cytology is found at the one- or two-year visit, or if ASC-H is persistent at the two-year visit, then a diagnostic excisional procedure is recommended.

Preceded by ASC-H cytology



Persistent for two years

- Persistent CIN 1 has a low risk of progression to CIN 3+
- Observation is preferred. Co test in 1 year
- Treatment with a diagnostic excisional procedure (LEEP, cold knife cone, and laser cone biopsy) or ablation (with cryotherapy, laser ablation, and thermo ablation)

CIN 2,3

- Prompt treatment is recommended, with the exception of pregnant patients and patients younger than 25 years of age
- Patient compliance is another factor to consider when deciding whether to treat or manage expectantly

nonpregnant patients ≥ 25 years

- If histologic HSIL is unspecified (reported as histologic HSIL or HSIL [CIN 2,3] without distinction of CIN 2 or CIN 3):
 - Treatment is preferred; in these patients, CIN 3 cannot be excluded, and, therefore, patients are managed as if CIN 3 were present.
 - Observation (with colposcopy and HPV testing at 6 and 12 months) is acceptable.

If CIN 2 is specified

Treatment is recommended

Observation (with colposcopy and HPV testing at 6 and 12 months for up to two years) is acceptable if all of the following are present:

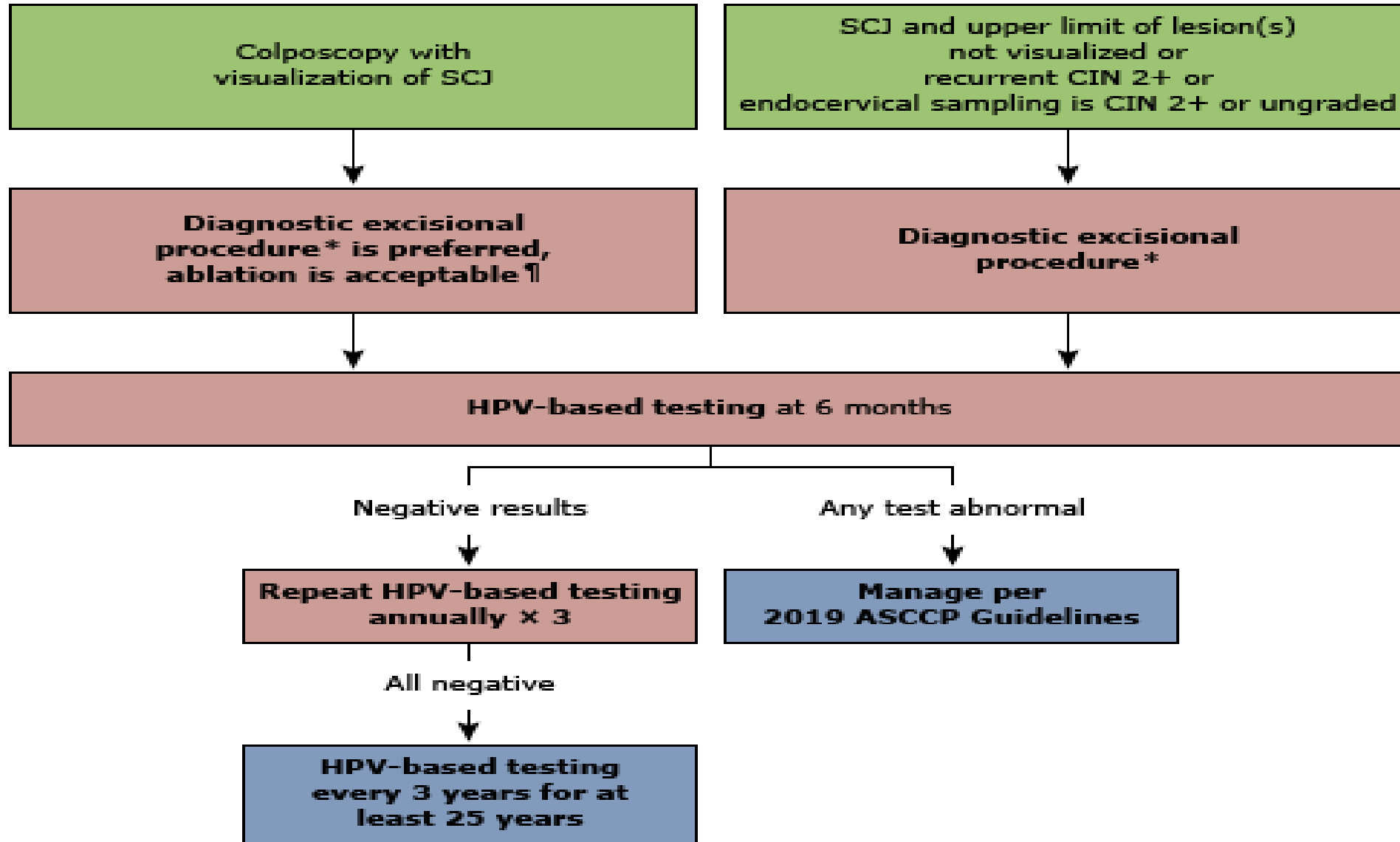
- The patient's concerns about potential adverse pregnancy outcomes after an excisional procedure outweigh the concerns about cancer
- The entire SCJ and lesion are visible on colposcopy, and ECC does not demonstrate CIN 2+ or ungraded CIN.

If CIN 3 is specified, if the entire SCJ or lesion are not visible on colposcopy, or if the ECC is CIN 2+:

Treatment is recommended

Hysterectomy is not acceptable for the primary treatment of HSIL (CIN 2 or 3).

clinical management of histologic HSIL



CIN 2 specified
Observation preferred <25 years
Acceptable ≥25 years if concerns about treatment effects on future pregnancy outweigh concerns about cancer

HSIL, unspecified
Observation acceptable <25 years
Treatment preferred ≥25 years

CIN 3 specified; any histologic HSIL with SCJ or upper limit of lesion(s) not visualized; or ECC with CIN 2+ or ungraded

Observation:
▪ Colposcopy & cytology <25 years
▪ Colposcopy & HPV-based testing ≥25 years at 6 and 12 months

Diagnostic excisional procedure

2 consecutive evaluations both <ASC-H cytology and <CIN 2 histology

Colposcopy remains CIN 2 or cytology ASC-H, AGC, or HSIL with biopsy <CIN 2

HPV-based testing (≥25 years) or cytology (<25 years) in 1 year

Test results negative

Any test abnormal

HPV-based testing annually × 3 total years, then test at 3-year intervals for at least 25 years

Continue observation:
▪ Colposcopy & cytology <25 years
▪ Colposcopy & HPV-based testing ≥25 years at 6-month intervals up to a total of 2 years since first CIN 2 diagnosis

CIN 3 develops at any point or CIN 2 histology or ASC-H, HSIL, or AGC cytology persists for 2 years

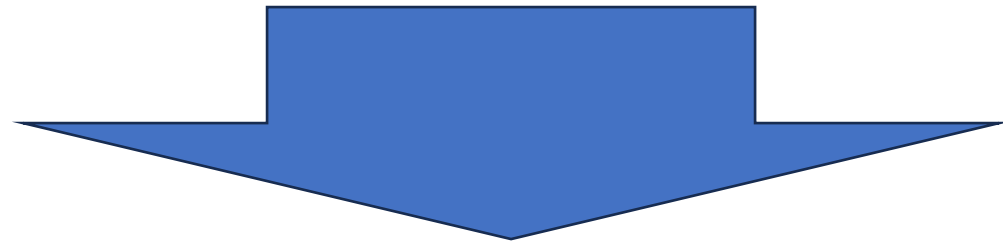
Diagnostic excisional procedure

RECOMMENDATIONS

- New-onset CIN 1 and (ASC-US), (LSIL), or (ASC-H), we recommend observation rather than treatment
- **Follow-up for these patients is with HPV testing in one year**
- Treatment rather than observation may be reasonable in some patients
 - ❖ long-term follow-up may be difficult,
 - ❖ completed childbearing and are not concerned about future obstetric complications

ASC-US

- CIN 1 , Age > 25y



co test 1y

RECOMMENDATIONS

Persistent CIN 1 (lesions present for ≥ 2 years), we continue to prefer observation, but treatment is also acceptable

RECOMMENDATIONS

- CIN 1 and a preceding lesion of high-grade squamous intraepithelial lesion (HSIL) or CIN 2, treatment or observation is acceptable
- For most patients, we suggest treatment rather than observation

Dr. Harald zur Hausen



Identified Human papillomavirus as the etiologic agent in cervical cancer

Received the Nobel Prize in 2008



THE HPV
VACCINE IS
CANCER
PREVENTION