

The role of colposcopy in the diagnosis and treatment of cervical precancerous lesions



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Overview

According to the World Health Organization (2000), there were 500,000 new cervical cancer cases worldwide each year, 80% of which were in developing countries. About 30% (150,000) of the global new cases were in China.

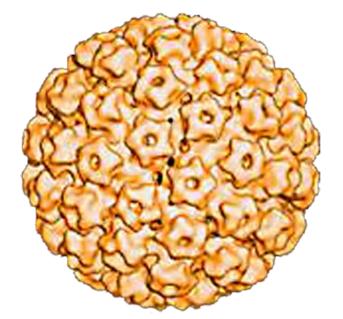
270,000 women worldwide died of cervical cancer

Incidence: the U.S. 1,1000 / year; China 135,000/year

Mortality: the U.S. 3900 / year; China 5,3000/year

Preface Development of cervical cancer screening

Time	Events
1928	Papanicolaou proposed vaginal cytology smears in screening, which was ignored at that time
1934	A study conducted by Papanicolaou and Traub demonstrated the use of cytology to detect cervical precancerous lesions
1950S	The ideas in the article were widely accepted, and screening was introduced in the United States and Canada
1955	Scheffey introduced colposcopy, initially thinking it could be an alternative to Pap smear; 10 years later, it was recognized as a further examination to abnormal cytology
1960S	Pap smear is widely accepted as the standard screening method for early detection of cervical precancerous lesions
1990s	HPV is recognized as a major cause of cervical cancer, and HPV testing has become a screening technique for cervical cancer



Cervical cancer and HPV



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Harald zur Hausen

1/2 of the prize

Germany

German Cancer Research Centre Heidelberg, Germany



Photo: Sakutin/SCANPIX

Françoise Barré-Sinoussi

9 1/4 of the prize

France

Regulation of Retroviral Infections Unit, Virology Department, Institut Pasteur Paris, France



Photo: Magunia/SCANPIX

Luc Montagnier

9 1/4 of the prize

France

World Foundation for AIDS Research and Prevention Paris, France

b. 1936 b. 1947 b. 1932

Colposcopy

 A type of endoscope that refers to clinical use of a magnifying instrument between the visual inspection and a low-power microscope to directly visualize lesions in cervix and lower genital tract under strong light illumination

The occurrence and development of cervical cancer

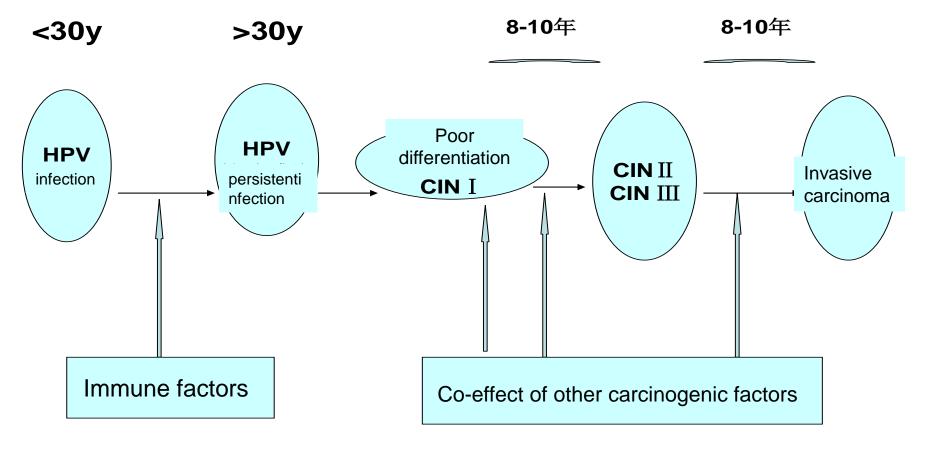
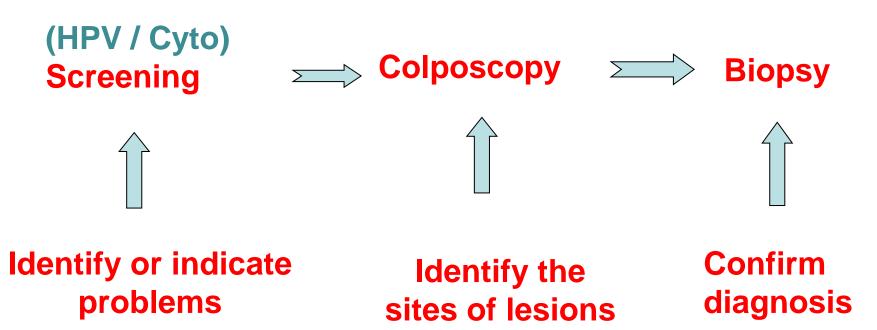


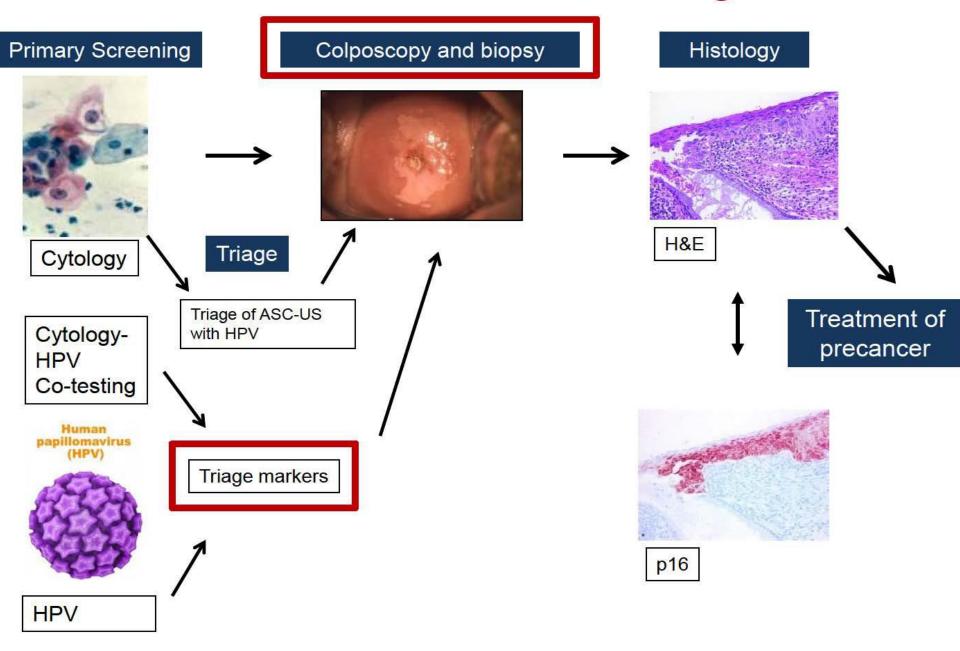
Fig 30-2-1 The occurrence and development of cervical cancer

Preface

Three-step approach

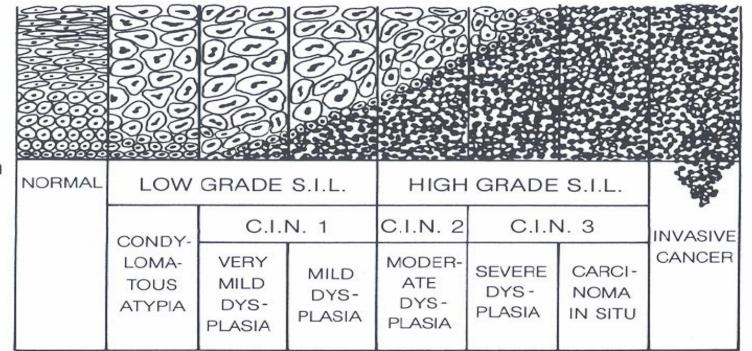


Cervical cancer screening



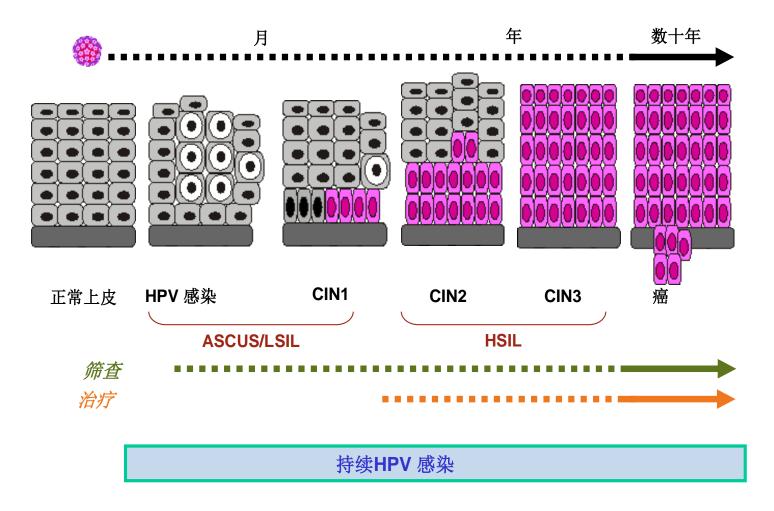
pithelium

Basal epithelium





HPV感染与子宫颈癌的自然史



• HPV(+)==子宫颈癌

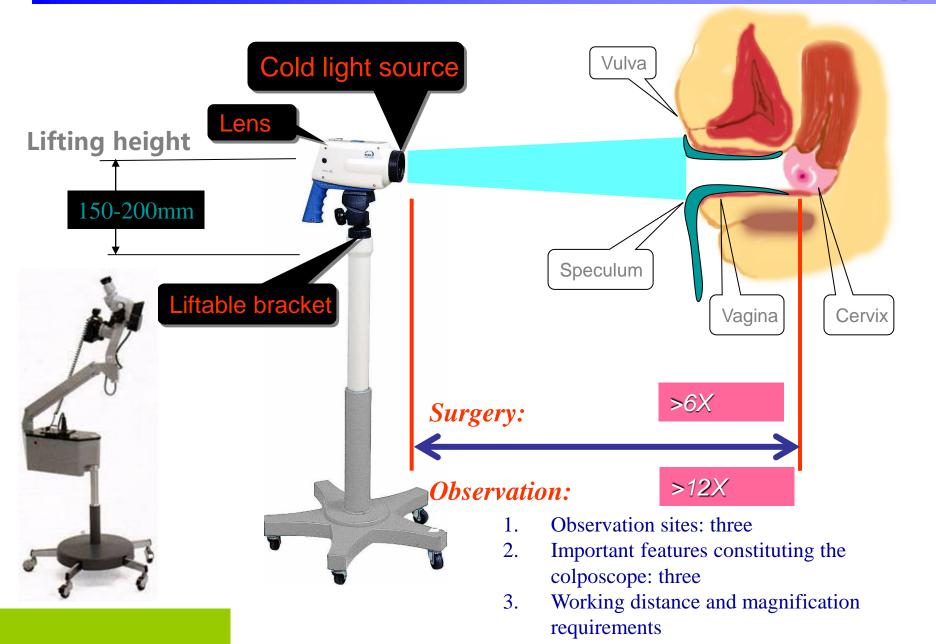
Preface

 Colposcopy can detect subclinical lesions invisible to naked eyes and localize biopsies at suspected lesions, thus increasing the positivity and accuracy of biopsies.

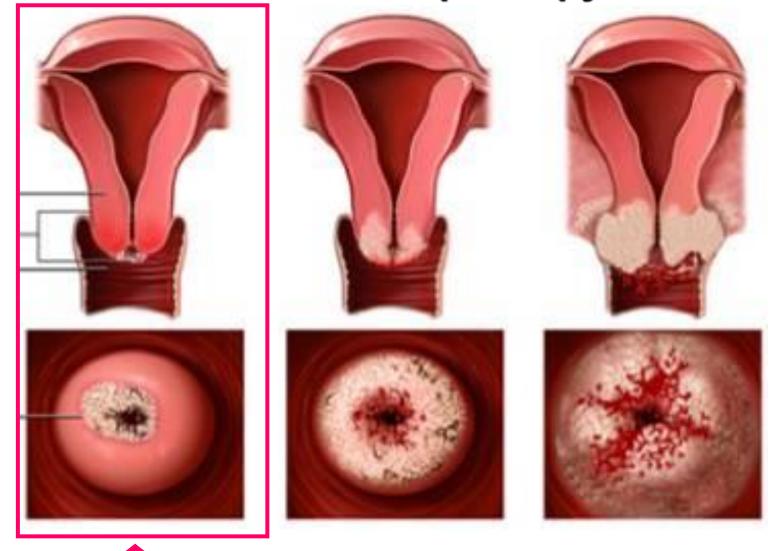
 Combined with cytology, it can be used for patients with abnormal or suspicious vaginal cytology.

 One of the important auxiliary methods for early detection of cervical cancer and precancerous lesions

Composition and principle of colposcopy



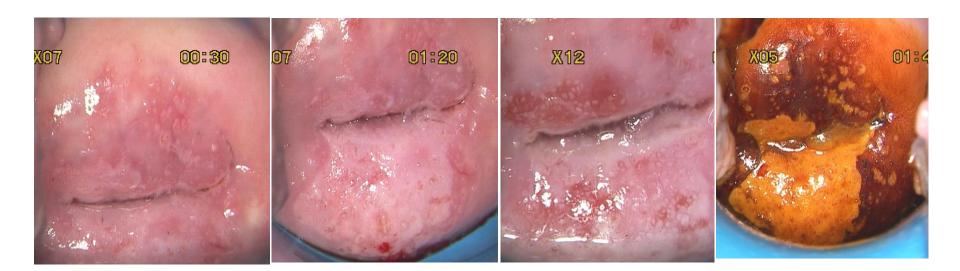
The development of cervical cancer and the role of colposcopy



Early detection and treatment of precancerous lesions

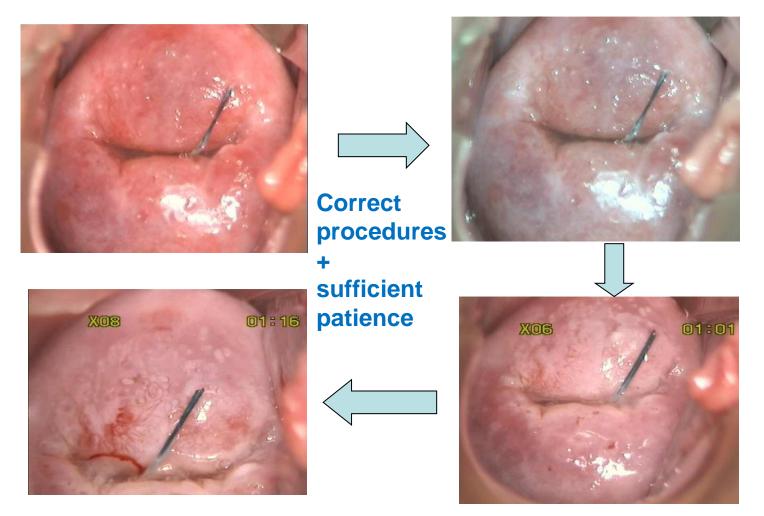
The complexity of colposcopy

- ◆Colposcopy technique is an imaging technique based on histomorphology, but differs from conventional imaging as it involves visual inspection of morphological changes of the epithelium and vessels of cervix for a limited period of time (10s-3min) with acetic acid or compound iodine solution.
- ◆The conditions for such reversible changes depend on the content of cellular nucleic acid protein and the concentration of keratinocytes.
- ◆Therefore, the results of colposcopy images are greatly influenced and limited by the concentration and duration of acetic acid.
- ◆The establishment of a method based on a quantifiable control of operating procedure is the key to the quality control of colposcopy techniques and the availability of it in primary hospitals.

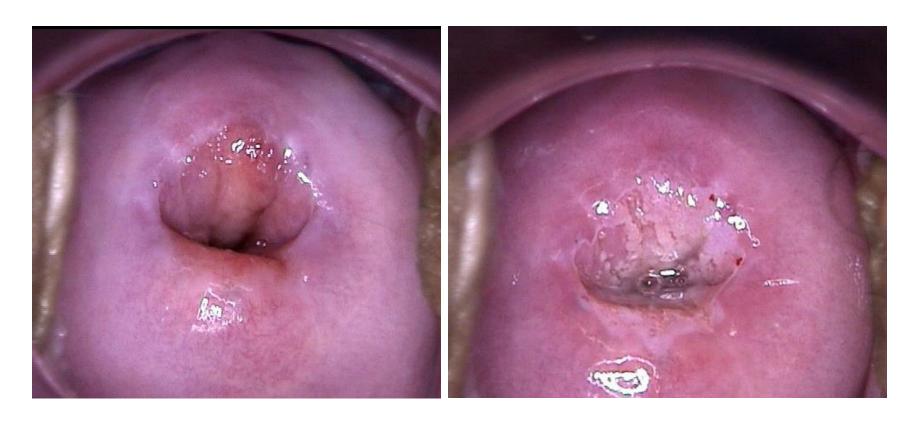


Preface

 Purpose of colposcopy: accurate detection of abnormal proliferative lesions



How to distinguish metaplastic epithelium from white epithelium?



before applying acetic acid

after applying acetic acid

Differentiation of benign/malignant lesions





The mosaic on the white epithelium is obvious after the application of acetic acid but disappears quickly within a short period of time

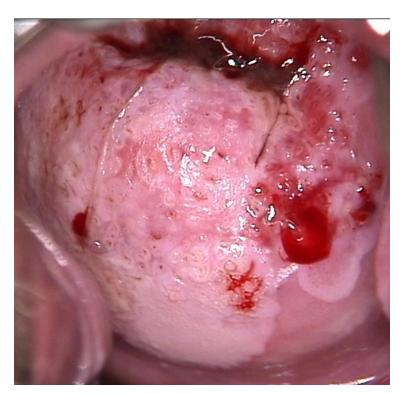
GOLDWAY INC.

The same image appearance may have different lesion results









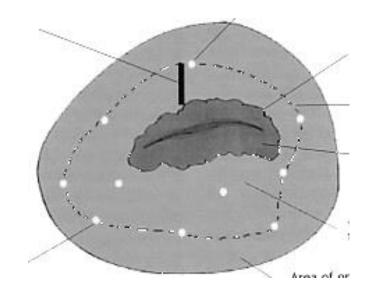


Preface

- Focus problems of colposcopy in the diagnosis of cervical cancer and precancerous lesions
- Detect lesions and instruct biopsy
- Biopsy is the 'gold standard' for diagnosis, but there are still problems with its accuracy
- Continuity and multi-correlation of lesions

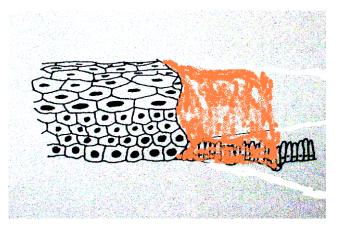
Limitations of colposcopy and cytology

- Physiological characteristics of cervical epithelium
- Formation of the transformation zone (or transition zone) and the primary site of developing cervical cancer



Attention while diagnosis:

Unsatisfactory colposcopy and cytology, VIA/VILI misdiagnosis



Excessive treatment of cervical "erosion"

- A misconception that cervical "erosion" is a high risk factor for cervical cancer
- Serious overtreatment of cervical "erosion":

Various physical therapy:

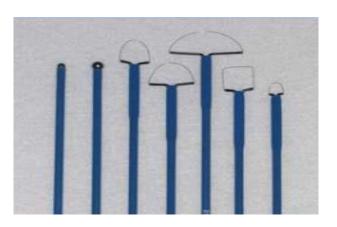
Loop electrosurgical excision procedure (LEEP) and conization

Leep and conization under colposcopy

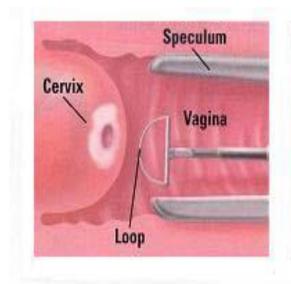
cervical "erosion" ≠ precancerous lesions

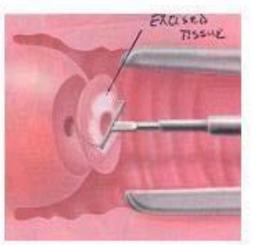
Evolution of treatment

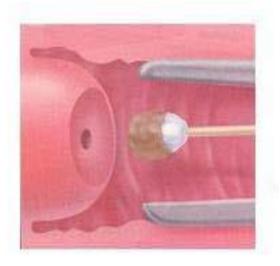
• • LEEP











Thanky ou



Question ???



Factors affect colposcope

The transition zone and the lesions are well exposed



- Cervical canal lesions are poor exposed
- Peripheral cervical lesions are easily ignored



Factors affect colposcope

- Readability of images
- Light sources and filters
- Inspection area and viewfinder angle
- Depth of field
- Magnification
- Focus ---- sharpness

Pay attention to approaches of image acquisition; Inform the content and focus of observation





Factors affect colposcope

- Concentration, duration, and distribution of acetic acid
- Quality of Iodine Test

Indications for colposcopy



Abnormal cervical cytology

ASC

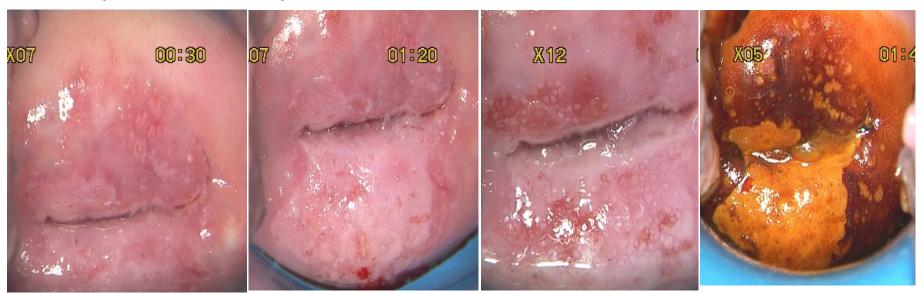
AGUS

LSIL, HSIL, Suspicious cancer

(Or Pap Test 2+)

The complexity of colposcopy

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Limitations of colposcopy and cytology

- Colposcopy has some limitations
- Specificity of colposcopy: 10%-48%; sensibility: 96%

Screening test

Positive

Sensibility

Specificity

self-sampling

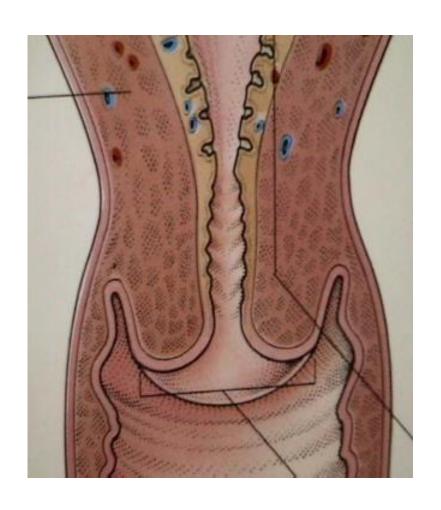
Fluorescence spectroscopy

Pap

physician sampling

Visual inspection
(any abnormality)
Colposcopy
(any abnormality)

Normal anatomy of the cervix



The cervix is a cylinder or cone.

Length: 2.5-3.5 cm

It connects uterine isthmus and vagina.

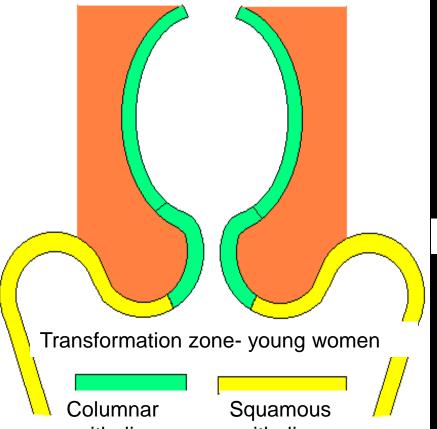
It can be divided into the vaginal part of the cervix and the upper vaginal part of the cervix.

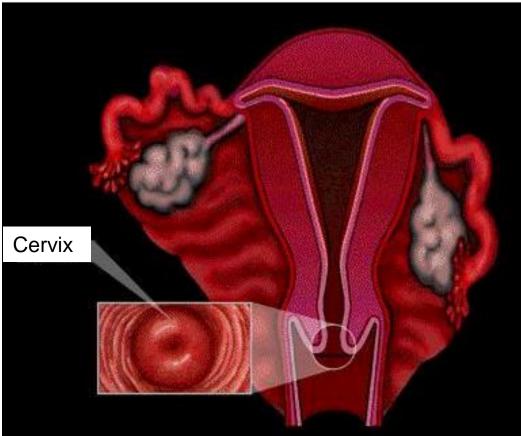
The cervical canal is a conical tract connecting the vagina and the uterine cavity.

^{*} The size of cervix changes with age and endocrine status

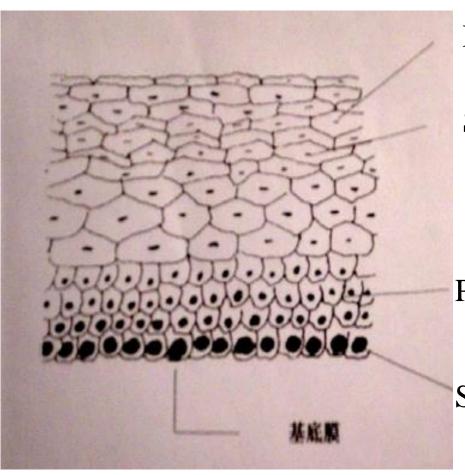
Cervical histology

 There are two types of epithelium in the cervix: stratified squamous epithelium in the vaginal part of cervix, and simple columnar epithelium in the cervical canal





Histological images of stratified squamous epithelium



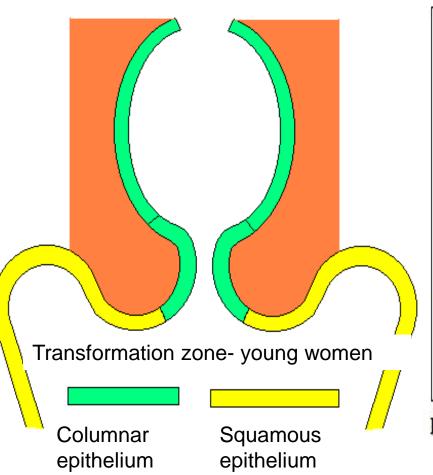
Epidermal cell layer

Stratum spinosum

Para-stratum basele

Stratum basele

Histological images of columnar epithelium



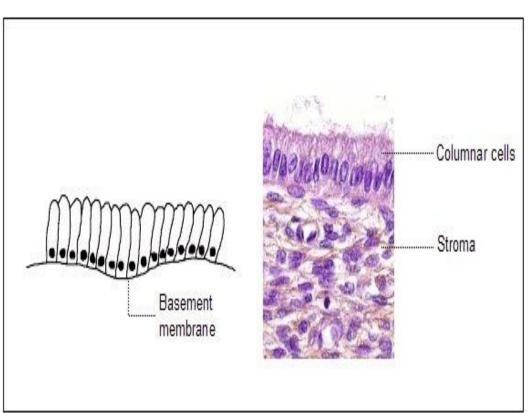
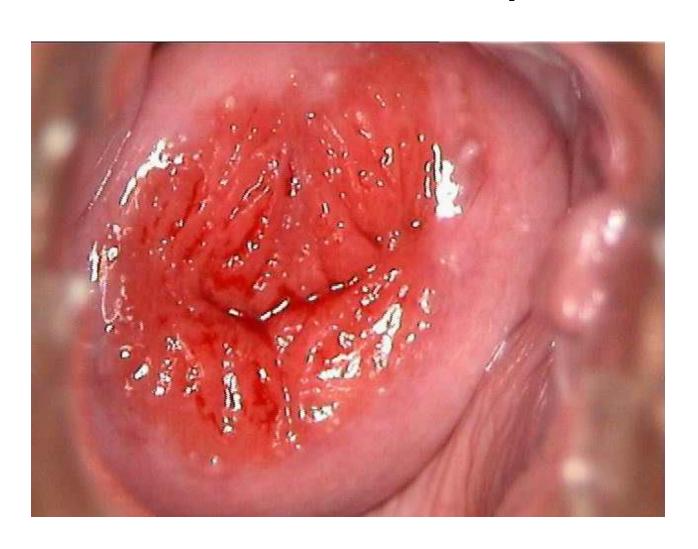


FIGURE 1.3: Columnar epithelium (×40)

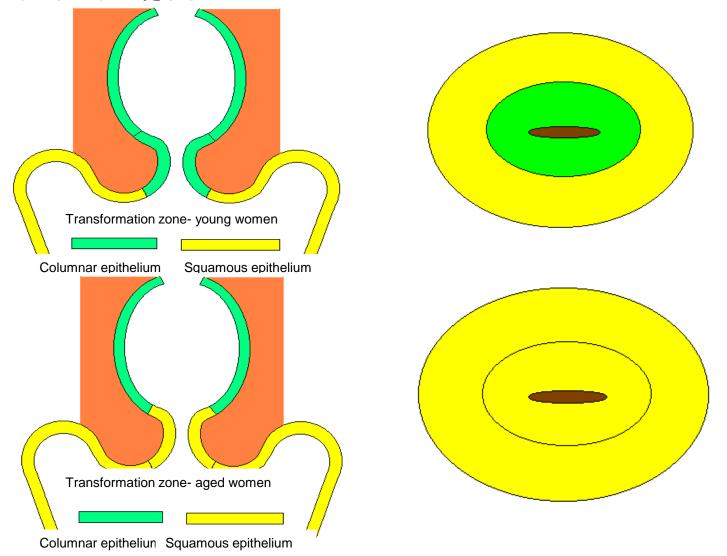
Non-keratinized stratified squamous epithelium

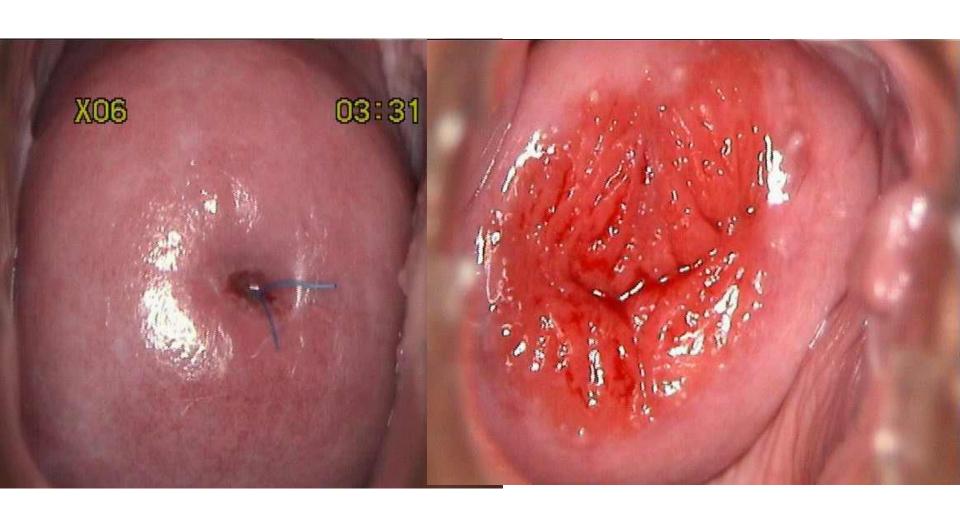


Cervical columnar epithelium



Changes in cervical squamocolumnar transition zone and cervical morphology in women of different ages

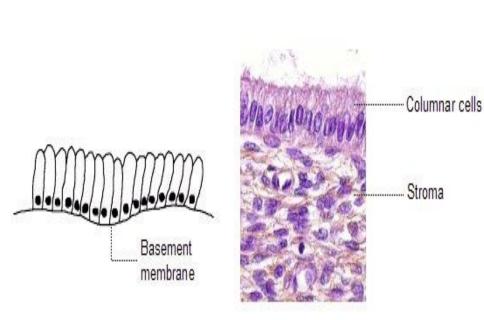


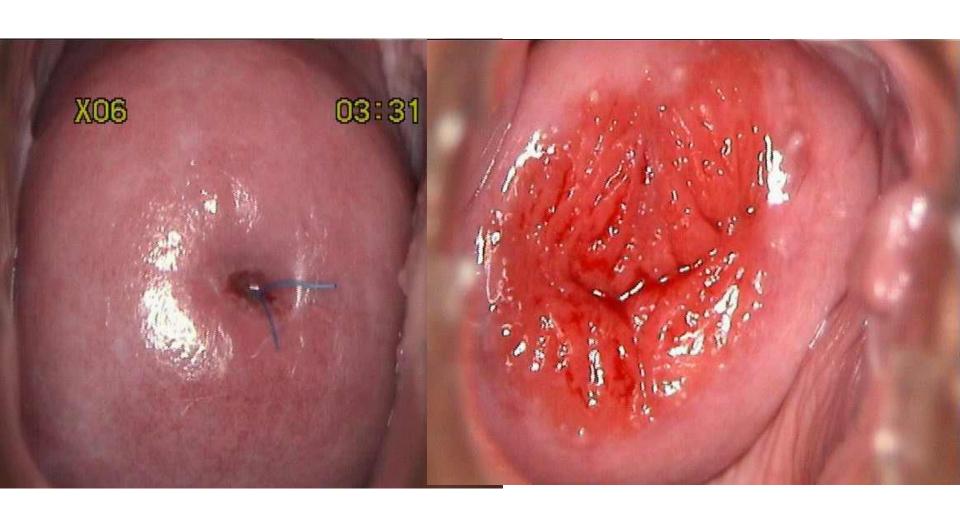


The mechanism of squamous metaplasia of covered columnar epithelium in the transformation zone

 Squamous metaplasia: the columnar epithelium at cervix and vagina is affected by the acid environment at vagina, and thus the undifferentiated reserve cells under the columnar epithelium proliferate and transfer to squamous epithelium, and then the column epithelial will shed and replaced by the stratified squamous.







Key technologies of colposcopy

Key - recognize the transformation zone (TZ)

- Definition of TZ the zone between new and old squamocolumnar junction
- TZ the primary zone for developing CIN and cervical cancer
- The important zone for colposcopy
- * The essential technique for colposcopist



Key technologies of colposcopy

Key - recognize the abnormal hyperplasia focus

Image of abnormal colposcopy:

- White vinegar epithelium
- Punctation
- Inlay
- Abnormal blood vessels



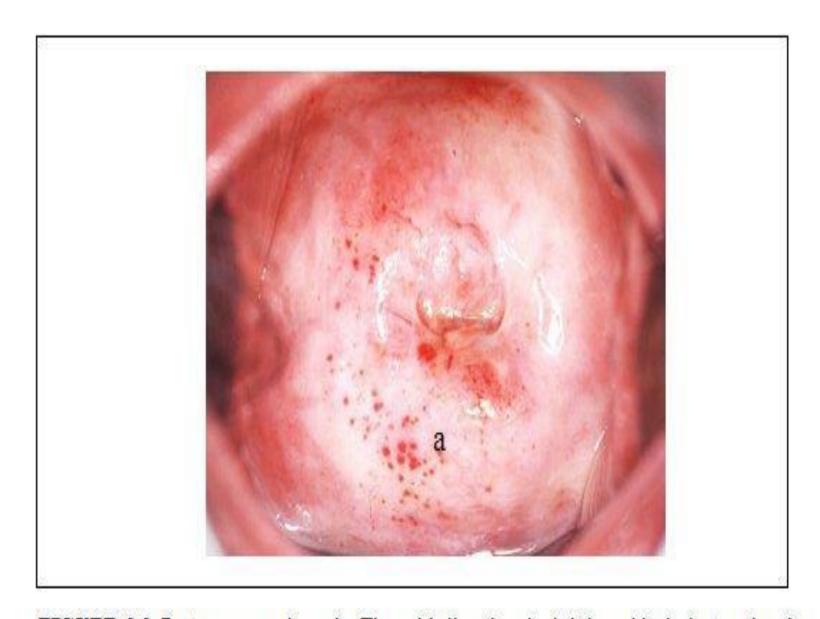


FIGURE 6.6: Postmenopausal cervix: The epithelium is pale, brittle and lacks lustre, showing sub-epithelial petechiae (a). Squamocolumnar junction is not visible.



FIGURE 6.7: The colour changes in the columnar epithelium after the application of 5% acetic acid. The columnar villi turn white, obliterating the red colour of the columnar epithelium.

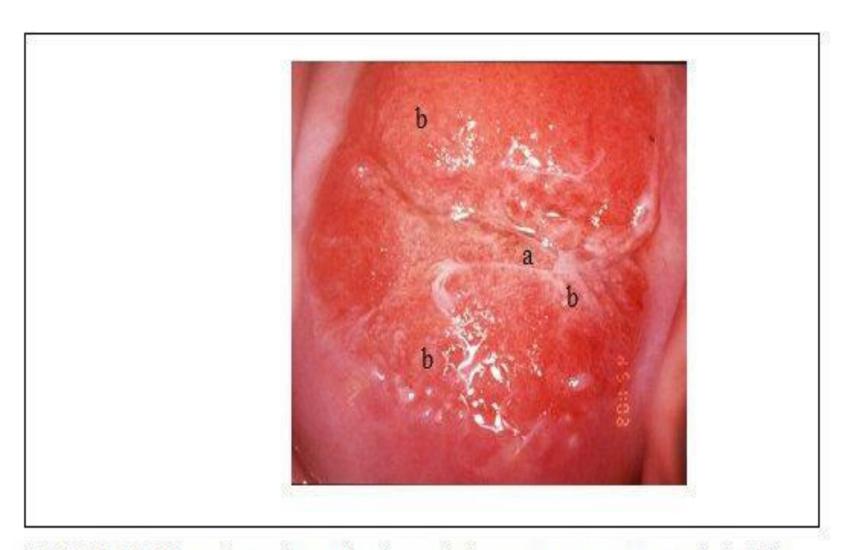


FIGURE 6.8: The earliest colposcopic changes in immature squamous metaplasia (after application of 5% acetic acid) in which the tips of the columnar villi stain white (a) and adjacent villi start fusing together (b).

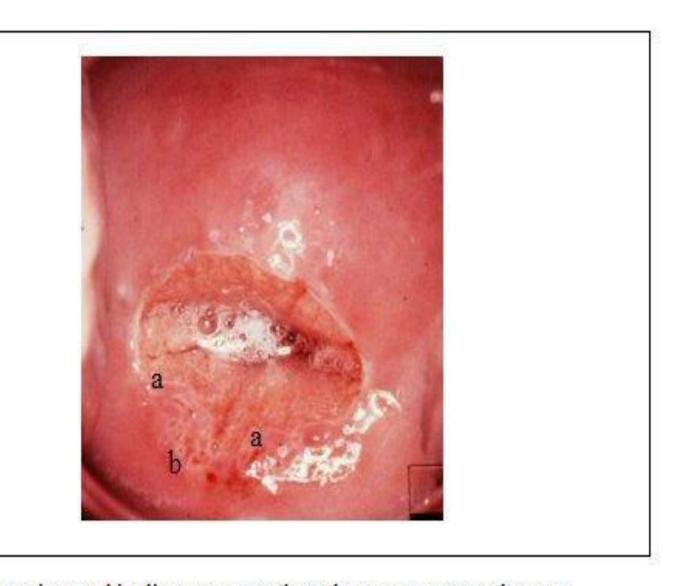


FIGURE 6.11: The prominent white line corresponds to the new squamocolumnar junction and tongues of immature squamous metaplasia (a) with crypt opening at 4-8 o'clock positions (b) (after application of 5% acetic acid).

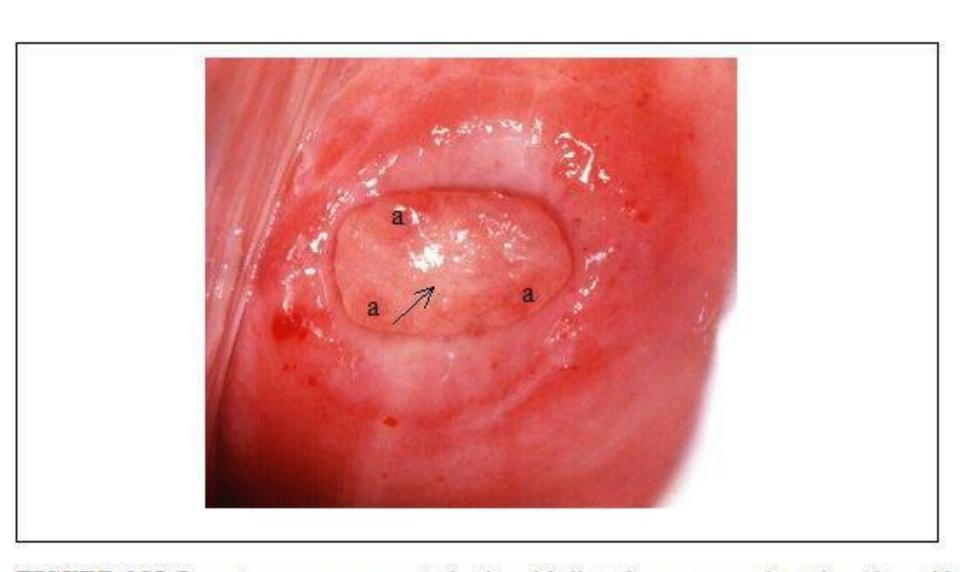


FIGURE 6.15: Immature squamous metaplastic epithelium (narrow arrow) on the polyp with intervening areas of columnar epithelium (a), after application of 5% acetic acid.

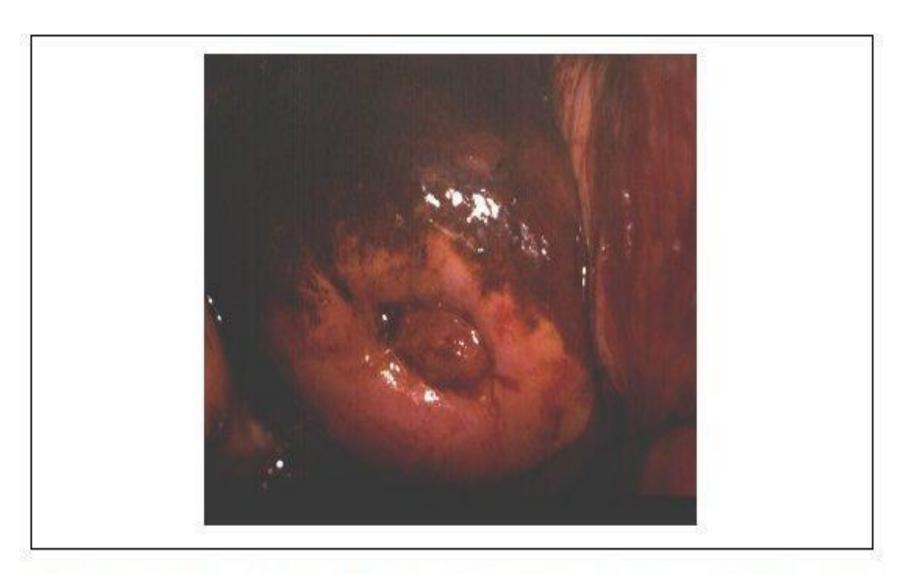


FIGURE 6.18: After application of Lugol's iodine solution, the endocervical polyp and the immature squamous metaplasia surrounding the os partially take up iodine.



FIGURE 7.2a: Fine punctation (a) and coarse mosaic (b) seen afterapplication of normal saline.

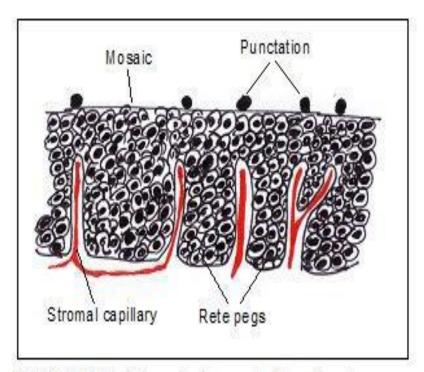


FIGURE 7.2b: Schematic diagram to show the rete pegs and the stromal capillaries which on end-on view appear as punctations.

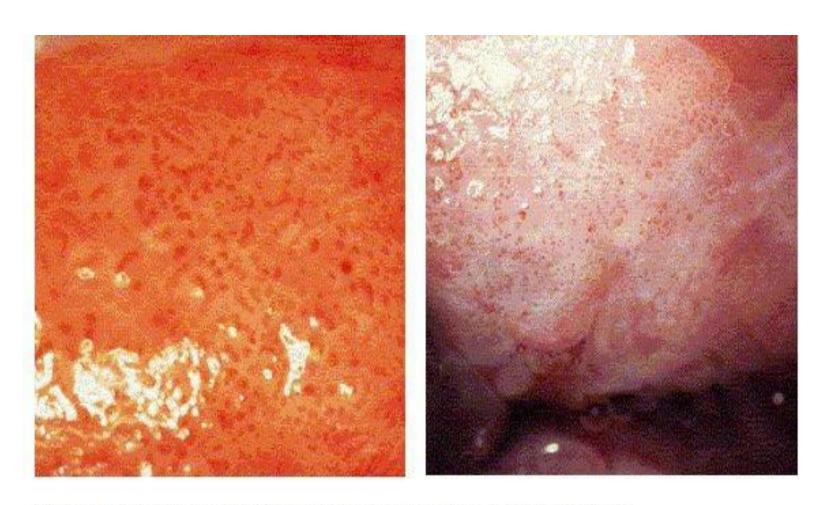


FIGURE 7.3: Coarse punctation before and after application of acetic acid

Histology of cervix

- Under normal circumstance, cervix and vagina are covered by non-keratinized stratified squamous epithelium mostly
- Non-keratinized stratified squamous epithelium:
- Primitive squamous epithelium: formed during the embryonic period
- Metaplasia of squamous epithelium: metaplasia during physiological process
- * Note: both squamous epithelium share common histology characteristics. The squamous epithelium of cervix is similar to the one of vagina, rich in glycogen, and with multi-layered cells

Squamocolumnar junction SCJ

The junction between squamous epithelium and columnar epithelium of cervix

Original squamocolumnar junction

New squmaocolumnar junction (physiological squmaocolumnar junction)



Distribution of cervix squamocolumnar epithelium

- Concept of cervix transformation zone
- Transformation zone means the zone where cervix columnar epithelium has been or is replaced by new squamous epithelium, located between the primitive squamocolumnar junction and physiological squamocolumnar junction
- Clinical meaning: >90% cervical cancer occurred at transformation zone; the primary zone for colposcopy examination

Transformation zone

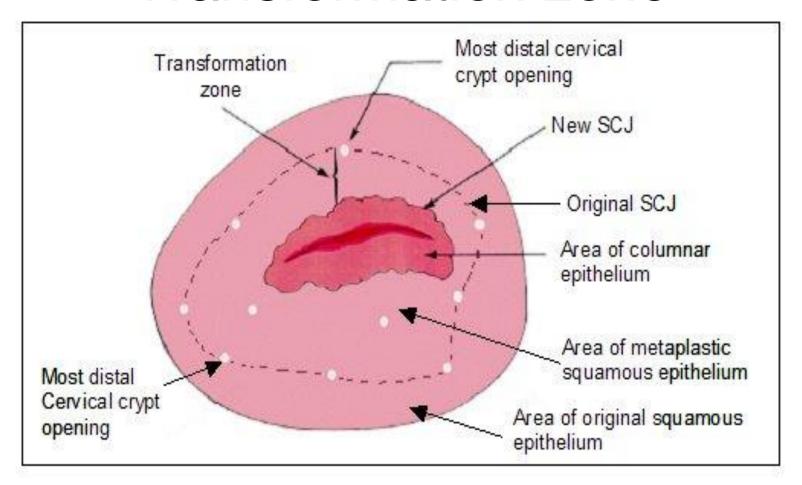


FIGURE 5.1: A method of identifying outer and inner borders of the transformation zone (SCJ: Squamocolumnar junction)

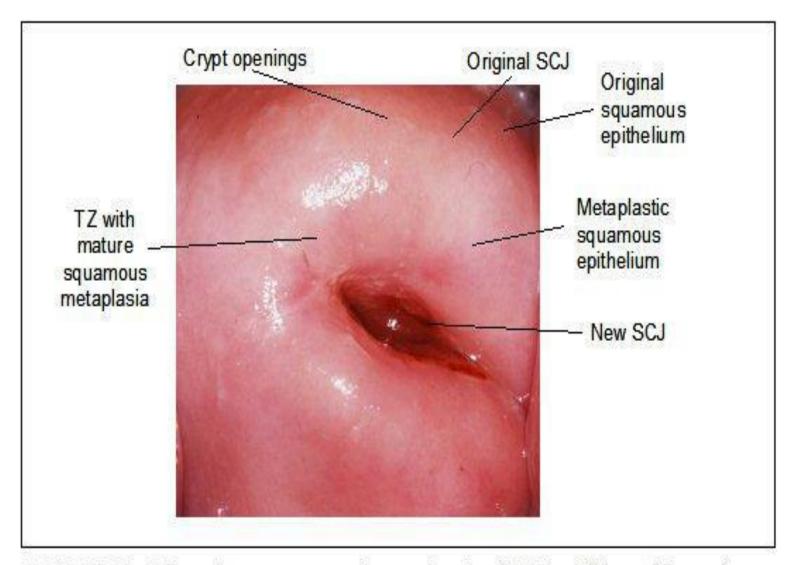


FIGURE 6.1: The entire new squamocolumnar junction (SCJ) is visible, and hence the colposcopic examination is satisfactory; the transformation zone (TZ) is fully visualized. The metaplastic squamous epithelium is pinkish-white compared to the pink original squamous epithelium

Transformation zone

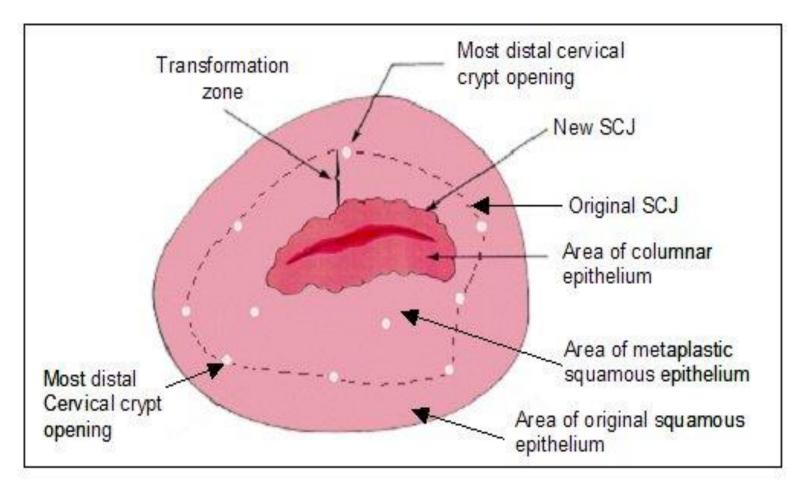


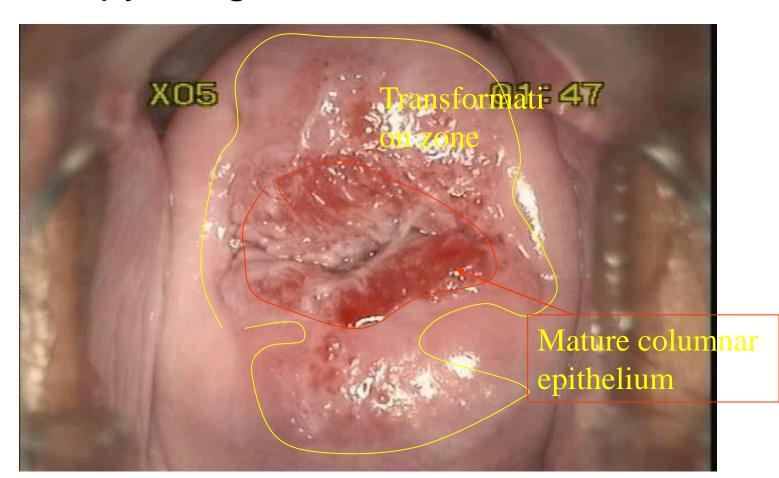
FIGURE 5.1: A method of identifying outer and inner borders of the transformation zone (SCJ: Squamocolumnar junction)

Colposcopy image of transformation zone

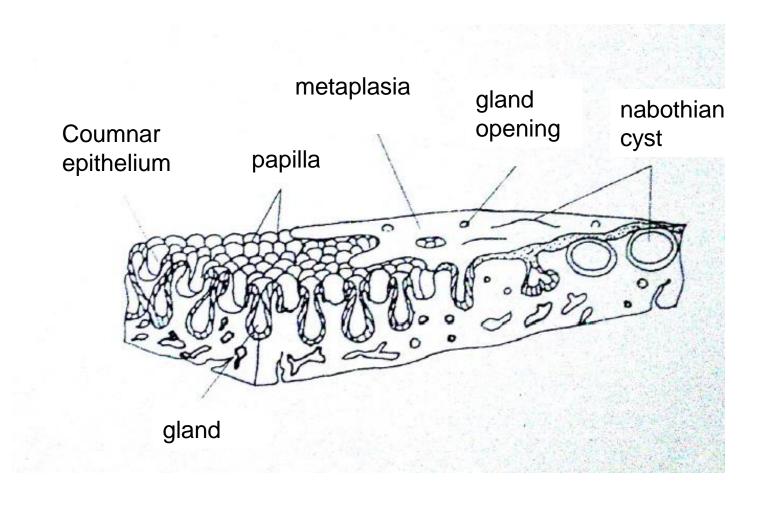


The part
beween the
yellow and red
line is
transformation
zone

Colposcopy image of transformation zone



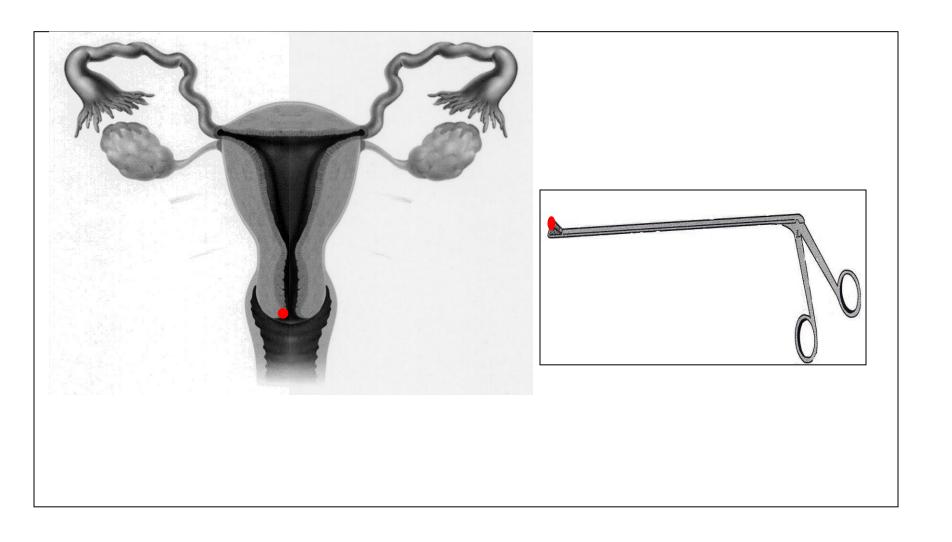
Stereoscopic diagram of transformation zone



Application value of colposcopy

- Early diagnosis of cervical cancer
- Guide localized biopsy, improve accuracy of early diagnosis
- Distinguish benign and malignant lesions under colposcopy, avoid overtreatment
- Lesion observation and long-term follow-up tool
- Diagnose subclinical cervix HPV infection

Cervix biopsy



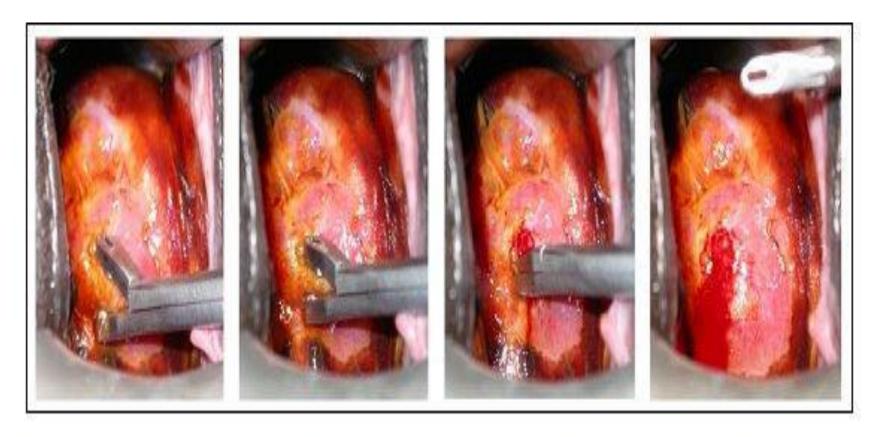


FIGURE 5.2: Biopsy technique: A toothed and sharp cutting biopsy forceps should be used for biopsy. Firmly apply the biopsy punch onto the cervix with the jaws wide open; fix the lower lip of the biopsy punch and close the jaws completely. Cutting the specimen should be carried out by quick and firm closure of the jaws. Repeated cutting and rotation of the forceps should be avoided, as this can crush the tissue sample. The removed specimen should be immediately placed in formalin. The biopsy site may be cauterized with Monsel's paste.

Indications for colposcopy

- Abnormal cytology: Pap smear ≥ □ or TBS ≥ ASC/AGC; or ASC with positive high risk HPV-DNA
- Suspicious clinical medical history or signs, e.g. contact bleeding, abnormal discharge, abnormal cervix, e.g. chronic cervicitis, polypus, white spots, red zone, or suspicious cancer et.al.
- Visual inspection positive acetic acid test with or without magnify
- Non-staining visual lodien test
- Positive high-risk HPV-DNA
- Suspicious lesions of vulvae and vagina
- Condyloma of the lower reproductive tract
- Follow-up after treatment of CIN and cervical cancer
- Follow-up and observe the dynamic changes of cervix, vagina and vulvae.
- Others such as understanding the vaginal wall before CIN or early diagnosed cervical cancer, management of pregnancy with CIN et.al.

Auxiliary equipment of colposcopy



FIGURE 4.3: Colposcopy instrument tray

- 1: Kidney tray
- 4: Bottle containing formaline
- 7: Cotton-tipped fine swab sticks
- 10: Vaginal speculum
- 13: Endocervical speculum
- 16: Punch biopsy forceps

- 2: Bottles with normal saline, 5% acetic acid and Lugol's iodine
- 5: Local anæsthetic syringe
- 8: Cervical cytology brushes
- 11: Sponge-holding forceps
- 14: Endocervical curette

- 3: Monsel's solution
- 6: Jar containing alcohol for cervical smear fixation
- 9: Larger cotton-tipped swab sticks
- 12: Vaginal side-wall retractor
- 15: Dissecting forceps

Cervical expanding forceps

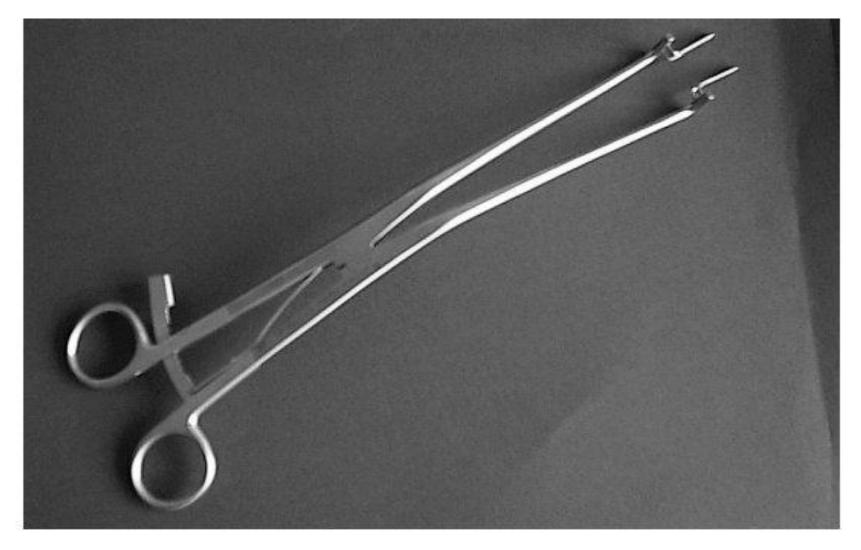


FIGURE 4.6: Endocervical speculum

5% acetic acid

- Component: Acetic acid, 5ml
- Distilled water: 95ml
- Mixed 5% solution, stored in the sealed glass bottle

Logol's iodine solution

- Component: Iodine 5mg
- Potassium iodide 10mg
- Distilled water 100ml
- After preparation stored in sealed brown glass bottle. After 6-8 months of utilization, reprepare refresh solution to prevent deterioration

Cervical intraepithial neoplasia

• It is a group of precancerous lesions closely related to cervical invasive carcinoma.

Normal vessels

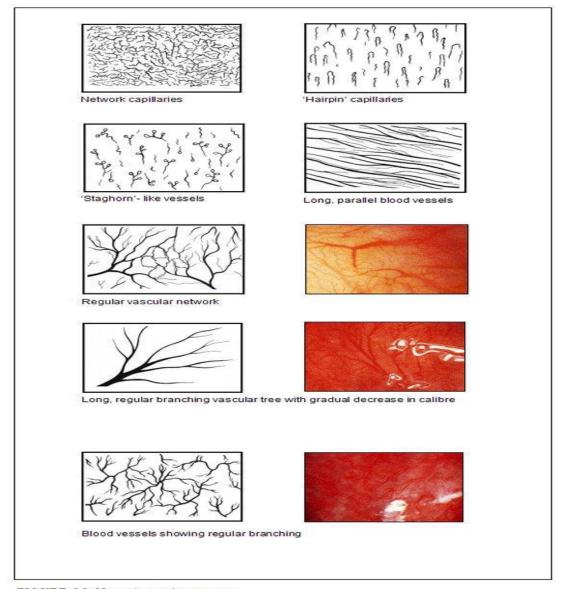


FIGURE 6.2: Normal vascular patterns.

Normal vessels

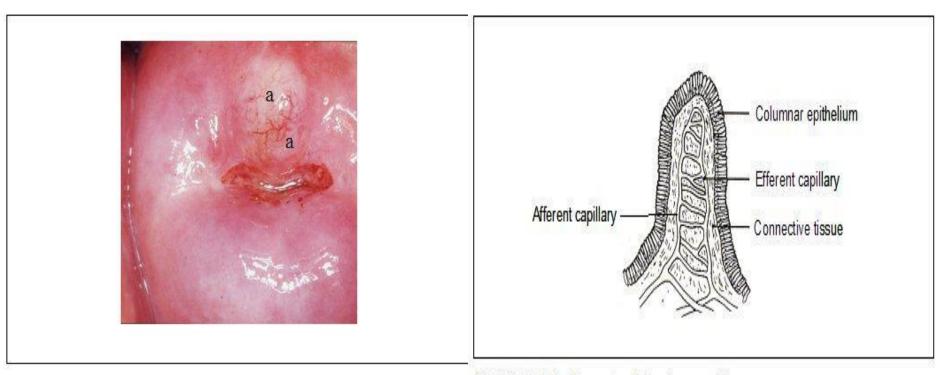
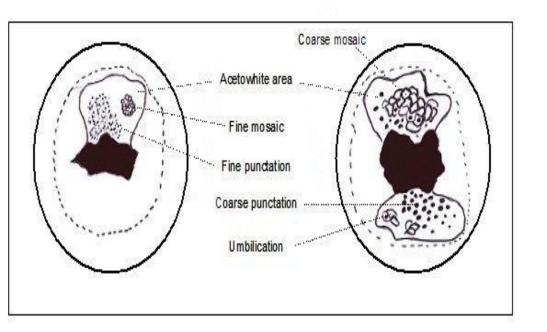


FIGURE 6.3: Nabothian cyst with regularly branching tree-like vessels (a).

FIGURE 6.4: Capillary network in columnar villi



Punctation & mosaic

FIGURE 7.1: A schematic representation of punctation and mosaics.

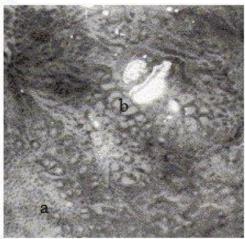


FIGURE 7.2a: Fine punctation (a) and coarse mosaic (b) seen afterapplication of normal saline.

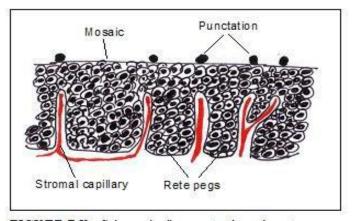


FIGURE 7.2b: Schematic diagram to show the rete pegs and the stromal capillaries which on end-on view appear as punctations.

Coarse punctation

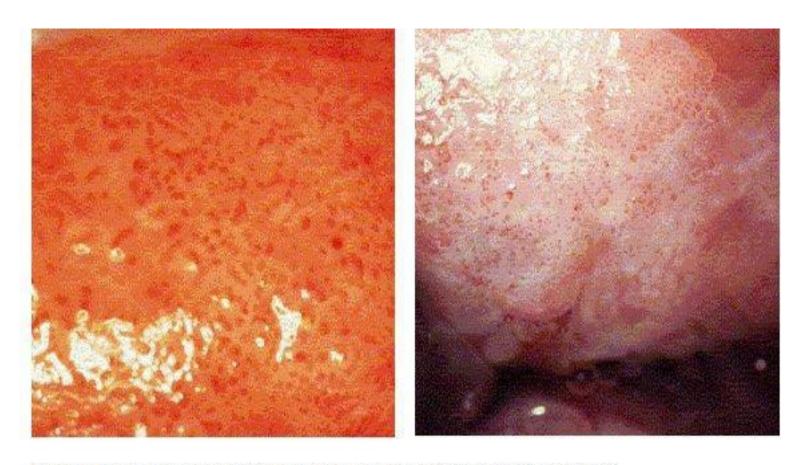


FIGURE 7.3: Coarse punctation before and after application of acetic acid

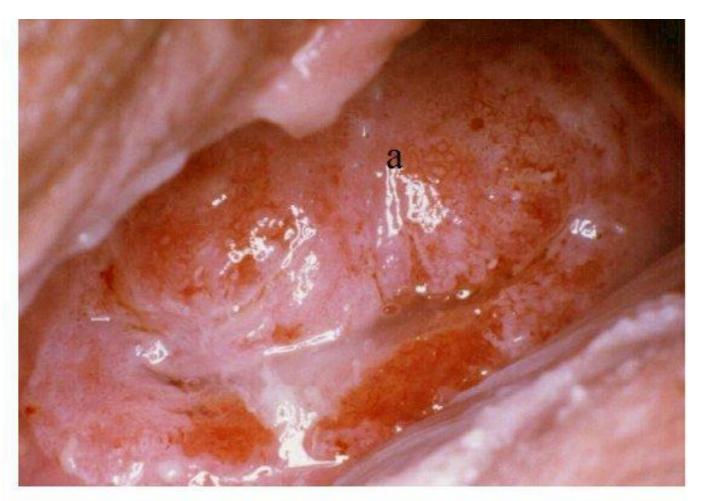


FIGURE 7.24: Coarse mosaics (a) in a CIN 3 lesion.

Atypical vessels



FIGURE 8.5: Atypical vessel patterns

- According to the degree of lesion, CIN is divided into three grades:
- CIN I grade: mild dysplasia, nucleo-cytoplasmic ratio is slightly larger, cell polarity is normal
- CIN II grade: moderate dysplasia
- CIN III grade: severe dysplasia + cancer in situ (CIS)
- All grades have the potential to develop into invasive cancer.
 Generally, the higher the grade, the easier to develop into invasive cancer. According to relative statistics, there are 10% ~15% in mild and moderate, 75% in severe cases to develop into cancer. (Not fixed, reversible)

Procedure for colposcopy



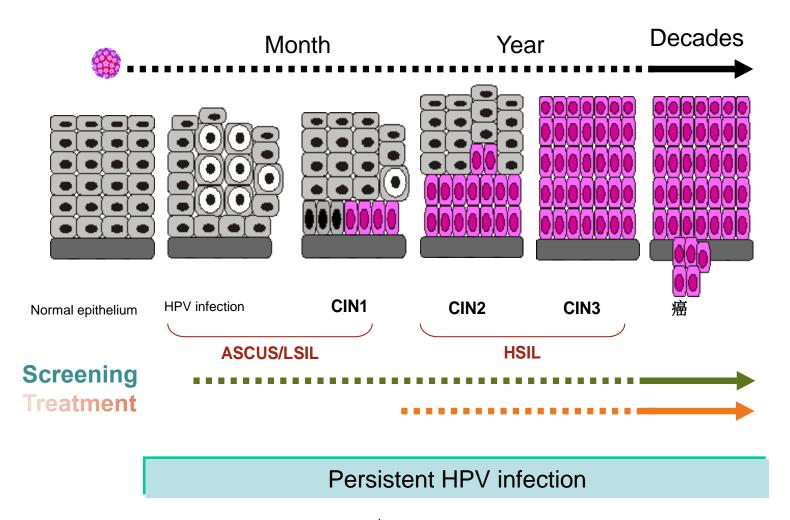
Electronic colposcopy technology

- Observe changes of cervical morphology and structure
- Observe distribution of cervical squamous and columnar epithelium
- Observe subepithelial vessel changes
- Observe epithelium histology
- Assist biopsy localization
- Graphic record of observations mentioned above

5% acetic acid - key to colposcopy

 Principle: Acetic acid causes swelling of cervical epithelial tissue, reversible coagulation or precipitation of nuclear protein and keratin, most obvious at columnar epithelium and any abnormal squamous epithelial areas.

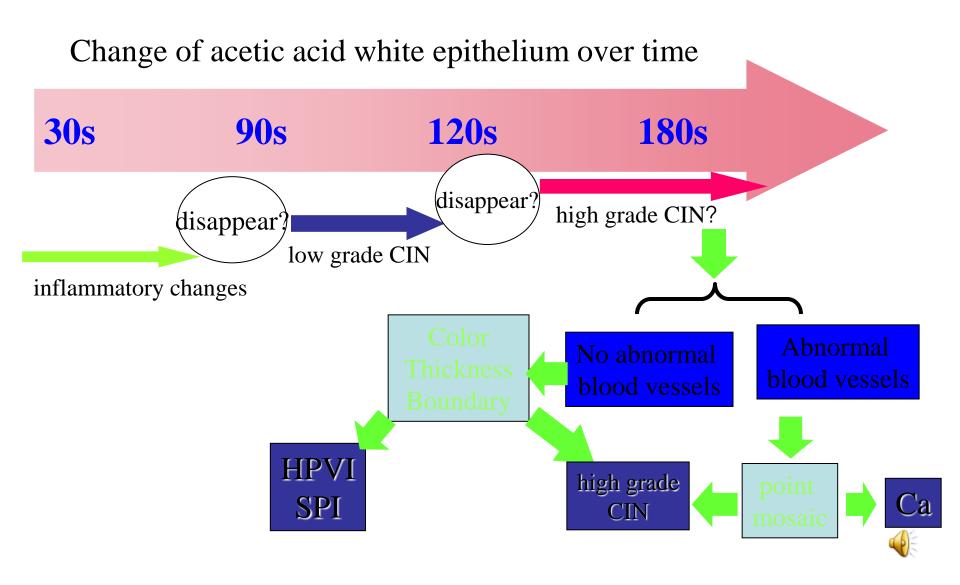
Development of HPV infection and cervical caner



• HPV(+)==cervical cancer

Based on 5% acetic acid

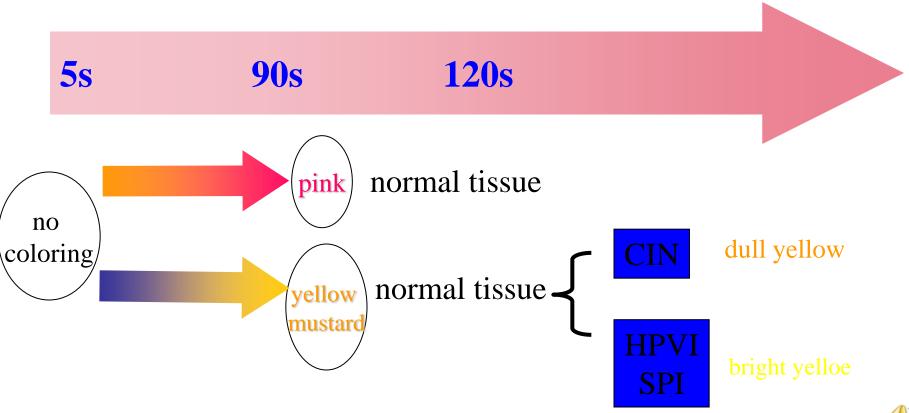
——Time control method and control process



Based on Lugol's dyeing

——Time control method and control process

Changes in epithelial staining over time after Lugol 'dyeing





Colposcopy

- •Intracervical neoplasia (CIN) must be confirmed by tissue biopsy
- •Through colposcopy, the appearance of the cervix was examined, and the changes in intraepithelial glycogen and keratin caused by CIN were observed. Tissues that reacted abnormally to acetic acid and iodine solution were excised and sent for medical examination, so that accurate sampling could be taken to prevent missed diagnosis or blind sampling
- •Colposcopy testing must strictly follow the operating procedures

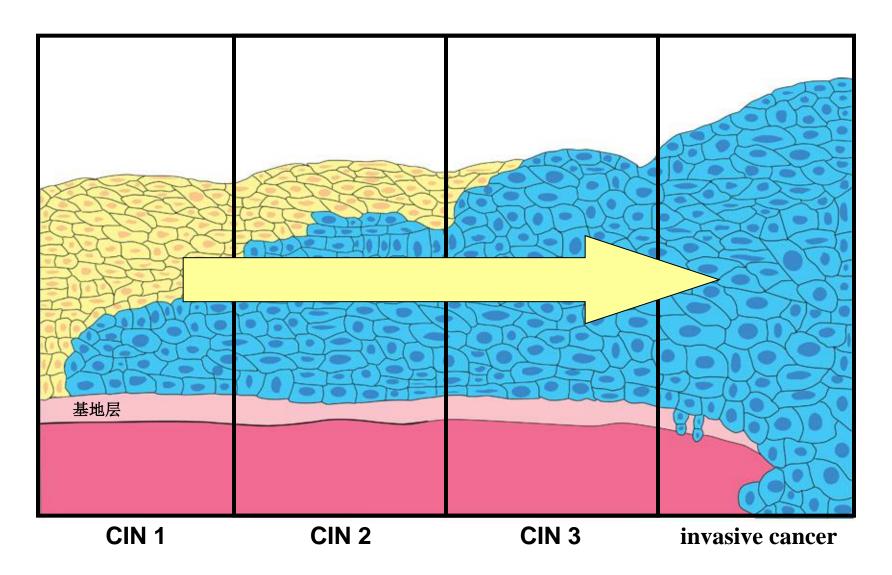
Diagnostic terms for colposcopy (2002)

- Normal colposcopy findings: primitive squamous epithelium, columnar epithelium, transformation zone
- Abnormal colposcopy findings: inside and outside the transformation zone: flat acetic white epithelium, thick acetic white epithelium, dense vinegar white epithelium, fine mosaic, thick mosaic, fine punctate blood vessels, thick punctate blood vessels, negative iodine test, atypical blood vessels,
- Suspected invasive carcinoma under colposcopy
- Dissatisfied with colposcopy: the squamous-columnar junction is invisible, severe inflammation, severe atrophy, injury, and the cervix cannot be exposed
- Others: condyloma, keratosis, erosion, inflammation, atrophy, shedding, polyps et.al.

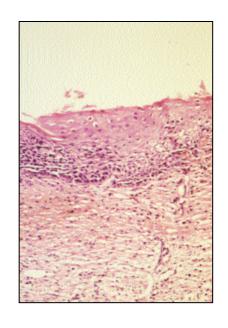
Cervical intraepithelial neoplasia CIN

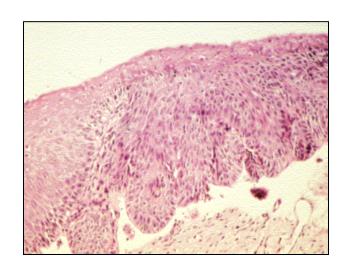
- A group of precancerous lesions closely related to cervical cancer.
- Reflects the continuous process of cervical cancer development.
- Usually occurs in women aged 25-35 years

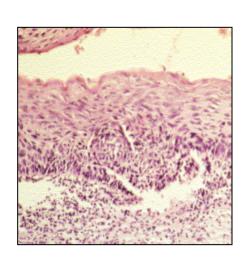
Natural development of cervical cancer



Pathological process







CIN₁

CIN₂

CIN₃

CIN lesions under colposcopy

- CIN contains a large number of nuclei, and the nucleoprotein will undergo a reversible coagulation reaction under the action of acetic acid. As a result, it affects the light transmittance of the epithelium and prevents light from passing through the epithelial layer, making it difficult to see the subcutaneous blood vessels, thereby forming white epithelium.
- CIN lesions showed mustard yellow after iodine test due to lack of glycogen.

Colposcopy image of CIN changes

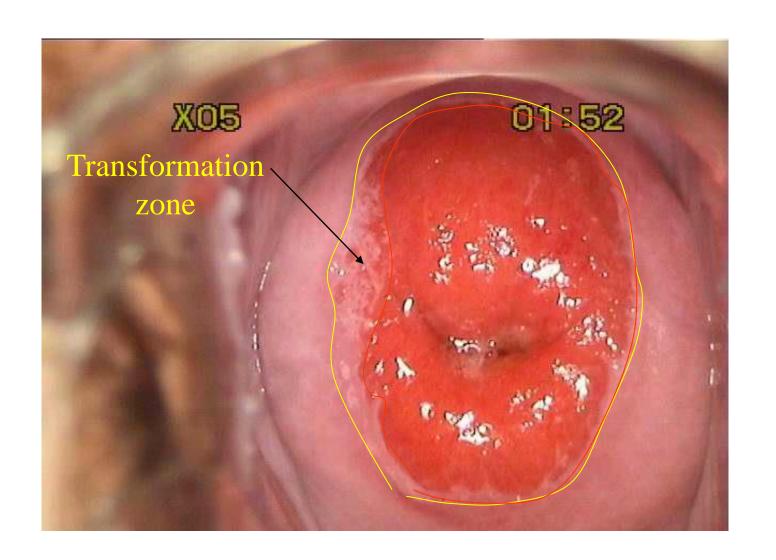
Distinguish the degree of lesions, by:

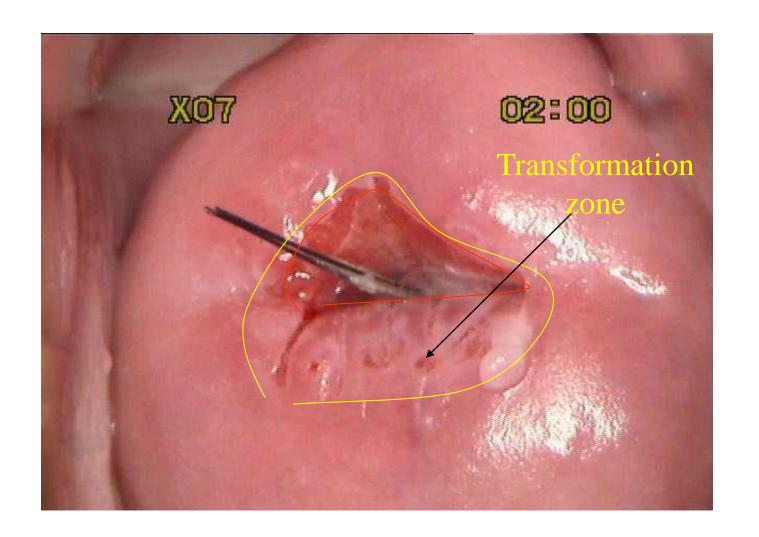
- 1. Acetate white epithelium, its color, transparency, boundary, and surface contour characteristics.
- 2. Relationship between vinegar white and shape, number, and distribution of blood vessels.
- 3. Overlap and boundary between the iodine-negative area and the acetic acid white.
- 4. Determine the relationship between tissue and CIN lesions according to the area where the characteristics appear.

Examples of colposcopy image

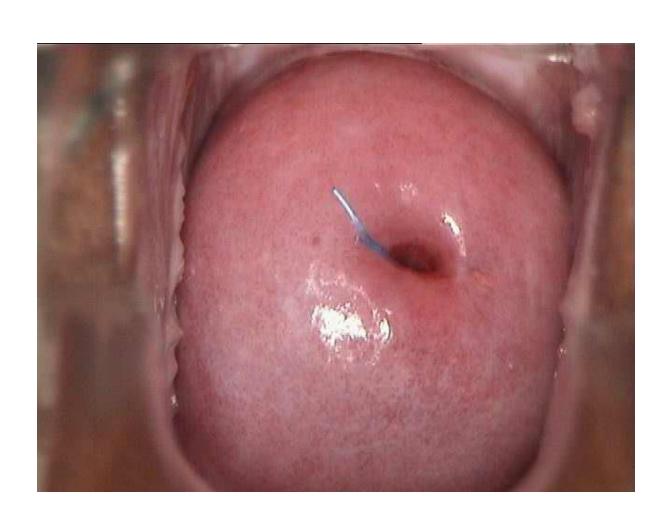
Where to exam for colposcopy?

First colposcopy diagnosis:
Satisfactory colposcopy
Unsatisfactory colposcopy





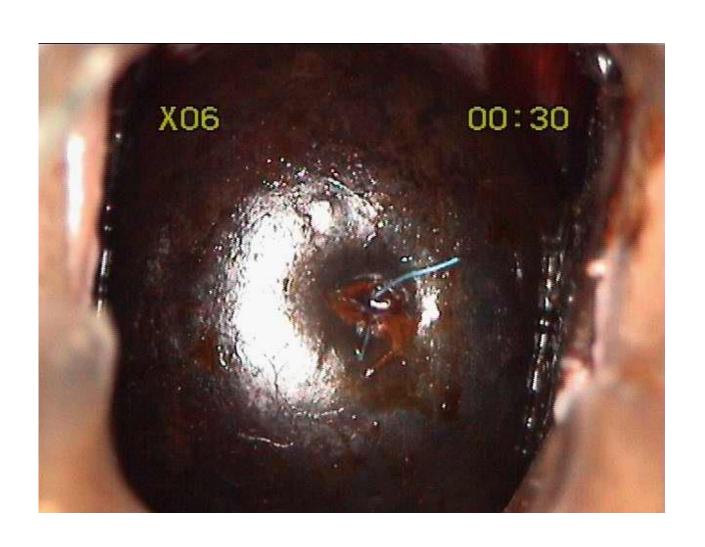
Normal cervical image



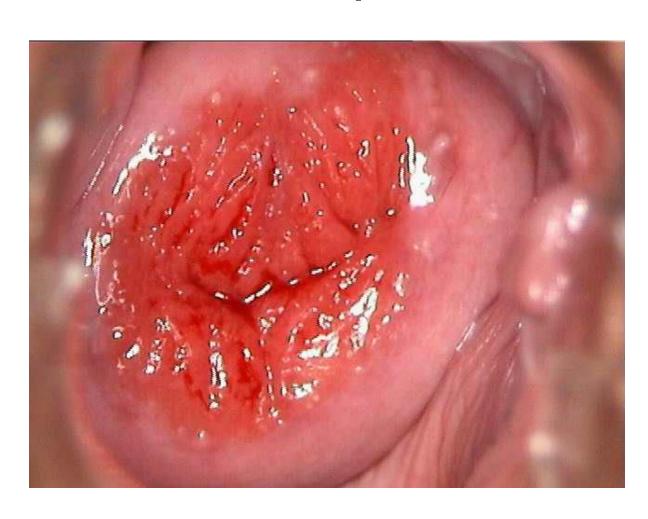
Normal green light image of the cervix



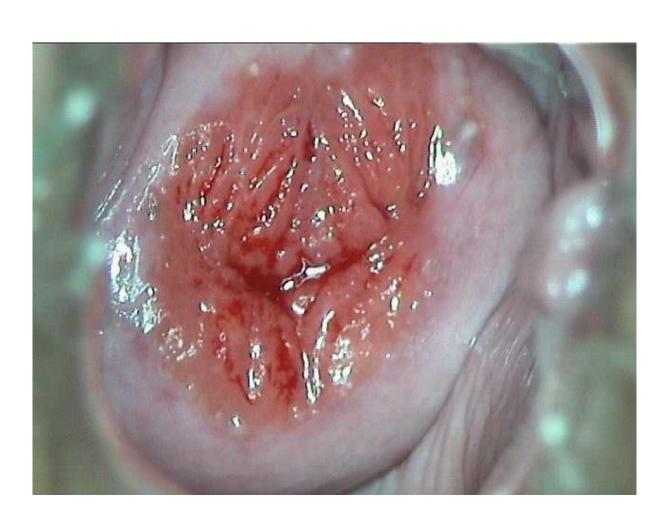
Normal iodine stain of the cervix



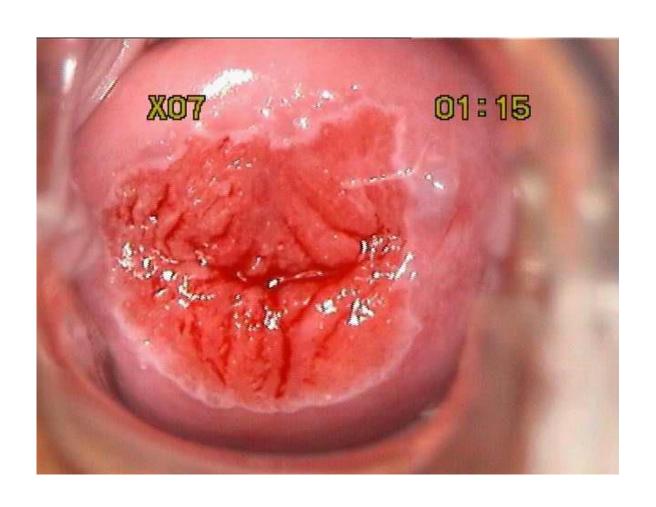
Extroversion of cervical columnar epithelium



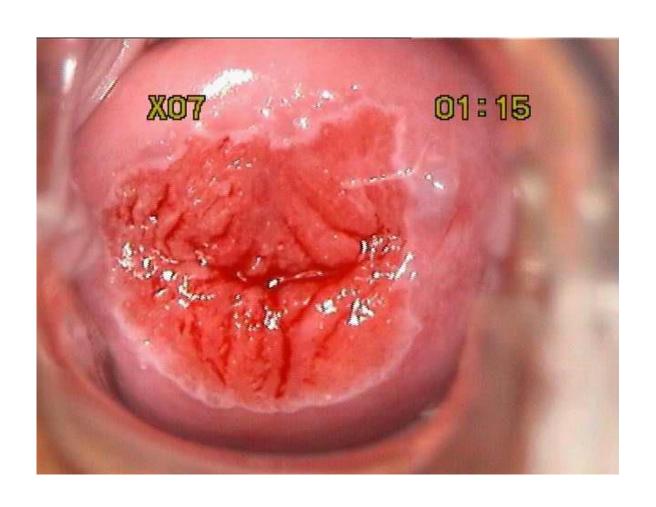
Extroversion of cervical columnar epithelium/Green light



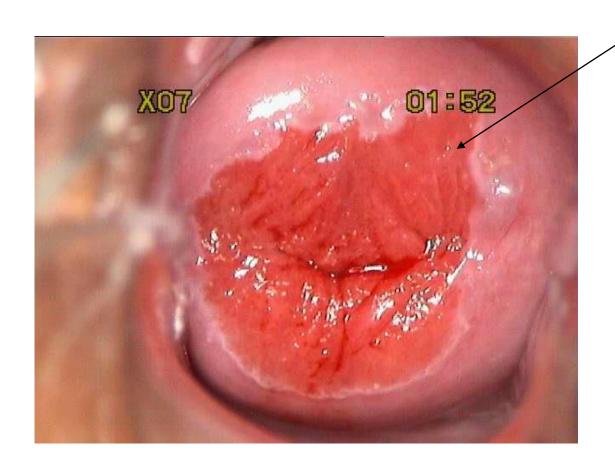
Extroversion of cervical columnar epithelium/Acetic acid reaction for 60 seconds



Extroversion of cervical columnar epithelium/Acetic acid reaction for 60 seconds

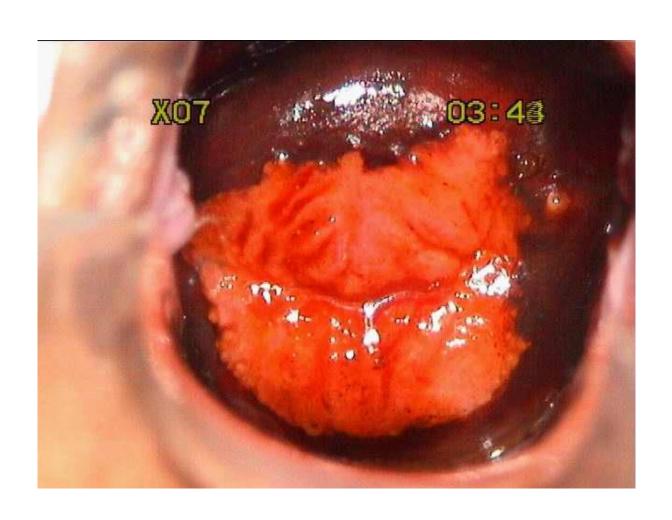


Extroversion of cervical columnar epithelium/Acetic acid reaction for 120 seconds

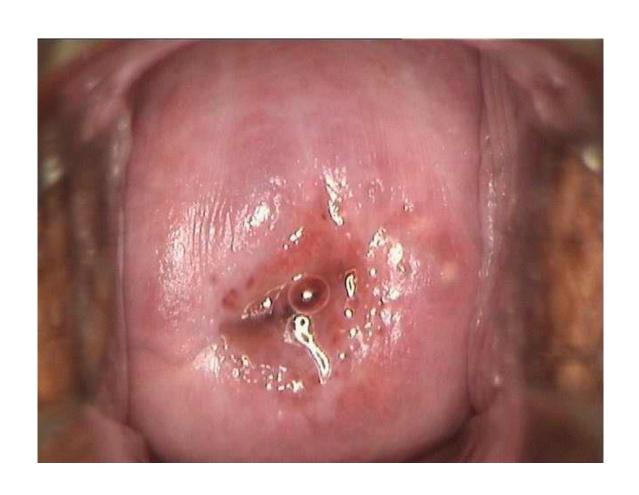


Columnar epithelium

Extroversion of cervical columnar epithelium/lodine staining



CIN1(Thin vinegar white gradually aggravated)

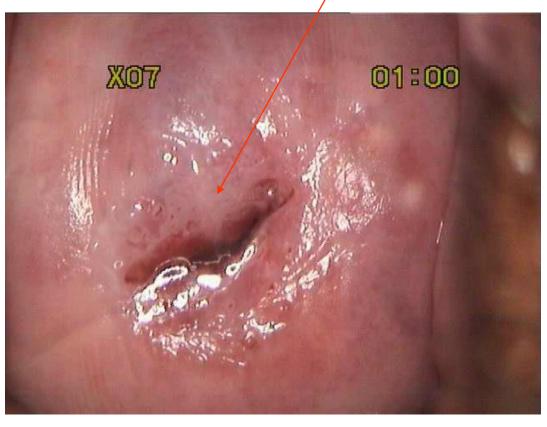


CIN1/Green light



CIN1/Acetic acid reaction for 60 seconds

Thin acid white epithelium

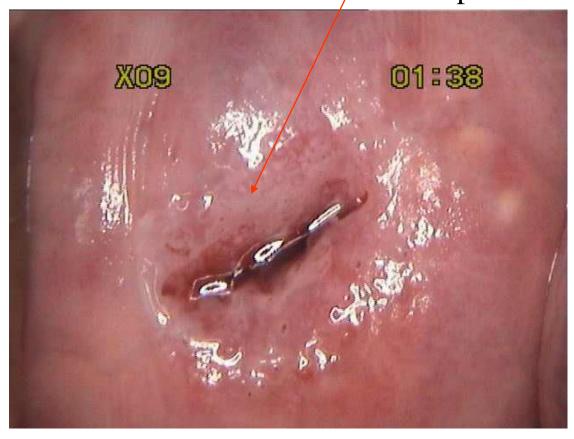


Normal image with cervical acetic acid reaction



CIN1/Acetic acid reaction for 90 seconds

White epithelial thickening



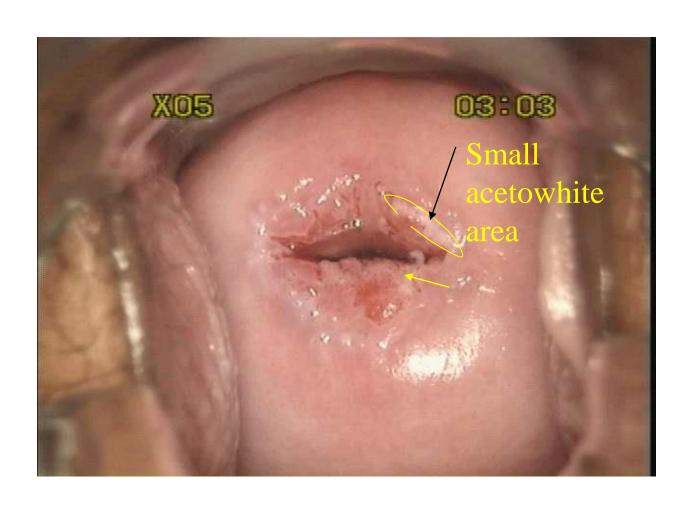
CIN2(Atypical)



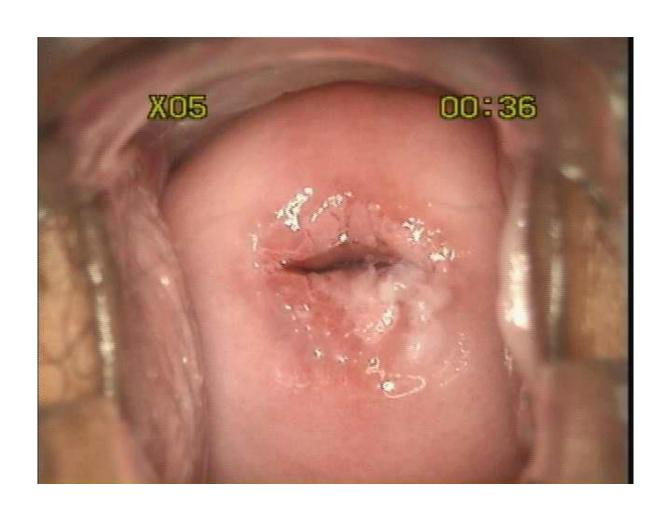
CIN2(Atypical)/Green light



CIN2(Atypical)

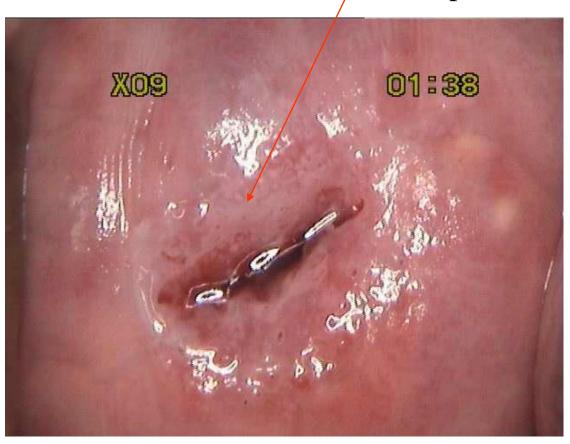


CIN2(Atypical)/Acetic acid reaction for 30 seconds



CIN1/Acetic acid reaction for 90 seconds

White epithelial thickening





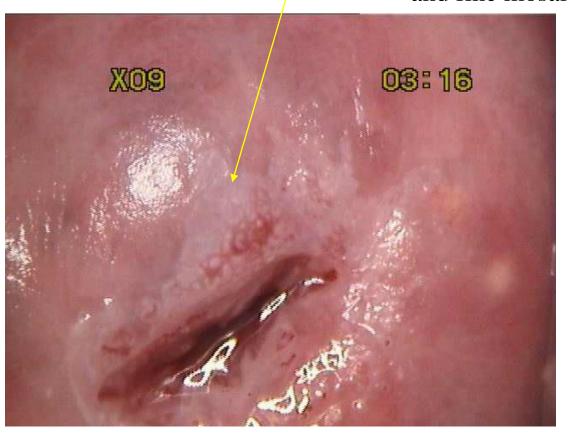
White epithelium with incomplete boundary, ECC are required.





CIN1/Acetic acid reaction for 180 seconds

The white epithelium with clear boundary and fine mosaic



CIN1/lodine staining

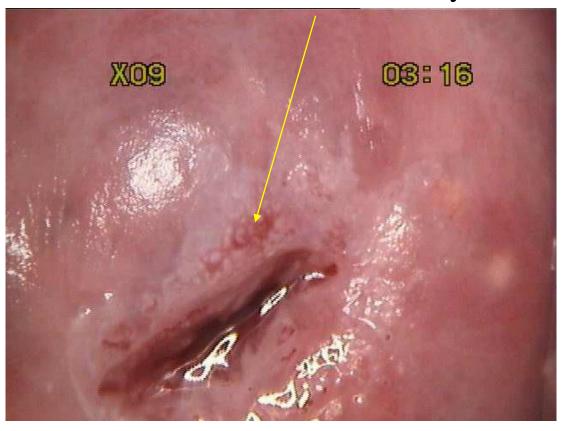


CIN2(Atypical)/Acetic acid reaction for 90 seconds

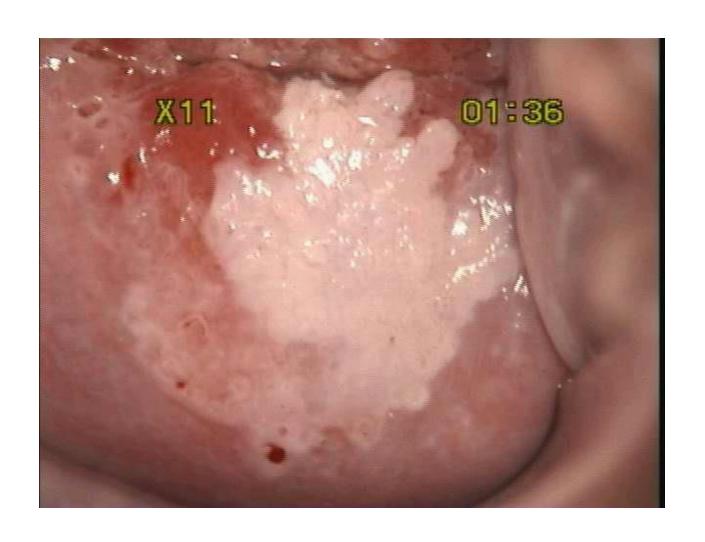


CIN1/Acetic acid reaction for 180 seconds

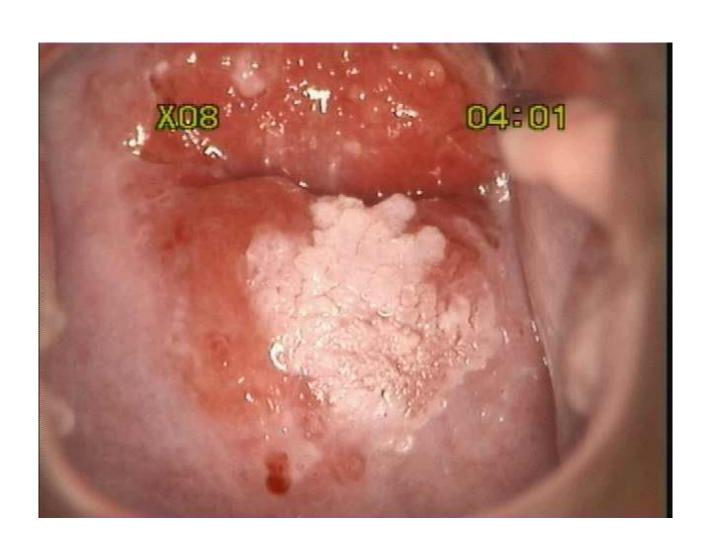
The white epithelium with clear boundary and fine mosaic



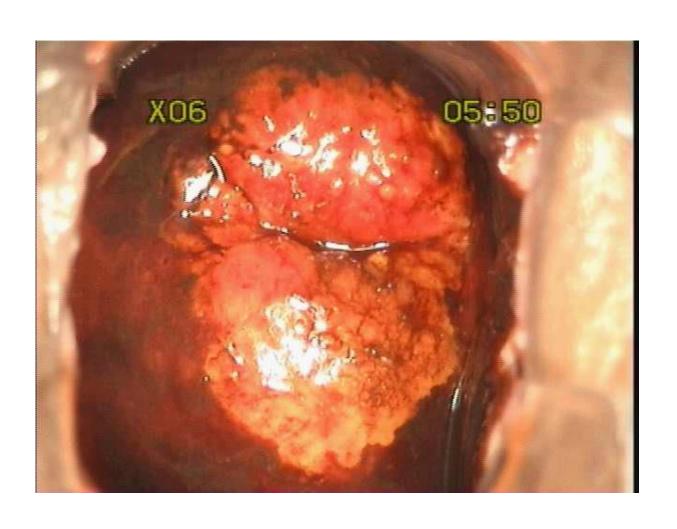
CIN2/Acetic acid reaction for 90 seconds



CIN2/Acetic acid reaction for 4 min



CIN2/Iodine staining



Distinguish metaplasia epithelium from white epithelium



Before applying acetic acid

After applying acetic acid

GOLDWAY INC.

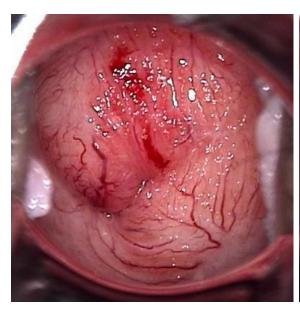
Differentiation of benign / malignant lesions



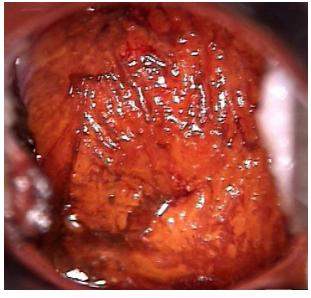


The mosaic on the white epithelium is obvious after applying acetic acid, but it disappeared rapidly in a short time

Differentiation of benign / malignant lesions





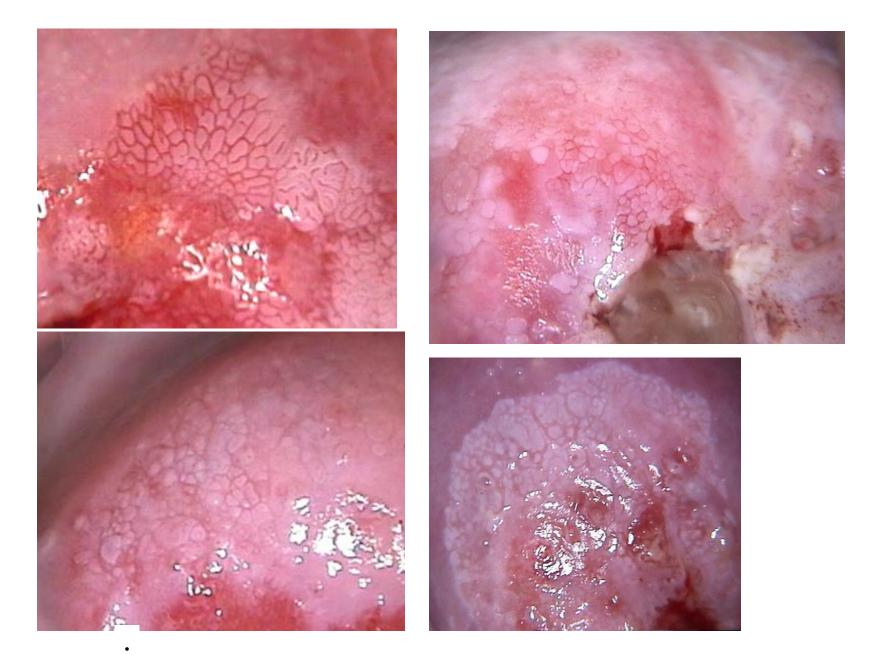


Before applying acetic acid

After applying acetic acid for 2 minutes

After applying compound iodine solution

The same image appearance may have different pathological results



Thanky ou

