Colposcopy

Chris DeSimone, M.D.
Gynecologic Oncology
Images from *Colposcopy Cervical Pathology*, 3rd Ed., 1998
Colposcopy was pioneered in Germany by Dr. Hinselmann during the 1920’s. He sought to prove that microscopic examination of the cervix would detect cervical cancer earlier than 4 cm. His work identified several atypical appearances which are still used today:

- Luekoplakia
- Punctuation
- Felderung (mosaicism)
History

Through the 30’s and 40’s breakthroughs were made regarding which appearances were more likely to progress to invasive carcinoma; HOWEVER,

These findings were difficult to interpret since they were not correlated with histology

One researcher would claim his patients with X findings never had carcinoma while another emphatically believed it did

World wide colposcopy was underutilized as a diagnostic tool secondary to these discrepancies
History

► Papanicolaou and Traut revolutionized screening of cervical cancer with cytology
► It was easy to collect and provided a more objective findings than colposcopy
► Pap testing was rapidly accepted in North America and Western Europe as the screening test of choice
► Its acceptance in Germany was poor

Papanicolaou, Traut: Diagnosis of uterine cancer by the vaginal smear, 1943
History

- During the 60’s colposcopy made a resurgence
- New studies showed that detection of carcinoma-in-situ (CIS) or invasive carcinoma were better detected by combining cytology with colposcopic directed biopsies
  - Total 838 cases
  - Colposcopy 663 (79%)
  - Cytology 729 (87%)
  - Combination 828 (99%)
Today colposcopy has been accepted as a diagnostic tool in evaluating abnormal pap tests.

Colposcopy elegantly identifies the location of abnormal lesions allowing the practitioner to obtain histologic samples.

Its utility as a screening test is likely finished in westernized nations.
Overview

- Cytologic indications for colposcopy
- Cytologic correlation with histology
- Tools, Techniques and stains of colposcopy
- Normal colposcopic anatomy
- Abnormal colposcopic anatomy
- Unusual colposcopic anatomy
- Treatment of abnormal histology
Indications for Colposcopy

► Abnormal pap tests suggestive of cervical dysplasia
► Types are classified according to Bethesda 2001 nomenclature
► Best to delineate which pap tests correlate with mild dysplasia and those which are more severe
2001 Bethesda Nomenclature

- **Mild dysplasia**
  - **HPV** effect (Human Papilloma Virus)
  - **ASC-US** (Atypical Squamous Cells of Unknown Significance)
  - **LSIL** (Low Grade Squamous Intraepithelial Lesion)

- **Severe dysplasia**
  - **ASC-H** (Cannot rule out HGSIL)
  - **HSIL** (High Grade Squamous Intraepithelial Lesion)
  - **CIS** (Squamous Carcinoma In-Situ)
2001 Bethesda Nomenclature

- Glandular abnormalities
- Should be handled with utmost caution
  - **AGC** (Atypical Glandular Cells of Unknown Significance)
  - **AIS** (Adenocarcinoma In-Situ)
- Biopsy medial to the transformation zone
Frequency of Abnormal Pap Tests

- Estimated 50 million pap tests are performed each year
- 5% are abnormal
- 2-3 Million ASCUS
- 1 Million LSIL
- 600,000 HSIL
CIN (Cervical Intraepithelial Neoplasia)

- CIN 1 corresponds to mild dysplasia
- CIN 2 corresponds to moderate dysplasia
- CIN 3 corresponds to severe dysplasia
- CIS and CIN 3 are the same entity
Histopathology

Development of Cervical Cancer

Abnormal Cells

Moderate Dysplasia (CIN II)

Severe Dysplasia, or Carcinoma-in-Situ (CIN III)
Overview

► Cytologic indications for colposcopy
► **Cytologic correlation with histology**
► Tools, Techniques and stains of colposcopy
► Normal colposcopic anatomy
► Abnormal colposcopic anatomy
► Unusual colposcopic anatomy
► Treatment of abnormal histology
Histologic correlation

- As a colposcopist, histology is more important than cytology

- The cytology is important for two reasons:
  - 1) indication to perform colposcopy
  - 2) gives the colposcopist a “hint” of the histology

- Histology is important for determining patient treatment

- Cytology does not equal histology
Histologic correlation

► ASC-US

- Most common type of abnormal pap
- Is it a premalignant change?
- No! Roughly 70% of ASC-US paps are related to vaginitis, atrophy, granulation tissue, chronic cervicitis, etc
- Only 30% are dysplastic in nature
  - 90% are CIN 1
  - 5-10% are CIN 2-3

Histologic correlation

► LSIL

- Common, 1 million paps diagnosed each year
- Most erroneously managed pap test. Why?
  ► Pap repeated frequently
  ► HPV testing
- 30% of LSIL paps harbor CIN 2 and CIN 3 on colposcopic directed biopsies
- Colposcopy needs to be done first and foremost to ascertain histologic diagnosis
Histologic correlation

► ASC-H

- 28-40% of these pap tests are CIN 2-3 on histologic biopsy
- Accordingly, HPV testing is positive 70-86%
- Colposcopic examination will reveal a wide range of findings

► HSIL & CIS

- Expect worrisome colposcopic abnormalities with these pap tests
Colposcopic Correlation

► Mild dysplasia
  - Acetowhite changes
  - Bright white
  - Clear demarcation between normal and abnormal epithelium
  - Fine punctations

► Severe dysplasia
  - Dull, pearly grey epithelium
  - Faint to difficult to interpret demarcation between abnormal and normal epithelium
  - Coarse punctations
  - Mosaicism
  - Abnormal vessels
Overview

► Cytologic indications for colposcopy
► Cytologic correlation with histology
► **Tools, Techniques and stains of colposcopy**
► Normal colposcopic anatomy
► Abnormal colposcopic anatomy
► Unusual colposcopic anatomy
► Treatment of abnormal histology
Tools, Techniques & Stains

► Colposcope

- Stereoscopic binocular microscope
- Magnification from 8× to 40×
- Generally panoramic view at 10× most useful
- A green filter
  - Used to highlight vascular patterns
  - Demarcate color differences between normal and abnormal tissue
Colposcope
Tools, Techniques & Stains

► Instruments
  - Kevorkian-Younge biopsy forceps
  - Endocervical curette
  - Endocervical brush
  - Cytology brush
  - Silver Nitrate stick
  - Monsel’s solution
Instruments

- Curette
- Kevorkian
Instruments

- Cytology Broom
- Endocervical Brush
- Lugol’s
- Monsel’s
- Silver Nitrate Stick
Stains

- 3% Acetic Acid
- Works as a desiccant
- The cellular cytoplasm is reduced enhancing a prominent nucleus
- The nucleus is enlarged secondary to HPV replication
- This nuclear enlargement is seen as acetowhite changes
Acetic Acid
Tools, Techniques & Stains

► Stains

- Lugol’s iodine solution (Schiller test)
- Works by staining glycogen
- Dysplastic tissue has an increased metabolic rate thereby lowering cellular glycogen
- Normal tissue stains black/brown while dysplastic tissue appears highlighted or yellow
- Useful stain for hard to see lesions
Lugols Solution
Tools, Techniques & Stains

▶ Technique

- Orient colposcope so that a panoramic view is obtained
- Start with normal light and 10× magnification
- Entire cervix should be visualized
- Apply generous amount of acetic acid while cleaning off obscuring mucous or discharge
- You can never apply too much acetic acid
Tools, Techniques & Stains

Evaluate the squamocolumnar junction (SCJ) or transformation zone (TZ)

- Dysplasia originates from this boundary and spreads lateral to this junction
- Medial to this border are columnar cells/glandular cells
- A large volume of glandular cells are called ectropion
- Young women and pregnant women generally have ectropion
3% Acetic acid applied to cervix
Cervix viewed under magnification and green light
Entire transformation zone must be visualized

Dysplastic epithelium will be “acetowhite” due to higher nuclear/cytoplasmic ratio
Squamocolumnar Junction

SCJ
Tools, Techniques & Stains

► Evaluate areas of acetowhite changes
  - Are they small or large patches?
  - Does it have a sharp or indistinct border?
  - Is it a bright white or a dull, pearly grey?

► Evaluate areas of punctation
  - Are the punctations small or large caliber?
  - Are the punctations sparse or numerous?

► Evaluate areas of mosaicism

► Evaluate areas of abnormal blood vessels
  - Are the blood vessels uniform or sporadic?
  - Are the vessels large caliber or small caliber?
Adequacy of Colposcopy

- Must evaluate the entirety of the lesion
  - Can you follow the entire lesion?
  - Does it go past the SCJ and into the endocervix?
  - Does it move into the vagina?

- Must evaluate the entirety of the SCJ
  - Is it obscured by prior treatments?
  - Does it recede into the endocervix?

- Proper evaluation of both the lesion and the SCJ is an adequate colposcopy

- Failure of either criteria is an inadequate colposcopy and leads to changes in treatment NOT diagnosis of histopathology
Biopsies

- Best to obtain biopsy of worst area
- Try to incorporate SCJ if at all possible
- Multiple biopsies are recommended but should be kept within reason (2-3)
- Endocervical curettage (ECC) should generally be included as part of each colposcopy
- Having the patient cough during biopsy is good distraction
To ECC or not to ECC

► Never wrong to perform
► However, ECC can be avoided if entire lesion is visible on ectocervix
► This position is strengthened since squamous dysplasia is continuous; it does not skip
► Others proclaim it evaluates occult endocervical dysplasia
► Ultimate decision lies with wisdom and expertise of practitioner

Williams. Obstet Gynecol, 2000
Most uncomfortable portion of colposcopic directed biopsies

Good to have patient take NSAID 30 min before colposcopy

Apply curette at four cardinal directions

Swirl curette in fixative then take endocervical brush to collect rest of sample

Prospective randomized trial showing better results with curette and brush than either alone

Tate. Obstet Gynecol, 1997
Overview

- Cytologic indications for colposcopy
- Cytologic correlation with histology
- Tools, Techniques and stains of colposcopy
- **Normal colposcopic anatomy**
- Abnormal colposcopic anatomy
- Unusual colposcopic anatomy
- Treatment of abnormal histology
Normal Colposcopy
Normal Histology
Normal Colposcopy/Ectropion
Normal Colposcopy
Normal Colposcopy
Normal Colposcopy
Close-up of SCJ
Overview

- Cytologic indications for colposcopy
- Cytologic correlation with histology
- Tools, Techniques and stains of colposcopy
- Normal colposcopic anatomy
- Abnormal colposcopic anatomy
- Unusual colposcopic anatomy
- Treatment of abnormal histology
Abnormal Colposcopic Anatomy

- Acetowhite epithelium or changes
- Punctations
- Mosaicism
- Abnormal Vessels
- Invasive carcinoma
Abnormal Colposcopic Anatomy

► Acetowhite changes
  - Mildest changes of cervical dysplasia
  - Caused by desiccation of cytoplasm from acetic acid leading to increased nuclear /cytoplasmic ratio
  - Other areas of abnormal change can be found within acetowhite lesions
  - Often times very clear area of demarcation from normal to abnormal
Normal versus Abnormal
Post Acetic Acid
Acetowhite changes
Acetowhite changes
Acetowhite changes

- Mosaicism
- Line of demarcation
Line of demarcation
Acetowhite changes

Punctations
Faint Acetowhite
Lesion Found
Punctations are vessels that run perpendicular to the portio of the cervix. They are end on end to the colposcopist. The green filter removes red light thus vessels are darkened. Punctuation can be small vessels (fine punctation) or large vessels (coarse punctation).
Punctations

Coarse Punctations

Coarse Punctations
Punctations

Fine Punctations
Bright acetowhite lesion with coarse punctations
Mosaicism

- A mosaic is a large image pieced together by smaller usually colorful tiles
- In colposcopy it is essentially the same - a larger lesion made of small heaped epithelial islands and tiny vessels
- These islands look like a cobblestone road
- Islands are separated by vessels running parallel to the portio or colposcopist
Mosaicism

Large lesion composed of multiple islands and intervening small vessels.
Microscopic Mosaicism
Mosaicism
Mosaicism

Area of mosaicism with large punctations consistent with CIN 3
In the natural progression of dysplasia to invasive cervical cancer, many genetic and pathologic changes occur.

One important change is angiogenesis.

The evolving carcinoma needs oxygen and nutrients to grow at an exponential rate.

In order to achieve maximal growth, new blood vessels are synthesized.
Abnormal Vessels

- The newly created vessels are perfect for pooling blood.
- They have low flow, little pulsatility and poor resistance.
- The above factors are caused by multiple tributaries arising from any one vessel.
- End result is like a delta from a river, lots of nutrients are brought in but blood is slow to return.
Examples of Normal Vessels
Abnormal Vessels
Normal versus Abnormal
Abnormal Vessels
Abnormal Vessels
Invasive Cancer

- Conglomeration of all colposcopic finding: acetowhite, punctations, mosaicism, and vessels
- Necrotic tissue results in anaerobic odors
- Think ahead when performing biopsies: Monsel's, packing and even suture might be necessary to control hemorrhage
- Shoot for a good tissue collection, often time not enough tissue is obtained for pathologist to document invasion!!!
Invasive Cancer
Microscopic Invasion
Invasive Cancer
Overview

- Cytologic indications for colposcopy
- Cytologic correlation with histology
- Tools, Techniques and stains of colposcopy
- Normal colposcopic anatomy
- Abnormal colposcopic anatomy
- Unusual colposcopic anatomy
- Treatment of abnormal histology
Polyps
Polyps
Nabothian Cysts

Normal Vessels
Nabothian Cysts

Prominent vessels of normal caliber surrounding multiple Nabothian cysts
Condylomas

Heaped vaginal/cervical condyloma in a gravid female
Overview

- Cytologic indications for colposcopy
- Cytologic correlation with histology
- Tools, Techniques and stains of colposcopy
- Normal colposcopic anatomy
- Abnormal colposcopic anatomy
- Unusual colposcopic anatomy
- Treatment of abnormal histology
Treatment Modalities

- Cryosurgery
- Loop Electricosurgical Excision Procedure (LEEP)
- Laser Ablation
- Cold Knife Conization
- Hysterectomy
Cryosurgery

- Inexpensive, easy to perform, tolerated well by patients
- Cells are destroyed by (cold) thermal damage
- 3 minute freeze/1 minute thaw/3 minute freeze
- Well documented technique
- Does cause 2-3 weeks of malodorous discharge
- Does hinder repeat colposcopy (SCJ often obscured)
LEEP

- Procedure of choice for most OB/GYN’s
- Easy to perform, well tolerated and provides specimen for pathologic evaluation (Margins)
- Good rule to keep specimens less than 4 cm wide and 2 cm tall
- Concern that multiple excisions or one large excision will increase rate of preterm labor/incompetent cervix
Preterm Delivery and LEEP

► Meta-analysis of 27 studies
► Studies chosen had to have a control group
► Evaluation of CKC, LEEP and laser for:
  ▪ preterm delivery (<37 weeks gestation)
  ▪ Low birth weight (<2500 g)
  ▪ Cesarean delivery
Preterm Delivery and LEEP

► CKC
- Preterm delivery- RR 2.59 (95% CI 1.80-3.72)
- Low birth weight- RR 2.53 (95% CI 1.19-5.36)
- Cesarean section- RR 3.17 (95% CI 1.07-9.40)

► LEEP
- Preterm delivery- RR 1.70 (95% CI 1.24-2.35)
- Low birth weight- RR 1.82 (95% CI 1.09-3.06)
- Cesarean section- RR 2.69 (95% CI 1.62-4.46)

► Laser
- NS for Preterm delivery- RR 1.71 (95% CI 0.93-3.14)
Preterm Delivery and LEEP

► Summary

► CKC patients are 2.5 times more likely to have a preterm delivery, low birth weight infant and/or cesarean section

► LEEP 1.5 times more likely

► Incidence of preterm delivery is 2-3%
  - CKC ~ 7.5% (1 in 15 women)
  - LEEP ~ 4.5% (1 in 20 women)
Margins and LEEP

- Margin status helpful in predicting recurrence of cervical dysplasia
- Negative margins ~15%
- Positive margins ~30-60%
- Re-excision not needed. Follow patient with serial pap tests and treat accordingly if patient recurs
Laser

- CO2 laser works by vaporizing cervical cells
- Very precise method; only need 5-7 mm of vaporization for treatment
- Heals great, spares cervical excisions
- COST major problem
- No pathology specimen
Cold Knife Conization (CKC)

- Used to be the treatment of choice before LEEP
- Surgically excises dysplasia with scalpel/scissors
- Large cost to patient from physician, anesthesia, and hospital charges
- Incompetent cervix an issue
- Indications to perform are few
Hysterectomy

► The final treatment for cervical dysplasia
► Comes with significant morbidity/ mortality and lengthy recovery (6 weeks)
► Complications include: hemorrhage, infections, bowel & bladder injuries, MI, pulmonary embolus, stroke, death
► 10-20% of patients will continue to have abnormal pap tests: vaginal dysplasia
Efficacy of treatment

► Randomized controlled trial between cryosurgery, LEEP and laser showed no statistical difference in efficacy
► Recurrences were measure from 6-37 months
► Cryosurgery 19%
► LEEP 13%
► Laser 13%

Efficacy of treatment

► Reich et al. performed two retrospective studies on cold knife conization
► 4417 women with CIN 3 were treated with CKC and followed for median 107 months (negative margins)
► Only 15 women developed recurrence (0.35%)
► 390 women with CIN 3 were treated with CKC and followed for a median of 19 years (positive margins)
► 84 women developed recurrence (22%)

Reich, Obstet Gynecol. 2001 and 2002
Which method to chose?

► Several factors to consider: age, desire for fertility, size of lesion, size of the cervix, severity of dysplasia, and prior therapies

► Generalizations:
  - Cryosurgery - best for young women with few finances and CIN 1 or 2.
  - LEEP - the majority of women with CIN 2 or 3. Women with endocervical lesions also suited for LEEP
Which method to chose?

- Laser - women who have had multiple recurrences of CIN 2 or 3 and who want to retain fertility. Example: a 19 year old G₀ who has CIN 3, prior LEEP, and a small cervix.
- CKC - glandular abnormalities (AIS) or early invasive cancer
- Hysterectomy - women finished with childbearing and who have persistent CIN. Often best utilized with other gynecologic problems like pelvic pain or abnormal uterine bleeding
Unknowns
Unknowns