PAP SMEARS & HPV

Kelly Gdovic WHNP
Papanicolaou Smear

- Pap smears first introduced to the public in the 1950’s
- Encouraged to be done annually by the 1960’s
- 1980’s American Cancer Society recommends testing every three years after 2 negative tests
- 2001 guidelines started to assist with management strategies based on cytologic findings
- 2006 guidelines added management guidelines for HPV positive specimens and adolescent/young women
Pap Smear

- 2012 guidelines extended the length of screening intervals.
- American Society for Colposcopy and Cervical Pathology (ASCCP)
  - American Cancer Society
  - US Preventative Services Task Force
- Cervical Cancer rates:
  - By the 1950’s cervical cancer was the #1 cancer causing death in women
  - Between 1955 and 1992 cervical cancer death rates dropped by 70%
- 2014 ACS estimates are: 12,360 new cases of invasive cervical cancer will be diagnosed and 4,020 deaths
Bethesda System

- Classification of pap smear results
- First introduced 1988
- Revised 2001 to include liquid based sample collection and HPV testing
2001 Bethesda System

- **SPECIMEN TYPE**
  Indicate conventional smear (Pap smear) vs. liquid-based preparation

- **SPECIMEN ADEQUACY**

  - **Satisfactory for evaluation**
    (describe presence or absence of endocervical/transformation zone component and any other quality indicators, e.g., partially obscuring blood, inflammation, etc.)

  - **Unsatisfactory for evaluation**
    - Specimen processed and examined, but unsatisfactory for evaluation of epithelial abnormality
2001 Bethesda System

• INTERPRETATION/RESULT

• NEGATIVE FOR INTRAEPITHELIAL LESION OR MALIGNANCY

• Organisms
  • *Trichomonas vaginalis*
  • Fungal organisms morphologically consistent with *Candida* spp
  • Shift in flora suggestive of bacterial vaginosis
  • Bacteria morphologically consistent with *Actinomyces* spp
  • Cellular changes consistent with Herpes simplex virus

• Other non-neoplastic findings
  • Reactive cellular changes associated with:

• Inflammation
  • Radiation
  • Intrauterine contraceptive device (IUD)
  • Glandular cells status post hysterectomy
  • Atrophy
2001 Bethesda System

- OTHER
  - Endometrial cells (in a woman >= 40 years of age)

- EPITHELIAL CELL ABNORMALITIES
  - Squamous cell
    - Atypical squamous cells Of undetermined significance (ASC-US)
      - Cannot exclude HSIL (ASC-H)
    - Low grade squamous intraepithelial lesion (LSIL)
      Encompassing: HPV/mild dysplasia/CIN 1
    - High grade squamous intraepithelial lesion (HSIL)
      Encompassing: moderate and severe dysplasia, CIS; CIN 2 and CIN 3
        - With features suspicious for invasion
    - Squamous cell carcinoma
2001 Bethesda System

- **Glandular cell**
  - Atypical
    - Endocervical cells, NOS or specify in comments
    - Endometrial cells, NOS or specify in comments
    - Glandular cells, NOS or specify in comments
  - Atypical
    - Endocervical cells, favor neoplastic
    - Glandular cells, favor neoplastic
    - Endocervical adenocarcinoma *in situ*
- **Adenocarcinoma**
  - Endocervical
  - Endometrial
  - Extrauterine
  - Not otherwise specified (NOS)
Human Papilloma Virus

- Wart virus
- Over 150 related strains (numbered)
- Lives in epithelial cells
- About 75%: Common warts, Plantar warts
- About 25%: mucosal types associated with being sexually transmitted (genital warts (condyloma), laryngeal papillomas, cervical dysplasia/cancer)
HPV

- High risk and low risk groups

- High risk: 16 & 18 associated with >90% of cervical cancers (linked to CA of vulva/vagina/anus/penis/throat)

- Low risk: 6 & 11 associated with genital warts/laryngeal papilloma

- Most common STI in the U.S.: approximately 50% of sexually active men and women have/have had HPV. 20 million people in the U.S have current HPV infection.

- Approximately 90% will be cleared within 2 years
HPV

- 10% with persistent infection has 300 times the risk of developing high grade lesions

- Can take 15-20 years to develop into cancer in women with healthy immune system.

- 5-10 years to develop into cancer in immunocompromised women (HIV+, pregnancy).

- Risk factors for being infected:
  - Sexual activity
  - Multiple partners or partner who has/had multiple partners
  - Unprotected sex (not 100%)
HPV

- Risk factors for persistent infection to progress to high grade lesion/cancer:
  - Smoking
  - Pregnancy (multiparity)
  - Immunosuppression
  - HPV 16 infection

- Vaccine:
  - **Gardasil**: aimed at types 6,11,16,18
    - Series of 3 over 6 months
    - Girls and boys ages 9-26
  - **Cervarix**: aimed at 16 and 18 only
    - Series of 3 over 6 months
    - Girls only
Cervical Cancer Screening

- Highlights:
  - Paps start at age 21 (regardless of sexual activity onset)
  - Co-testing
  - No paps after hysterectomy (unless hyst was done for CIN2/3)
  - Screening for women <30y/o and ≥ 30y/o differ
  - Discontinue paps after 65y/o (unless specific history exists)
  - Guidelines are NOT for immunosuppressed women/ DES exposed women
Cytology NILM* but EC/TZ Absent/Insufficient

Ages 21-29†
- HPV Negative
  - HPV Testing Preferred

Routine Screening

Age ≥ 30
- HPV Unknown
  - Repeat Cytology @ 3 years Acceptable

HPV Positive or
- Genotyping
  - Manage per ASCCP Guideline
  - Cytology & HPV Test @1 year
Management of Women ≥ Age 30, who are Cytology Negative, but HPV Positive

- **Repeat Cotesting** @ 1 year
  - Acceptable
  - Cytology Negative and HPV Negative
  - ≥ ASC or HPV Positive
  - Repeat Cotesting @ 3 years

- **HPV DNA Typing** Acceptable
  - HPV 16 or 18 Positive
  - HPV 16 and 18 Negative
  - Repeat Cotesting @ 1 year

- **Colposcopy**
  - Manage per ASCCP Guideline
Management of Women with Atypical Squamous Cells of Undetermined Significance (ASC-US) on Cytology*

- **Repeat Cytology**
  @ 1 year
  Acceptable
  - Negative
  - ≥ ASC
    - Routine Screening†

- **HPV Testing**
  Preferred
  - HPV Positive
    (managed the same as women with L.SIL)
  - HPV Negative
    Repeat Cotesting
    @ 3 years

- **Colposcopy**
  Endocervical sampling preferred in women with no lesions, and those with inadequate colposcopy; it is acceptable for others
  - Manage per ASCCP Guideline

* Management options may vary if the woman is pregnant or ages 21-24
† Cytology at 3 year intervals
Management of Women Ages 21-24 years with either Atypical Squamous Cells of Undetermined Significance (ASC-US) or Low-grade Squamous Intraepithelial Lesion (LSIL)

- **Repeat Cytology** @ 12 months Preferred
  - Negative, ASC-US or LSIL
    - Repeat Cytology @ 12 months
      - Negative x 2
      - ≥ ASC
        - Colposcopy
  - ASC-H, AGC, HSIL
    - HPV Positive
      - Reflex HPV Testing Acceptable for ASC-US only
        - HPV Negative
          - Routine Screening

© Copyright, 2013, American Society for Colposcopy and Cervical Pathology. All rights reserved.
Management of Women with Low-grade Squamous Intraepithelial Lesions (LSIL)**

**LSIL with negative HPV test among women ≥ 30 with cotestoning**

Preferred

Repeat Cotestoning @ 1 year

Cytology Negative and HPV Negative

Repeat Cotestoning @ 3 years

**LSIL with no HPV test**

Acceptable

≥ ASC or HPV positive

Colposcopy

Non-pregnant and no lesion identified
Inadequate colposcopic examination
Adequate colposcopy and lesion identified

Endocervical sampling “preferred”
Endocervical sampling “preferred”
Endocervical sampling “acceptable”

No CIN2,3

Manage per ASCCP Guideline

CIN2,3

Manage per ASCCP Guideline

* Management options may vary if the woman is pregnant or ages 21-24 years
† Management women ages 25-29 as having LSIL with no HPV test

© Copyright, 2013, American Society for Colposcopy and Cervical Pathology. All rights reserved.
Management of Pregnant Women with Low-grade Squamous Intraepithelial Lesion (LSIL)

Colposcopy
Preferred

No CIN2,3*

Postpartum Follow-up

CIN2,3

Manage per ASCCP Guideline

Defer Colposcopy
(Until at least 6 weeks postpartum)
Acceptable

* In women with no cytological, histological, or colposcopically suspected CIN2,3 or cancer

© Copyright, 2013, American Society for Colposcopy and Cervical Pathology. All rights reserved.
Management of Women with Atypical Squamous Cells: Cannot Exclude High-grade SIL (ASC-H)*

- **Colposcopy**
  Regardless of HPV status

- No CIN2,3
  - Manage per ASCCP Guideline

- CIN2,3
  - Manage per ASCCP Guideline

* Management options may vary if the woman is ages 21-24

© Copyright, 2013, American Society for Colposcopy and Cervical Pathology. All rights reserved.
Management of Women Ages 21-24 yrs with Atypical Squamous Cells, Cannot Rule Out High Grade SIL (ASC-H) and High-grade Squamous Intraepithelial Lesion (HSIL)

**Colposcopy**
Immediate loop electrosurgical excision is unacceptable

- **No CIN2,3**
  - **Observation with Colposcopy & Cytology**
    - @ 6 month intervals for up to 2 years
  - **Other Results**
    - **HSIL**
      - Persist for 24 months with no CIN2,3 identified
    - **CIN2,3**
      - Persist for 1 year
      - **Biopsy**
      - **CIN2,3**
        - (If no CIN2,3, continue observation)
    - **Manage per ASCCP Guideline for Young Women with CIN2,3**

- **CIN2,3**
  - **Manage per ASCCP Guideline**

* If colposcopy is adequate and endocervical sampling is negative. Otherwise a diagnostic excisional procedure is indicated.
† Not if patient is pregnant

© Copyright, 2013, American Society for Colposcopy and Cervical Pathology. All rights reserved.
Management of Women with High-grade Squamous Intraepithelial Lesions (HSIL)*

Immediate Loop Electrosurgical Excision†

Or

Colposcopy with endocervical assessment

No CIN2,3

CIN2,3

Manage per ASCCP Guideline

* Management options may vary if the woman is pregnant, postmenopausal, or ages 21-24
† Not if patient is pregnant or ages 21-24
Initial Workup of Women with Atypical Glandular Cells (AGC)

All subcategories (except atypical endometrial cells)

Colposcopy with endocervical sampling and Endometrial sampling (if ≥ 35 yrs or at risk for endometrial neoplasia*)

Atypical Endometrial Cells

Endometrial and Endocervical Sampling

No Endometrial Pathology

Colposcopy

* Includes unexplained vaginal bleeding or conditions suggesting chronic anovulation
Subsequent Management of Women with Atypical Glandular Cells (AGC)

Initial Cytology is AGC - NOS

No CIN2+, AIS or Cancer

Cotest @ 12 & 24 months

Both Negative

Cotest 3 years later

Any Abnormality

Colposcopy

CIN2+ but no Glandular Neoplasia

Manage per ASCCP Guideline

No Invasive Disease

Diagnostic Excisional Procedure*

Initial Cytology is AGC (favor neoplasia) or AIS

* Should provide an intact specimen with interpretable margins. Concomitant endocervical sampling is preferred.

© Copyright, 2013, American Society for Colposcopy and Cervical Pathology. All rights reserved. ASCCP
Management of Women with No Lesion or Biopsy-confirmed Cervical Intraepithelial Neoplasia — Grade 1 (CIN1) Preceded by “Lesser Abnormalities” *

Follow-up without Treatment

- **Cotesting** @ 12 months
  - HPV Negative
  - Cytology Negative
  - Age appropriate† retesting 3 years later
  - Cytology Negative +/- HPV Negative
  - Routine Screening‡

- > ASC or HPV Positive
  - Colposcopy
  - No CIN
    - Manage per ASCCP Guideline
  - CIN2,3
    - If persists for at least 2 years
  - CIN1
    - Follow-up or Treatment∞

* “Lesser abnormalities” include ASC-US or LSIL Cytology, HPV 16+ or 18+, and persistent HPV
† Management options may vary if the woman is pregnant or ages 21-24.
‡ Cytology if age <30 years, cotesting if age ≥30 years
∞ Either ablative or excisional methods. Excision preferred if colposcopy inadequate, positive ECC, or previously treated.

© Copyright, 2013, American Society for Colposcopy and Cervical Pathology. All rights reserved.
Management of Women with No Lesion or Biopsy-confirmed Cervical Intraepithelial Neoplasia — Grade 1 (CIN1) Preceded by ASC-H or HSIL Cytology

- **Cotesting @ 12 & 24 months**
  - **HPV Negative**
    - Age-specific Retesting @ 3 years
  - **HPV Positive or Any cytology abnormality except HSIL**
    - **HSIL at either visit**
      - **Colposcopy**

- **Or**
  - **Diagnostic Excision Procedure**
    - **Review of cytological, histological, and colposcopic findings**
      - **Manage per ASCCP Guideline for revised diagnosis**

* Only if colposcopy was adequate and endocervical sampling is negative
† Except in special populations (may include pregnant women and those ages 21-24)
‡ Cytology if age < 30, cotesting if age ≥ 30 years

© Copyright, 2013, American Society for Colposcopy and Cervical Pathology. All rights reserved.
Management of Women Ages 21-24 with No Lesion or Biopsy-confirmed Cervical Intraepithelial Neoplasia — Grade 1 (CIN1)

**After ASC-US or LSIL**
- Repeat Cytology @ 12 months

- < ASC-H or HSIL
  - Repeat Cytology @ 12 mos
  - Negative
    - Routine Screening
  - ≥ ASC
    - Colposcopy

- ≥ ASC-H or HSIL

**After ASC-H or HSIL**
- Manage per ASCCP Guideline for Women Ages 21-24 with ASC-H or HSIL using postcolposcopy pathway for No CIN2,3
Management of Women with Biopsy-confirmed Cervical Intraepithelial Neoplasia — Grade 2 and 3 (CIN2,3)*

* Management options will vary in special circumstances or if the woman is pregnant or ages 21-24

+ If CIN2,3 is identified at the margins of an excisional procedure or post-procedure ECC, cytology and ECC at 4-6mo is preferred, but repeat excision is acceptable and hysterectomy is acceptable if re-excision is not feasible.

Adequate Colposcopy

- Either Excision† or Ablation of T-zone*

2x Negative Results

- Repeat cotesting @ 3 years

Routine Screening

Inadequate Colposcopy or Recurrent CIN2,3 or Endocervical sampling is CIN2,3

- Diagnostic Excisional Procedure†

Cotesting @ 12 & 24 months

Any Test Abnormal

Colposcopy With endocervical sampling

© Copyright, 2013, American Society for Colposcopy and Cervical Pathology. All rights reserved.
Management of Young Women with Biopsy-confirmed Cervical Intraepithelial Neoplasia — Grade 2,3 (CIN2,3) in Special Circumstances*

**Observation — Colposcopy & Cytology***
@ 6 month intervals for 12 months

2x Cytology Negative and Normal Colposcopy

**Cotest @ 1 year**

Either Test Abnormal

Both Tests Negative

**Cotest @ 3 years**

**Treatment using Excision or Ablation of T-zone***

Colposcopy Worsens or High-grade Cytology or Colposcopy Persists for 12 Months

Repeat Colposcopy/Biopsy Recommended

CIN3 or CIN2,3 persists for 24 months

**Treatment Recommended**

* Either treatment or observation is acceptable, provided colposcopy is adequate. When CIN2 is specified, observation is preferred. When CIN3 is specified, or colposcopy is inadequate, treatment is preferred.

© Copyright, 2013, American Society for Colposcopy and Cervical Pathology. All rights reserved.
Management of Women Diagnosed with Adenocarcinoma in-situ (AIS) during a Diagnostic Excisional Procedure

- **Hysterectomy**
  - Preferred

- **Conservative Management**
  - Acceptable if future fertility desired

- **Margins Involved or ECC Positive**
  - Re-excision
    - Recommended

- **Margins Negative**
  - Re-evaluation*
    - @ 6 months
    - Acceptable
  - Long-term Follow-up

* Using a combination of cotesting and colposcopy with endocervical sampling

© Copyright, 2013, American Society for Colposcopy and Cervical Pathology. All rights reserved.
Conclusion

• THE major contributing factor to developing cervical cancer is not maintaining adequate cervical screenings.

• Provider’s judgment is prudent if patient’s hx/results don’t fall into an exact category

• Most insurance companies are still covering annual Pap smears (not HPV testing)

• Questions
Resources

- ASCCP.org
- CDC.gov
- WHO.int
- Cancer.org (American Cancer Society)
- Cancer.gov (National Cancer Institute)