

## **Abnormal Pap Smears**

**Satellite Conference  
Wednesday, December 8, 2004  
2:00-4:00 p.m. (Central Time)**

Produced by the Alabama Department of Public Health  
Video Communications Division

## **Faculty**

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## **Cervical Cancer Facts and Figures- Worldwide**

- Third most common cancer worldwide.
- Second most common cause of cancer-related deaths in women (200,000/yr).
- >450,000 cases are diagnosed annually.
- 80% of cases occur in developing countries.

## **Cervical Cancer Facts and Figures- U.S.**

- Ninth most common cause of cancer death in women.
- 13,000 new cases in 2002, 4100 deaths.
- Usually occurs in fifth or sixth decade.
- About 50% of US women in whom cervical cancer develops have never been screened.

## **Natural History**

- Cervical cancer evolves in a continuum of change:
  - Well-differentiated low-grade lesions
  - Undifferentiated high-grade intraepithelial lesion
  - Cellular intraepithelial neoplasia
  - Invasive cancer

## **Why Screen?**

- Long pre-invasive state
- Cytological screening can detect pre-invasive stage
- Treatment for pre-invasive disease is effective
- Untreated pre-invasive disease can progress to invasive cancer

### **Pap Smear**

- Designed to detect precursor lesions in cervical epithelium.
  - Until 30 years ago, 75% cervical cancer invasive.
  - Today: 78% diagnosed at in situ stage.
- No randomized control trials on effectiveness.
- Observational data from Northern Europe.
- Mortality in US decreased by 70% between 1947 and 1984 with mass screening.

### **Missed Opportunities**

- Only 1/3 of eligible women are screened yearly.
- 8% of women age 45 or older and 17% age 65 or older (42% of poor women) have **NEVER** had a Pap smear.
- Half of women diagnosed with cervical cancer in the U.S. have **NEVER** been screened and more than 60% have not had a Pap smear in more than 5 years.

**Any health care encounter should be viewed as an opportunity to provide cervical cancer screening.**

### **Risk Factors for Cervical Cancer**

- Genital HPV infection
- Low socioeconomic status
- Multiple sexual partners
- Early onset of sexual intercourse
- Smoking

### **When to Start Screening**

- Within three years of initiating sexual activity.
- By age 21 regardless of reported sexual activity.

### **When To Stop Screening**

- Advanced age (65+)
- Serious co-morbidities
- After total hysterectomy for benign reasons
  - If cervix still present, screen as for all other women

### How Often?

- Annual vs. q 2-3 years (no controlled studies)
  - High risk: multiple partners, promiscuous partners, early initiation of intercourse, partners with previous partners with cervical cancer, current or prior HPV, HIV, h/o STDs, h/o dysplasia/cervical CA.

### How Often?

- Immunocompromised women
  - Prevalence of cervical cancer higher in HIV+ women.
  - 1993: inclusion of invasive cervical CA in case definition of AIDS.
  - Twice in first year after dx and annually thereafter if normal.

### Qualities of a Good Screening Test

- Effective
- Safe
- Practical
- Affordable
  - Since 1998 Medicare has covered Pap testing q3 yrs
- Available

### The Pap Smear: An Effective Screening Test?

- Efficacy dependent on:
  - quality of the specimen
  - accuracy of the cytologic interpretation

### The Pap Smear: An Effective Screening Test?

- Sampling errors in 12% of cases (primary cause of false negatives).
- ~15% of patients with intraepithelial, precancerous lesions have “normal” Pap smear results.
- 20-50% of patients with cervical cancer have “normal” pap or “inflammation”.

### Pap Smear: An Effective Screening Test?

- Burden of suffering.
- Effectiveness of early detection.
- Accuracy of screening test.
  - Screen all women every year for 3 years, will miss 15% of 15% of 15% of precancers- 3/1000 women.
  - Only 20% of women will have precancer, we will miss 6/10,000.

### **Achieving Maximum Benefit- Patient Factors**

- Patient should ideally avoid coitus, lubricant, or douching for 24 hours before the exam.
- Avoid tampon use for 48 hours before.
- Should not be done during full menstrual flow (do not delay for abnormal bleeding).

### **Achieving Maximum Benefit- Practitioner Factors**

- Pap smear should be done at the start of the exam, before any cultures or the bimanual exam.
- Technique- adequate sampling of the transformation zone using both spatula and endocervical brush.
- Fix immediately to avoid air drying.

### **Fluid Based Cytology**

- Use of a fluid medium to capture and preserve cells collected from the cervix.
- Developed and promoted with increasing awareness of imperfect sensitivity of conventional pap smears.
- May increase sensitivity (90 vs 79%) at cost of decreased specificity (85 vs 89%).
- Offers advantage of doing HPV testing on the same Pap specimen.

### **How to Further Decrease Deaths from Cervical Cancer**

- Increase the rate of Pap testing in previously unscreened women.
- Minimize sampling errors- inadequate preparation of the slide (two-thirds of false-negative results).
- Decrease screening errors- errors in interpretation of the slide.

### **Cervical Cancer: A Sexually Transmitted Disease?**

### **Human Papilloma Virus (HPV)**

- HPV is highly prevalent, found in nearly two-thirds of female college students.
- Sexually transmitted virus.
- Most HPV infections are transient, with median duration of 8 months.

## Human Papilloma Virus (HPV)

- Risk for persistent HPV infection (>6 mos):
  - Older age
  - Infection with multiple types of HPV
  - High risk type infection
  - Duration of infection

## Role of HPV in Cervical Cancer

- Causal relationship identified between genital HPV infection and cervical dysplasia and cervical cancer.
- Several types of HPV
  - Low risk are types 6 and 11
  - Highest risk are types 16, 18, 33, 52, 59
- Infection with 16 and any other high risk type further increases the risk for developing cervical cancer.

## Role of HPV in Cervical Cancer Screening

- HPV testing can help identify with a single smear which women with ASCUS should undergo colposcopy.

## Interpretation of Pap Smears 2001 Bethesda System

The Bethesda System	Interpretation
<b>Specimen adequacy</b> Satisfactory for evaluation With presence or absence of endocervical/transformation zone component noted Unsatisfactory for evaluation  <b>Optional general categorization</b> Negative for intraepithelial lesion or malignancy Epithelial cell abnormality Other	Negative for intraepithelial lesion or malignancy <b>Organisms</b> <b>Inflammation</b> <b>Other reactive changes</b> Epithelial cell abnormalities Squamous cell Atypical squamous cells (ASC) -undetermined significance (ASC-US) Cannot exclude high grade (ASC-H) Low-grade squamous intraepithelial lesion (LSIL) High-grade squamous intraepithelial lesion (HSIL) Squamous cell carcinoma Glandular cell Atypical glandular cells ( AGC ) (endocervical, endometrial, or not otherwise specified) Atypical glandular cells, AGC favor neoplastic (endocervical or not otherwise specified) Endocervical adenocarcinoma in situ (AIS) Adenocarcinoma Other Endometrial cells in a woman aged $\geq 40$

Patient Care, June 2004

## Management of Abnormal Pap Smear Results

## **ASCUS**

- Most common abnormal finding (~3.5% of Pap smears).
- 5-17% chance of having CIN 2, 3 confirmed by bx.
- History of abnormal Pap smears or previous treatment for cervical dysplasia increases risk for finding neoplasia.

## **Intermediate Triage-Advantages**

- Allows triage based on initial Pap specimen.
- Decreases repeat Pap examinations.
- Reduces patient anxiety.
- Minimizes the loss of high-risk cases during follow-up.

## **ASCUS: Special Circumstances**

- Pregnancy
  - Manage the same as non-pregnant women except **NO ENDOCERVICAL SAMPLING**
- Immunosuppression (incl. HIV/AIDS)
  - Immediate colposcopy

## **AGUS**

- Relatively rare- 0.2-0.6% of all Pap smears.
- Between 17-52% of women will have significant cervical lesions.
- Prompt diagnostic workup indicated.
- Refer for colposcopy with biopsy.
- Endocervical curettage also recommended.

## **Low Grade SIL (LSIL)**

- 15-35% of women with LSIL have histologic CIN 2-3.
- Majority have no cervical lesion or CIN 1.
- Often transient HPV infection.

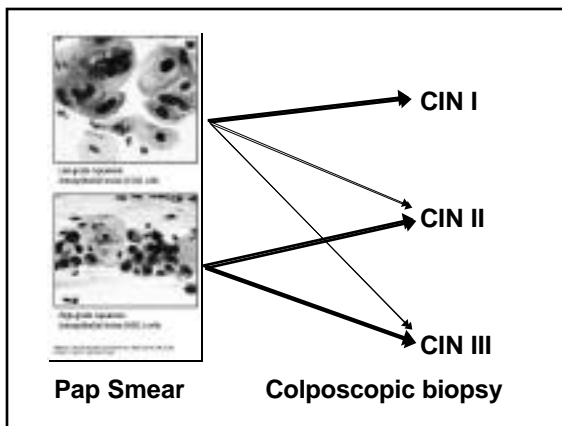
## **LSIL: Adolescents**

- Follow-up cytology at 6 and 12 months or
- Repeat HPV DNA testing at 12 months

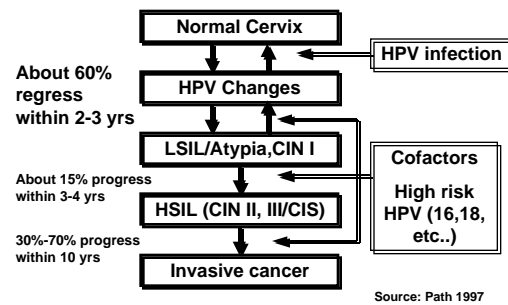
## High Grade SIL (HSIL)

- Uncommon- 0.45% of all Pap smears.
- 70-75% risk of having histologic CIN 2-3.
- 1-2% risk of having invasion.

## Treatment of CIS and CIN



## Progression



## Role of Colposcopy

- Identify cervical lesions
- Allow directed biopsies to identify invasive cancer or its precursors
- Sensitivity 96%
- Specificity 48%

## CIN I

- Most common and mildest form of cervical dysplasia.
- Corresponds to LSIL cytology.
- 12% progression to invasive cancer.
- Majority spontaneously resolve.
- TREATMENT OPTIONS:
  - Watchful waiting
  - Cryotherapy

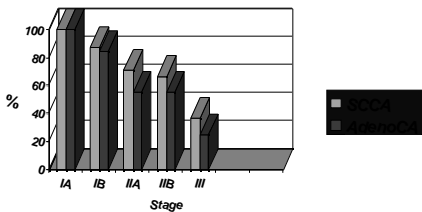
### CIN II or III

- Usually corresponds to pap smear of HSIL.
- Requires treatment to prevent subsequent invasive disease.
- TREATMENT OPTIONS:
  - Cryotherapy
  - Laser vaporization
  - Loop excision
  - Cone biopsy
  - Hysterectomy

### Cervical Cancer: Symptoms/Signs

- Abnormal vaginal bleeding
- Abnormal vaginal discharge
- Local organ impingement
- Red, friable, exophytic lesion
- Firm, enlarged cervix

### Five-Year Survival



### The Beginning Of The End For Cervical Cancer?

- Persistent infection with HPV is associated with the development of cervical cancer.
- HPV-16 is present in 50% of cervical cancers and HGSIL, 25% of LGSIL.
- 2002- development of vaccine against HPV 16.

### The Beginning of the End for Cervical Cancer?- Caveats

- Nearly 20 types of HPV associated with cervical cancer
- Vaccination will not reverse infection or cervical neoplasia once developed
- Duration of protection remains uncertain
- Goal: vaccinate against five HPV types (16,18, 31, 33,45) responsible for most cervical cancers before becoming sexually active

### Conclusion

- Overall mortality rate is decreasing because more patients are having their cancers diagnosed in early stages of disease.
- With early diagnosis and appropriate referral, providers can make great strides to protect women from this deadly disease.



## **Resources**

- **Abnormal Pap Consensus Guidelines**
  - <http://www.asccp.org/pdfs/consensus/algorithms.pdf>
  - JAMA, April 24, 2002- Vol 287, No. 16
  - Patient Care, June 2004
- **Cervical Cancer Screening**
  - NEJM Vol 344, No. 21- May 24, 2001

## **Upcoming Programs**

**Crisis & Emergency Risk  
Communication:  
by Leaders for Leaders (Part 2)  
Tuesday, December 14, 2004  
1:00-3:30 p.m. (Central Time)**

**For a complete listing of all upcoming  
programs, visit our website:  
[www.adph.org/alphtn](http://www.adph.org/alphtn)**