Welcome to CAP’s “Hot Topics in Pathology” Webinar Series sponsored by the Personalized Health Care Committee

This webinar on “Biomarkers in HPV-associated Lower Anogenital Squamous Lesions from the CAP-ASCCP Lower Anogenital Squamous Terminology Project” is presented by Mark H Stoler, MD, FCAP

Your host is Jill Kaufman, PhD. For comments about this webinar or suggestions for upcoming webinars, please contact Jill Kaufman at jkaufma@cap.org

THE WEBINAR WILL BEGIN MOMENTARILY. ENJOY!
Mark H. Stoler, MD, FCAP

- Professor of Pathology and Clinical Obstetrics and Gynecology at the University of Virginia Health System
- Associate Director of Surgical Pathology and Cytopathology
- Board of Directors and Past-President of the American Society for Clinical Pathology
- Steering Committee and Pathology Quality Control Committee for the NCI-sponsored ASCUS-LSIL Triage Study

© 2012 College of American Pathologists. All rights reserved.
Disclaimer

The College does not permit reproduction of any substantial portion of the material in this Webinar without its written authorization. The College hereby authorizes attendees of the CAP Webinar to use the pdf presentation solely for educational purposes within their own institutions. The College prohibits use of the material in the Webinar – and any unauthorized use of the College’s name or logo – in connection with promotional efforts by marketers of laboratory equipment, reagents, materials, or services.

Opinions expressed by the speaker are the speaker’s own and do not necessarily reflect an endorsement by CAP of any organizations, equipment, reagents, materials or services used by participating laboratories.
## Disclosure Information: Dr. Stoler

<table>
<thead>
<tr>
<th>Speaker</th>
<th>Interest /Activity Type</th>
<th>Entity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mark H. Stoler</td>
<td>Board or Advisory Board</td>
<td>Merck</td>
</tr>
<tr>
<td></td>
<td>Consultancy</td>
<td>Merck, Roche/Ventana/mtm, BD, Gen Probe/Hologic, Qiagen,</td>
</tr>
<tr>
<td></td>
<td>Royalties</td>
<td>Wolters Kluwer/Lippincott</td>
</tr>
</tbody>
</table>
Webinar Objectives

• Understand the biologic basis of the LAST recommendations: Axioms

• Understand how select biomarkers are used to improve accuracy and reproducibility of diagnosis in the revised terminology

• Understand the appropriate use for select molecular markers for HPV-related lesions of the lower anogenital tract body sites
44 Members and 13 advisors: Multidisciplinary panel of experts and thought leaders in the field, including...

- Expertise in pathology specialties, e.g.
  - Cytopathology
  - Dermatopathology
  - Gynecologic pathology
  - Surgical pathology

- Expertise in clinical specialties, e.g.
  - Dermatology
  - Gynecology & Gynecologic Oncology
  - Internal Medicine, Infectious Diseases & Medical Oncology
  - Colorectal Surgery & Urology
  - Epidemiology & Public Health

Project Overview
Webinar Objectives

• Understand the biologic basis of the LAST recommendations: Axioms

• Understand the how select biomarkers are used to improve accuracy and reproducibility of diagnosis in the revised terminology

• Understand the appropriate use for select molecular markers for HPV-related lesions of the lower anogenital tract body sites
What do we really know? = Axioms

- There is unified epithelial biology to HPV-related squamous neoplasia
  - Morphology is the visual synthesis of biology
  - Cytology and Histology are both valid representations of underlying biology
HPV Infection and Life Cycle

Differentiation Dependent HPV Expression: virion production & lesional transience

CIN1

LSIL
Condyloma

- Male vs Female
- Young vs Old
  - Same Histology
  - Same anatomic distribution
  - Same HPV types
PRECANCERS

• *The* precursor to HPV associated squamous carcinomas

• CIN2/3

• VIN2/3

• PIN2/3

• AIN2/3

• TIN2/3
HPV expression patterns in lesions of increasing severity

Doorbar J. Clinical Science 2006; 110, 525–541
Proliferative Phenotype Driven by E6/E7 Expression: no virions, persistence, risk of cancer
- Male vs Female
  - Same histology
  - Same anatomic distribution
  - Same HPV types
  - Same resulting cancers types
High Grade or High Risk or Precancer

CIN3

AIN3

AIN3

PIN3
IN2/3 is Noninvasive cancer

• Clear precursor relationship
• HPV types the same
• Invasive cancer develops from IN3
HSIL p16
**Morphology: Spectrum**

### Schematic Representation of SIL

<table>
<thead>
<tr>
<th>Condition</th>
<th>CIN/AIN grade 1</th>
<th>CIN/AIN grade 2</th>
<th>CIN/AIN grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Very mild to mild dysplasia</td>
<td>Moderate dysplasia</td>
<td>Severe dysplasia</td>
</tr>
<tr>
<td>Condyloma</td>
<td></td>
<td></td>
<td>In Situ carcinoma</td>
</tr>
<tr>
<td>LSIL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HSIL</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Morphologic Continuum**
### Biology: Infection vs Precancer

#### Schematic Representation of SIL

<table>
<thead>
<tr>
<th>Condition</th>
<th>Condyloma</th>
<th>CIN/AIN grade 1</th>
<th>CIN/AIN grade 2</th>
<th>CIN/AIN grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Very mild to mild dysplasia</td>
<td>Moderate dysplasia</td>
<td>Severe dysplasia</td>
</tr>
</tbody>
</table>

**Legend:**
- **Normal**
- **Condyloma**
- **CIN/AIN grade 1**: Very mild to mild dysplasia
- **CIN/AIN grade 2**: Moderate dysplasia
- **CIN/AIN grade 3**: Severe dysplasia
- **In Situ carcinoma**

**Notes:**
- Biology & Management
What do we know? = Axioms

• There is unified epithelial biology to HPV-related squamous neoplasia

• Each patient sample is only a statistical representation of the patient’s true biology
  • Clinical, Sampling and Diagnostic variation are all real issues
Sampling: A sample from one area does not necessarily represent the most significant disease.

Colposcopy
- **Not a gold standard** – significant variability in accuracy and sensitivity based on size, location and physical characteristics of the lesion and the skill and experience of the colposcopist.

Biopsy
- **Not a gold standard** – significant variation in diagnosis based on terminology used and training.
The Pathology is Geographically Linked to Sample Location: Lesions are Localized
Accuracy of Colpo Biopsy?

- OVERALL PERFECT AGREEMENT: 42%
- BX UNDERESTIMATES: 21%
- OVERESTIMATE or REMOVE: 36%
- Overall underestimation of CIN3+ = 42%
- Overall underestimation of CIN2+ = 26%
- **Biopsy is somewhat inaccurate and also potentially therapeutic**

H&E morphology
Interobserver Agreement

Robertson study

- Benign  Kappa 0.52
- CIN1    Kappa 0.24
- CIN2    Kappa 0.20
- CIN3+   Kappa 0.61

Kappa values: Strength of agreement

- < 0.20 Poor
- 0.21 - 0.40 Fair
- 0.41 - 0.60 Moderate
- 0.61 - 0.80 Good
- 0.81 - 1.00 Very good


What do we know? = Axioms

- There is unified epithelial biology to HPV-related squamous neoplasia
- Each patient sample is only a statistical representation of the patient’s true biology
- The more samples or data points available, the closer you get to the patient’s “true” biology
These results show that across various types of medical training, colposcopic impressions and colposcopically guided biopsies demonstrate similar sensitivities.

Colposcopy, like cytology and histology, is subjective, and the number of colposcopically guided biopsies taken is most strongly associated with sensitivity.

As women are referred to colposcopy based on increasingly sensitive screening tests, there is a need to have a diagnostic examination with the best accuracy possible.
**What do we know? = Axioms**

- There is unified epithelial biology to HPV-related squamous neoplasia
- Each patient sample is only a statistical representation of the patient’s true biology
- The more samples or data points available, the closer you get to the patient’s “true” biology
- The true biology represents “risk” for “cancer” at the current time and to a lesser extent “risk” over time
Classification systems for cervical squamous dysplasia

Bethesda 2001

CIN nomenclature

Dysplasia nomenclature

Papanicolaou classification
Risk assessment to guide clinical management
What do we know? Axioms / Truths

• The true biology represents “risk” for “cancer” at the current time and to a lesser extent “risk” over time
  • It is this “cancer risk” that drives clinical management
  • Clinical management choices are simple and limited:
    • routine follow-up = Normal
    • follow more closely = Productive HPV
    • Treat = Precancer
What do we know? = Axioms

- There is unified epithelial biology to HPV-related squamous neoplasia
- Each patient sample is only a statistical representation of the patient’s true biology
- The more samples or data points available, the closer you get to the patient’s “true” biology
- The true biology represents “risk” for “cancer” at the current time and to a lesser extent “risk” over time
- CIN2 is like ASCUS: an indistinct poorly defined entity
WHAT’S THE PROBLEM?
Histology: ‘CIN 2’

Not reflective of biology of HPV-related lesions

- CIN2 is poorly reproducible
- In ALTS, clinical site vs study pathologists
  - Only 46%, CIN2→CIN2
  - 27% upgraded to CIN3
  - 27% downgraded to CIN1 or normal

CIN2?

- The ASCUS of CIN
- An equivocation that is NOT reproducible
- A representation of bad sampling
- ~2/3s HSIL; ~1/3 LSIL
- A management safety net
CIN2

- A DISTINCT BIOLOGIC STAGE?
- UGLY LOOKING CIN1?
- NOT SO UGLY CIN3?
What do we know? = Axioms

- There is unified epithelial biology to HPV-related squamous neoplasia
- Each patient sample is only a statistical representation of the patient’s true biology
- The more samples or data points available, the closer you get to the patient’s “true” biology
- The true biology represents “risk” for “cancer” at the current time and to a lesser extent “risk” over time
- CIN2 is like ASCUS: an indistinct poorly defined entity
- Diagnostic variation can be improved by:
  - Limiting the number of tiers
  - The use of biologic markers
What do we know? Axioms / Truths

- Diagnostic variation can be improved by:
  - Limiting the number of tiers
  - The use of biologic markers, such as:
    - p16
    - Ki-67 or
    - ProEx C
WHAT IF?
ARE BIOMARKERS THE SOLUTION?

DATA ON ~1500 ADJUDICATED BIOPSIES WITH 3+ P16 STAINING: AJSP, August 2010

- NIL 5%
- CIN1 39%
- CIN2 77%
- CIN3 99%
THE AXIOMS

- There is unified epithelial biology to HPV-related squamous neoplasia

- Each patient sample is only a statistical representation of the patient’s true biology

- The more samples or data points available, the closer you get to the patient’s “true” biology

- The true biology represents “risk” for “cancer” at the current time and to a lesser extent “risk” over time

- CIN2 is like ASCUS: an indistinct poorly defined entity

- Diagnostic variation can be improved by:
  - Limiting the number of tiers
  - The use of biologic markers
False Premises: The Anti-Axioms

- Biopsy is perfect representation and contains everything you need to know to manage the patient
- Everybody reads the biopsy the same way
- CIN2 is a distinct biologically defined category
- Interpretative variation can be eliminated through education on morphologic criteria alone
False Premise

- Change is easy
Work Group 4 - Members

David Wilbur, M.D. – Co-Chair
Mark Stoler, M.D. – Co-Chair
Joel Bentz, M.D.
Christina Kong, M.D.
Bradley Quade, M.D.
Mary Schwartz, M.D.
Sarah Bean, M.D. - advisor
WG 4 Issues

- Assess the use of molecular markers in conjunction with morphology for HPV-related lesions
- Potential markers?
- Which are ready for primetime?
- How should they be used?
- Does marker use define any classification?
- Do markers affect interobserver variability?
- Single marker vs. combinations of markers?
- Does marker use affect clinical management?
Comprehensive literature review

- 2291 relevant articles identified (1985-2012)
- Pre-specified criteria
  - Study type
  - Scope
  - Number of subjects
- Systematic title/abstract and full text review process
- 72 articles for data extraction (53 for p16)
- Vast majority – cervix related
- Prospective and histology-adjudicated studies given most weight
Quality of evidence review

• Only WG with this review

• Independent evaluation of the evidence quality (18 articles)

• Conducted by Evan Myers, M.D., M.P.H.

• Use of terminology for qualification of the recommendations
  - “recommend” – WG’s recommendation is unlikely to change based on future studies
  - “suggest” – WG’s recommendation is most likely correct but could be better supported by additional data
Key Question #1

- What (if any) are the molecular markers and when should they be used?
- Utility on histologic specimens
- Aid to differential diagnosis
- Potentially definitional of the patient’s biologic state
Markers evaluated after 1\textsuperscript{st} tier review

- p16
- Ki67 (Mib1)
- ProExC
- L1
- HPV 16/18 mRNA
- Telomerase (TERC)
- HPV genotyping
Adaptability across lower anogenital tract

- Most studies focus on cervix
- Few studies available for other sites

- All studies for other sites show similar results to cervix.
- Given similarity of underlying HPV-associated biology;
- WG4 concludes that recommendations should apply across all HPV-related lower anogenital tract lesions.
Key Question #2

• Is any biomarker ready for prime time use?
  • It could be used commonly
  • It is reliable
  • Refines diagnostic issues
WG4 Biomarkers

1. **p16 IHC is recommended** when the H&E morphologic differential diagnosis is between precancer (—IN 2 or — IN 3) and a mimic of precancer (e.g., processes known to be not related to neoplastic risk such as immature squamous metaplasia, atrophy, reparative epithelial changes, tangential cutting).

   - Strong and diffuse block-positive p16 results support a categorization of precancerous disease.
cap.org

High-Grade SIL

Follow-up Clinical Management

Increasing Cancer Risk

Histologic Interpretation

LAST Terminology Diagnosis

A

HSIL vs. Mimic

p16 IHC

Negative

Increasing Cancer Risk
Transitional Cell Metaplasia
2. If the pathologist is entertaining an H&E morphologic interpretation of –IN 2 (under the old terminology, which is a biologically equivocal lesion falling between the morphologic changes of HPV infection [low-grade lesion] and precancer), p16 IHC is recommended to help clarify the situation.

- Strong and diffuse block positive p16 results support a categorization of precancer. Negative or non-block-positive staining strongly favors an interpretation of low-grade disease or a non-HPV associated pathology.
Increasing Cancer Risk

CIN1 → Low-Grade SIL

CIN2 → p16 IHC

CIN3 → High-Grade SIL

Histologic Interpretation

LAST Terminology Diagnosis

Follow-up Clinical Management

Treatment
Recommendation #2 Notes

- p16 should not be used if the H&E morphologic differential diagnosis is between low grade disease (CIN 1) and negative, as CIN 1 can be either p16 negative or positive.

- If the pathologist’s histologic diagnosis is “obvious” CIN 1, the WG does not recommend further IHC.
  - There is insufficient evidence to determine whether there is a difference in the natural history between p16 positive and p16 negative CIN 1. Hence at the present time, it is recommended that clinical management of CIN 1 be based on the histologic diagnosis alone.
Rationale for recommendations #1 and #2

• In the largest prospective adjudicated study and other supporting studies, diffuse strong (block positive) staining with p16 showed similar accuracy for high grade disease when compared to an adjudicated histology standard.

• p16 IHC improves the accuracy of a single pathologist’s interpretation of high grade vs. low grade disease relative to an adjudicated pathology panel.

• Addition of a p16 result leads to a more accurate prediction of the patient’s risk for high grade disease.
Recommendations #1 & 2

• Strength of Evidence – Dr. Myer

• “The quality of the evidence for the test characteristics of H&E + p16 is moderate-high.”

• “The quality of the evidence for improved consistency of readings with p16 is high.”
Biomarkers in HPV-Associated Lower Anogenital Squamous Lesions Recommendation 1

** Strong and diffuse block positive p16 results support a categorization of precancerous disease.

* Mimic of HSIL means: morphologies that can be confused with HSIL such as immature squamous metaplasia, atrophy, repair/regeneration due to inflammation; all of which are within the broad NILM category

** Strong and diffuse block positive p16 results support a categorization of precancerous disease.
Biomarkers in HPV-Associated Lower Anogenital Squamous Lesions

**Recommendation 2**

- **BIOPSY**
  - Morphologic
  - IN 2

- **p16 stain**

  * Strong and diffuse block positive p16 results support a categorization of precancerous disease.

- **p16-negative LSIL or non-HPV-associated pathology**

- **p16-positive* HSIL**

* Copyright © 2012 College of American Pathologists and American Society for Colposcopy and Cervical Pathology. All rights reserved.
3. p16 is recommended for use as an adjudication tool for cases in which there is a professional disagreement in histologic specimen interpretation, with the caveat that the differential diagnosis includes a precancerous lesion (−IN 2 or −IN 3).
A number of studies address interobserver variability in the interpretation of lower anogenital tract squamous lesions. These studies all show that there is substantial improvement in agreement between observers when p16 IHC is used. Therefore in association with recommendation #1, the addition of p16 provides a more objective adjudication of the differential diagnosis than does H&E histologic assessment alone.
Recommendation #3

- Strength of Evidence – Dr. Myer

- “The quality of the evidence is high.”
Biological markers in HPV-associated lower anogenital squamous lesions

Recommendation 3

- **p16 negative LSIL or HSIL mimic or non-HPV-associated pathology**
- **p16 positive* HSIL**

*Strong and diffuse block positive p16 results support a categorization of precancerous disease.
4. **WG4 recommends against** the use of p16 IHC as a routine adjunct to histologic assessment of biopsy specimens with morphologic interpretations of negative, –IN 1, and –IN 3.
4. SPECIAL CIRCUMSTANCE

a) p16 IHC is recommended as an adjunct to morphologic assessment for biopsy specimens interpreted as ≤ IN 1 that are at high risk for missed high-grade disease, which is defined as a prior cytologic interpretation of HSIL, ASC-H, ASC-US/HPV16 +, or AGC (NOS).

- Any identified p16 positive area must meet H&E morphologic criteria for a high-grade lesion to be reinterpreted as such.
Based on the high sensitivity of p16 for precancerous lesions, areas of small or equivocal high grade disease have been identified on histologic sections using p16, which were not readily identifiable on H&E sections alone.

In a “high risk” situation, p16 block positive areas are most likely to represent precancerous disease.
Galgano et al, 2010; figure 4 (high risk biopsy, initially read as negative)
Recommendation #4

- Strength of Evidence – Dr. Myer

- “...., the quality of the evidence for superior sensitivity of H&E + p16 is high-moderate.”
Biomarkers in HPV-Associated Lower Anogenital Squamous Lesions
Recommendation 4

BIOPSY
Morphologically unequivocal NILM -IN 1 -IN 3

NO
p16 stain

NILM
LSIL
HSIL
Biomarkers in HPV-Associated Lower Anogenital Squamous Lesions

Recommendation 4a

**BIOPSY**
Morphologic < -IN 1 identified as high risk:

Prior cytology of HSIL, ASC-H, ASC-US/HPV16 +, or AGC (NOS)

* Strong and diffuse block positive p16 results support a categorization of precancerous disease. Any identified p16-positive area must meet H&E morphologic criteria for a high-grade lesion to be reinterpreted as such.

**p16 stain**

- p16-negative LSIL or non-HPV-associated pathology
- p16-positive* HSIL
Biomarkers in HPV-associated Lower Anogenital Squamous Lesions

- Any identified p16-positive area must meet H&E morphologic criteria for a high-grade lesion to be reinterpreted as such.

- Strong and diffuse block positive p16 results support a categorization of precancerous disease.
Upcoming LAST Sessions

• CAP-ASCCP LAST Project will be presented in full (including terminology + biomarker usage):
  • ASCP Meeting, Boston, MA, Course 1007, Nov 1, 2012: 4:15 pm
  • ASC Meeting, Las Vegas, NV, Current Issues, Nov 5, 2012: 8 am
Next in the “Hot Topics in Pathology” Webinar Series

• The Legal Status of Patents on Laboratory Tests
  Wednesday, October 10, 11:00-12:00 PM Central
    o Jack Bierig, JD

• This webinar will focus on the conceptual underpinnings of the United States patent laws, explain how these laws diverge from medical ethics, and explore their application in the area of laboratory medicine. These issues have inherent intellectual interest for pathologists and important economic consequences for genetic and other forms of laboratory testing.
### Archived Webinars on Getting Started and Taking Next Steps in Molecular Pathology

- **The Why, What, and How of Identifying Patients at Risk for Hereditary Cancer Syndromes in Surgical Pathology Practice** (Alexis Carter, MD, FCAP) + other alexis

- **Molecular Tests and Pathology Practice: What Every Community Pathologist Should Know**/Clinical Requests for Molecular Tests (Alexis B Carter, MD, FCAP)

- **How to Build and Fund a Viable Molecular Lab** (Frederick Kiechle, MD, PhD, FCAP)

- **Cancer: The Critical Role of Pathology in Personalized Health Care** (Eric Walk, MD, FCAP)

### Archived Webinars on Genomic Analysis, Large Molecular Panels, Exome, Genome

- **Whole Genome Analysis as a Universal Diagnostic: A Pathologist’s Perspective** (Mark Boguski MD, PhD, FCAP)

- **Clinical Use of Whole Genomic and Whole Exome Today** (Paula North, MD, FCAP and David Bick MD)

- **Next-Generation Sequencing for the Clinical Laboratory** (Karl V. Voelkerding, MD, FCAP)

- **Next-Generation Sequencing** (John Pfeifer, MD, FCAP)
## Archived Webinars on Organ Based Pathology

<table>
<thead>
<tr>
<th>Topic</th>
<th>Speaker(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Diagnosis for Lung Cancer Patients</td>
<td>Philip T. Cagle, MD, FCAP</td>
</tr>
<tr>
<td>Molecular Diagnosis for Colorectal Cancer Patients</td>
<td>Antonia R. Sepulveda MD, PhD, FCAP</td>
</tr>
<tr>
<td>Molecular Markers in Breast Cancer</td>
<td>David G. Hicks, MD, FCAP</td>
</tr>
<tr>
<td>Molecular Testing Guidelines for Selection of EGFR and ALK Tynsine</td>
<td>Neal I. Lindeman, MD, FCAP and Marc Ladanyi, MD, FCAP</td>
</tr>
<tr>
<td>Karnase Inhibitors in Non-Small Cell Lung Cancer</td>
<td></td>
</tr>
<tr>
<td>Molecular Diagnostics of Lung Cancer</td>
<td>John Iafrate, MD, PhD</td>
</tr>
<tr>
<td>Breast Cancer and Molecular Tests</td>
<td>Kenneth J. Bloom, MD, FCAP</td>
</tr>
<tr>
<td>Molecular Testing and Hematopathologic Conditions</td>
<td>David Czuchlewski, MD, and Mohammad Vasef, MD, FCAP</td>
</tr>
<tr>
<td>Molecular Genetics of Pancreatic Neoplasms</td>
<td>Ralph Hruban, MD- also on Genomic Analysis</td>
</tr>
</tbody>
</table>

© 2012 College of American Pathologists. All rights reserved.
Coming Soon…

- CAP/IASLC/AMP Molecular Testing Guidelines for Selection of Lung Cancer Patients for EGFR and ALK Tyrosine Kinase Inhibitors
  - Archives of Pathology and Laboratory Medicine
  - Journal of Thoracic Oncology
  - The Journal of Molecular Diagnostics
The CAP has created the Pathology Resource Guides, a new tool to assist pathologists in understanding key emerging technologies. These Resource Guides are a new CAP member benefit available at no charge.

**Genomic Analysis (large molecular panels, exome, genome)**  
**Digital Pathology**  
**In Vivo Microscopy**  
**Molecular Diagnostic**—LAUNCHED AT CAP ‘12

Register through the [CAP member tab](#). You will receive periodic updates for two years.

Questions? Contact [capguides@cap.org](mailto:capguides@cap.org).
A New CAP Tool- Short Presentations On Emerging Concepts (SPECs)

• **Pathology SPECs are:**
  - Prewritten PowerPoint presentation on emerging topics where molecular testing plays a key role in patient management.
  - Designed for pathologists to customize and use for educating other physicians and health care leaders in their communities.
  - Focused on molecular tests that are actionable to patient care today.

• **Now Available:**
  - Emerging Concepts in the Workup of Colorectal Cancer
  - Emerging Concepts in Therapeutic Guidance for Metastatic Melanoma
  - Emerging Concepts in the Diagnosis and Workup of Thyroid Cancer
  - Emerging Concepts in Colorectal Cancer Hereditary Non-Polyposis Cancer (Lynch Syndrome)
  - Emerging Concepts in the Workup of Polycythemia and Thrombocytethemia: JAK2

• **To register**, go to the [Reference Resources and Publications](http://cap.org) tab on cap.org. You do **not** need to be a member to utilize this free tool.
# CAP Learning – HPV

<table>
<thead>
<tr>
<th>Course</th>
<th>Learning Objectives</th>
</tr>
</thead>
</table>
| **Archives Applied – HPV (SAM Eligible)** CME/SAM – 1.0                | - List appropriate uses of HPV testing both in cytology triage and screening.  
- Propose an appropriate follow-up strategy and indicate whether HPV testing is appropriate when given a defined clinical scenario and cytology result.  
- Describe why inappropriate HPV testing may lead to patient harm and increased costs.                                                                                                                                                                                                                                              |
| **Testing for Human Papillomavirus in the Vaccine Era (SAM Eligible)**  CME/SAM – 2.5 | - Discuss the basic molecular biology of HPV and the natural history of HPV infection.  
- Explain the epidemiology of HPV and cervical cancer.  
- Describe how the new vaccines for HPV are used clinically and the potential impact of their use on the incidence of cervical cancer.  
- Explain the methods utilized to detect HPV with the operating characteristics of each.  
- Ensure proper test validation and quality assurance practices related to test performance.                                                                                                                                                                                                                   |
| **CAP 2012 PAP PT: Online Education Activity** CME/CE – 5.0            | - Select the correct General Category for a PAP test using The Bethesda System.  
- Interpret a PAP test given the clinical information, history, and virtual slides.  
- Determine an appropriate management strategy using the 2006 ASCCP guidelines.                                                                                                                                                                                                                                                                                  |
| **CAP Practical Guide to Gynecologic Cytopathology: Morphology, Management and Molecular Methods – Chapter 3: HPV** CME/SAM/CE – 0.0 | Image-rich guide that extensively covers the principles of gynecologic cytopathology. The 270-page reference volume takes a thorough look at practical matters such as evaluations of patients and their specimens as well as criteria to determine specimen adequacy. You will find comprehensive reviews of the morphology of the vast majority of entities both benign and malignant that are routinely identified in Pap tests.                                                                 |

© 2012 College of American Pathologists. All rights reserved.
The CAP Learning Portal landing page on the cap.org website replaces the previous Education Programs page design. A user must log into cap.org in order to access further information.

The CAP Learning Portal includes new tools to support the learning needs of pathologists such as:

- Learning Options search/catalog
- Competency Model for Pathologists
- Personal Progress Check (member only tool)
- My Learning Plan (member only tool)
- Help Center

Benefits
- Increase effectiveness to plan and manage learning
- Increase efficiency to target learning needs and identify premium learning solutions
- Increase satisfaction with learning solutions that meet specific learner needs
- Increase capability to maintain professional certifications

© 2012 College of American Pathologists. All rights reserved.
To learn more...

- For more details and to register for/access to HPV educational offerings:
  1. Log in to the cap.org website
  2. Click on Launch Portal
  3. Click on the Learning Options tab
  4. Type HPV in the Search box. A list of available learning options displays
See, Test & Treat® brings cancer screenings to women in need!

- See, Test & Treat is a CAP Foundation-funded program that brings free, same-day cervical and breast cancer screening, diagnoses and follow-up care to women in medically underserved communities across the U.S.

- CAP member pathologists’ partner with gynecologists, radiologists and other medical professionals to lead See, Test & Treat programs in hospitals, clinics and other facilities

- Women learn the importance of preventive care through annual exams, a Pap test, Mammogram and a healthy lifestyle

See, Test & Treat Needs Your Financial Support
Visit foundation.cap.org and click on DONATE!
THANK YOU!

Thank you for attending our webinar “Biomarkers in HPV-associated Lower Anogenital Squamous Lesions from the CAP-ASCCP Lower Anogenital Squamous Terminology Project” by Mark H. Stoler, MD, FCAP.

For comments about this webinar or suggestions for upcoming webinars, please contact Jill Kaufman, PhD, Director of Personalized Health Care at jkaufma@cap.org

NOTE: There is no CME/CE credit available for today’s free webinar.