WOMEN'S HEALTH 2020:
Beyond the Annual Visit

Advances in Cervical Cancer Screening

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omnia EDUCATION

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Learning Objectives

- Discuss current updated recommendations for cervical cancer screening (CCS)
- Describe the unmet needs associated with current CCS triage options
- Explain the diagnostic benefits provided by novel dual-staining cytology in CCS triage
- Formulate strategies that maximize the diagnostic accuracy of CCS triage in clinical practice

ACS/ASCCP/ASCP
2012 Cervical Cancer Screening Guidelines[1]

- Cervical cancer screening should begin at age 21 with cytology alone every 3 years until age 29
- 30-65 yrs: "co-testing" (Pap & HPV) every 5 years (preferred)
- 30-65 yrs: cytology alone every 3 years (acceptable)
- *Primary HPV testing is not recommended for most clinical settings*

1. *CA Cancer J Clin*. 2012:62(3);147-172.

US Preventive Services Task Force (USPSTF)
2018 Cervical Cancer Screening Guidelines[1]

Population	Recommendation	Grade (What's This?)
Women aged 21 to 65 years	The USPSTF recommends screening for cervical cancer every 3 years with cervical cytology alone in women aged 21 to 29 years. For women aged 30 to 65 years, the USPSTF recommends screening every 3 years with cervical cytology alone, every 5 years with high-risk human papillomavirus (hrHPV) testing alone, or every 5 years with hrHPV testing in combination with cytology (cotesting).	A

1. https://www.uspreventiveservicestaskforce.org

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American Cancer Society (ACS)
2020 Cervical Cancer Screening Guidelines[1]

- Cervical cancer screening should begin at age 25
- Those aged 25-65 should have a primary HPV test every 5 years
- If primary HPV testing is not available, screening may be done with either a co-test (Pap and HPV) every 5 years or a Pap test alone every 3 years

1. https://www.cancer.org/cancer/cervical-cancer

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Risk-based Clinical Management
Utilized for Two Decades

- Original 2001 ASCCP Consensus Guidelines for cervical cancer screening results were risk-based
- Fundamental premise is that women with the same risk of CIN3+, regardless of the combination of conditions causing the risk, are managed equivalently
- New 2019 ASCCP Guidelines incorporate clear risk-based thresholds and a new management app

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2019 ASCCP Management Options[1]
Cervical Cancer Screening Results

- 6 management options based on risk of ≥CIN3:

Expedited treatment	**≥60%** *(immediate risk)*
Treatment or colpo	**25% - <60%** *(immediate risk)*
Colposcopy	**4% - <24%** *(immediate risk)*
Retest – 1 yr	**0.55% - <4%** *(5-yr / immed risk)*
Retest – 3 yrs	**0.15% - <0.55%** *(5-yr risk)*
Retest – 5 yrs	**<0.15%** *(5-yr risk)*

1. Cheung LC, et al. *J Low Genit Tract Dis*. 2020;24(2):90-101.

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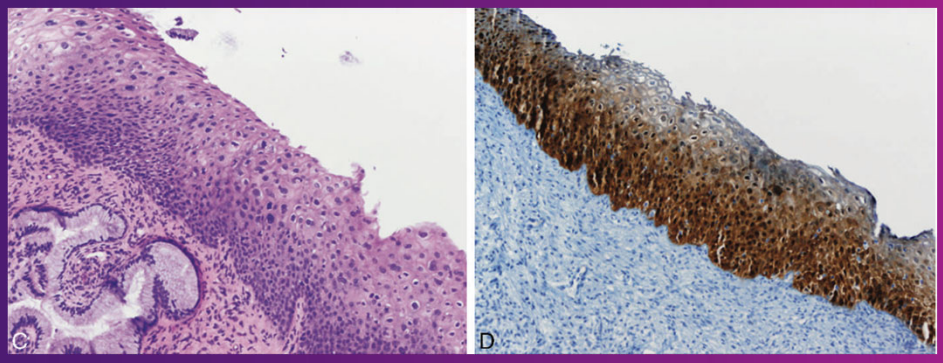
p16^{INK4a} Immunohistochemistry – CIN 2



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p16^{INK4a} Immunohistochemistry
Differences when using it for histology and cytology

- When used for histology, there are architectural features available – classify as positive when there is diffuse, block-like staining of basal/parabasal layers
- In non-neoplastic cervix, there are often individual epithelial cells that stain strongly with p16 – these present a problem for p16 IHC of cytology specimens
- Lack of architecture in cytology specimens is overcome by utilizing dual staining with Ki-67

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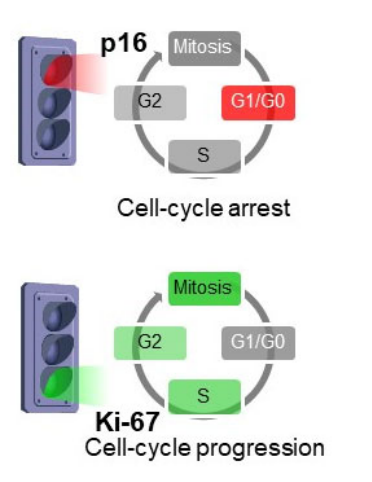
p16/Ki-67 Dual-Staining Cytology

Detecting the molecular driver event



Co-expression of p16 and Ki-67:

- Indicates cell cycle deregulation
- Hallmark of transforming HPV infections

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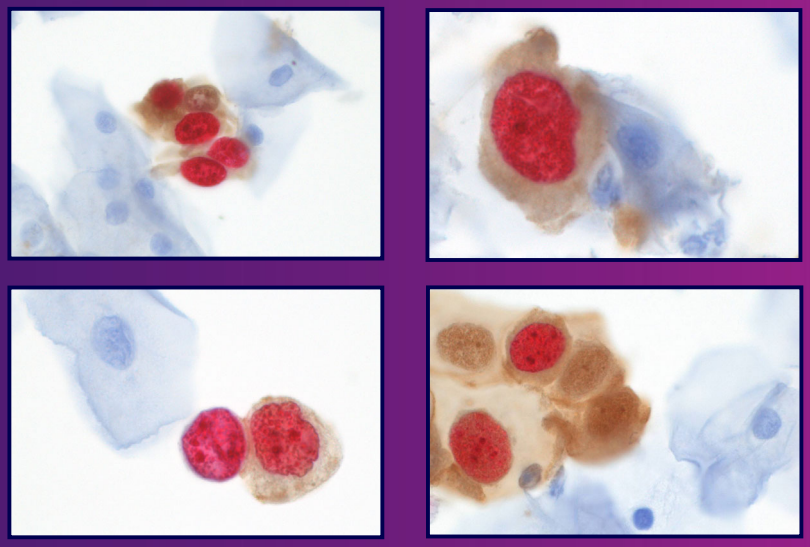
p16/Ki-67 Dual-Staining Cytology



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IMPACT – Primary HPV Screening (25-65 yrs)

Dual stain vs. cytology performance in 12 "other" HPV(+)

Measure	CPR Result ≥CIN3		
	Dual Stain	Pap Cytology	Difference
Sensitivity (%)	**86.2**	**67.0**	**19.1** (9.8, 28.4)
Specificity (%)	**55.6**	**64.8**	**-9.2** (-11.3, -5.8)
PPV (%)	**6.1**	**6.0**	**0.1** (-0.7, 0.9)
1 - NPV (%)	**0.8**	**1.7**	**-0.8** (-1.3, -0.3)

CINtec PLUS Cytology. Package Insert. FDA;2020.

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IMPACT – Primary HPV Screening (25-65 yrs)

Dual stain vs. cytology performance in HPV 16(+)

Measure	CPR Result ≥CIN3		
	Dual Stain	Pap Cytology	Difference
Sensitivity (%)	**94.0**	**78.6**	**15.4** (7.98, 23.4)
Specificity (%)	**39.2**	**55.1**	**-15.9** (-20.7, -11.0)
PPV (%)	**27.5**	**30.1**	**-2.6** (-5.4, 0.2)
1 - NPV (%)	**3.6**	**8.7**	**-5.1** (-8.3, -1.7)

CINtec PLUS Cytology. Package Insert. FDA;2020.

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Dual Stain *(CINtec PLUS Cytology)*
Indications for primary HPV screening – 25-65 yrs

- To be used in women 25-65 yrs with 12 other hrHPV (+) test results in primary HPV screening to determine need for referral to colposcopy
- To be used in women 25-65 yrs with HPV 16/18 (+) test results in primary HPV screening where the CINtec PLUS Cytology results will be used in conjunction with the physician's assessment of patient screening history, other risk factors, and professional guidelines to guide patient management

CINtec PLUS Cytology. Package Insert. FDA;2020.

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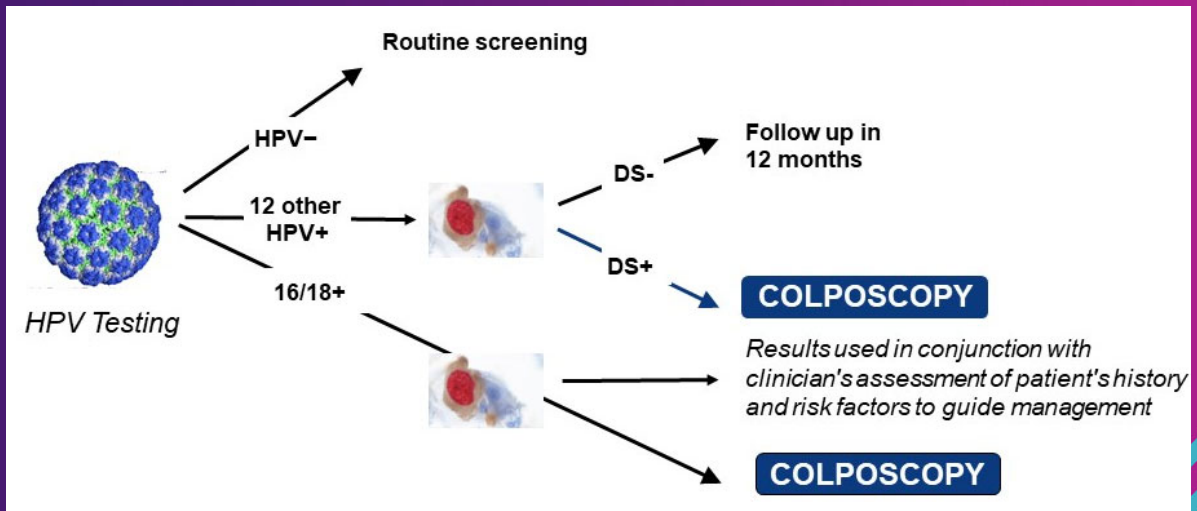
Primary HPV Screening *(25-65 yrs)*
Dual-staining algorithm



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Case #1
Use when "co-testing"

- 35-year-old G2P0 with no previous cervical disease
- Her cytology result was NILM and her HPV test came back as positive for 12 "other" HPV genotypes
- You request dual staining be performed, and the lab calls the sample "positive"
- Based on the recommended protocol, you schedule a colposcopy

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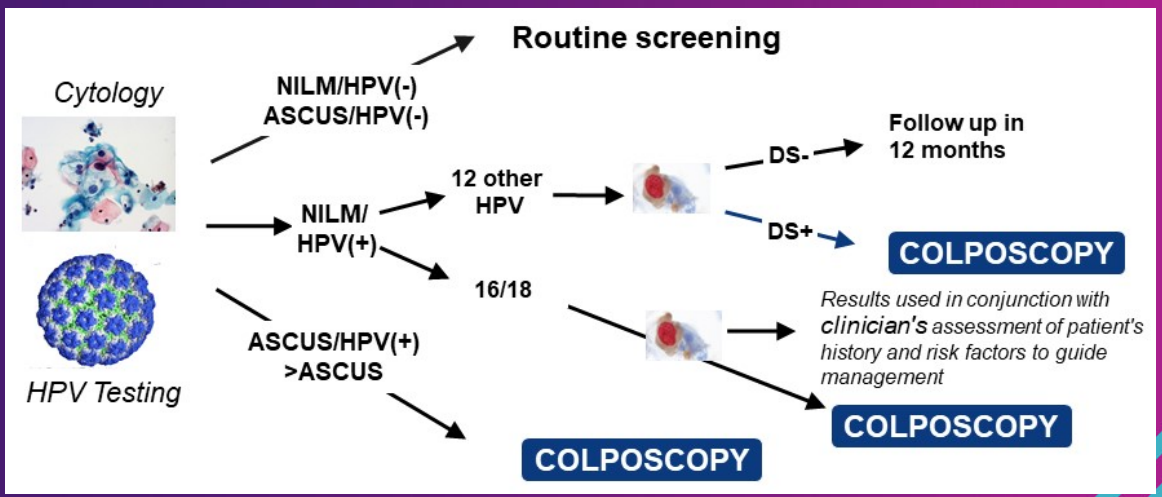
Co-testing with Cytology & HPV *(30-65 yrs)*
Dual-staining algorithm



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Case #2
Use with HPV primary screening

- 47-year-old G3P2 with history of CIN 2,3 four years ago and had a LEEP – margins unknown
- She is HPV positive for HPV 16
- Dual staining was performed, and the lab calls the sample "positive"
- After discussing options with the patient, you decide to go straight to a LEEP

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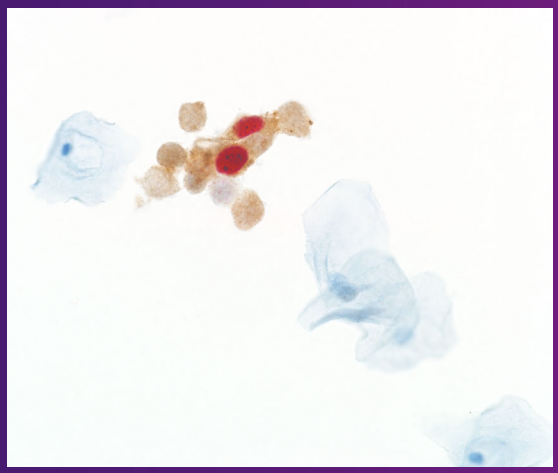
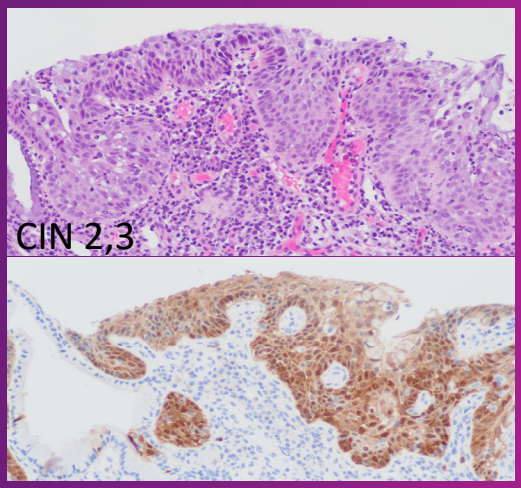
Case #2
Use with HPV primary screening





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Primary HPV Screening *(25-65 yrs)*
Dual-staining algorithm