

# **Cervical Cancer Screening in the 21<sup>st</sup> Century**

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# Conflict of Interest

**I have no investment in, nor do I receive research funding, consulting fees or honoraria from any drug or device manufacturer.**

# Cervical Cancer

**Worldwide 3<sup>rd</sup> most common cancer**

**Rare in developed countries**

**Pap test screening**

**Treatment of CIN**

# Cervical Cancer

## Etiology

**1900's Agent transmitted by sex**

**1960's GC or Chlamydia**

**1970's HSV**

**1980's HPV**

# **Pap Test Screening**

**Introduced in the 1950s in the US**

**Yearly testing became routine despite  
lack of data**

**Colposcopy and cryosurgery early  
1970s**

# **Pap Test Screening**

**70% Reduction**

**In**

**Cervical Cancer**

# Pap Test Screening

**Will never eliminate cervical cancer**

**Poor compliance**

**Immigrant populations**

**Disease factors**

**No insurance for prevention (USA)**

# Colposcopy

**Introduced USA 1970**

**Identify CIN lesions**

**Office treatment (cryotherapy)**

**Goal was to eliminate all CIN!!!**

**70% reduction in cervical cancer**

# CIN 3



# Colposcopy

**1970s: Large lesions**

**2000+: Many small, insignificant lesions**

**Are we over-treating?**

# **Cervical Cancer 2000+**

**Uncommon enough to consider  
changing strategies of  
Yearly cytology  
Treatment of all lesions**

# 2006 Consensus Conference

All major US specialties

OB-Gyn

Pathology

Gyn Oncology

Cytology

Am Cancer Soc

NCI

Family Med

NIH

Internal Med

etc

# **2006 Consensus Conference**

**Guidelines in Am Journal OB-Gyn**

**Best source:**

**[www.asccp.org](http://www.asccp.org)**

# **Cervical Cancer Screening 2000+**

## **2006 Guidelines**

**Agreement that there should be selected changes to the philosophy of annual screening for all sexually active women.**

# **Cervical Cancer Screening 2000+**

## **2006 Guidelines: Screening Changes**

**Adolescents**

**Reproductive age**

**Post-hysterectomy**

**Menopause**

# **Cervical Cancer Screening 2000+**

## **Adolescent Screening**

**Incidence of Cervical Cancer**

**1 : 10<sup>6</sup> per year**

**Prevalence of HPV**

**30%**

**Result: Many abnormal cytology  
specimens but little significant  
disease**

# Cervical Cancer Screening 2000+

## Adolescent HPV

**91% regression of CIN I in 36 months**

(Moscicki 2004)

**Many infections disappear in < 3 mo**

(Castle, Sept 2006 pers comm)

**“Persistent disease” is new infection**

(Castle and Schiffman, Sept 2006 pers comm)

# **Cervical Cancer Screening 2000+**

## **Adolescent HPV**

**30% Prevalence**

**>90% resolve spontaneously  
in weeks to months**

**Frequent screening leads to  
over-treatment**

# Cervical Cancer Screening 2000+

## Adolescent HPV

HPV to cancer takes 20 years on average, with the longest interval from CIN 3 to cancer (Hildesheim, 1999)

# **Cervical Cancer Screening 2000+**

## **Adolescent Screening**

**Do not start screening immediately  
when sexually active  
(STDs and contraceptives)**

**Yearly cytology to age 30**

# **Cervical Cancer Screening 2000+**

## **Reproductive Age**

**Yearly cytology screening to age 30**

**Decrease screening interval > 30 yrs**

**Every 2 yr cytology**

**Every 3 yr cytology + HPV**

# Cervical Cancer Screening

## Sensitivity $\pm$ HPV-DNA\*

	Pap	HPV	Both
Germany	34	86	94
UK	72	97	100
Mexico	57	94	98
Costa R	80	86	92
So Africa	74	85	87
China	94	98	100
US	60	100	100

\* CIN2+, %

# **Cervical Cancer Screening**

## **Age 30+**

**Cervical Cytology + HPV testing q 3yrs**  
**Neg / Neg better predictor of no**  
**HSIL in next 3-5 years than 3**  
**neg cytology**

# **Cervical Cancer Screening 2000+**

## **Screening after hysterectomy**

**Vaginal cancer is extremely rare**

**Most abnormal paps are false +**

**Atrophy**

**Vaginal HPVs**

**Screening leads to anxiety and**

**over-treatment**

# **Cervical Cancer Screening 2000+**

**9,610 vaginal paps post-hysterectomy**

**1.1% abnormal**

**No VAIN III**

**Pearce, NEJM**

**1996**

# **Cervical Cancer Screening 2000+**

## **Post-Hysterectomy**

**Cease screening after total  
hysterectomy**

**(Immunocompromised)**

**(Recent CIN III)**

**(ACOG, ACS, USPSTF)**

# Cervical Cancer Screening 2000+

## Postmenopause

Cervical cancer is **rare** after age  
50 in frequently screened  
populations

### Exceptions:

Immunocompromised

Recent CIN 3

DES exposed

# **Cervical Cancer Screening 2000+**

**Stop screening at some age**

**Disagreement on age**

**Cx CA takes 20+ yrs to develop**

# **Cervical Cancer Screening 2000+**

**What is the future of Cervical  
Cytology testing?**

# **Cervical Cancer Screening 2000+**

**Prediction:**

**Cervical cancer screening will be  
accomplished with HPV testing**

# HPV Screening

## Costa Rica study \*

	HPV Neg	HPV Pos
Pap Neg	0.26%	5.24%
Pap ASC-US	0.00%	18.75%
Pap LSIL	0.00%	9.84%
Pap HSIL	7.41%	43.62%

\*>10,000 women, cum rate over 7 yrs,  
conven cytol

# HPV Screening

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conven cytol

# HPV Screening

Lessons from Costa Rica study

HPV Neg, ASC-US = Normal

HPV Neg, LSIL = Normal

# HPV Screening

## Kaiser study\*

	HPV Neg	HPV Pos
Pap Neg	0.23%	2.23%
Pap ASC-US	2.92%	6.15%
Pap LSIL	6.67%	10.53%
Pap HSIL	12.50%	69.57%

\*>5,000 women, cum rate over 10years,  
conven cytol

# HPV Screening

## ALTS\*

	HPV Neg	HPV Pos
Pap neg	0.79%	3.88%
Pap ASC-US	1.26%	6.94%
Pap LSIL	3.17%	16.39%
Pap HSIL	25.00%	40.28%

\*N>2K, cum rate HSIL+ over 2 yrs

# **Cervical Cancer Screening 2000+**

**Will cytology be available?**

**US Cytotech schools are closing  
(Computer interpretation)**

**Rarer abnormalities after vaccine  
? expertise**

# HPV Screening

## Current test

HR HPV types mixed

False neg and pos

(No clinical use for LR test)

# HPV Screening

Very likely that a **PCR-based HPV test** will supplant cytology screening within the next few yers

**Good performance characteristics**

# HPV Screening

**Future test problem**

**PCR based and type-specific**

**Too sensitive ?**

# HPV Screening

**Problem with HPV-only screening**

**Adolescent positives**

# HPV Screening

Adolescent screening

~30% positive

Over treatment = OB problems

# HPV Screening

Adolescent solutions ???

**Start screening later (eg, 21-25)**

**(No cancer before age 21)**

**Never treat unless CIN 3**

**CIN 1 >90% regress**

**CIN 2 ~50% regress**

**CIN 3 ~30% regress**

# HPV Screening

## Reproductive age

HPV less common >30 yrs

Type-specific testing

Many Pos regress spontaneously

Persistent Pos = Colpo

# HPV Screening

Post-Reproductive age

Type-specific testing

Many “vaginal types”

# **Cervical Cancer Screening 2000+**

**What is the effect of the  
HPV vaccine on the use of  
Cytology testing?**

# **Cervical Cancer Screening 2000+**

## **HPV Vaccination Limitations**

**Current vaccine misses 30%  
of the HR types**

**Vaccine must be given before  
exposure**

**>90% immunization before  
“herd immunity”**

# **Cervical Cancer Screening 2000+**

**HPV Vaccination Limitation  
Extreme cost!**

# Cervical Cancer Screening 2000+

## New vaccines

**Better multivalent vaccines are  
currently in research trials**

**>90% protection**

# **Cervical Cancer Screening 2000+**

## **HPV Vaccination Limitations**

**No changes in cytology screening  
for at least 20 years**

# **Cervical Cancer Screening 2000+**

## **Societal Changes**

# **Cervical Cancer Screening 2000+**

**Will cytology be available?**

**Cytotech schools are closing**

**(Computer interpretation)**

**Rarer abnormalities after vaccine**

**? Expertise**

# **Cervical Cancer Screening 2000+**

**What is the role of the annual pelvic exam?**

**No data to support its use as a screening test (asymptomatic women)**

# Cervical Cancer Screening 2000+

## Conclusions:

Cytology screening will slowly fade

HPV testing will be used for  
a few years

HPV vaccination **is** the future

**Thank You**



# Cervical Cancer Screening 2000+

# **Cervical Cancer Screening 2000+**

**Female preventive health exams: USA**

**Too few family practitioners**

**Too few general internists**

**Most female exams are and will be  
performed by OB-Gyns**



# Cervical Cancer Screening 2000+

## 2006 Guidelines

**Do not rush to screen newly  
sexually active teens**

**Do not screen women without uterus  
(unless recent CIN 3)**

**Less frequent screening after 3 neg**

**Stop screening at some age  
(? 65, ?70)**

# **Cervical Cancer Screening 2000+**

## **Changes**

**Test frequency**

**Type of test**

**Influence of vaccines**

**Societal influences**