Biomedical Engineering for Global Health

Lecture Thirteen

Outline

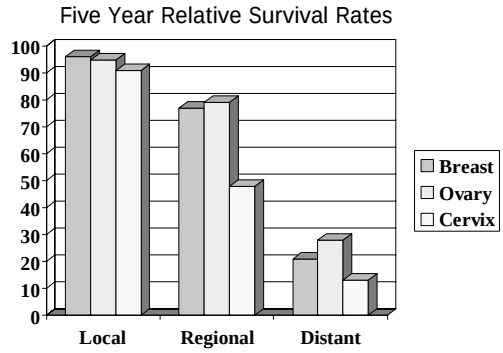
- The burden of cancer
- How does cancer develop?
- Why is early detection so important?
- Strategies for early detection
- Example cancers/technologies
  - Cervical cancer
  - Ovarian cancer
  - Prostate cancer

Statistics on cervical cancer

US data (2007)
- Incidence: 11,150
- Mortality: 3,670

World data (2004)
- Incidence: 510,000 (80% developing world)
- Mortality
  - 288,000 deaths per year worldwide

Importance of Early Detection



Screening

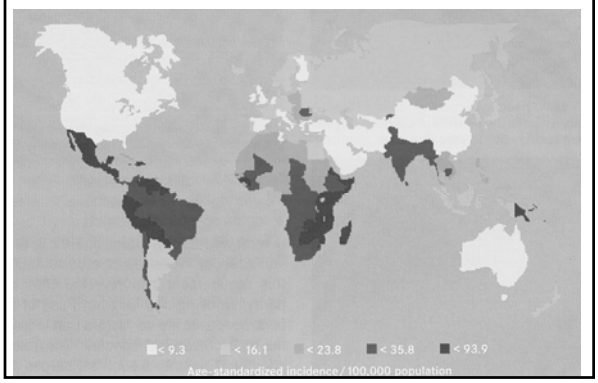
- Use of simple tests in a healthy population
- Goal:
  - Identify individuals who have disease, but do not yet have symptoms
- Should be undertaken only when:
  - Effectiveness has been demonstrated
  - Resources are sufficient to cover target group
  - Facilities exist for confirming diagnoses
  - Facilities exist for treatment and follow-up
  - When disease prevalence is high enough to justify effort and costs of screening

How do we judge efficacy of a screening test?

Sensitivity/Specificity

Positive/Negative Predictive Value

Global Burden of Cervical Cancer

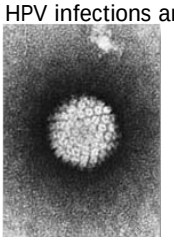


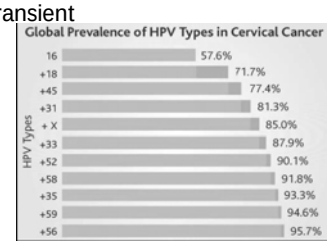
Risk factors

- HPV infection
  - HPV infection is the central causative factor in squamous cell carcinoma of the cervix
- Sexual behaviors
  - Sex at an early age
  - Multiple sexual partners
- Cigarette smoking

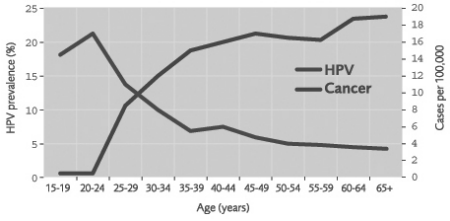
Human papilloma virus (HPV)

- Most common STD
- >70 subtypes
- Asymptomatic infections in 5-40% of women of reproductive age
- HPV infections are transient



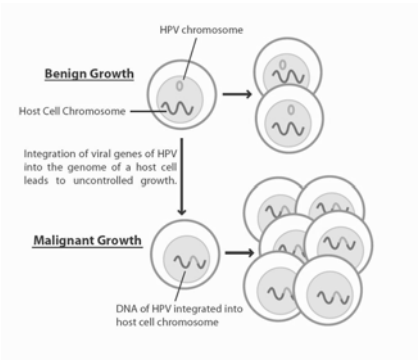


X. Bosch And N. Munoz/Iarc, Ibccs, And Multicentric Studies (N = 3045). From Science 29 April 2005: Vol. **308** no. 5722, pp. 618–621.

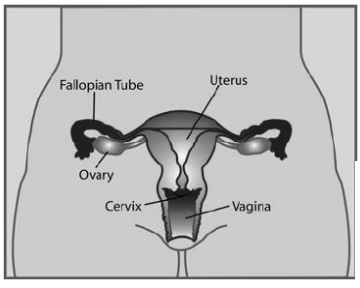


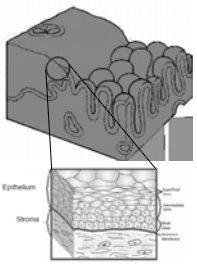
HPV and cervical cancer

What Initiates Transformation?

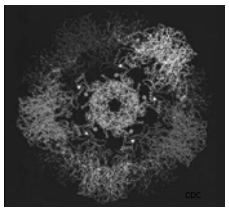


Pathophysiology





HPV vaccine

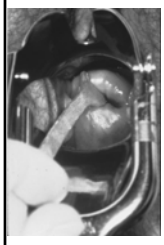


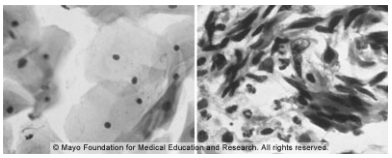
Virus-like particles (VLP) made from the L1 protein of HPV 16

- approved for use in girls and women aged 9 to 26 years in the US
- not effective to women already exposed to HPV
- Effective on 4 HPV isotypes
- Recombinant technology
- Alternative prevention technique to screening?

How Do We Detect Early Cervical Cancer?

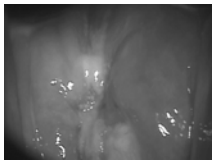
Pap Smear





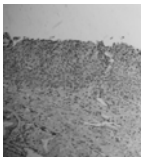
- 50,000-300,000 cells/per slide
- Cytotechnologists review slides (<100/day)
- Se = 62% → 3%
- Sp = 78% → $6B

Colposcopy and Biopsy



Colposcope

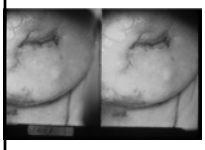
Se = 95%
Sp = 44%



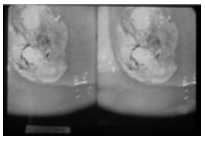
Biopsy sections

Colposcopy and Treatment

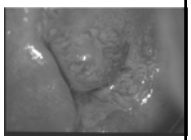
CIN 1/LGSIL



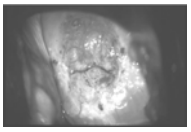
CIN 2/HGSIL



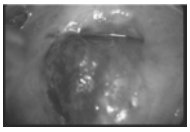
CIN 3/HGSIL



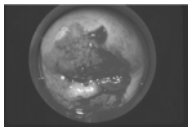
Microinvasive CA



Invasive CA



Invasive CA



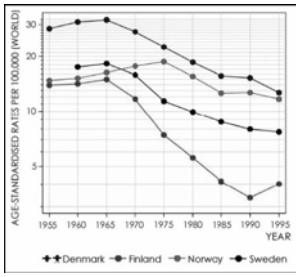
Detection and Treatment

- Screening:
  - Pap smear
- Diagnosis:
  - Colposcopy + biopsy
- Treatment:
  - Surgery, radiotherapy, chemotherapy
- 5 year survival
  - Localized disease: 92% (56% diagnosed at this stage)

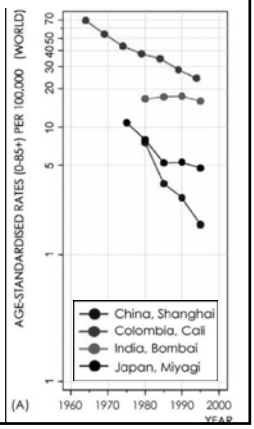
Screening Guidelines, ACS

- All women should begin cervical cancer screening about 3 years after they begin having vaginal intercourse, but no later than when they are 21 years old. Screening should be done every year with the regular Pap test or every 2 years using the newer liquid-based Pap test.
- Beginning at age 30, women who have had 3 normal Pap test results in a row may get screened every 2 to 3 years with either the conventional (regular) or liquid-based Pap test.
- Option for women over 30 is to get screened every 3 years with either the conventional or liquid-based Pap test, *plus* the HPV DNA test.

Trends in Screening Cervical Cancer



Vaccine, *Vol. **24S3**, D. Maxwell Parkin and Freddie Bray, The burden of HPV-related cancers, pp. S3/11–S3/25, c. Elsevier (2006)*



Challenge

- Developed and developing world
- Cost and infrastructure requirements for screening
- Need for appropriate technologies

New Detection Technologies

Aims:

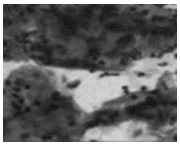
- Reduce the false positive and false negative rates
- Give instantaneous results
- Reduce the costs

New Technologies for Cervical Cancer

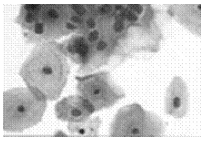
- Liquid Based Pap testing
- Automated Pap smear screening
- HPV Testing
- VIA
- HPV Vaccine

Liquid Based Pap Smear

- Rinse collection device in preservative fluid
- Process suspension of cells to deposit a monolayer of cells on a microscope slide



Conventional Pap



Liquid Based Pap

http://www.prlnet.com/ThinPrep.htm

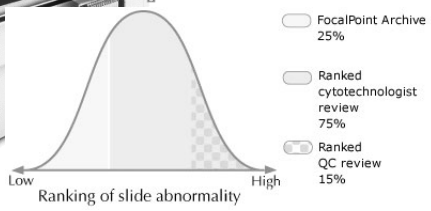
Liquid Based Pap Smear

- Gentle dispersion breaks up blood, mucous, non-diagnostic debris, and mixes sample
- Negative pressure pulse draws fluid through filter to collect a thin, even layer of cells
- Monitor flow through filter during collection to prevent cells from being too scant or too dense
- Cells then transferred to a glass slide

Automated Pap Smear Screening

http://www.tripathimaging.com/images/cutaway.gif

- TriPath Care Technologies
  - http://www.tripathimaging.com/usproducts/index.htm

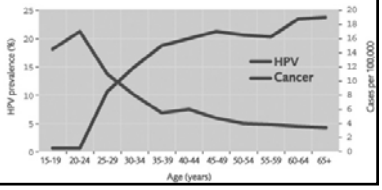


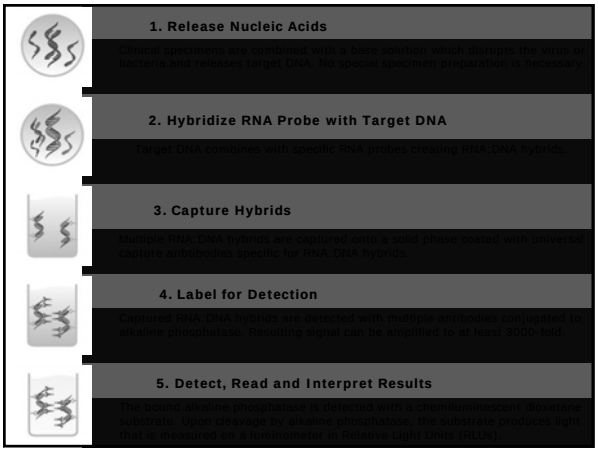
The Lancet Oncology, *2001, Vol. 2 No. 1, pp. 27–32*

HPV Testing

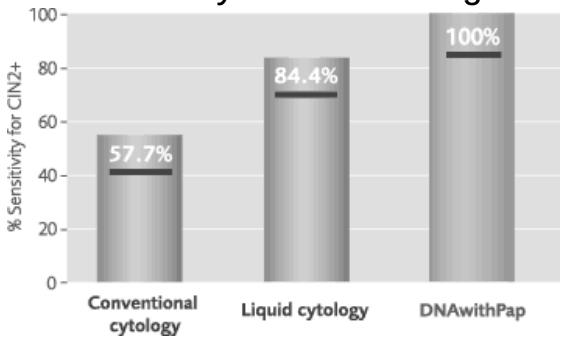
- The DNAwithPap Test is FDA-approved for routine adjunctive screening with a Pap test for women age 30 and older.
- Digene
  - http://www.digene.com

http://www.digene.com/PapXYLC-5301-30%20VER%20X.mpg





Sensitivity of HPV Testing



http://www.digene.com/images/sens.gif

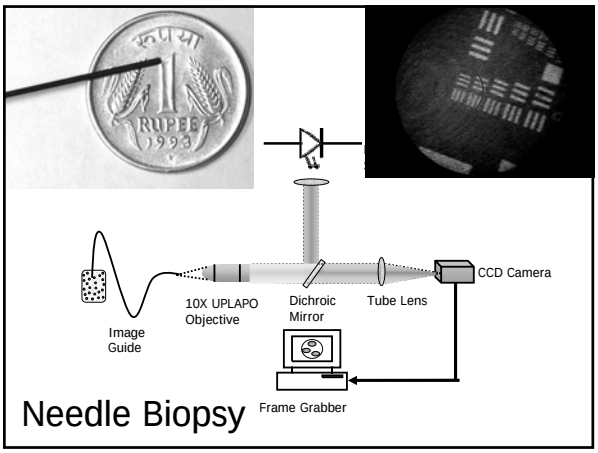
Study of 5,671 women age >30 years

Comparison of Various Techniques

	Sensitivity	Specificity
Pap smear	60-80%	45-70%
Colposcopy	90-100%	20-50%
Digene HPV Test	80-90%	57-89%
VIA	67-79%	49-86%

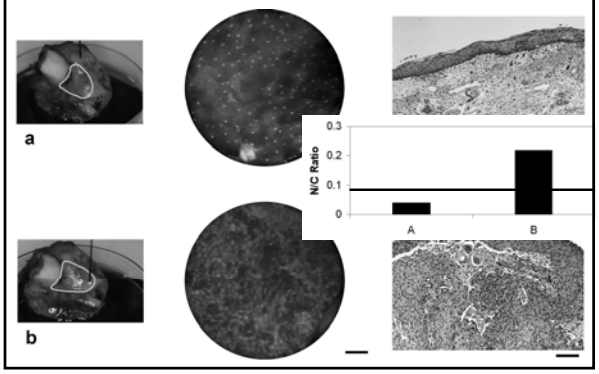
Costs

Pap Test	$10-20
Liquid-based Pap	$50
Automated Pap Smear Screening	$20-60
HPV DNA test	$90
HPV vaccine	$360

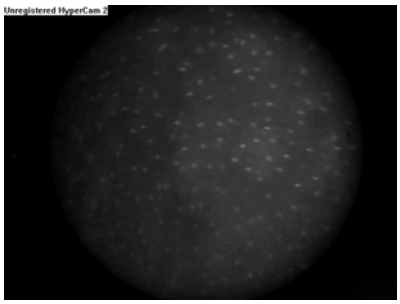


Needle Biopsy

Needle Biopsy



Needle Biopsy



Summary of Cancer

- The burden of cancer
  - Contrasts between developed/developing world
- How does cancer develop?
  - Cell transformation → Angiogenesis → Motility → Microinvasion → Embolism → Extravasation
- Why is early detection so important?
  - Treat before cancer develops → Prevention
- Accuracy of screening/detection tests
  - Se, Sp, PPV, NPV

Summary of Cervical Cancer

- Cervical cancer
  - 2nd Leading cause of cancer death in women in world
  - Caused by infection with HPV
  - Precancer→cancer sequence
  - Precancer is very common
- Screening & Detection
  - Pap smear; colposcopy + biopsy
  - Reduces incidence and mortality of cervical cancer
  - Insufficient resources to screen in developing countries
- New technologies
  - Automated reading of Pap smears → reduce FN rate
  - HPV testing
  - VIA

Global Inequities in Cancer Prevention