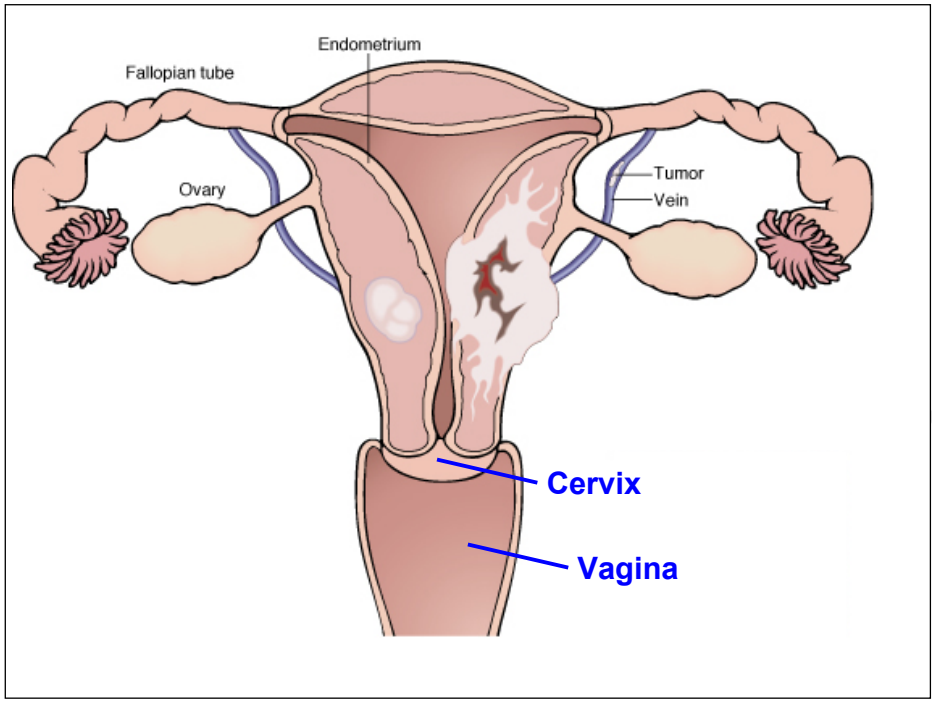
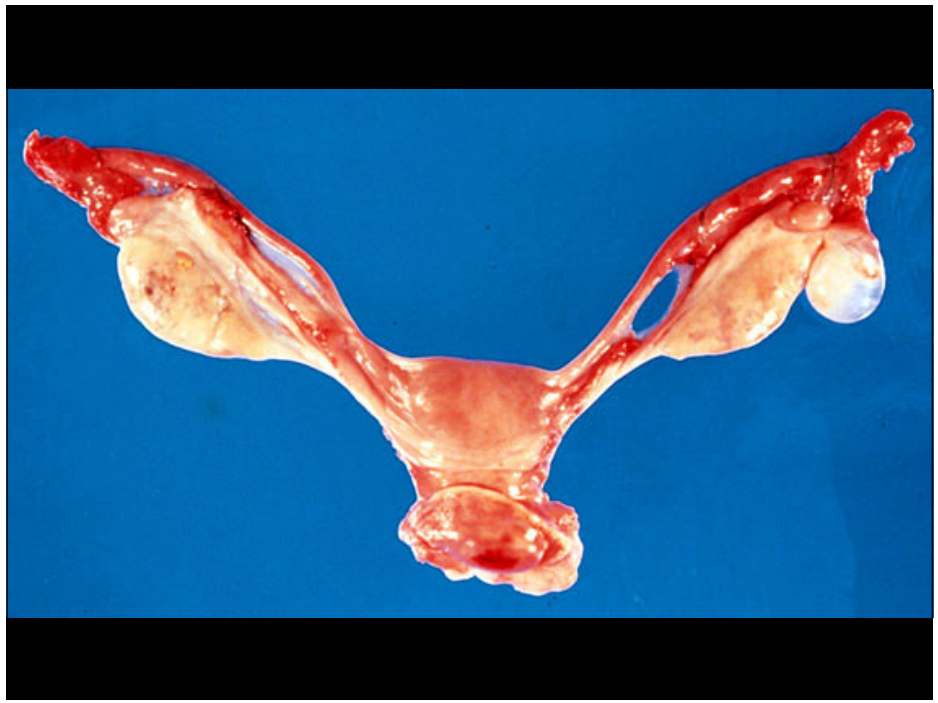
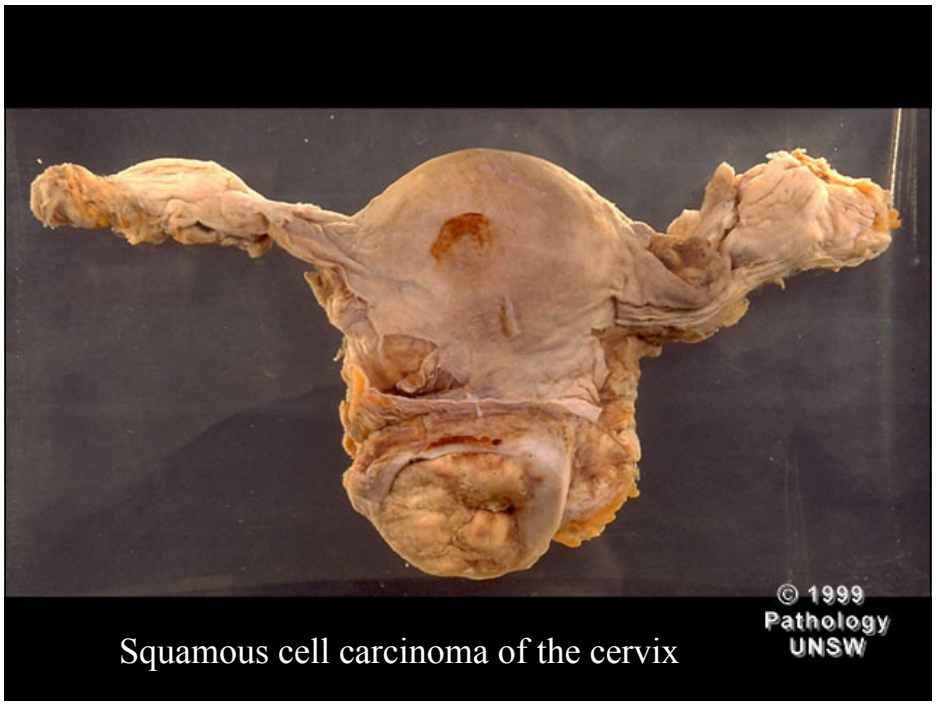
Cancer of the Cervix

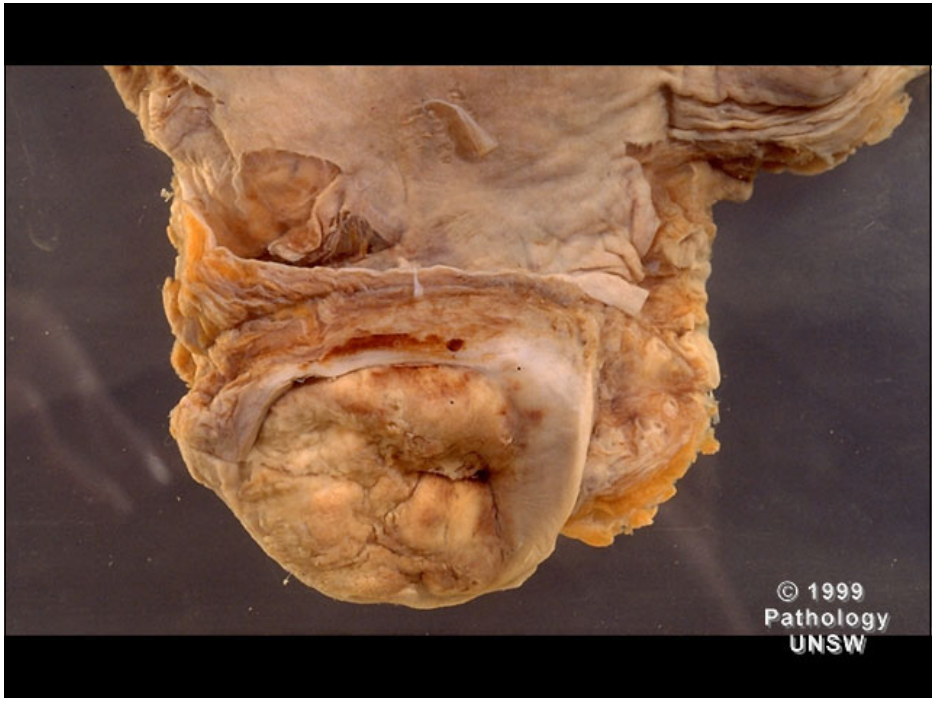
A Smear Campaign







Squamous cell carcinoma of the cervix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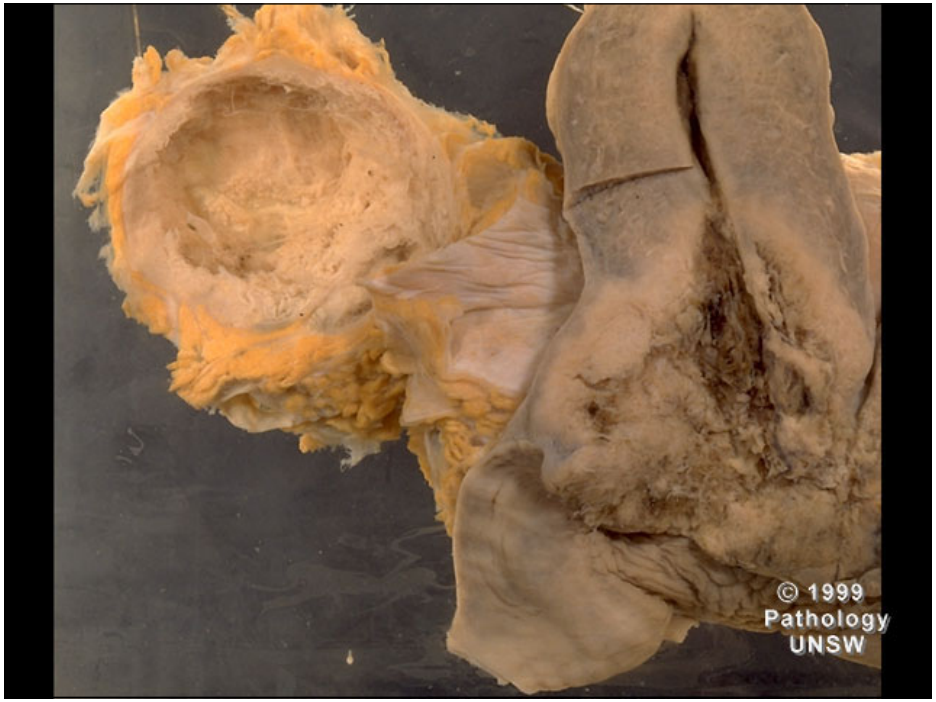
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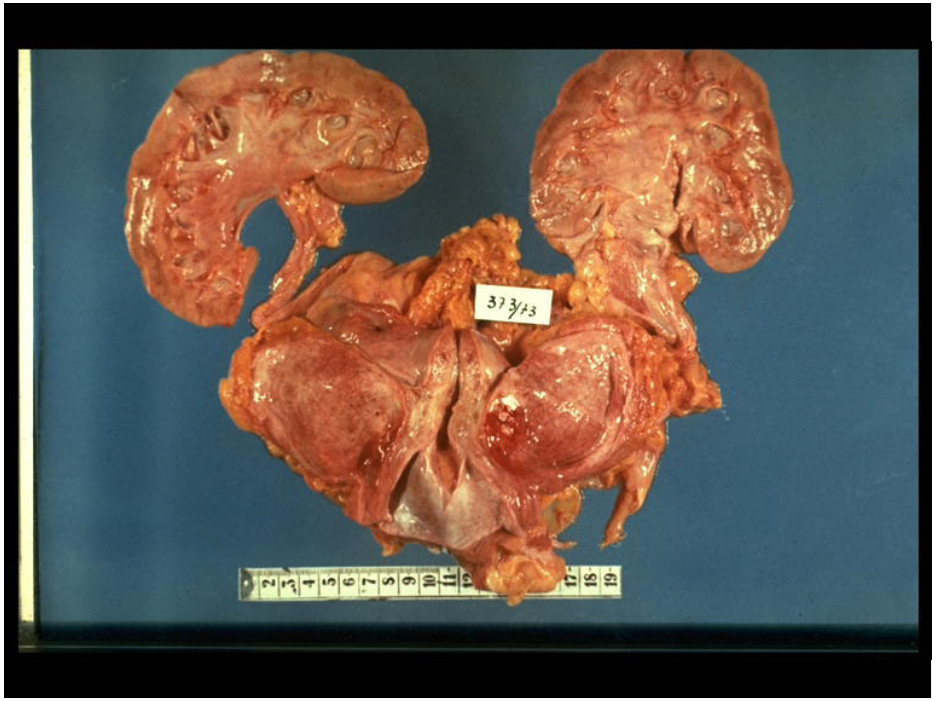
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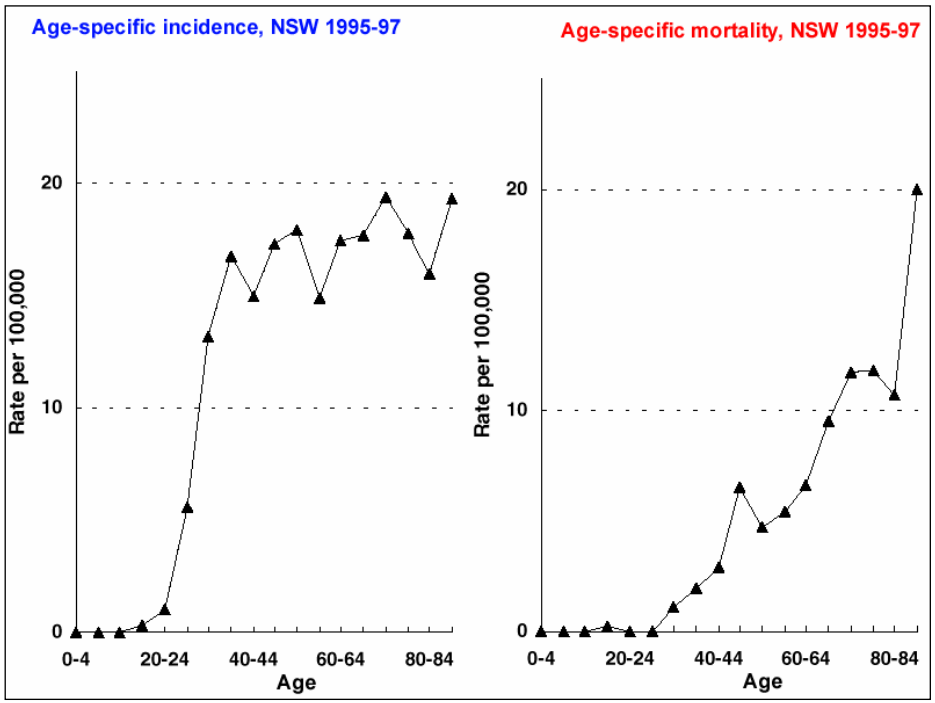
Epidemiology

- In NSW in 1997 there were
  - 285 new cases of cervical cancer (2% of cancers)
  - 100 deaths (2% of female cancer deaths)
- Ranking
  - 11th in incidence (4th in 1973)
  - 14th in mortality
- 1 in 144 females will develop cervical cancer by age 75

Variation with age

- Median age at diagnosis: 48 years
- New cases by age

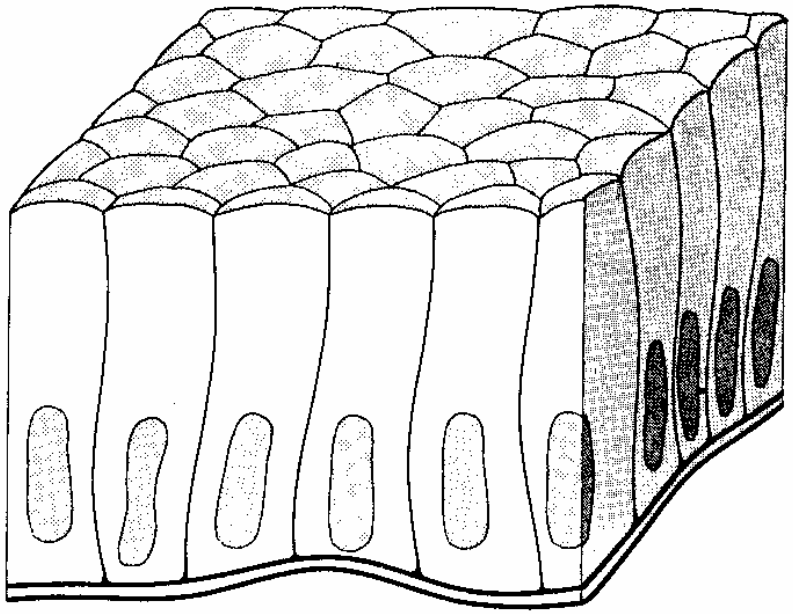
0-34	48
35-44	69
45-54	66
55-64	33
65-74	40
75-84	20
85+	9



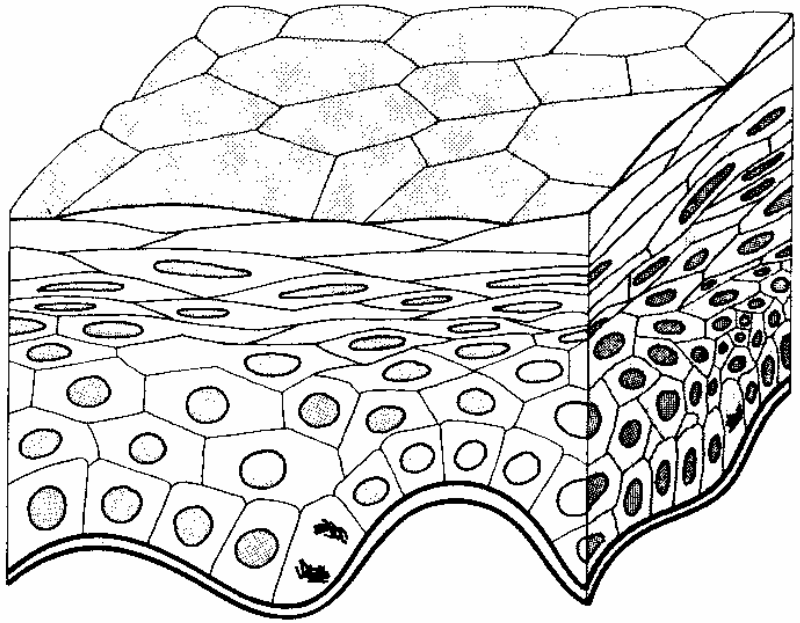
Risk Factors for Squamous cell carcinoma of cervix

- Multiple sexual partners
- Early age at 1st intercourse
- Human Papilloma virus (HPV) infection

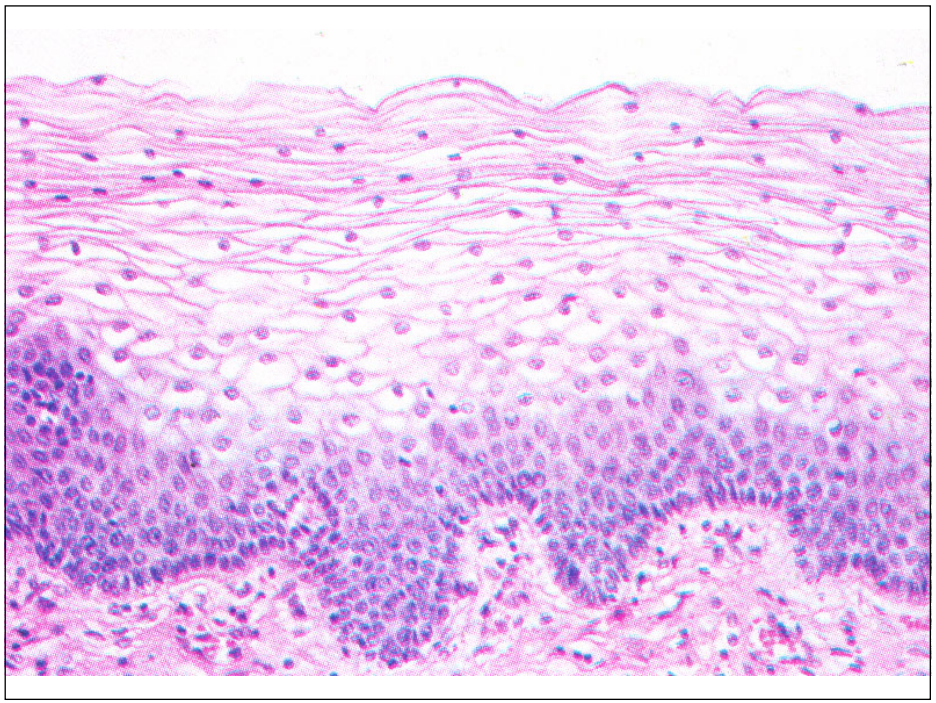
- *Other genital infections (HSV)*
- *Smoking*
- *Oral contraceptive use*
- *High number of live births*
- *Nutritional deficiency*
- *Immunosuppression*

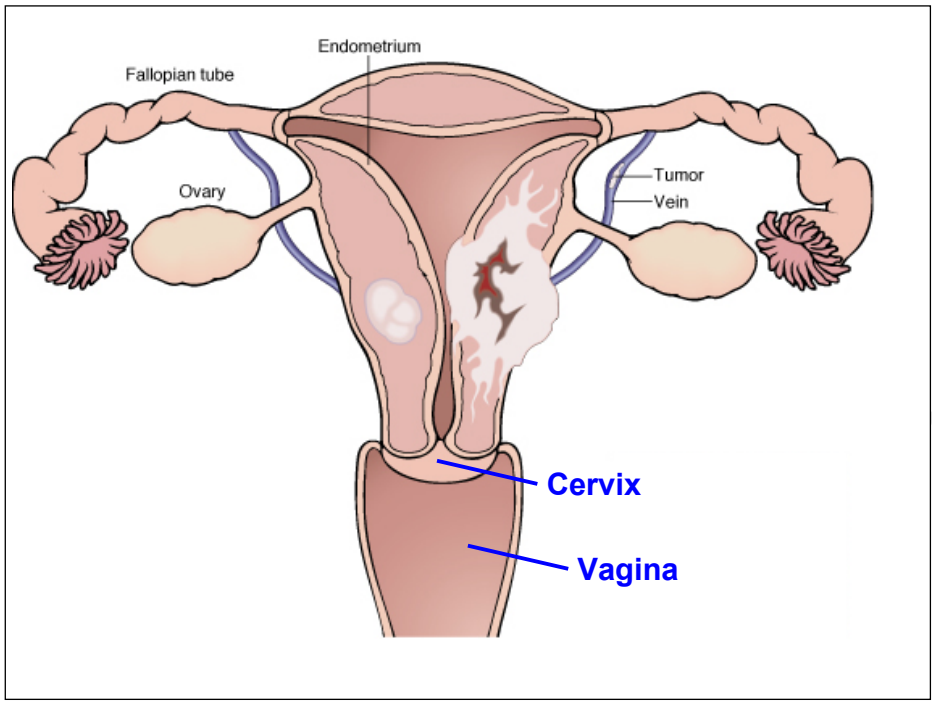


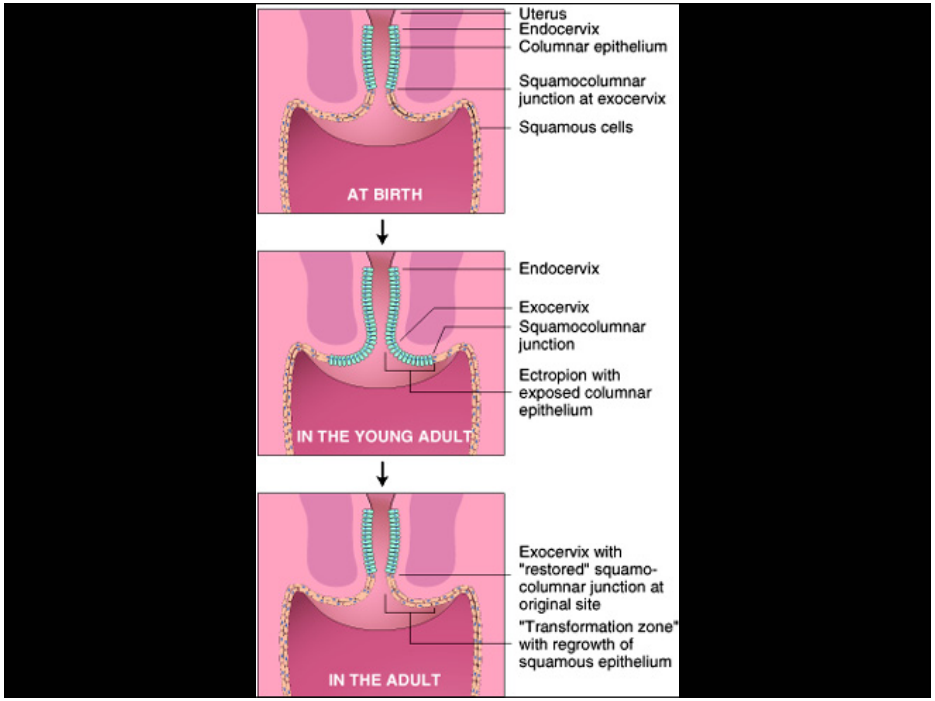
Simple columnar epithelium



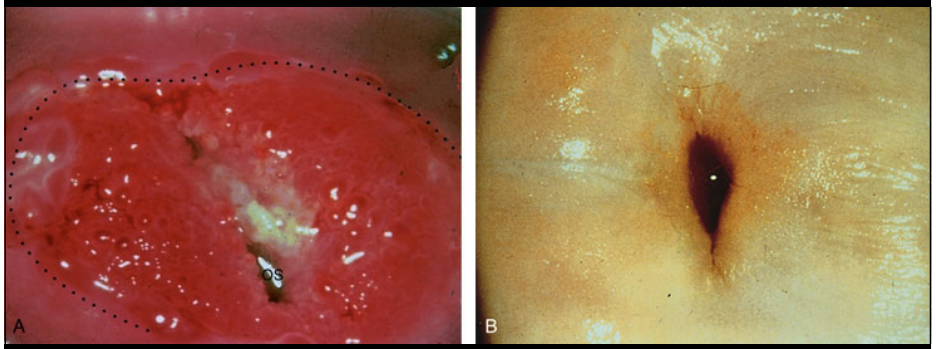
Stratified squamous epithelium





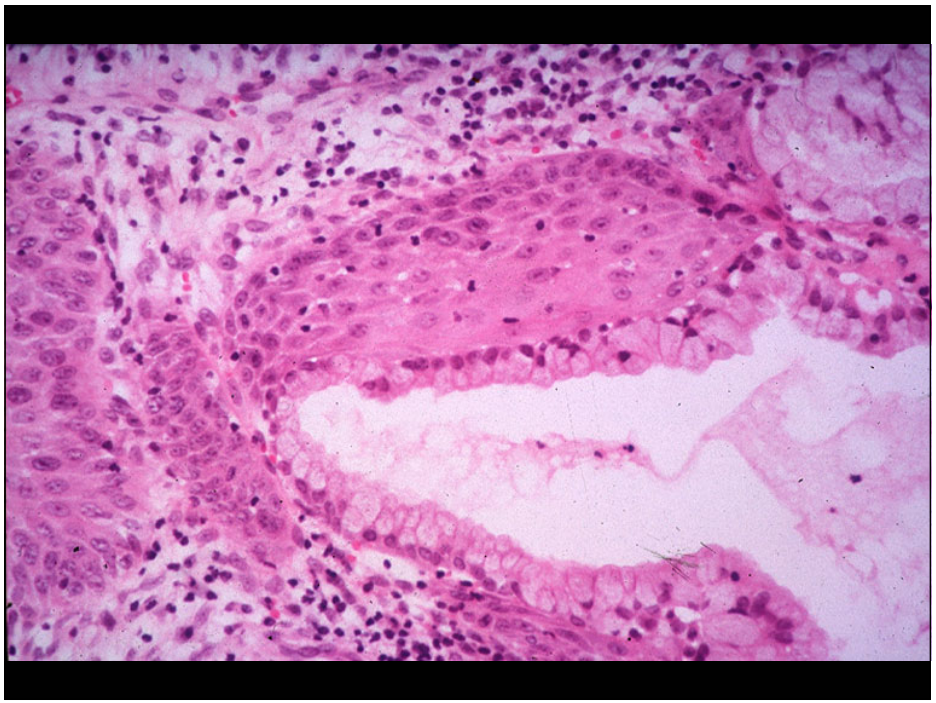


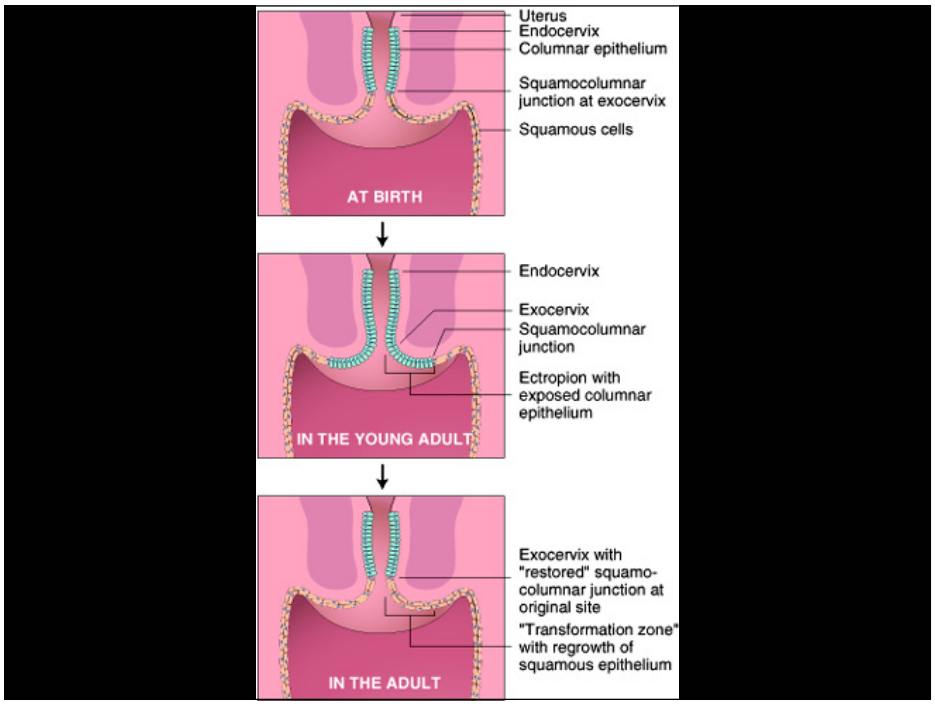
Colposcopy of Cervix

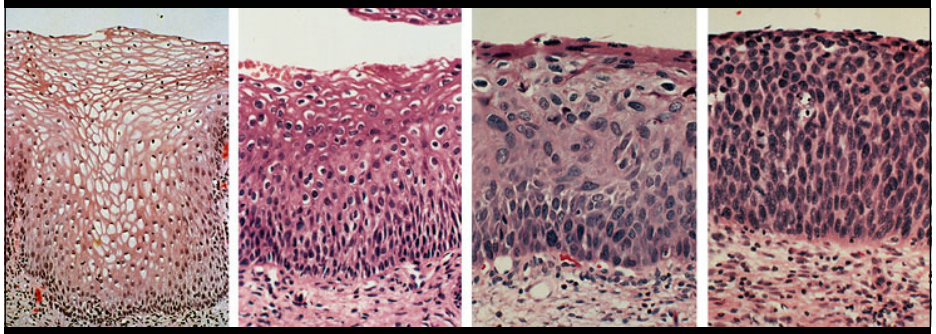


Reproductive age woman

Post-menopausal woman



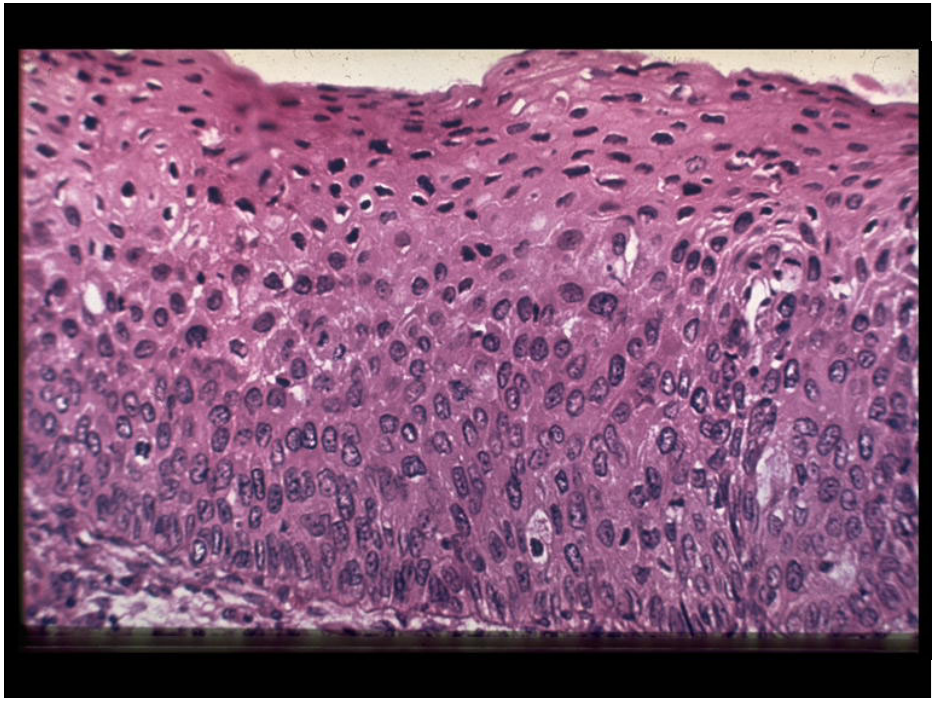


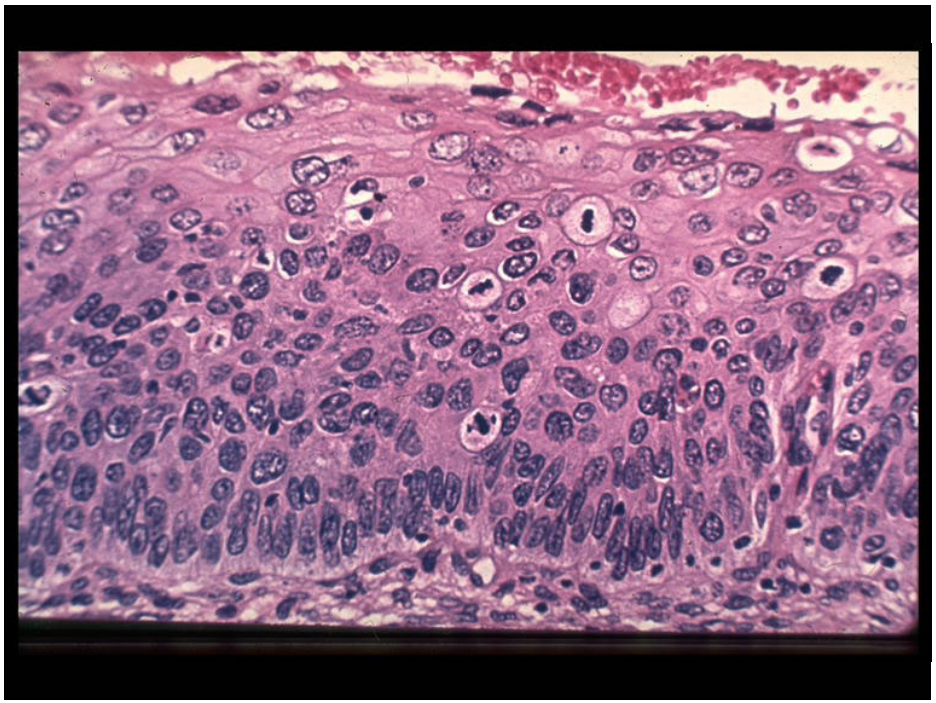


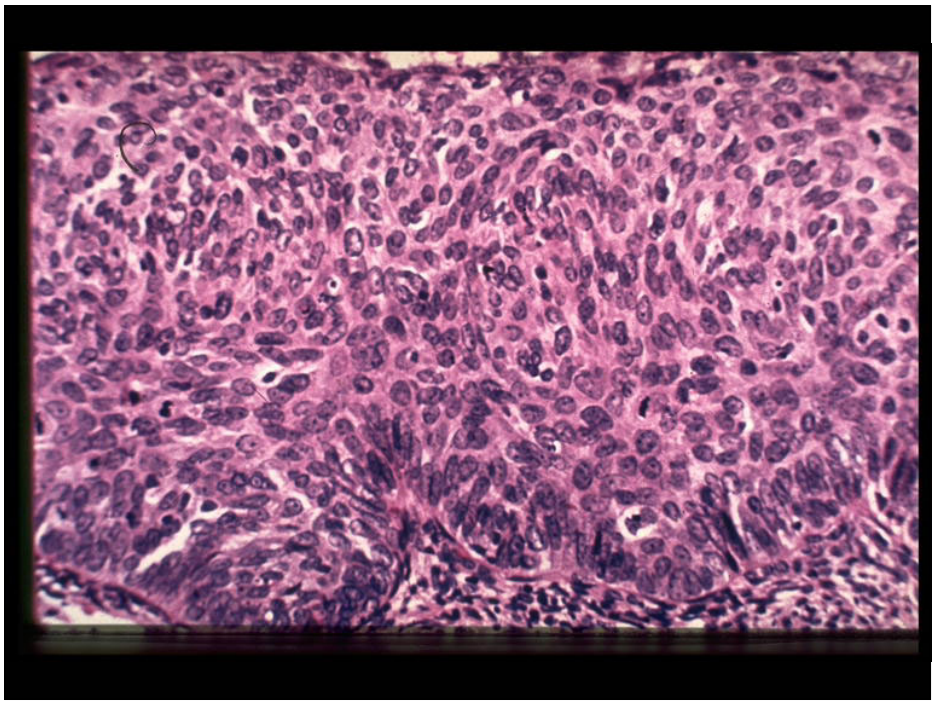
Normal CIN I CIN II CIN III

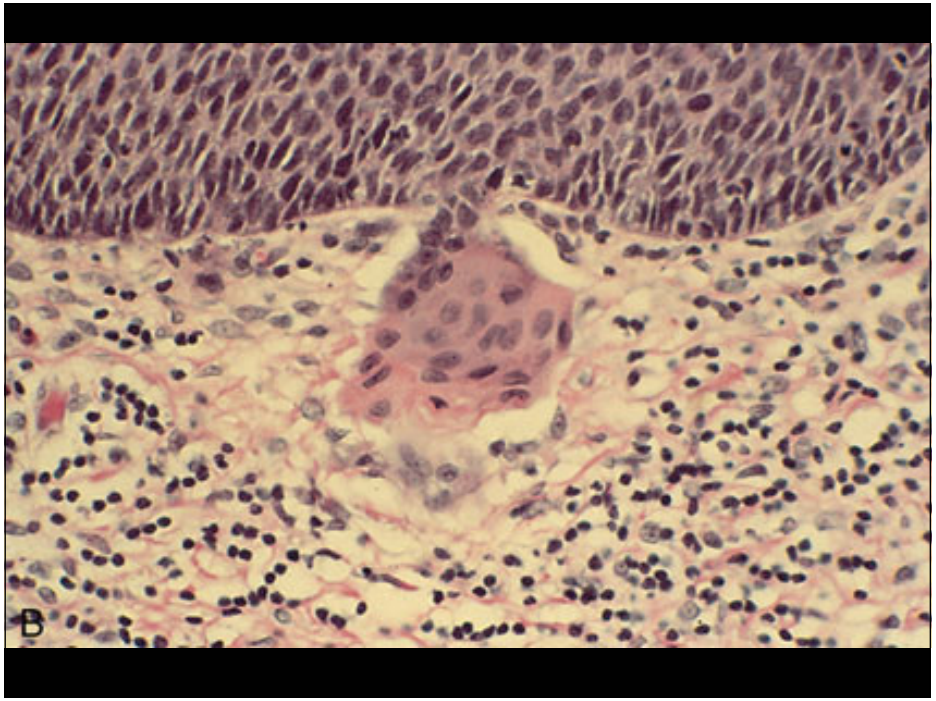
Cervical intraepithelial neoplasia

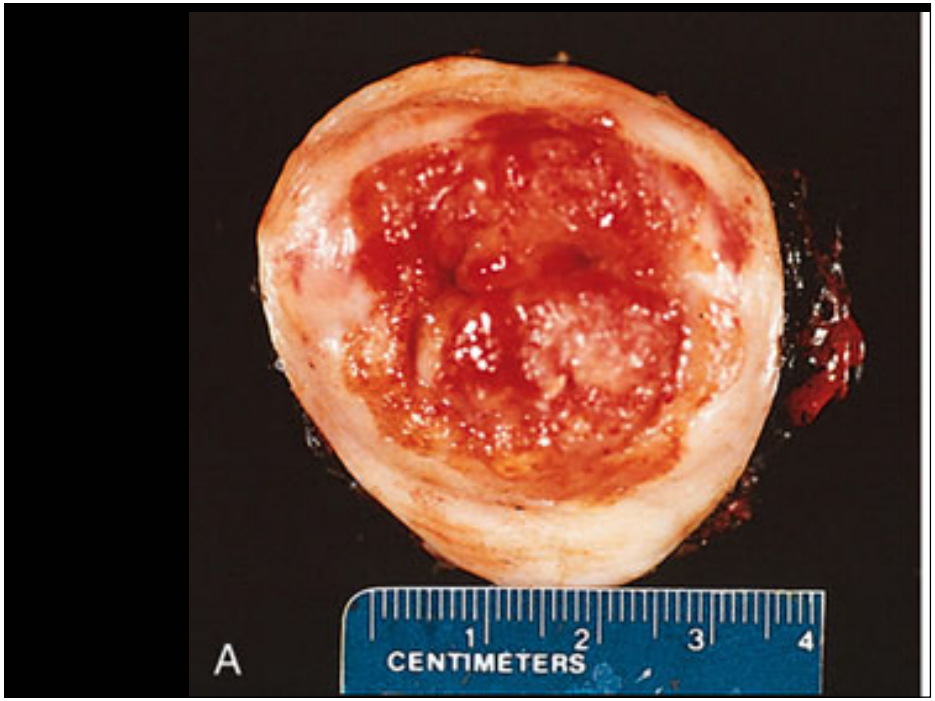
Squamous intraepithelial lesions

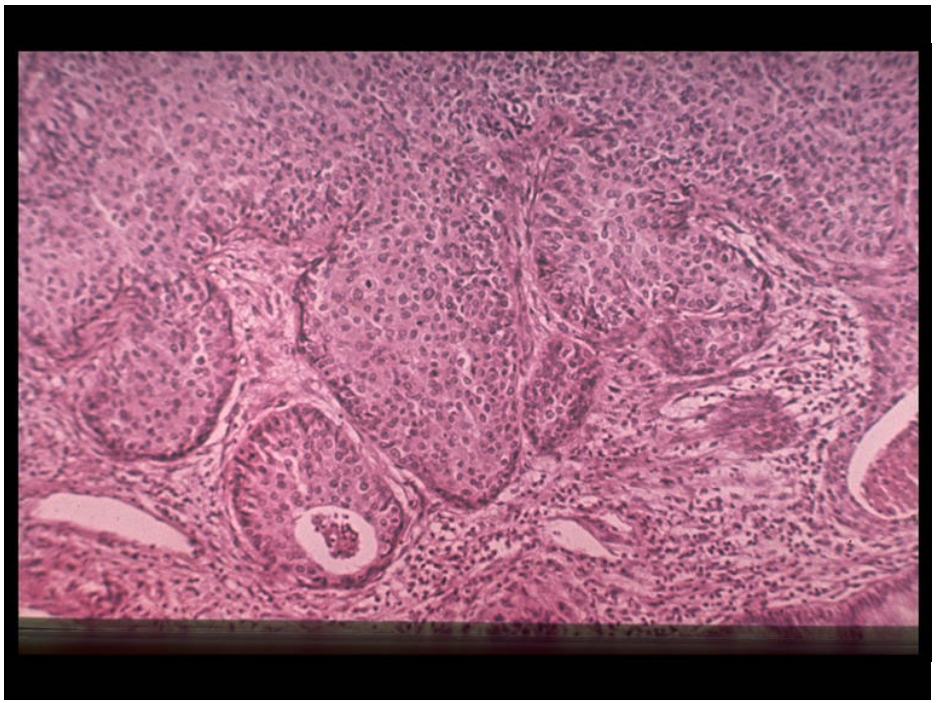










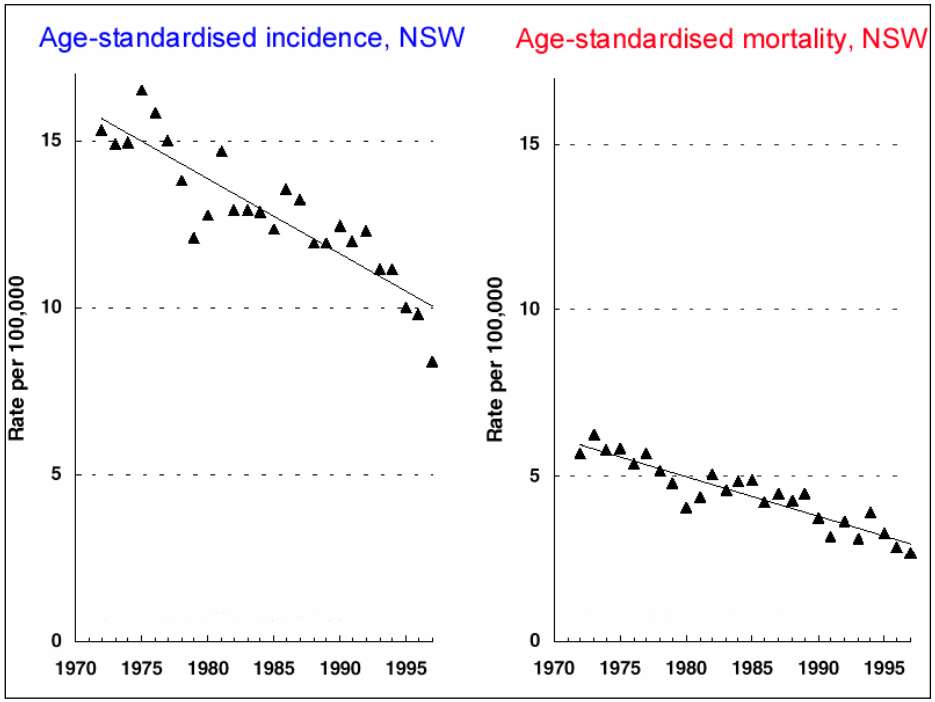


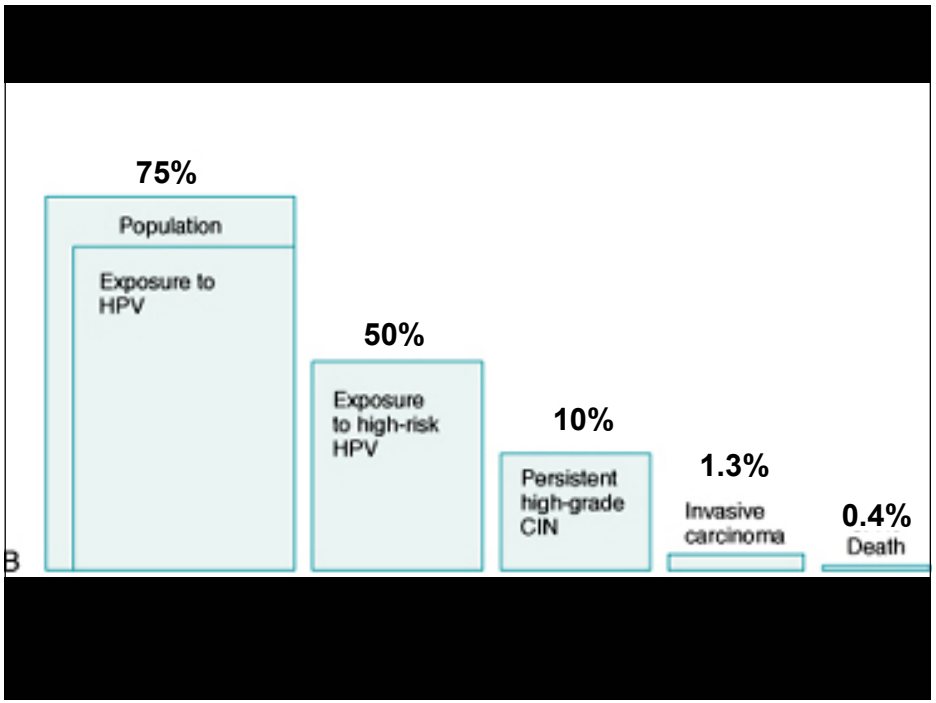
International comparison

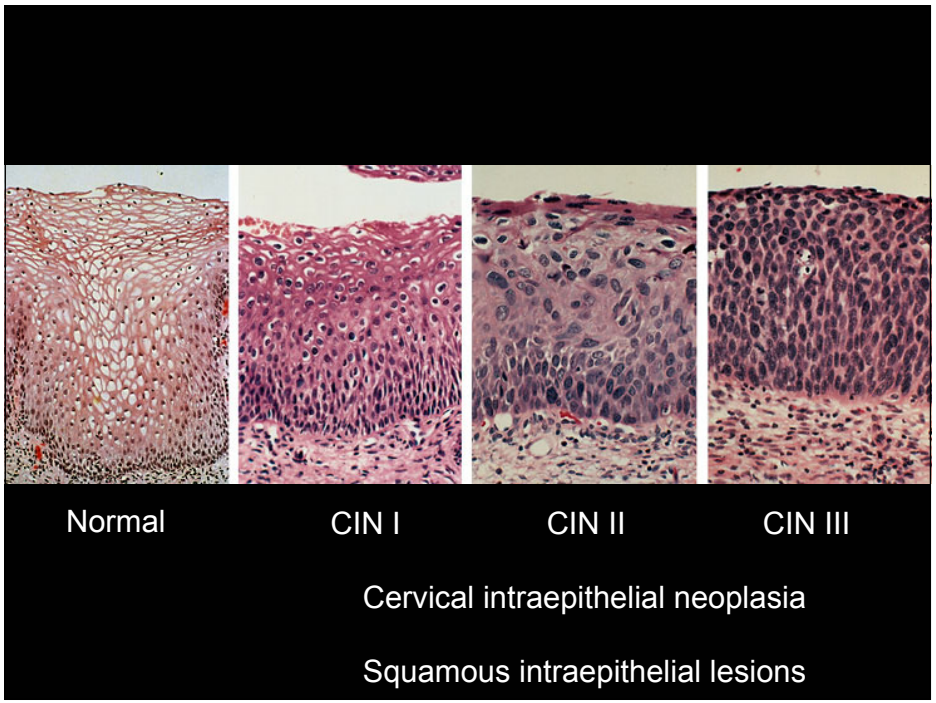
- 2nd ranking worldwide (both incidence and mortality) among cancers in women (~470,000/year)
- Incidence rates for cervical cancer (per 100,000)
  - NSW 9.9
  - NZ Maori 32.2
  - South America >50
- Lower than UK, Denmark, USA (black), NZ, South America, SE Asia
- Higher than Canada, Japan, USA (white)

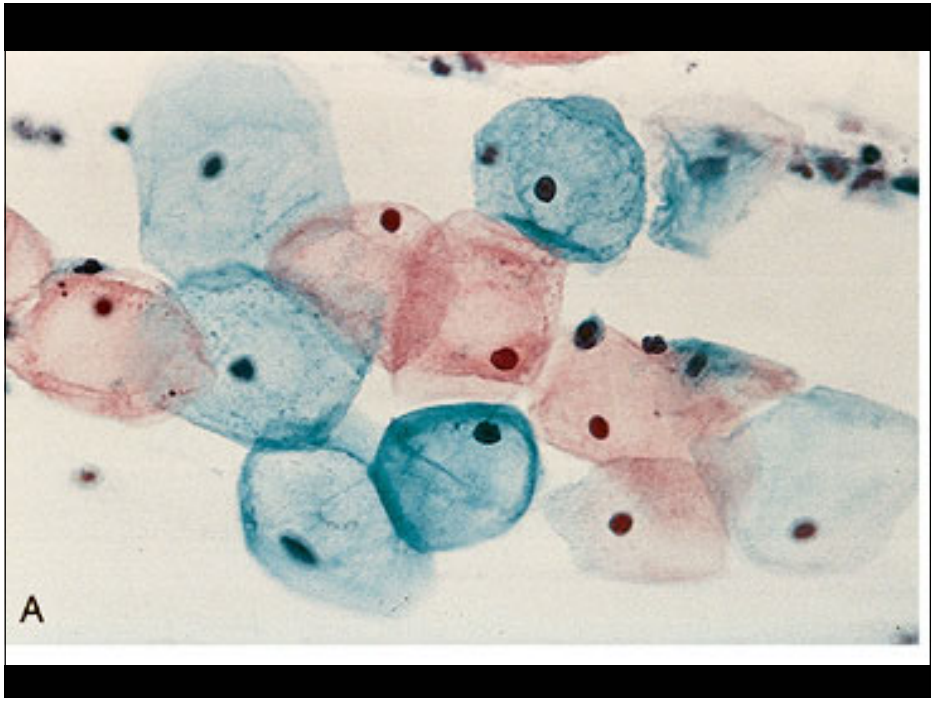
Time trends

- Between 1987 and 1997
  - 29% decrease in incidence
  - 37% decrease in mortality
- Incidence rate has been decreasing throughout period 1972-1997; annual % decrease has been higher over past 10 years





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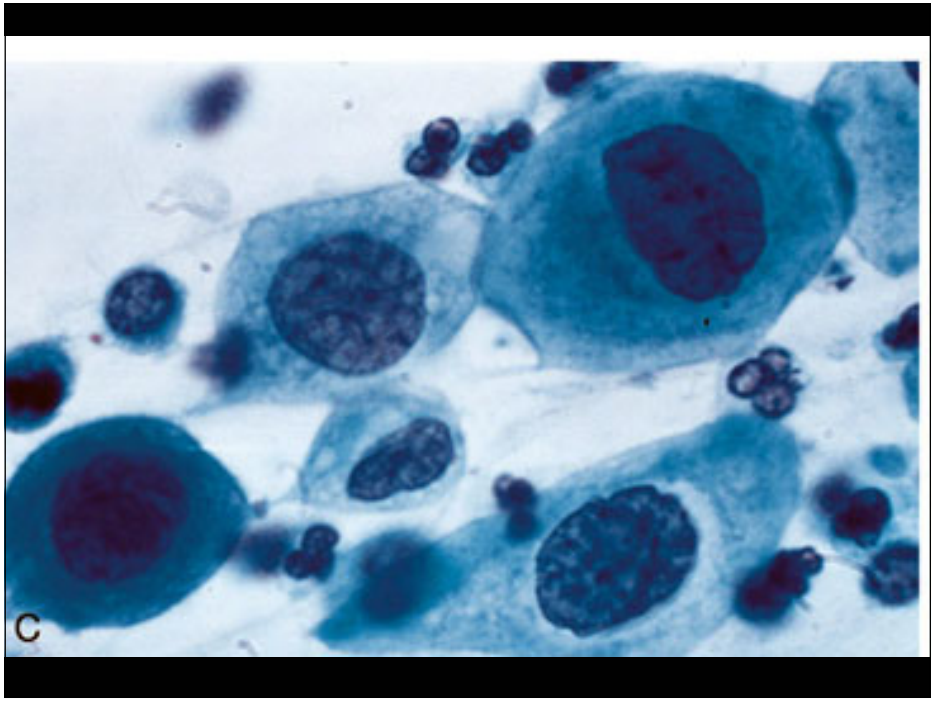
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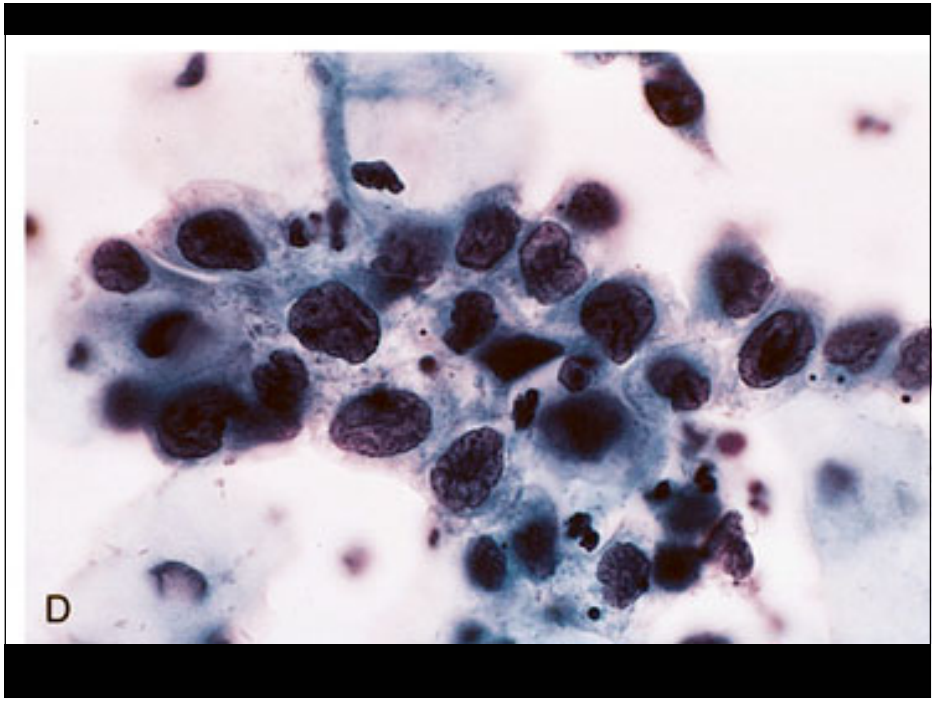
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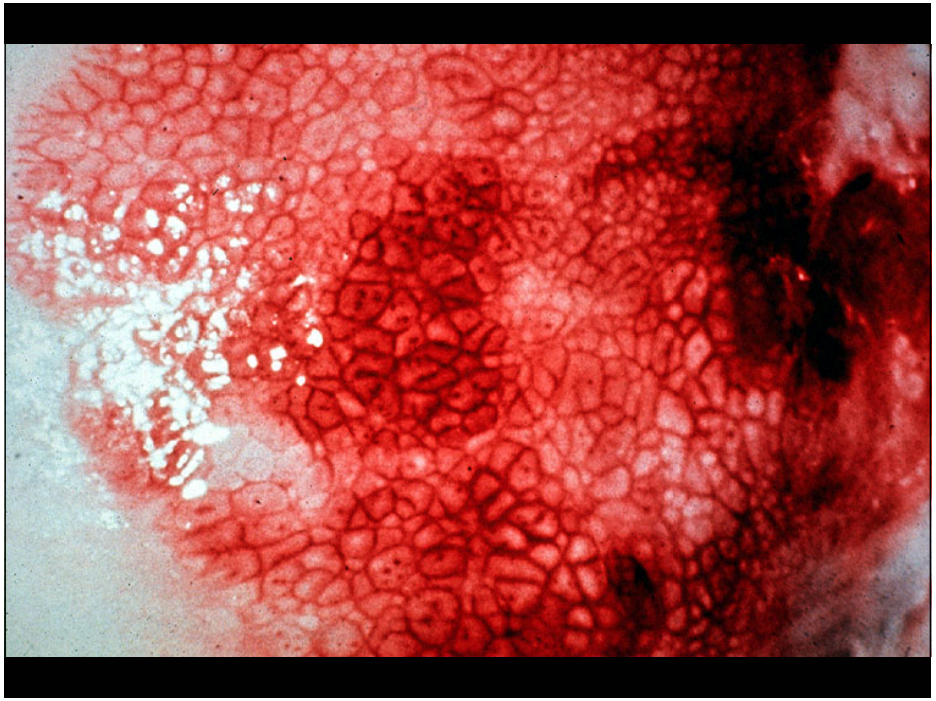
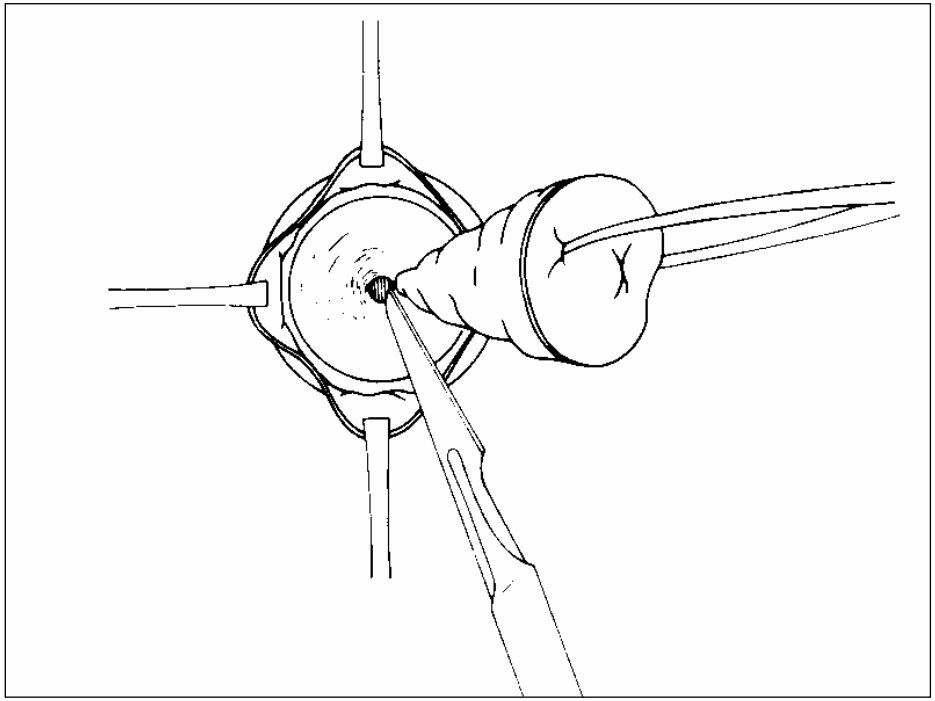
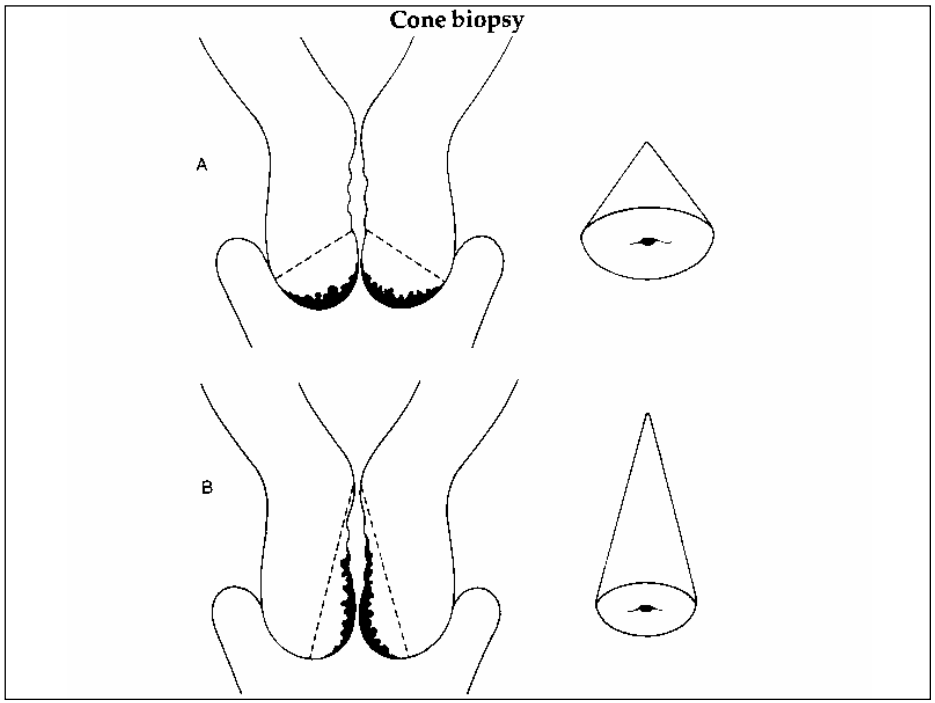
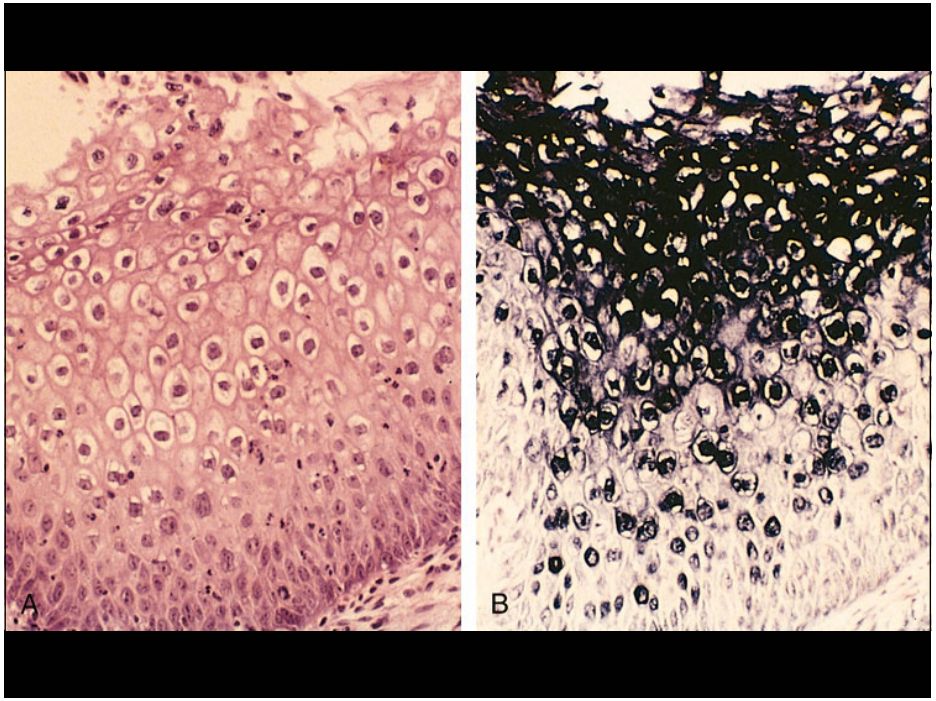


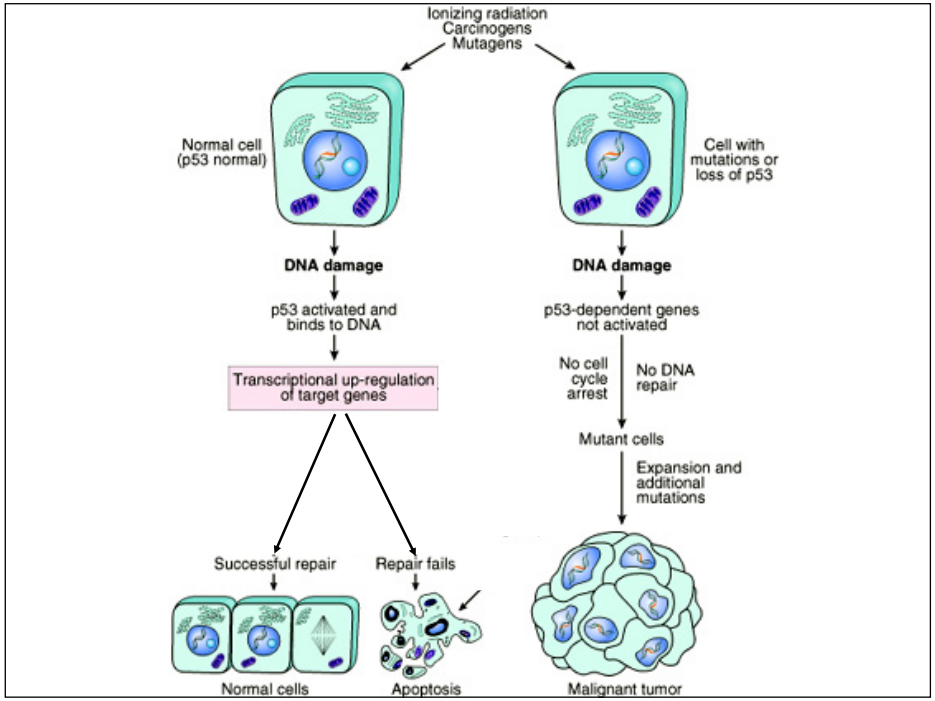




Human Papilloma virus

- HPV DNA is present in >90% of cervival carcinomas
- HPV genes E6 and E7 are integrated into the host's genetic material
- The proteins encoded by the E6 and E7 genes are tumourigenic





E6 and E7 proteins

- E6 protein binds to the protein product of the p53 tumour suppressor gene and inactivates it.

Cells with mutations avoid apoptosis

- E7 protein binds to the protein product of the Rb tumour suppressor gene and inactivates it.

Cells divide more rapidly

The Unfortunate Experiment at National Women's Hospital

The Report of the Cervical Cancer Inquiry
1988
(Cartwright Report)

The 1984 paper

McIndoe, McLean, Jones & Mullins. *The invasive potential of carcinoma in situ of the cervix* (Obstet Gynecol 64:451, 1984)

- Retrospective statistical analysis of women with carcinoma in situ of the cervix managed at National Women's Hospital, Auckland between 1955 & 1976
- Women divided into 2 groups
  - Group 1: negative (normal) cytology after treatment
  - Group 2: continuing positive cytology

1984 paper - Results

- Group 1
  - 1.5% developed invasive cancer; 0.5% died
- Group 2
  - 22% developed invasive cancer; 6% died
- Compared with Group 1 women, Group 2 women had:
  - 24.8x risk of developing invasive cancer
  - 12x risk of dying

- " I don't recall a single one of my colleagues who from that time [1960] to the present did not regard carcinoma in situ as a precursor and who did not treat patients with the lesion"
- Petersen et al (1955) – 33% of 127 untreated women with abnormal cervical cells [suggestive of carcinoma in situ] developed invasive cancer.
- Mid 60's opinion – carcinoma in situ progresses to invasion in 33% to 100% of cases

"Who said they became invasive? Just because Dr McLean [chief pathologist] says they're invasive does not mean they are."

"When would you accept a case is invasive?"

"When you have an ulcerating or fungating lesion or the woman dies of the disease"

"The practical outcome is …. there is no need for concern even if she continued to have positive smears….. For your peace of mind I would suggest that you did not take any further smears."

Correspondence with GP

"We would see the same cells over and over…. Sometimes I would just about cry from upset and frustration."

Cytology screener

"a well-planned and managed method of treatment which ultimately saved many patients from unnecessary traumatic surgery"

Professor Bonham, 1988

"It merged into general treatment. It stopped being a study and became general treatment"

Professor Bonham, when asked when the 1966 study was terminated.

Continuing education

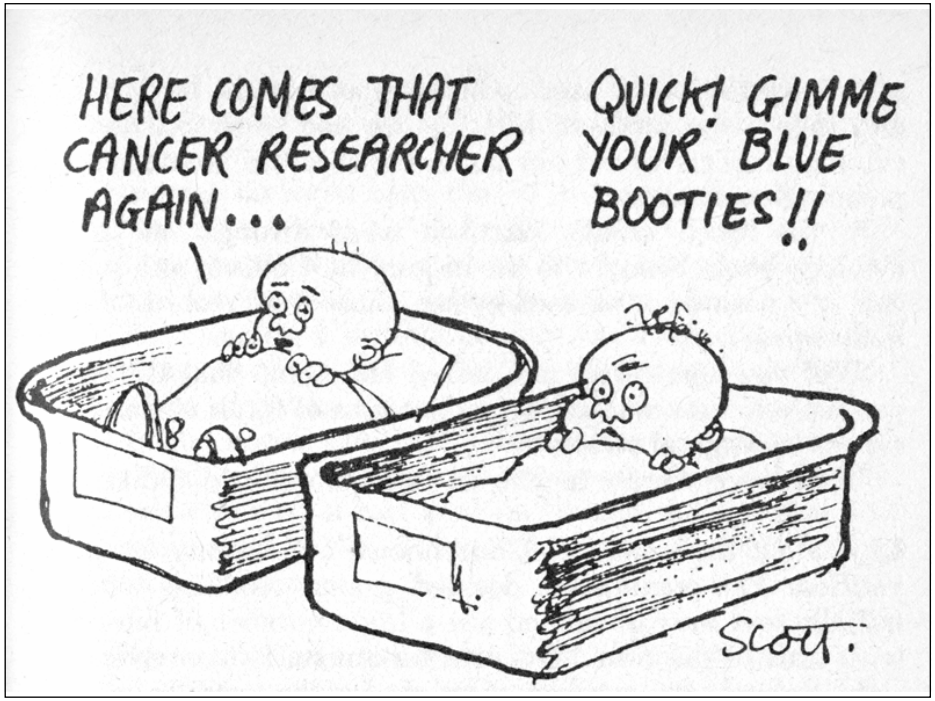
- Papers Green had written for the postgraduate school in the late 60's and early 70's were still being handed out to diploma students in 1984 & 1986.

" True the victims are not eaten by worms, but gnawed away by cancer (or fear of it) they are. The wages of sex is a positive smear"

Jamieson & Skrabanek "Eaten by Worms: a Comment on Cervical Screening". Letter to the editor, NZMJ, 1985

Smear tests on neonates

- Vaginal vault smears taken from female infants < 5days old, without parental consent
- Dr Green lost interest in the trial after 200 babies had smears taken
- His decision to discontinue the trial was not communicated to nursing staff – more than 2000 further smears were taken



Gisborne Cervical Cancer Inquiry

- Investigated pathology reporting of Dr M. Bottrill during the period 1990-1996
- 22978 cervical smear slides were sent to Australia for rescreening
  - 616 women had at least one smear which showed high grade abnormalities
  - Bottrill's laboratory had reported a high grade lesion in the smears of less than 100 of these women

Reasons for under-reporting

- Systemic problems with NZ's National Cervical Screening Programme
  - Laboratories not required to follow quality control procedures or be accredited with an independent authority
  - No monitoring and evaluation of performance of laboratories
  - No central computerised registration system to link cytology, histology and and cancer morbidity and mortality data