Menstrual Disorders and HPV Workshop

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Heavy Menstrual Bleeding (HMB)

- HMB is excessive menstrual blood loss which interferes with a woman's physical, social, emotional and/or material quality of life. It can occur alone or in combination with other symptoms.
- In the early 1990s, over 60% of women presenting with HMB went on to have a hysterectomy

Management of Heavy Menstrual Bleeding

- History
- General and abdominal examination
- Bimanual, Speculum +/- smear
- FBC
- TFTs only if hypothyroidism suspected
- Tests for coagulopathy only if suspected
- TVS and / or pipelle if ‘high risk’

Background

- 5% GP consultations are for HMB
- 11 of gynaecologist referrals
- 80mls per cycle is the 90th centile
- 7000 hysterectomies per annum in NZ

History and Examination

- Age / parity
- Cycle, IMB, PCB
- Clots and Flooding
- Soiling of clothes
- Social function
- Family complete?
- Family History
- PMH (PCOS, Tamoxifen, ERT, Obesity)
- Symptoms of anaemia
- Anaemia?
- Obesity
- Pulse and BP?
- Signs of coagulopathy?
- Abdominal exam
- Bimanual
- Speculum (?should be mandatory)
- Smear if due

Investigation

Overall incidence of endometrial carcinoma in premenopausal women is 14.3/100,000 women years in one UK paper

- TVS

  12 mm or greater is abnormal for premenopausal women

  (For PMB, an endometrial thickness of < or equal to 5mm in post menopausal women means <4% risk of cancer. 'Virtually' zero if < or equal to 4mm but again beware!)

- Pipelle

  Quick, low risk, fairly accurate but ……

  Beware the 'inadequate' result

  Can miss focal cancers

  Pain (warn patient)

Investigation

- Hysteroscopy D & C

  The ‘gold’ standard, well tolerated and safe

  In a series of 2500 outpatient hysteroscopies; 10% of pre and 22% of post menopausal women had polyps. Fibroids played a part in 25%.

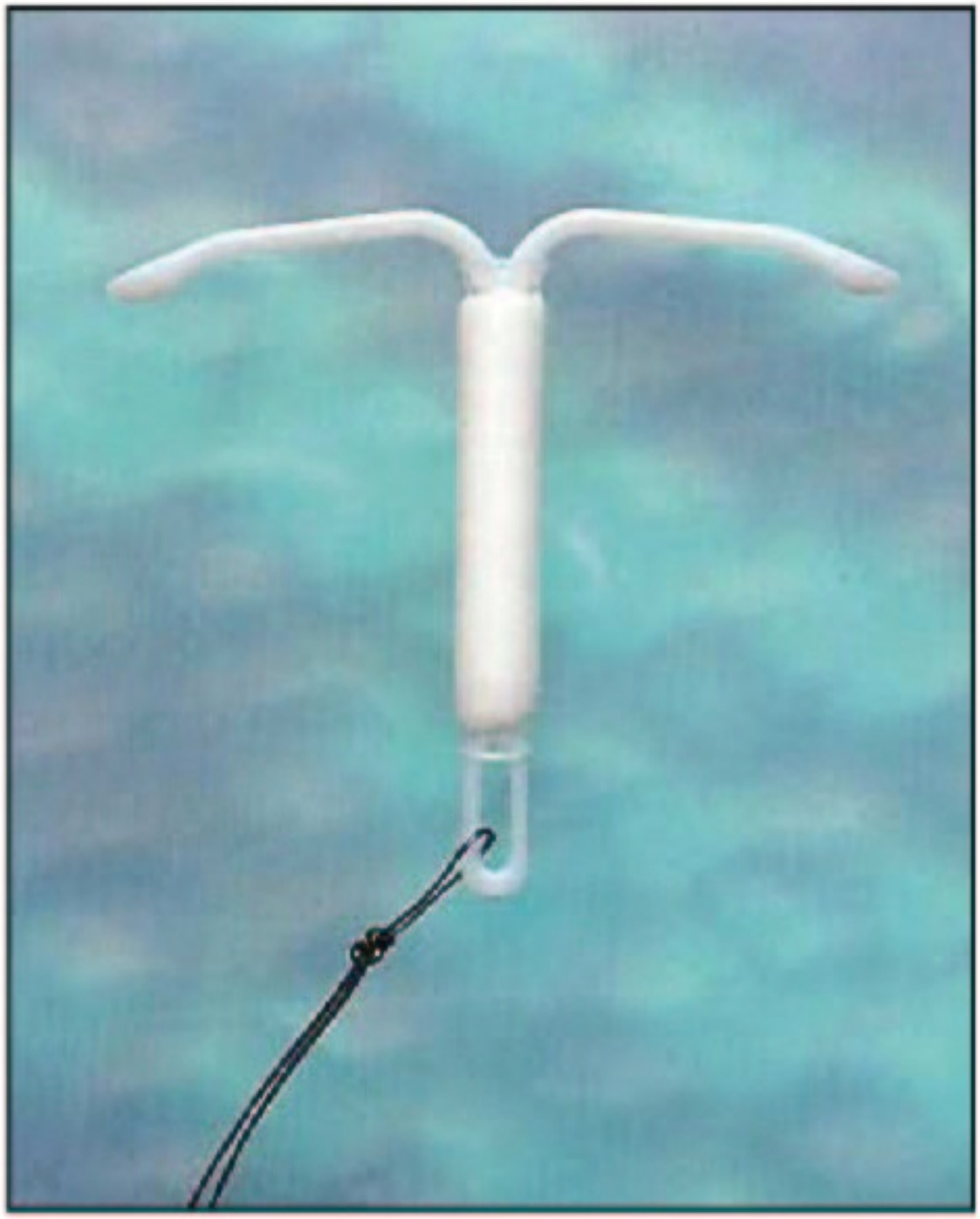
Treatment; Drugs

- **Mirena**
  pgs reduced, inactive endom, reduces fibrinolysis. Mbl down 86% after 3/12
- **Cyclokapron** 1-1.5 g up to qds during heavy days.
  Inhibits tissue plasminogen activator mbl down 50%
- **NSAIDS** e.g. Ponstan 250-500 mg tds during menses.
  Inhibits cyclo-oxygenase and blocks myo pge2 receptors mbl down 30%
- **Progestagens** e.g. NET 5mg tds
  For emergency use e.g. 30-50 mg provera/day for 3/52.
- **COCP**

  20-30% reduction MBL
- **Depo-provera / Implantable Prog**

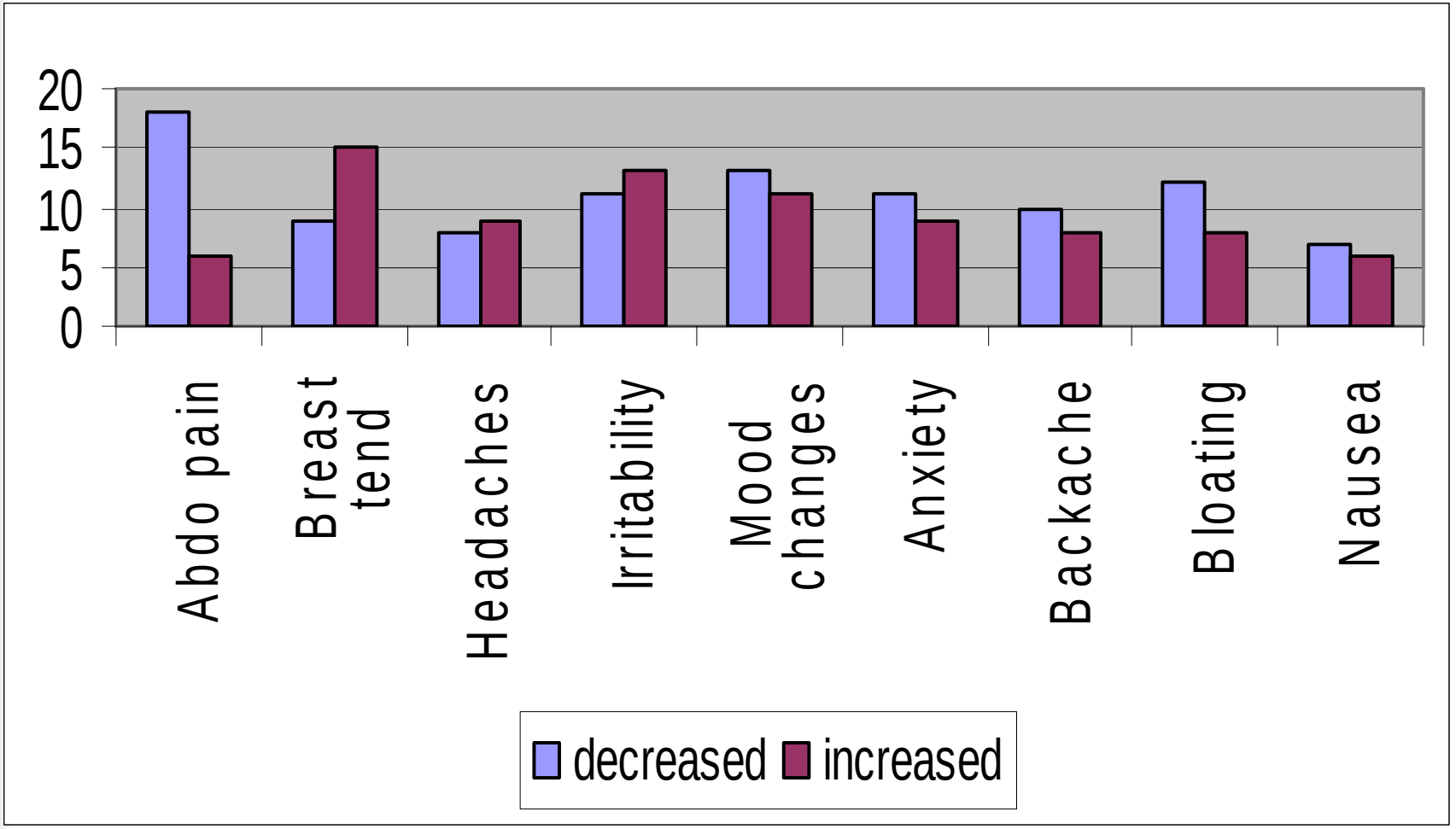
Mirena

- Efficacy for HMB and dysmenorrhoea
- Some endometriosis
- Endometrial protectant
- Fibroids…relative CI
- ?Side-effects
- Also able to prevent some other annoying things

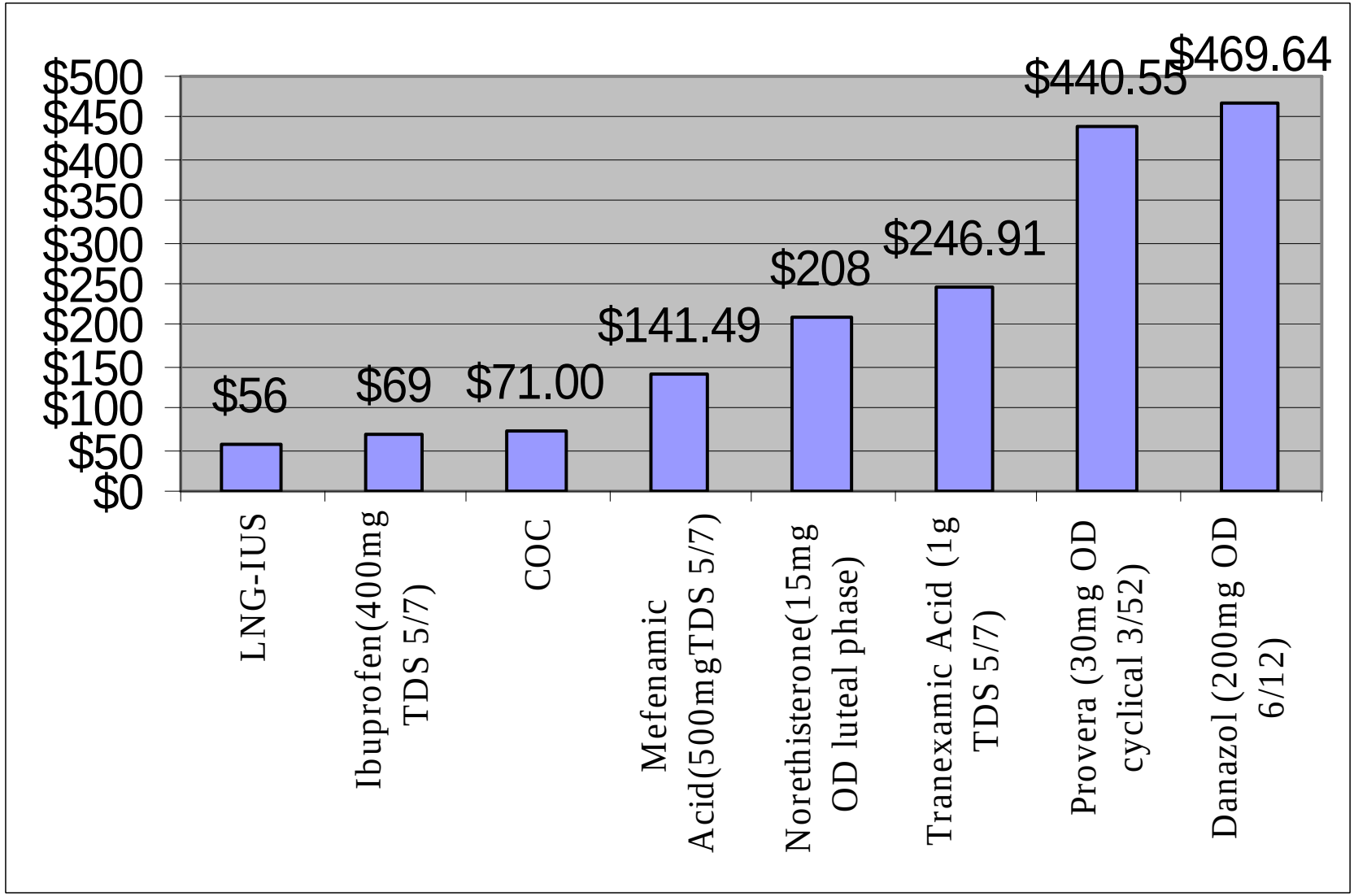


Effects

36/69 women continuing with it experienced ‘side-effects’, some experiencing more than one



Annual Costs of Medical Therapies



Surgical Therapy

- Endometrial ablation (2nd gen)
- Myomectomy;

  Open or hysteroscopic
- Hysterectomy

Novasure Endometrial Ablation

- Bipolar radio-frequency energy
- Impedance controlled
- Need for contraception
- GA vs LA
- 50-65% amenorrhoea at 5 years
- 10% hysterectomy at 5 years
- 90% satisfaction

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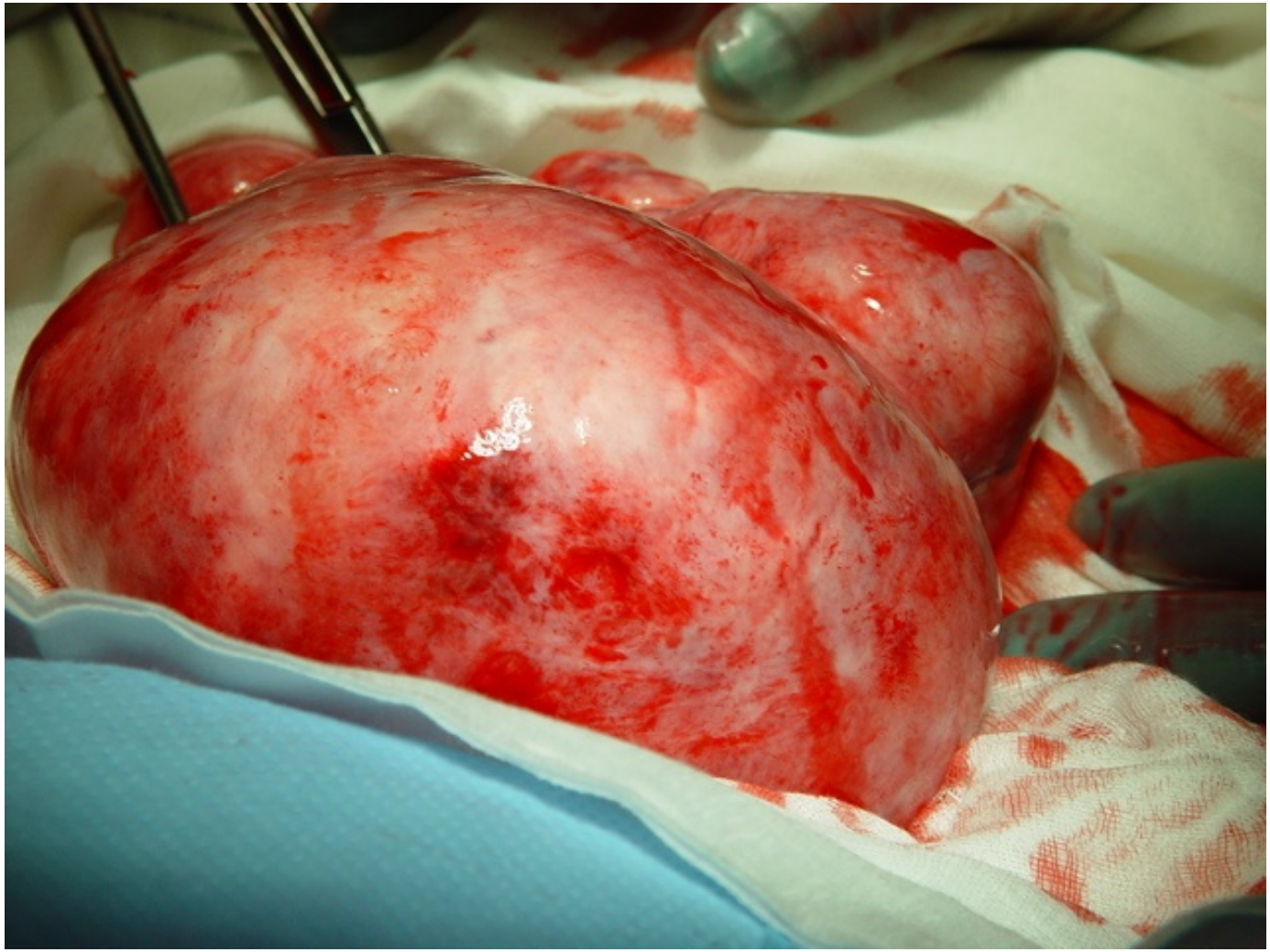

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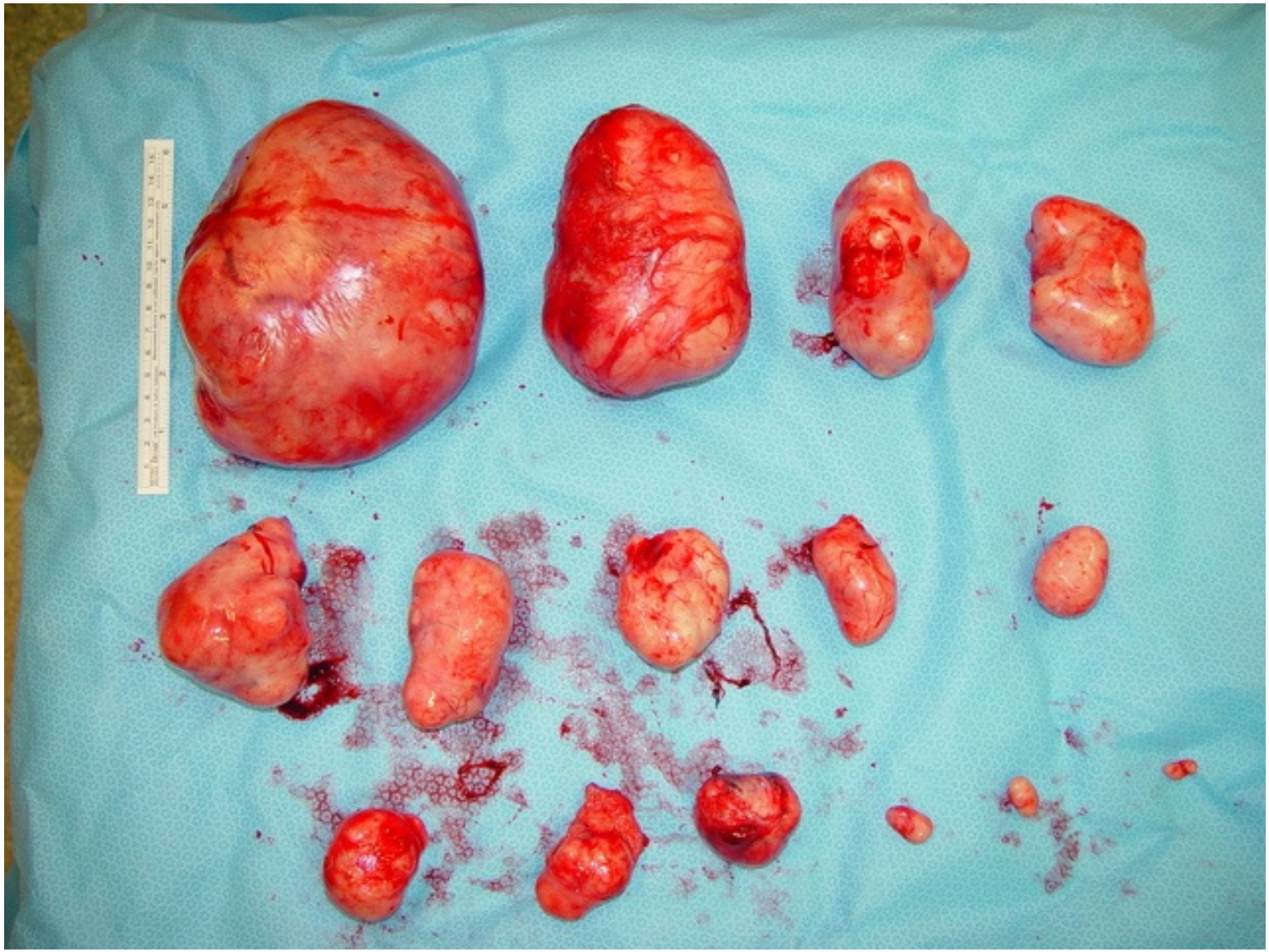

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Hysterectomy
VH, LAVH, TAH, LH

- Major op with mortality and morbidity
- Economic issues
- ?7% increased risk of prolapse
- Subtotal?
- BSO?
- 4% earlier menopause?
- However 100% cure rate for HMB

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Summary of Management

based on NZGG and RCOG

- History
- General and abdominal examination
- Bimanual, speculum +/- smear
- FBC and ferritin
- TFTs only if hypothyroidism suspected
- Tests for coagulopathy only if suspected
- TVS and ? pipelle

Assess Risk of Hyperplasia

The Risk is less than 2% if;

- <90kg
- <45 years
- Parous
- No Tamoxifen
- No PCO, no HNPCC or FH of Endometrial Cancer
- Not on unopposed ERT

Otherwise greater than 2%, maybe much more

Management in Primary Care

- Normal sized uterus on PV
- Hb above 80g/l (treat anaemia)
- Regular cycles
- Low risk of hyperplasia
- Treat women at low risk
- Refer treatment failures

Specialist Referral

- Irregular or prolonged periods
- Abnormal examination (abdo or pelvic)
- Hb < 80
- Inadequate response to initial treatment
- Endometrium > 12mm on scan
- All at ‘high’ risk of hyperplasia
- Abnormal pipelle

How to decide how to treat

- Patient bias
- Clinician bias
- Family complete? Smears normal?
- Contraceptive issues
- Hormone issues
- Burn issues
- Major surgery issues
- Read and sleep on it

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Cervical Cancer and Screening

- Cervical cancer 1 in 200 women. In NZ 180 new cases and 60 deaths p.a. (E&W, 2500,1000).
- NCSP NZ 1991 onwards
- Cartwright Enquiry
- Cervical cancer 12/100,000 1950-1991

  Reduced to 7/100,00 by 2002 (40%)

  (Cohort effect; women born 1940-1950s have a higher incidence Ca Cx, so real reduction is greater)
- HGSIL detection from 8 to 11/1000 women screened
- 73% coverage (women with current smear)

  Risk of cervical cancer reduced 90%
- Pacific / Asian 50%, Maori 65%,

  European 80% coverage

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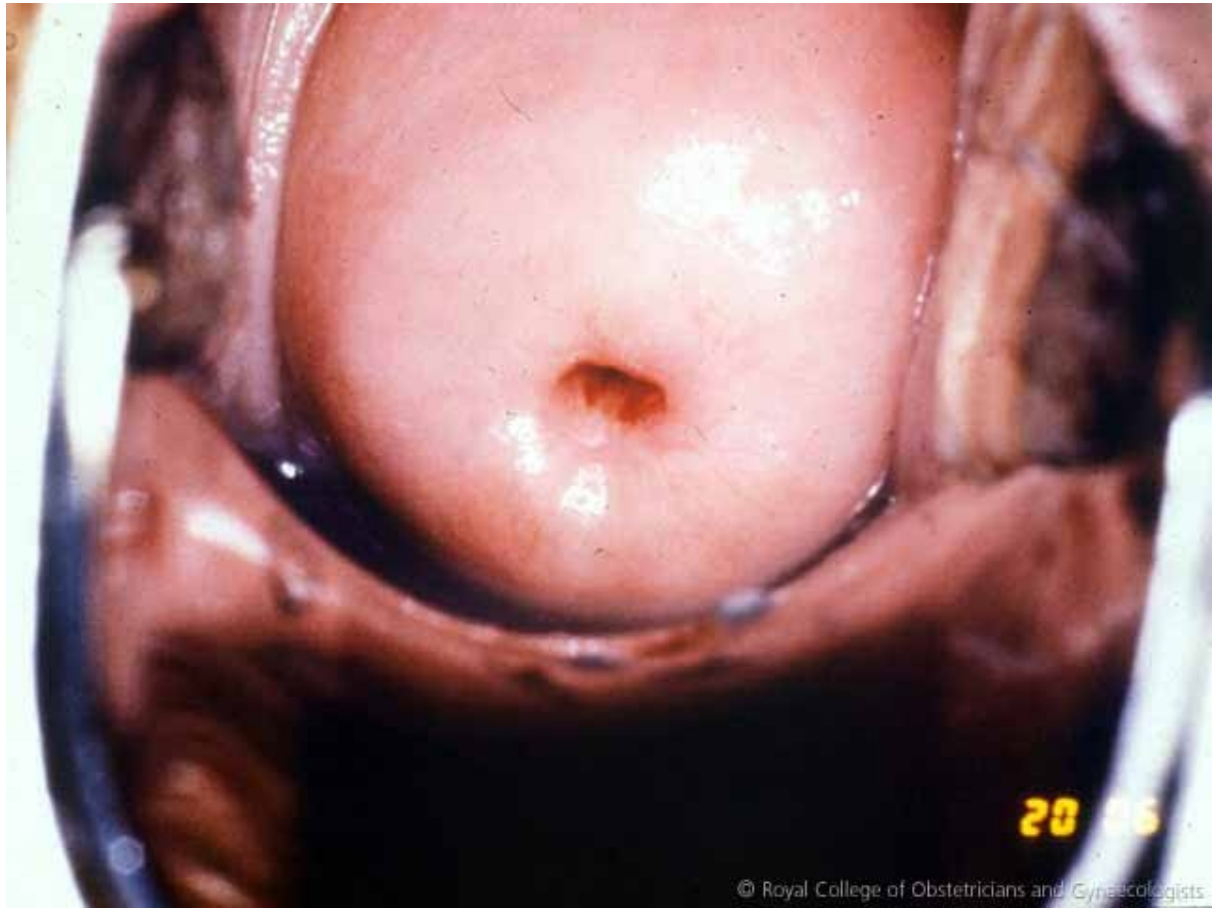
Normal cervix



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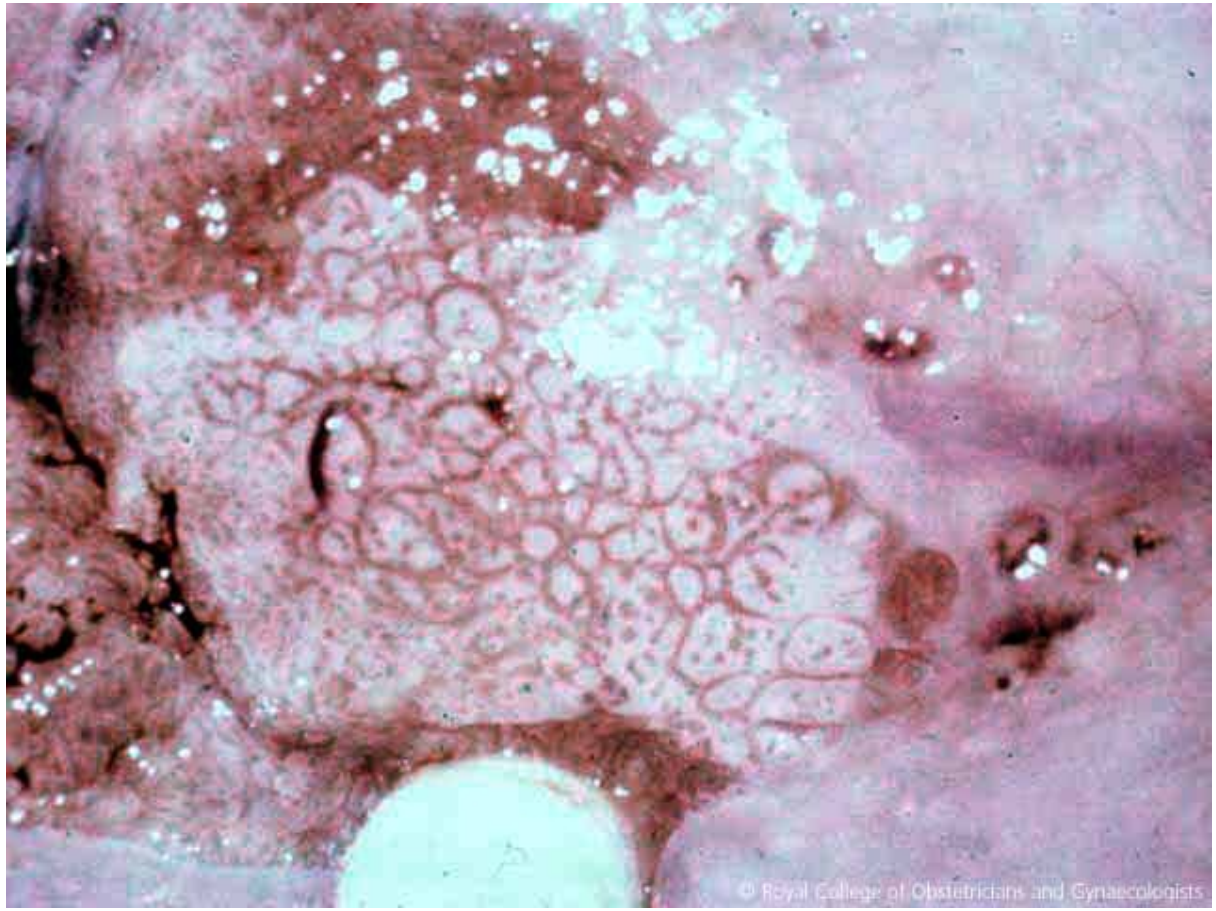
CIN 3



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Cervical Cancer

- Globally, cervical cancer is the second leading female cancer (after breast)
- Cervical cancer is the third most common cause of female cancer-related mortality worldwide.
- Age adjusted survival rates are around 65% in industrialised countries

Squamous vs Adeno Carcinoma

- Screening has reduced the incidence of squamous-cell carcinomas overall
- The incidence of adenocarcinomas has increased, because these cancers are more difficult to detect at a pre-invasive stage and because HPV prevalence is increasing.

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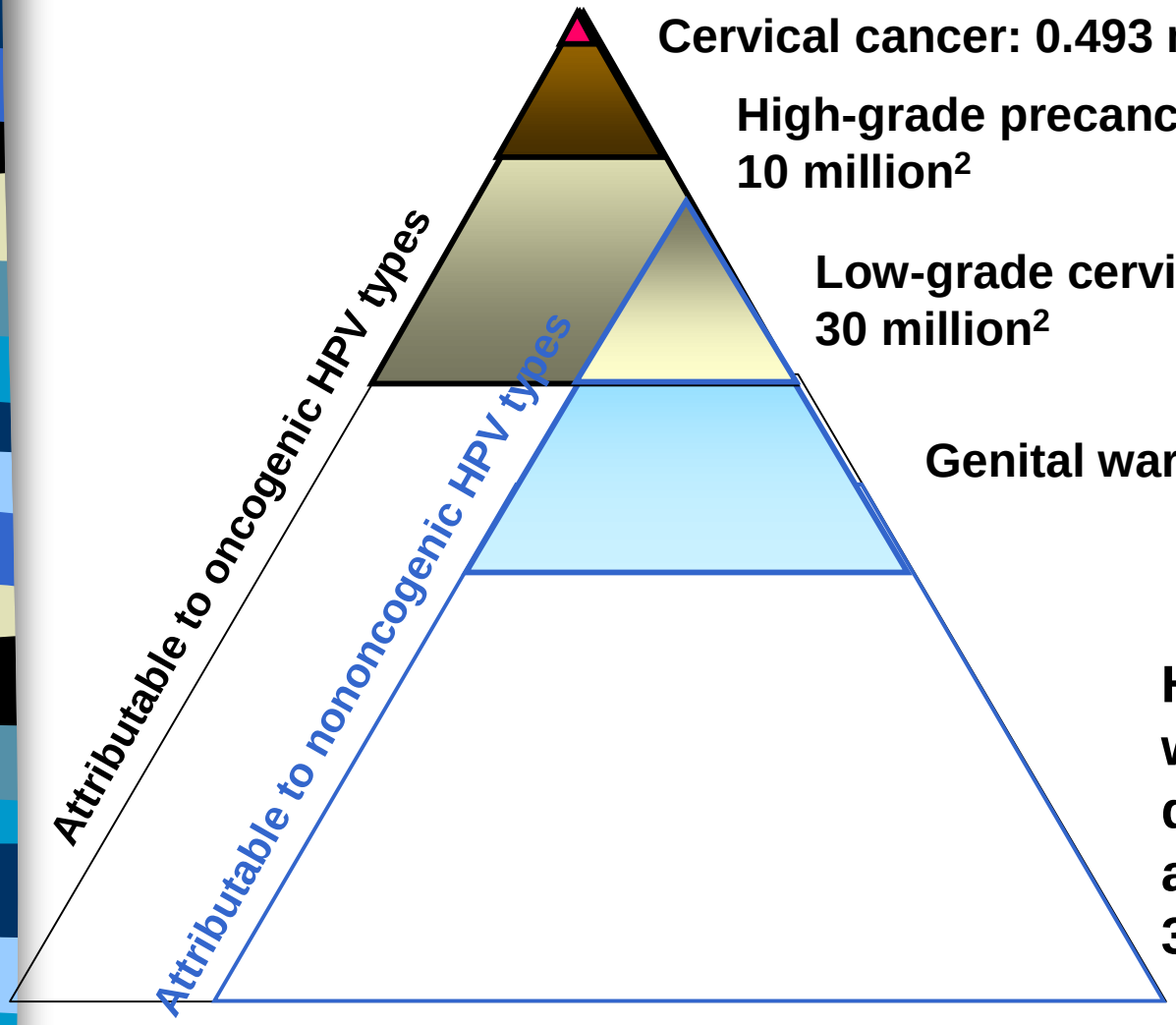
Estimated World Burden of HPV-Related Disease



Cervical cancer: 0.493 million in 2002[1]

High-grade precancerous lesions: 10 million[2]

Low-grade cervical lesions: 30 million[2]

Genital warts: 30 million[3]

HPV infection without detectable abnormalities: 300 million[2]

1. Parkin DM, Bray F, Ferlay J, Pisani P. *CA Cancer J Clin*. 2005;55:74–108.

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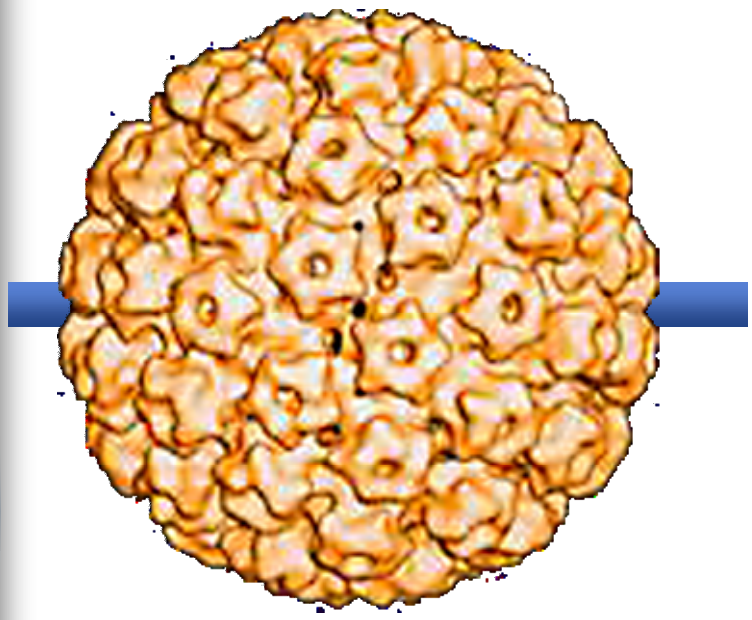
HPV

Nonenveloped double-stranded DNA virus[1]



- >100 types identified[2]
- ~30–40 anogenital[2,3]
  - ~15–20 oncogenic*[,2,3]
    - HPV 16 and HPV 18 types account for the majority of worldwide cervical cancers.[4]
  - Nononcogenic** types
    - HPV 6 and 11 are most often associated with external anogenital warts.[3]

*High risk; ** Low risk

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A few scary things about HPV

- Has evolved mechanisms to prevent exposure to the host's immune system
- Lifetime risk for sexually active men and women for HPV infection is 50%
- The highest risk of HPV infection occurs at age 15-19 years
- HPV infection is usually asymptomatic
- Sexual intercourse, manual-genital and oro-genital contact.
- Condoms are not foolproof in preventing infection.

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HPV continued

- Non-penetrative sexual transmission; 8% of virgins in one study being infected within 2 years
- Vertical transmission to a neonate is uncommon and fomite transmission rare but hypothesized (e.g. undergarments, surgical gloves).
- Infection is quickly acquired after sexual debut. In one study (with only one sexual partner) females under 19 years had a risk of acquiring cervical HPV of 46% at 3 years after first intercourse

Protection from HPV Infection

- Total abstinence from all genital contact
- Lifetime mutual monogamy between 2 (ex) virgins

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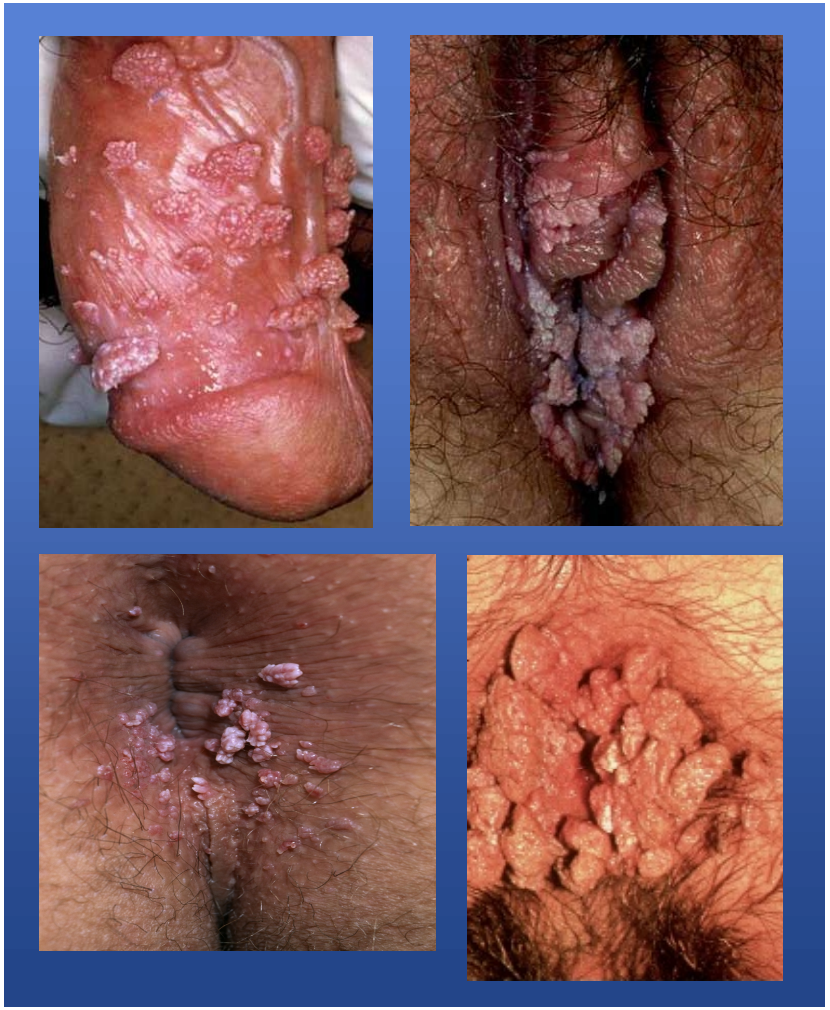
The Natural History of HPV

- Most HPV infections will clear
- Some with hrHPV may ultimately lead to cervical cancer via a number of intermediate steps
- Most low-grade lesions do not lead to cancer
- >90% of infections are spontaneously cleared by the immune system within approximately 1 year
- LSIL to HSIL and then to cervical cancer.
- However LSIL may progress directly to cervical cancer
- Some HPV infection may progress directly to HSIL
- One-third to two-thirds of women with HSIL will progress to cervical cancer if left untreated.

HPV and Anogenital Warts



- HPV 6 and 11 responsible for >90% of anogenital warts
- Clinically apparent in ~1% of sexually active US adult population
- Estimated lifetime risk of developing genital warts ~10%

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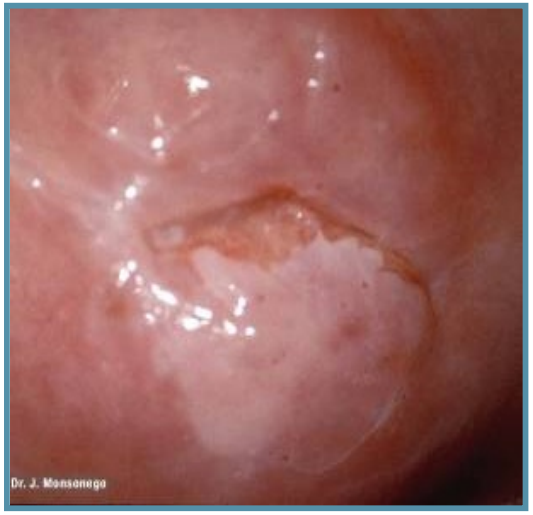
HPV & HPV Vaccine (Gardasil)

- 6, 11 cause warts. 16,18 cause CIN &75% Ca Cx
- PCR specific tests vs. hybrid capture
- Gardasil 3 injections over 0,2,6/12
- SE temp, local reactions
- 100% for 9-26 year old virgins (5 year)
- 40% if HPV status unknown
- Should Continue Cervical Screening Programme

CIN as Seen in Colposcopy

- CIN 1: Mild dysplasia; includes condyloma (anogenital warts)
- CIN 2: Moderate dysplasia
- CIN 3: Severe dysplasia; cancer in situ (CIS); FIGO Stage 0

CIN 1



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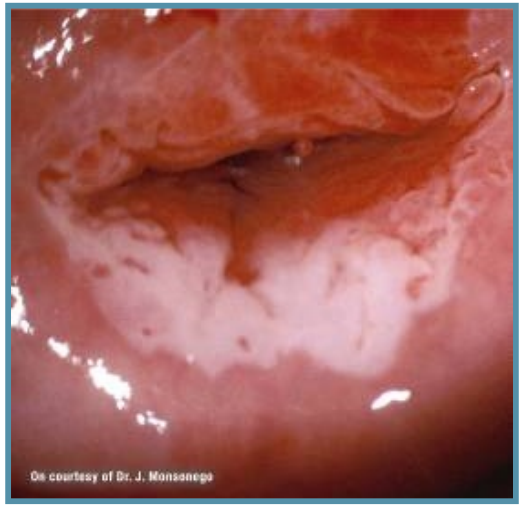

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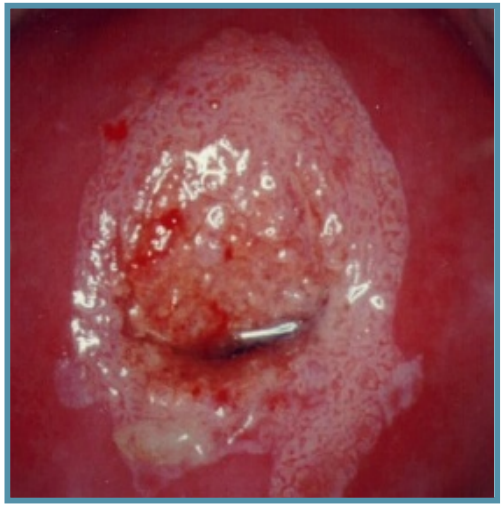

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The Role of HPV Testing in Practice

- Anyone over 30 years with normal smears who has a ASCUS or LSIL will have an HPV test as well.
- Under 30 HPV is common and usually clears.
- Smear taker to request HPV test 1 year PMH of treatment for CIN2/3 (If smears and HPV tests negative on 2 consecutive tests may return to 3 yearly follow-up).
- But can opt for annual smears without HPV test.
- For discordant cytology / colposcopy.

The Vaccine and Non-Virgins

- Vaccination after HPV infection is efficacious for the types that the patient has not been infected with.
- The likelihood of having been infected by both 16 and 18 is very low.
- Serotyping of the 22,500 women in the trials showed that only 20% of the women (sexually active women) had been infected by two types of HPV.
- The probability of the patient having been infected with all 4 types in Gardasil, is about 0.6%.
- Vaccination still has a place for sexually active women after appropriate counseling.

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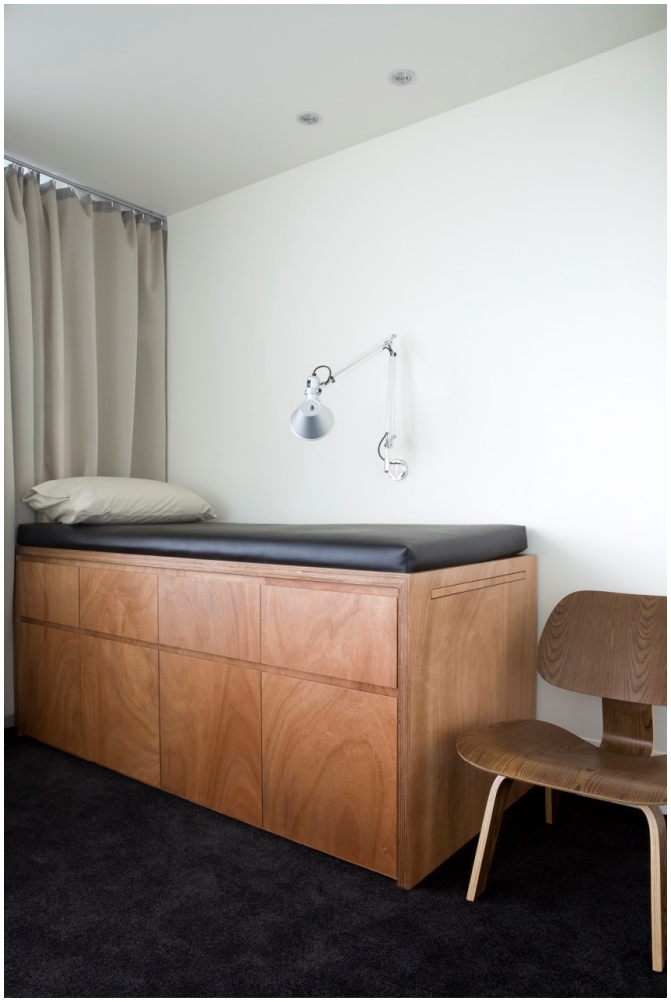
I have opinions of my own, strong opinions, but I don't always agree with them.

George W Bush



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Thank you

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