

## SEXUALLY TRANSMITTED VIRUSES

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 18 April 2011

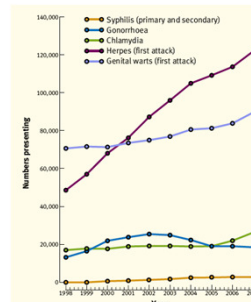
### Overview

- Introduction
  - Prevalence of sexually transmitted viruses (STIs)
    - Genital tract mucosa
- Individual viral STIs
  - Genital tract disease
  - No genital tract disease

### INTRODUCTION

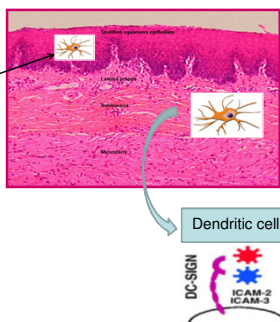
- > 30 bacterial, viral and parasitic pathogens are transmissible sexually
- Worldwide prevalence of **viral STIs** (sexually transmitted infections)
  - ~ 33.4 million people were living with HIV in 2008
  - ~ 400 million people with chronic hepatitis B virus (HBV)
  - ~ 170 million people with chronic hepatitis C virus (HCV)
  - HPV accounts for about 510 000 cases of cervical cancer annually
- People at high risk for STIs
  - men and women aged 15 - 49 years

### UK incidence of STIs from 1998 - 2007

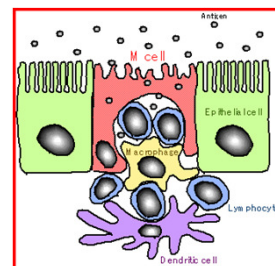
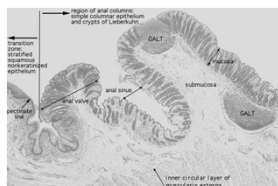


### STRUCTURE (genital mucosa)

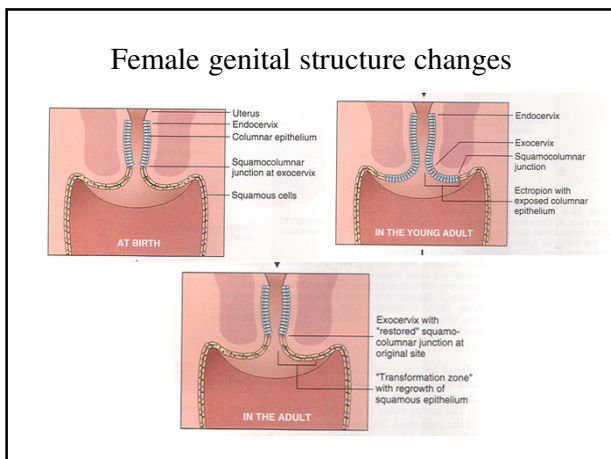
- Vagina, ectocervix, glans penis and inner foreskin, distal end of male urethra consist of:
  - stratified squamous epithelial cells interspersed with immature Langerhans cells (LC)
  - these LC overlie the lamina propria or submucosa
- LC in genital mucosa are:
  - motile and
  - readily emigrate from tissue to draining lymph nodes following contact with an antigen



### STRUCTURE (rectal & anal mucosa)



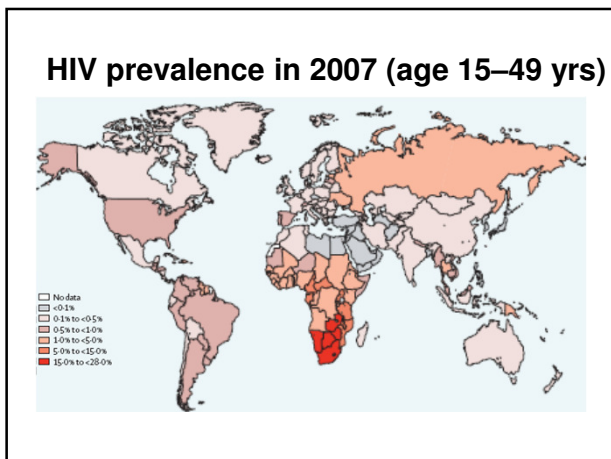
- Simple columnar epithelium
- M – cell
  - in rectal mucosa



### Viral STIs

- Common
  - HIV-1 & 2
  - HSV 1 & 2\*
  - HPV\*
  - HBV
- Less common
  - HCV
  - *Molluscum contagiosum*\*
  - CMV (in immunosuppressed individuals)\*
- Other viruses transmitted via seminal fluid
  - HTLV-I & II, EBV, HHV-8

\* Associated with disease/pathology of the genitalia



### HIV Transmission routes : Transmission risk (%)

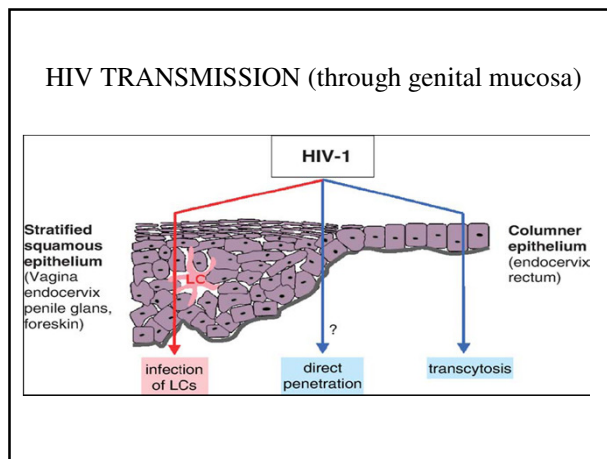
Route	Transmission risk (%)
Sexual	
penile-vaginal	0.001
penile-anal	1
Parenteral	
needle stick injury	0.3
IV drug use	1
blood products	100
Vertical	
in utero	~10
during labour	~60
breast-feeding	~30

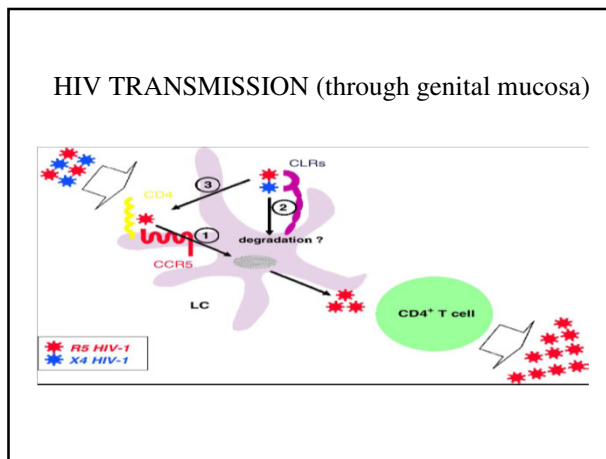
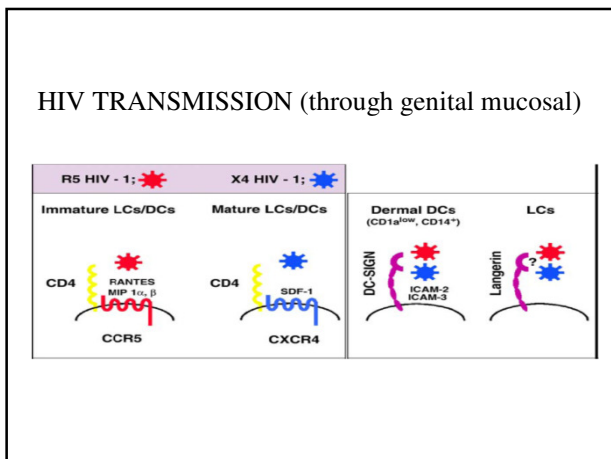
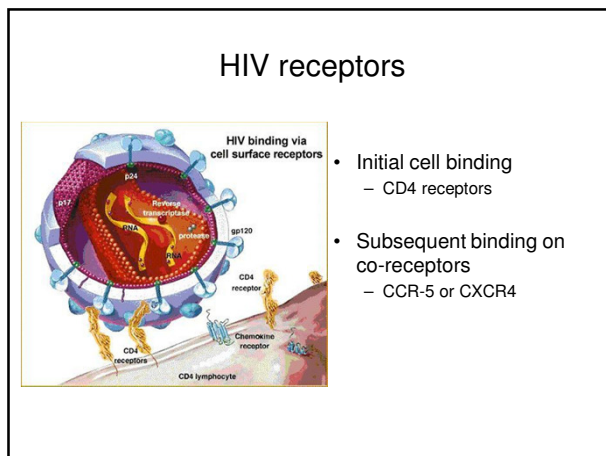
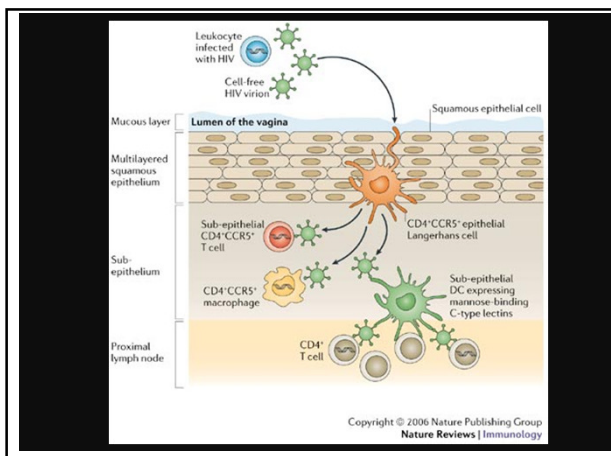
0.1 transmission per 1000 acts (Viral Load < 1700 copies/ml)

2-3 transmissions per 1000 acts (Viral Load > 38 500 copies/ml)

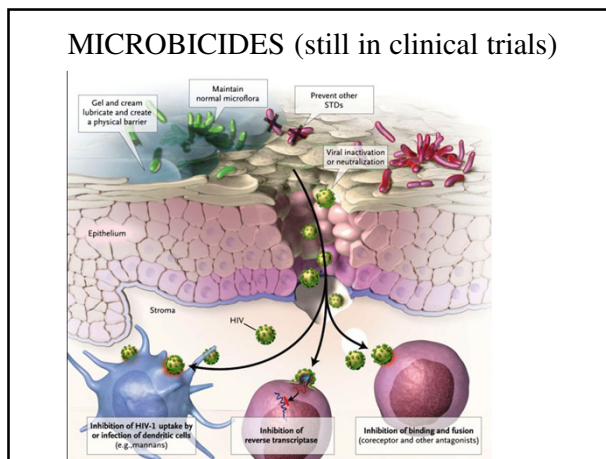
*Gray et al. Lancet 2001; 357: 1149-53.*

- ### Factors influencing sexual transmission of HIV
- High HIV viral load
  - Other STIs - ↑ CD4 lymphocytes - genital ulcers
  - Female gender – at ↑ risk than males
  - Circumcision status - ↑ risk in uncircumcised men
  - Vaginal tears – during sexual intercourse





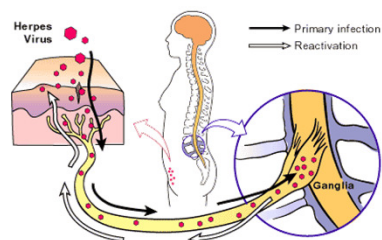
- ### HIV MANAGEMENT
- Diagnosis
    - HIV ELISA
    - HIV PCR - < 18 months
  - Treatment
    - antiretroviral drugs
    - ARV treatment monitoring – HIV viral load & CD4 count
  - Prevention
    - ABC – abstain, be faithful, condoms
    - Circumcision – ~ 60% effective
    - ARVs – stop mother to child transmission, for post exposure prophylaxis, and reduce infectiousness of HIV-positive individuals
    - Microbicides – topical agents designed to block HIV-1 infection (still in clinical trials)
    - No vaccine yet



## Genital herpes

- Herpes simplex virus 1 and 2 (HSV-1 and HSV-2)
- Latent infection → reactivation
  - HSV-2 more severe, more prone to reactivation
- The first episode presents with multiple painful genital ulcers
- Recurrent episodes occur in about a half of patients, tend to be less severe

## HSV - Pathogenesis



- Reactivation
    - Recurrent HSV infection
    - Asymptomatic viral shedding
- NB!!! HERPES IS FOR EVER!!!**

## Genital herpes - clinical

- Acute, very **painful** vesicle
  - 3 - 7 days after exposure
- Break to form **painful** shallow ulcers

## Genital herpes - clinical

- Regional lymphadenopathy
  - ± disuria
  - ± headache, fever, malaise & myalgia
- Healing takes 2-3 weeks
- Complications
  - aseptic meningitis
  - meningo-encephalitis
  - urinary retention

## Genital herpes and HIV

- Can be prolonged & extensive
  - >1 month = AIDS defining condition

## Neonatal herpes

- Acquired in utero or during birth
- Clinical features – refer to neonatology lectures

## HSV - Diagnosis

### Laboratory diagnosis for complicated cases

- Viral isolation in cell culture
  - Inoculate vesicular fluid / scrapings / swab from ulcer
- Direct detection : Electron microscopy (EM)
  - Collect vesicular fluid between 2 microscope slides
- PCR
  - CSF for meningitis / meningo-encephalitis
- Serology: - NOT the test of choice!
  - HSV IgM and IgG

## HSV

### – Treatment & prophylaxis

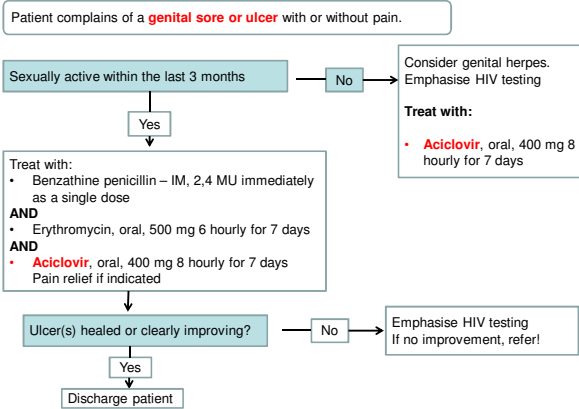
- Acyclovir, Valacyclovir\*, Famcyclovir for 7 days
  - *Early antiviral treatment alleviates symptoms & prevents serious complications*
- Resistant infections: Foscarnet, Cidofovir
- Depending on the frequency of recurrences
  - Episodic treatment
  - Long-term suppressive treatment
    - *Decreases attacks*

\* – longer t<sub>1/2</sub>, ↑ bioavailability

## HSV treatment & prophylaxis in pregnancy

- Treatment
  - acyclovir, valacyclovir, famcyclovir
  - intravenous acyclovir for severe infections
- Prophylaxis
  - daily suppressive acyclovir in the last 4 weeks of gestation
  - Caesarean section should be offered to all women with active genital herpes lesions at the time of delivery
    - not of benefit in reducing transmission for women presenting with ruptured membranes for greater than 4 hours

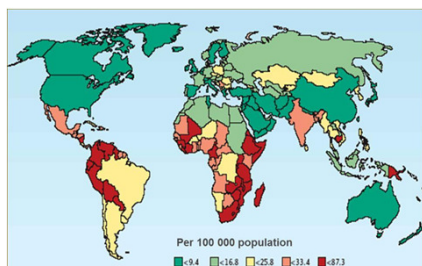
## SOUTH AFRICAN STI SYNDROMIC MANAGEMENT - 2009



## HUMAN PAPILLOMA VIRUS (HPV)

= causes **CERVICAL CANCER**

- ~ 510 000 new cases of invasive cervical cancer / year
- ~80% occurs in the developing world



## HUMAN PAPILLOMA VIRUS (HPV)

- >100 HPV subtypes have been described
- Anogenital HPV subtypes infect the epithelial lining
  - cervix, vagina, vulva, rectum, urethra, penis, and anus
- HPV subtypes 16, 18, 31 & 45
  - high risk types for **cervical cancer**
  - 16 & 18 – more common causes of cervical cancer
- HPV subtypes 6 & 11
  - commonly associated with genital warts

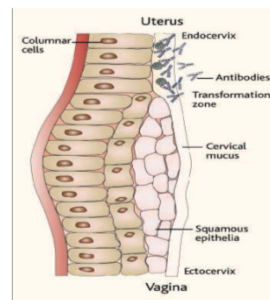
### CERVICAL CANCER RISK FACTORS

- Most significant factor is HPV infection
  - lifetime number of sexual partners influence HPV acquisition
- Persistent or latent infection with hrHPV
  - important determinant in the development of cervical cancer
- Other factors that may be associated with HPV persistence
  - 30 years or older
  - immunosuppression from any cause
  - cigarette smoking
  - Chlamydia infection

### HUMAN PAPILLOMA VIRUS

In the cervix

- HPV infects the basal epithelial cells of the squamous epithelia
- The viral types most responsible for causing cervical cancer
  - make proteins (E6 and E7) that bind two tumor suppressors, p53 and retinoblastoma protein
  - allows the squamous epithelial cells to divide abnormally = cancer



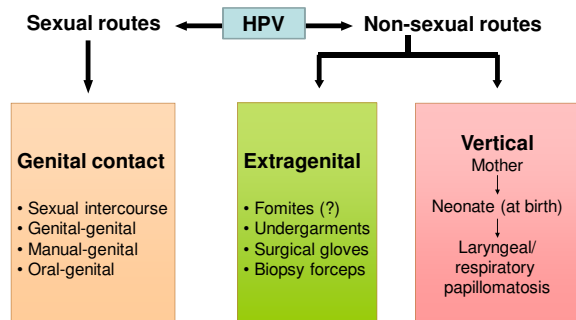
### Genital warts (types 6 & 11)

- ♂: penis or scrotum
- ♀: vulva, perineum, perianal area, vagina or cervix
- May be a marker for exposure to hrHPV
- Physical & psychological morbidity because of their recurrence & resistance to treatment

### Genital warts in HIV patients

- Severe disease

### HPV Transmission



### Recurrent respiratory papillomatosis (types 6 & 11)

- Pregnant ♀ with genital warts → vertical transmission of HPV during NVD → laryngeal papillomas in baby (rare)
  - Morbidity high
    - May lead to significant airway compromise
    - Repeated surgical procedures often necessary

## CERVICAL CANCER SCREENING

- Cytology (from cervical swab)
  - PAP smear – to look for abnormal cervical cells (koilocytes)
- Histology (from cervical biopsy)
- Molecular detection (HPV PCR)
  - hrHPV → present/absent
  - HPV genotyping → identify 37 different types

## HPV vaccines

- Gardasil® (Merck)
    - HPV 6, 11, 16 & 18 (quadrivalent)
    - 0, 2 & 6 months IM
  - Cervarix® (GlaxoSmithKline)
    - HPV 16 and 18 (bivalent)
    - 0, 1 & 6 months IM
- Efficacy 100% in ♀ who are HPV naïve
- Cross protection to types 31, 45 predominantly, & 33, 35, 52, 58

## Administration of HPV vaccine

- For optimal effect the vaccines should be given prior to sexual activity so that recipients will be naïve to all vaccine HPV types
  - The primary target are young ♀ aged 11-12 years
  - Can be given to ♀ 9-26 years of age
- ♀ who are sexually active
  - Should however still be given the vaccine, but they will only obtain protection against those vaccine HPV types to which they have not been exposed

## Viral STIs

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  - HSV 1 & 2\* ✓
  - HPV\* ✓
  - HBV
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## *Molluscum contagiosum*

- Pox virus
- Usually a disease of childhood
  - Shared towels
  - Direct bodily contact
- Adults
  - Sexually transmitted
  - Marker of more serious STDs
- Severe in patients with AIDS
  - Widespread
  - Recurrent infection

## *Molluscum* - Clinical Features

- Pearly, flesh coloured, raised nodules, small white core often seen
  - “umbilicated”
- 2 - 5 mm in diameter
- Painless
- Often persists for months

## Molluscum – Diagnosis

- Clinical diagnosis
- EM
  - Lesion material between to microscope slides

## Molluscum

### – Treatment & prevention

- No specific antiviral treatment available
- Resolves spontaneously with time
- Cryotherapy / surgical removal of core
- Imiquimod cream (immune modulator)
  - 80% effective

## HEPATITIS VIRUSES (HBV & HCV)

- South Africa has high prevalence of HBV, and much lower prevalence of HCV
- **Transmission:**
  - blood and blood products } parenteral
  - needles e.g. tattooing }
  - **sexual**
  - vertical (perinatally)
  - horizontal in families – only for HBV
- **Complications:**
  - Cirrhosis
  - Hepatocellular carcinoma
  - Extrahepatic complications, e.g. renal disease

## Hepatitis B VIRUS (HBV)

- Worldwide distribution
  - 400 million carriers worldwide



## MANAGEMENT OF HBV & HCV

- Diagnosis
  - Serology
  - PCR
- Treatment
  - HBV: pegylated interferon, lamivudine, tenofovir, and others
  - HCV: pegylated interferon plus ribavirin
- Prevention
  - HBV vaccine – part of EPI
  - No vaccine available for HCV

## HIV interactions with other STIs

- Impact of HIV on other viral STIs
  - ↑ HBV & HCV replication
  - ↑ persistence of HPV
  - ↑ recurrence & severity of HSV
  - ↑ genital CMV disease
- Impact of other viral STIs on HIV
  - HSV - ↑ transmission of HIV