Urogenital Tract / 3rd year
Syphilis , HPV

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What you need to know about syphilis?

Etiology of syphilis

Transmission & Epidemiology

Pathogenesis

Clinical manifestations

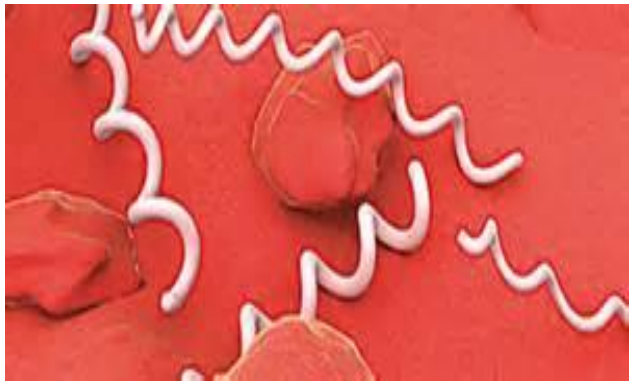
Diagnosis

Treatment & Prevention

Etiology of syphilis

Caused by *Treponema pallidum* which is:

- A member of the spirochete family
- Spiral-shaped (corkscrew shape)



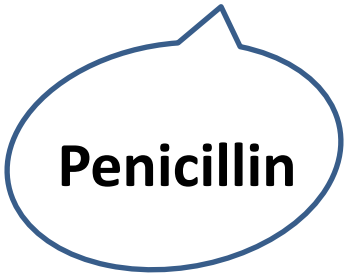
- Gram-negative, thin (0.1-0.2um in diameter) and 5 to 15um long
- Highly motile bacterium
- Rapidly die on drying
- killed by detergents and disinfectants
- Heat sensitive

Transmission & Epidemiology

- Direct contact with infectious lesions of skin and mucous membranes
- Most commonly occurs during sexual activity:
  - Unprotected vaginal, anal or oral intercourse
- Less commonly occurs during non sexual activity
  - Blood transfusions
  - Congenital: vertical transmission from mother to child during pregnancy
  - Direct contact with an infectious lesion
- Cannot be spread through contact with toilet seats, doorknobs, swimming pools, shared clothing, or eating utensils

Transmission & Epidemiology

- The infective dose 50 (ID_{50}) is only about 60 organisms
- ID50 = The dose of microorganisms required to cause infection in 50% of the experimental animals
- The prevalence and incidence have been decreasing since 1943 by 95%, Why?

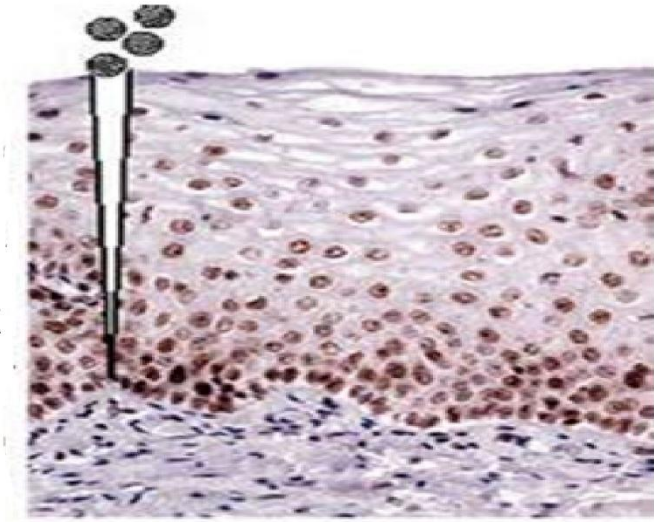


- Groups at risk are:
  - ✓ Homosexuals (MSM)
  - ✓ Individuals with HIV
  - ✓ Sex workers

Entry

The spirochete can reach the subepithelial tissues through

1. Minute abrasions that occurs during sexual intercourse
2. Passage between the epithelial cells of mucous membranes



ectocervix

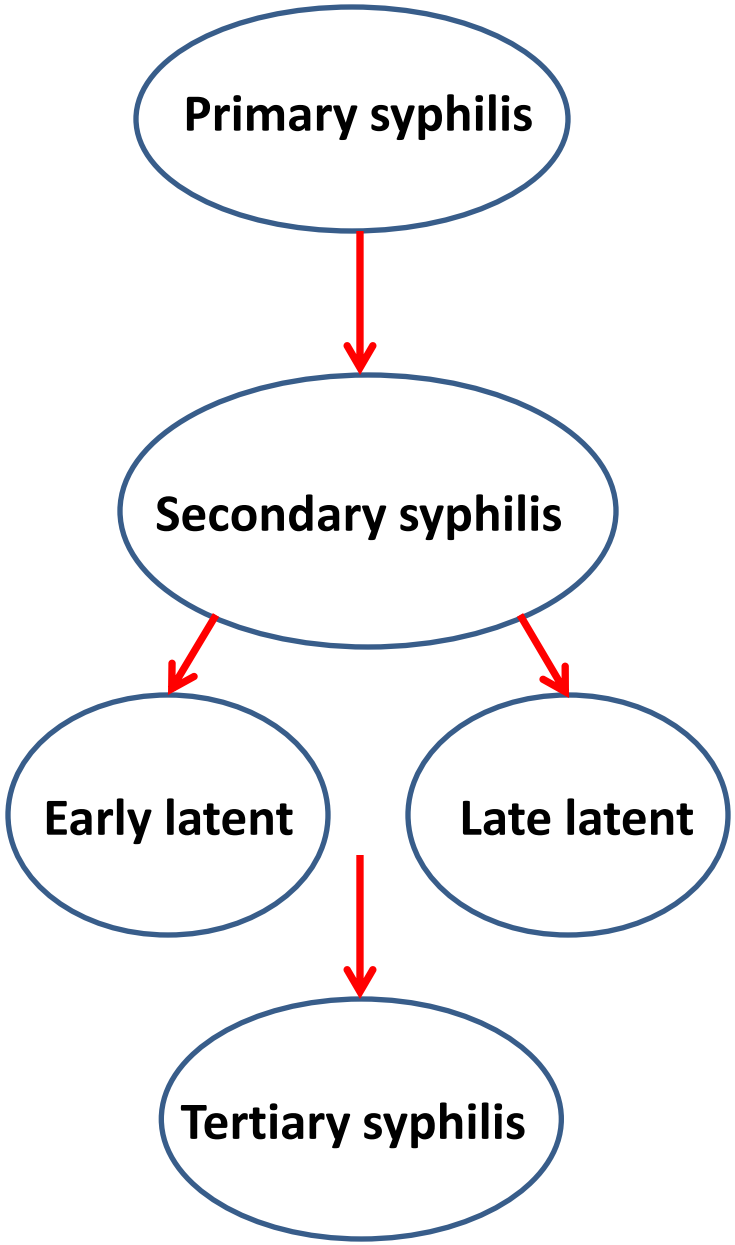
Then they replicate in the subepithelial tissue

From their they can escape to the systemic circulation

Endocervix

Pathogenesis and Clinical Manifestations

Stages of syphilis



!00 **untreated infected** patients with primary syphilis

↓

70% of them will undergo secondary syphilis

↓

1/3 of the 70% will undergo latent syphilis

↓

1/3 of them will develop tertiary syphilis

Pathogenesis and Clinical Manifestations

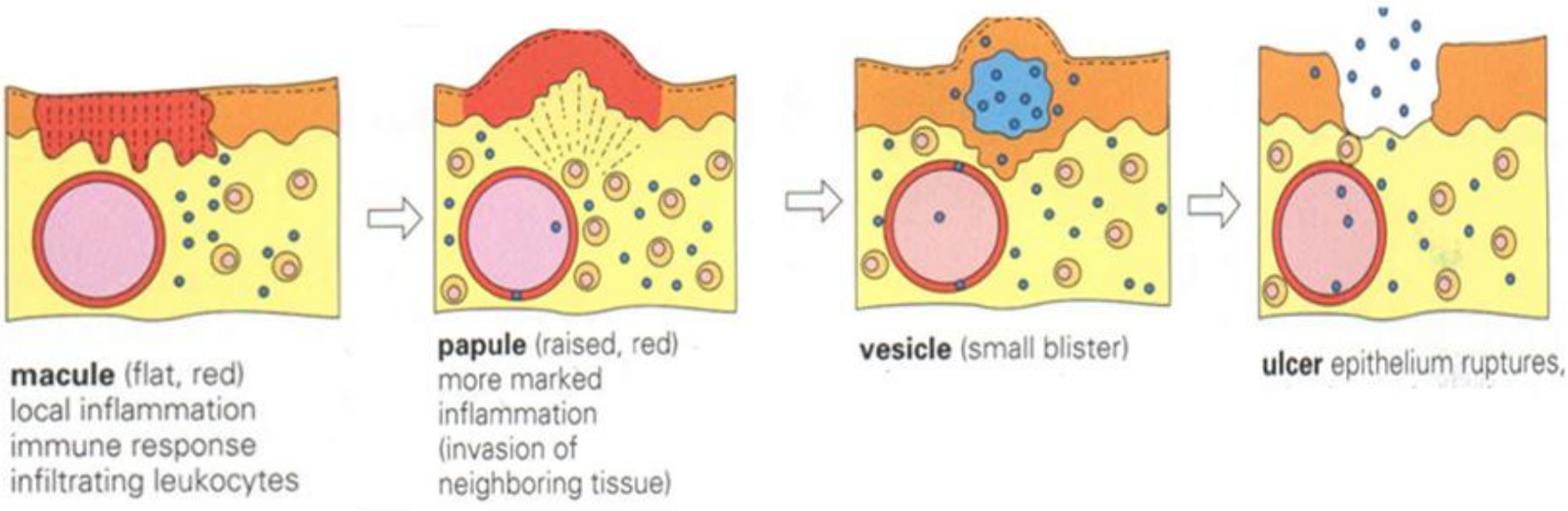
Stages of syphilis

- ***Treponema*** **causing obliterating endarteritis**
- Obliterating **endarteritis:** inflammation of the intima or inner lining of an artery) that results in an occlusion of the lumen. This obstruction eventually causing necrosis, ulcers, and death of the affected tissue

Pathogenesis and Clinical Manifestations

Primary syphilis

- The first symptom of syphilis is **chancre** (sore) develops between 10-90 days after exposure (mean of 21 days) at the site of infection
- The chancre is a **painless** ulcer, **moist** base with **well defined** and **indurated margins**
- Usually single unless immunocompromised



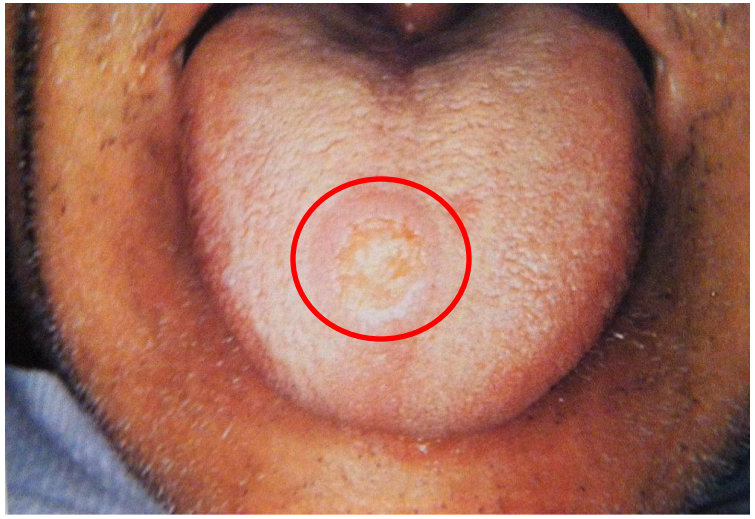
Pathogenesis and Clinical Manifestations

Primary syphilis

- Highly infectious
- Regional **painless** and **nontender** Lymphadenopathy (swollen glands)
- **Systemic dissemination** continues during this period
- The chancre resolves spontaneously over a period of 4-6 weeks without treatment
- Exudate from chancre used for diagnosis
- 1/3 heals spontaneously and 2/3 of untreated patients undergo the secondary syphilis

Pathogenesis and Clinical Manifestations

Primary syphilis



Pathogenesis and Clinical Manifestations

Secondary syphilis

Penetrate microabrasions

~ 21 days

The chancre resolves after 4-6 weeks

Secondary syphilis appears 2-10 weeks after the appearance of chancre

Constitutional symptoms

maculopapular skin rash

Other complications

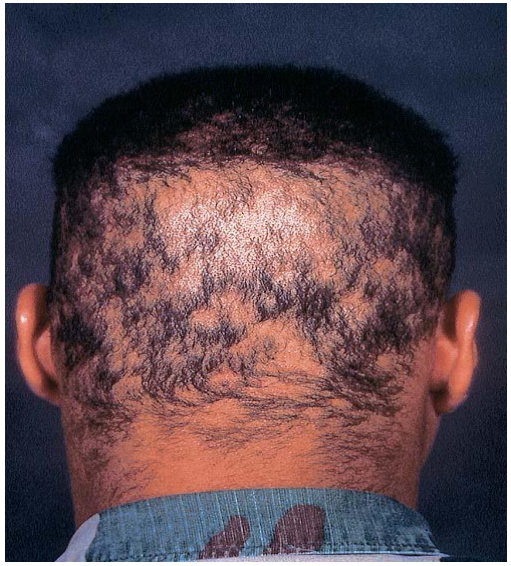
Pathogenesis and Clinical Manifestations

Secondary syphilis

- Secondary or disseminated syphilis **develops 2 to 10 weeks after the appearance of the chancre**
- Infection spreads through the blood and lymph system
- Common sings & symptoms include:
  - generalized **nontender lymph node enlargement**
  - **chancre may still be present**
  - fever, malaise and other manifestations of systemic infection
  - **mucocutaneous maculopapular and pustular skin rash**
    - palms & soles
    - Abdomen
    - Face
  - condyloma lata: painless, mucosal, warty like rash, develop in warm, moist sites of the genitals and perineum.

Pathogenesis and Clinical Manifestations

Secondary syphilis



- **Less common symptoms include:**
  - ✓ Hair loss
  - ✓ hepatitis, GI ulceration
  - ✓ Arthritis and joint problems
  - ✓ Renal symptoms, Eye and ear abnormalities

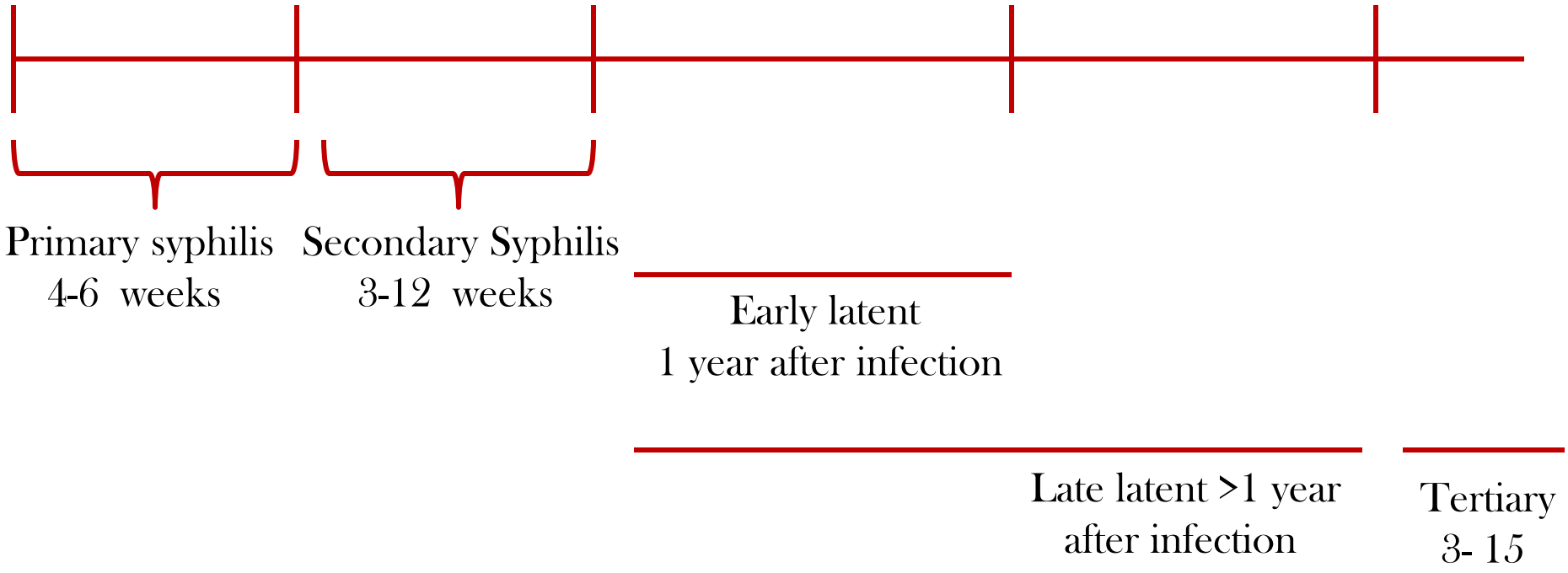
Because *Treponema* causing endarteritis it can damage anything has its own blood supply

- Lesions are **highly infectious**
- **Symptoms** resolve spontaneously **after 3-12 weeks**
- The illness enters the **latent** state in **1/3** of patients

Pathogenesis and Clinical Manifestations

Secondary syphilis

Pathogenesis and Clinical Manifestations



Pathogenesis and Clinical Manifestations

Latent Syphilis (hidden)

- Latent syphilis is defined as having serologic proof of infection without symptoms of disease
- Divided into:

On and off

a. <u>Early latent syphilis</u>

- One year or less post-infection.
- Occasional relapses of active lesions
- Transmittable from mother to child, resulting in congenital syphilis

b. <u>Late latent syphilis</u>

- is defined as asymptomatic infection of longer than one year post-infection.
- Transmittable from mother to child, resulting in congenital syphilis

- One third of patients with untreated latent syphilis develop tertiary syphilis

Pathogenesis and Clinical Manifestations

Tertiary syphilis

- The stage of end organ damage
- The major manifestations occur after 3 to 15 years of primary infection
- Three major forms

- Neurosyphilis: e.g Meningoencephalitis and paralysis
- Cardiovascular: aneurysm of ascending aorta, aortitis
- Skin and bone granulomatous lesions (Gummas)

Pathogenesis and Clinical Manifestations

Congenital syphilis

Congenital syphilis: acquired *in utero* (transmitted from mother to a child during gestation).

➢ **Early congenital syphilis**

- Early manifestations appearing in the first 2 years of life.
- Resembles severe symptoms of adult secondary syphilis.
- The first symptom seen in up to 50% of newborns with congenital syphilis is snuffles (a nasal discharge in infancy characteristic of congenital syphilis).

➢ **Late congenital syphilis**

- Late manifestations appearing after 2 years.
- E.g Ocular syphilis, arthropathy, gummas.

Diagnosis

Syphilis diagnosis relies on:

1. Dark-field microscopy:

Detection of the organism in the exudates and lesions using dark field E.M or phase contrast,

is the most specific technique for diagnosing syphilis when an active chancre present

2. Nonspecific serological testing (nontreponemal antibodies)
   - VDRL=Venereal Disease Research Laboratory, detecting anticardiolipin antibodies
   - RPR=Rapid Plasma Reagin
3. Specific treponemal tests (confirmatory test)
   - FTA Antibody-Fluorescent treponemal antibody absorption
   - TPHA test- Treponemal pallidum haemagglutination assay
   - TPPA test- Treponemal pallidum particle agglutination assay

Test / stage	Primary	Secondary	Latent	After treatment
VDRL/RPR	70%	99%	ZERO	ZERO
FTA-Abs	80%	100%	95%	100%
TPHA	70%	100%	90%	100%

Sensitivity of serological test in syphilis

Diagnosis

Congenital syphilis:

Testing for IgM and retesting at 6 months of age, by which time maternal antibody levels have waned. Antibody titers remain elevated in babies with congenital syphilis

Treatment & Prevention

Treatment:

- Penicillin G (2.4 million units I.M)
- If allergic, Doxycycline or erythromycin is a good alternative
- In neurosyphilis use penicillin and Doxycycline together

Prevention:

- No vaccine
- Early diagnosis and treatment of case and contact is important
- Test for syphilis if any STD exists

Harald zur Hausen
Nobel prize holder / 2008 / Medicine

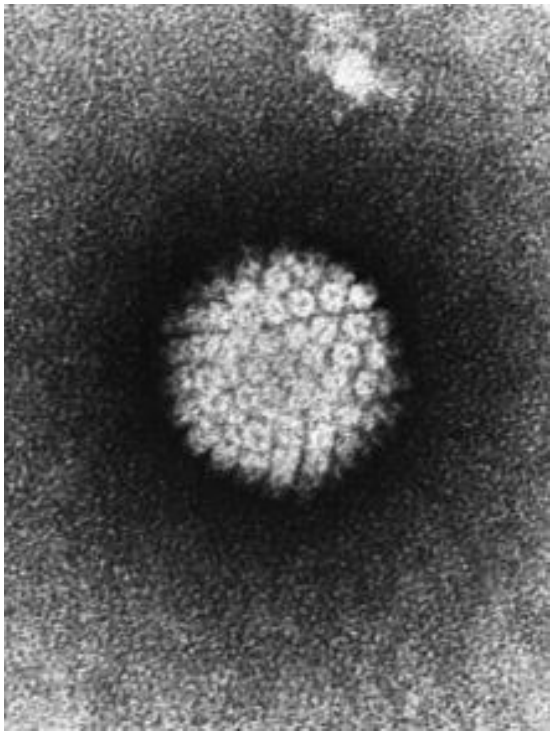
Human papillomavirus

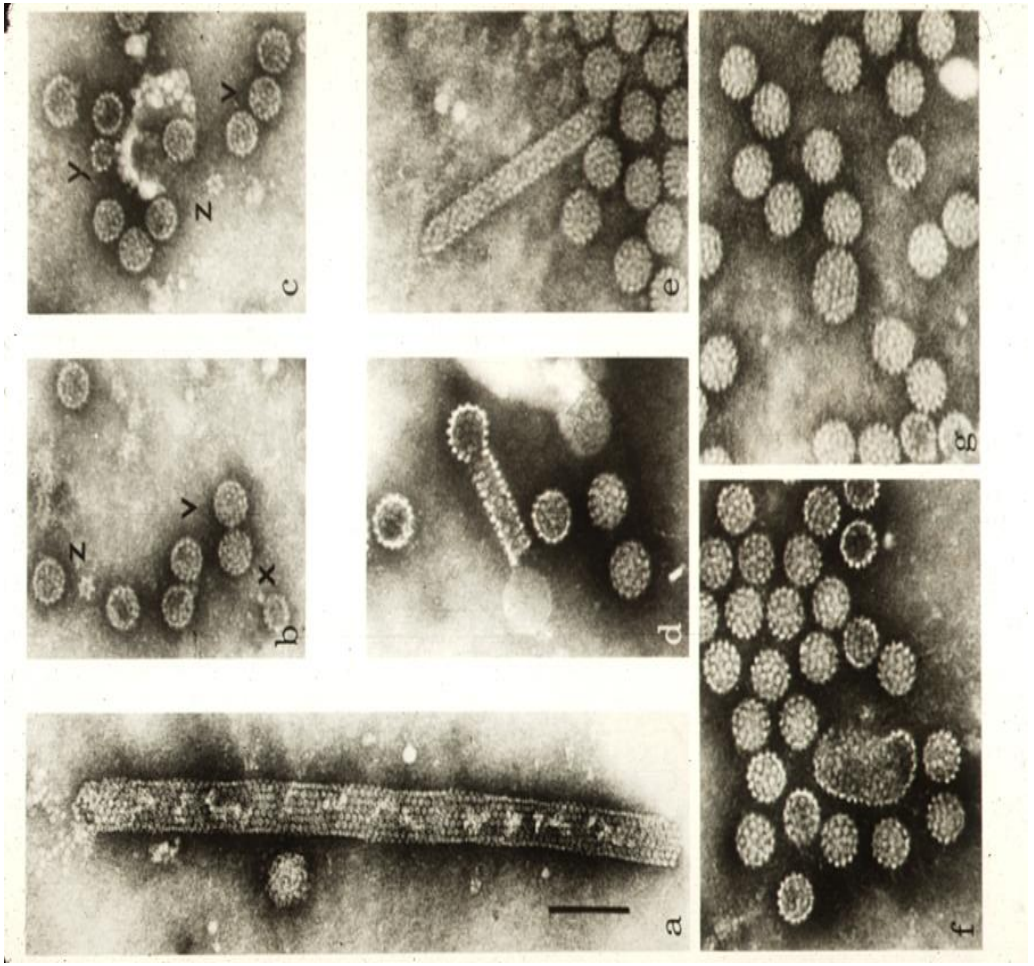
- Human papillomavirus (HPV) is a DNA virus.
- Non-enveloped

- sexually transmitted, also skin contact and perinatally.

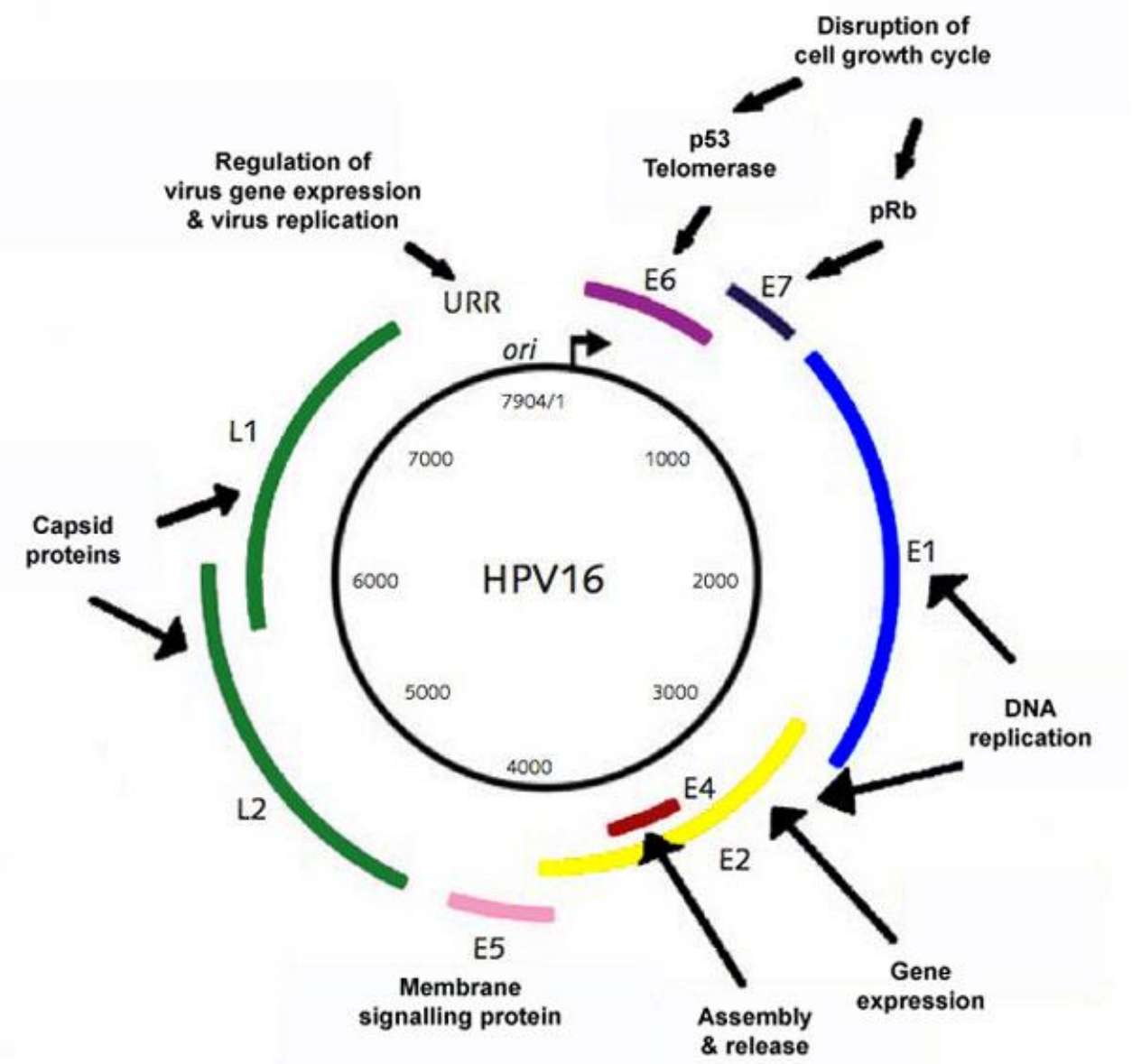
- >100 HPV genotypes.

HPV under E.M

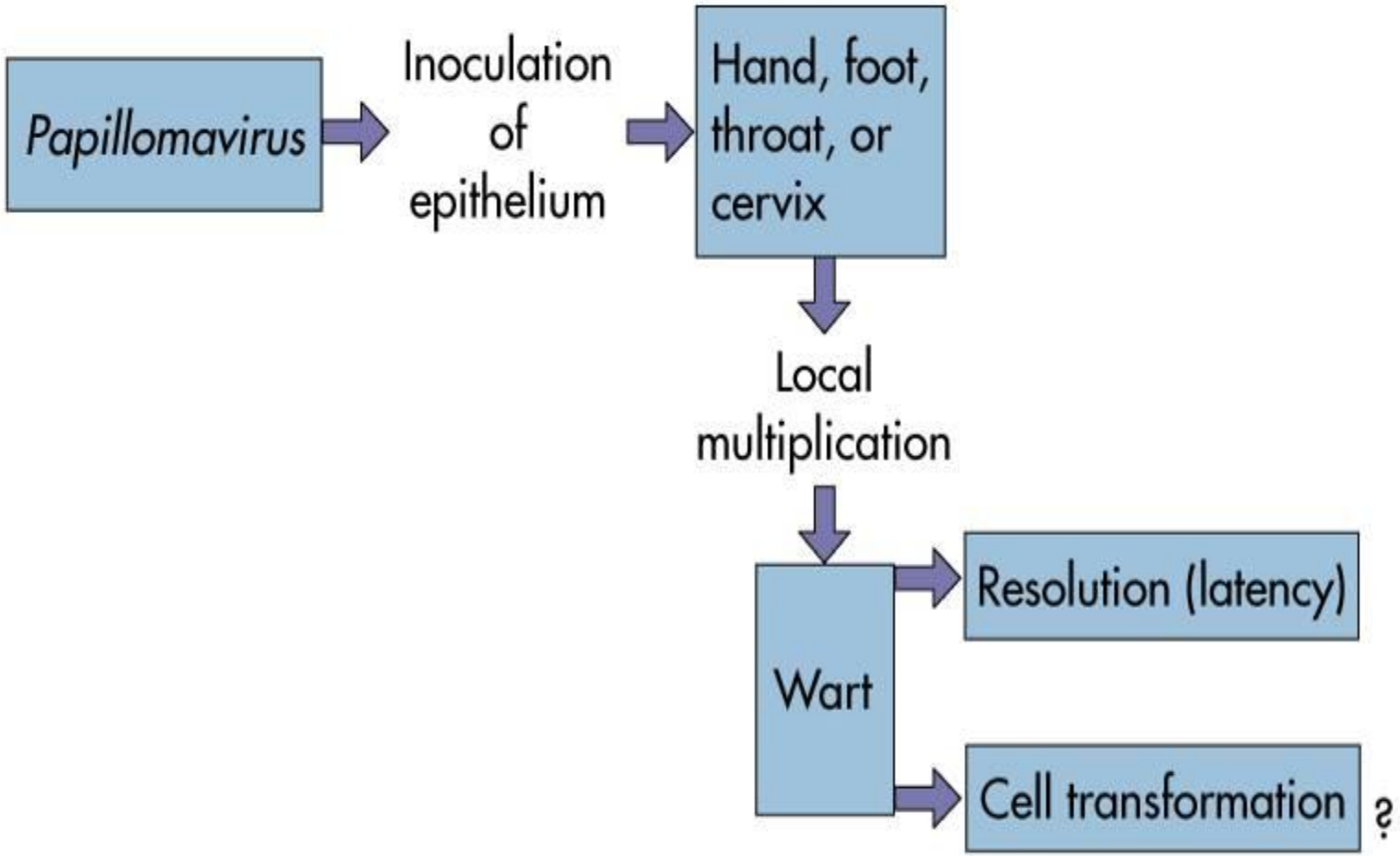




Human papillomavirus / genome



Human papillomavirus / pathogenesis



Human papillomavirus / Clinically

- **Risk factors:**
- Multiple sexual partners
- Combined oral contraceptive pills, Smoking.....

- **1. low risk HPV types (e.g types 6 and 11):**
- Papillomas are benign lesions that develop after a variable duration, usually weeks or months, of HPV infection.

- In a papilloma there is epidermal thickening with hyperkeratosis and parakeratosis.

- The lesions are called warts if they arise on the skin or condyloma if found on the genitalia.

Human papillomavirus / Clinically

- HPV 6 and 11 are also associated with laryngeal papillomas in children and other respiratory papillomas such as sino-nasal, tracheal, and lung papillomas

- Child presents with hoarseness, or even a life threatening airway obstruction

- These lesions are more common in infants and young children less than 5 years old who can acquire the infection during birth

Human papillomavirus / Clinically

Human papillomavirus / Clinically

Human papillomavirus

2. High risk genotypes: mainly types 16, 18, 31, 33 and 45.

(Cervical cancer)

- Persistent (HPV) infection > pre and malignant cervical CA (other cancers, laryngeal papilloma and genital warts).

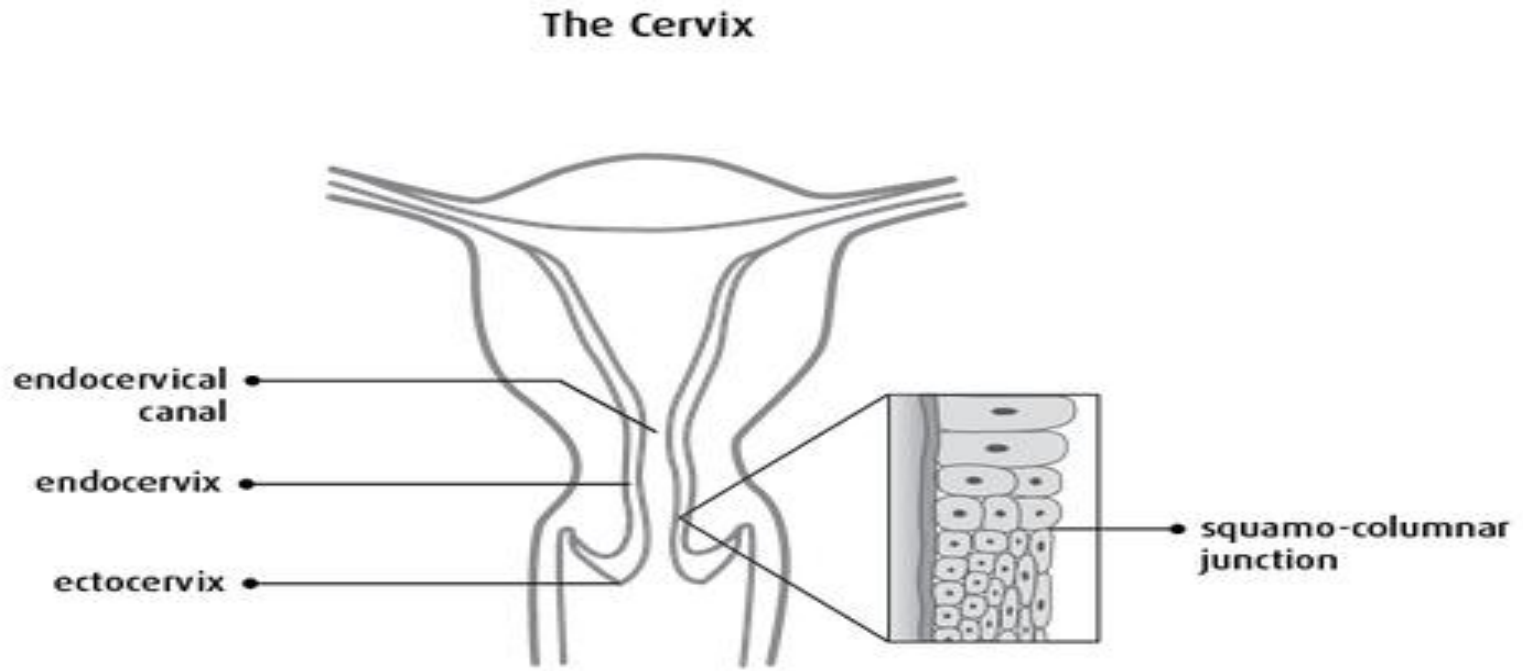
- E6 and E7 > inhibitions of P53 and RB genes respectively
- Approximately, ½ million cervical cancer cases are diagnosed annually worldwide, with 50% mortality.

- In the UK: 1600 deaths / year due to cervical cancer.

- The **endocervical canal** is the passageway from the uterus to the vagina.
- The 2 main types of cells in the cervix are:
- **Columnar cells** line the endocervical canal. They are glandular cells that make mucus. They are called columnar cells because they are tall and shaped like columns.
- **Squamous cells** line the ectocervix and vagina. They are flat and thin like the scales on a fish.

- The squamous cells join the columnar cells in an area of the cervix called the squamo-columnar junction.

This is also called the transformation zone because the tall columnar cells are constantly being changed into flat squamous cells, especially during puberty and child-bearing years. Precancerous changes of the cervix and most cervical cancers start in the transformation zone.



Transformation zone

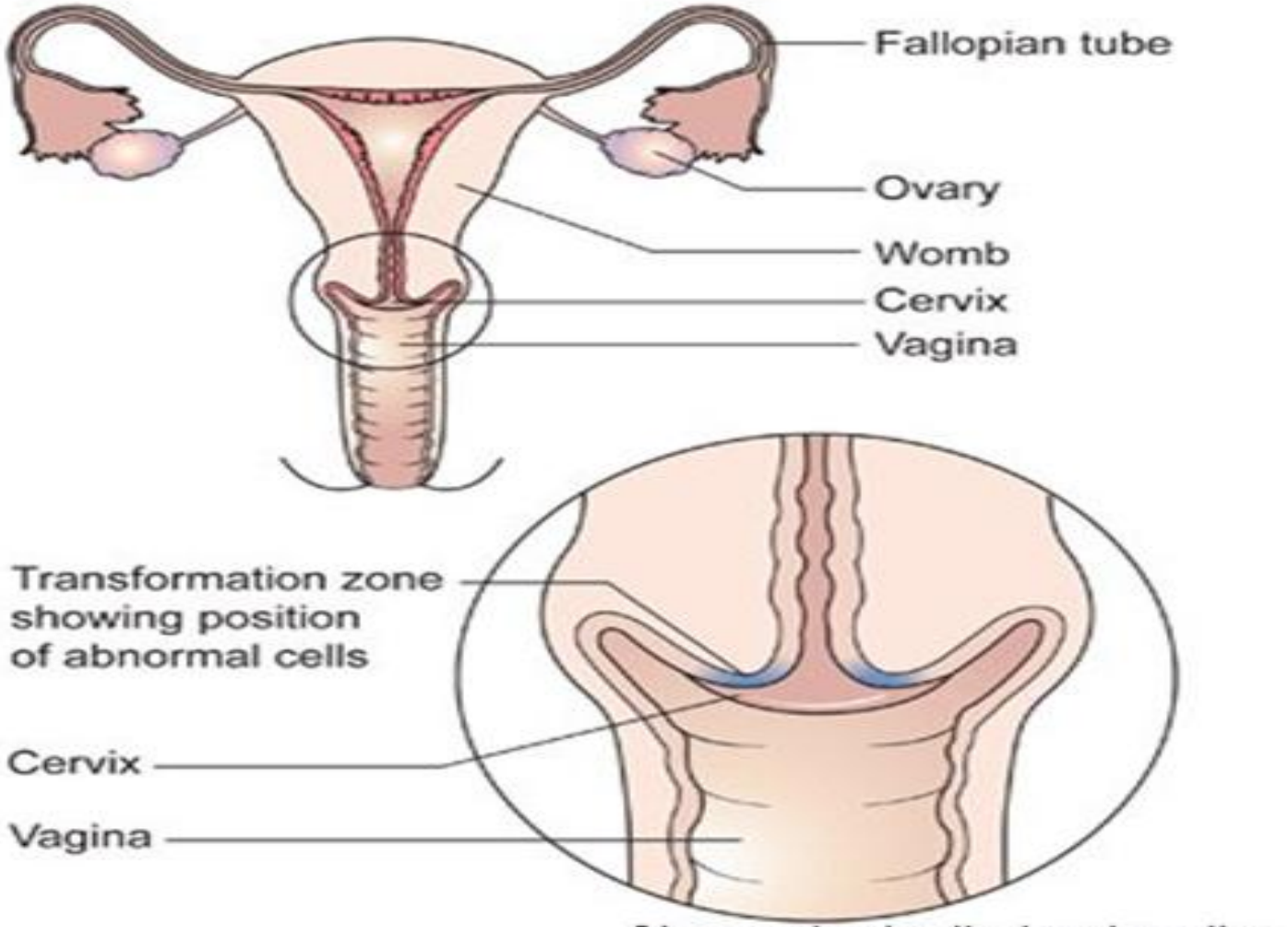


Diagram showing the transformation zone on the cervix

Human papillomavirus

- **Diagnosis:**

- Detecting the curable premalignant lesions.

- Mainly cytology / Pap smear > Colposcopy

- Molecular using PCR and HC2 ± genotyping.
- (FDA approved HC2 in 2003)

- Electron microscope

Treatment

- **Warts**

- Most warts are asymptomatic and regress spontaneously, particularly in immunocompetent patients. However, sometimes treatment is needed for cosmetic reasons.

- Treatment options for warts include podophyllotoxin, cryotherapy, and excisional therapy using surgical instruments

Treatment

- **Premalignant lesions:**
- carbon dioxide laser treatment or cold coagulation
- Excision

- **Malignant lesions:**
- Based on the stage of cervical cancer, treatment options include surgical excision, radiotherapy and / or chemotherapy

Human papillomavirus

- **Prevention:**

- Sexually transmitted > multiple partners > ABC.

- Screening by cervical smears to detect curable premalignant lesions.

- Vaccines: L1 expression > Viral Like Particles (VLPs) of the main high risk genotypes (Gardasil & Cervarix)

The End

Thank you