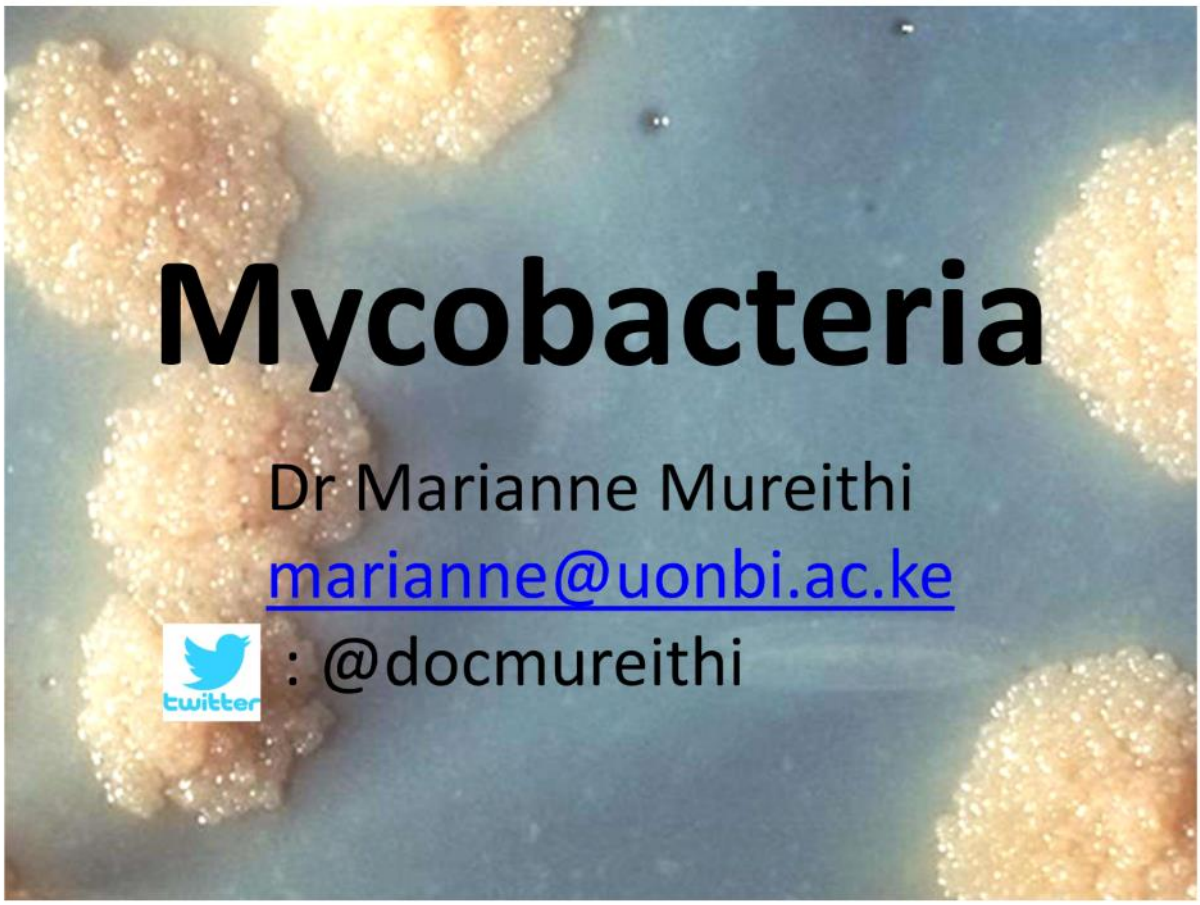
Mycobacteria: TB

Wednesday, August 1, 2018 8:20 PM



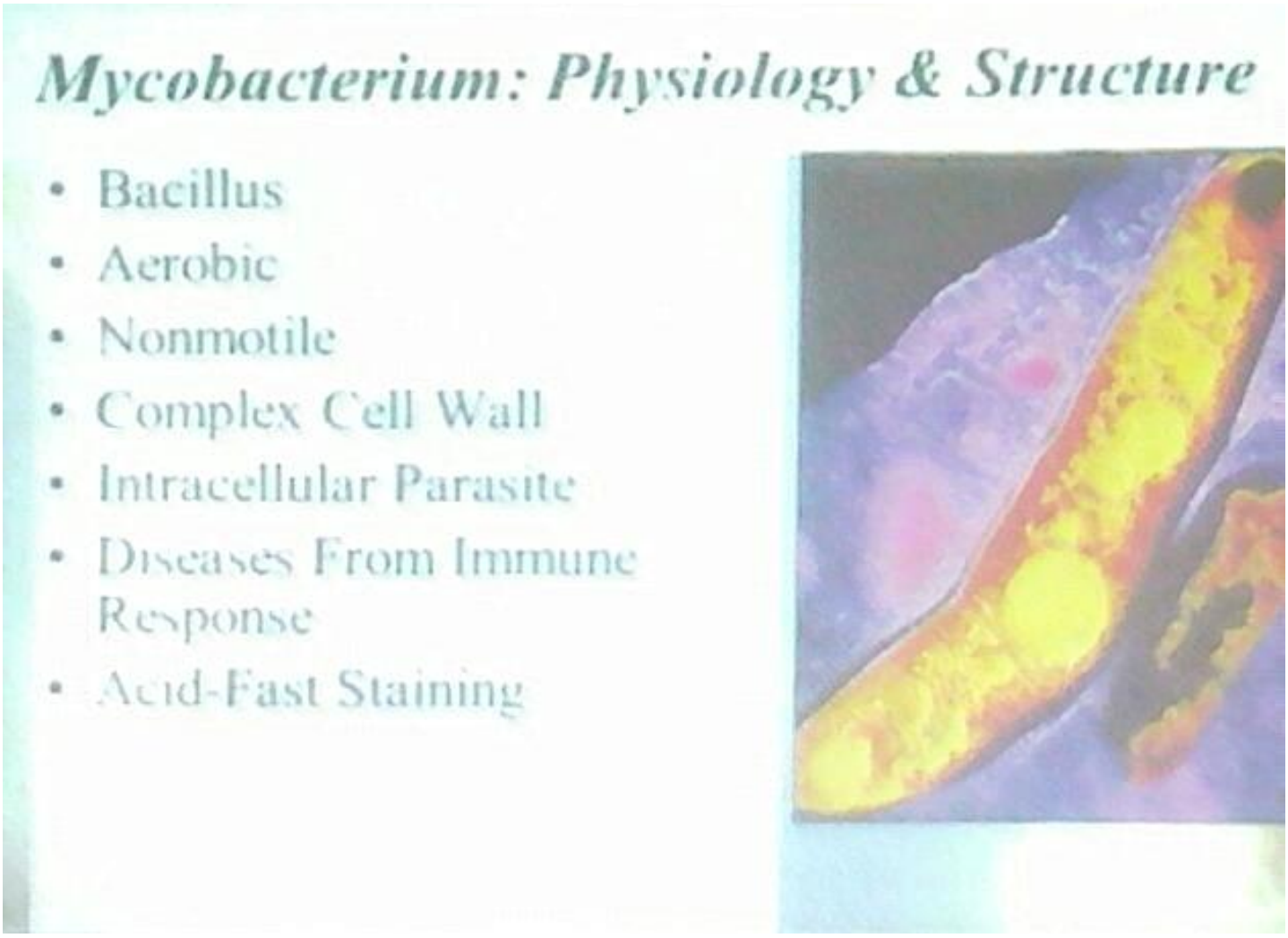
Learning Objectives

- Describe the structure, epidemiology and main pathogenic features & symptoms of Mycobacteria.
- Discuss Laboratory Diagnosis and treatment.
- MDR and XDR TB: what are they, how have they come about
- Prevention and treatment
- Leprosy
- Non-Tubercular Mycobacterium infections

Introduction

- >100 species of mycobacteria

- Major pathogens:
  - *Mycobacterium tuberculosis* (Koch, 1882) – Koch bacillus
  - *Mycobacterium leprae* (Hansen, 1874) – Hansen's bacillus
  - Rest are environmental organisms-collectively known as MOTTs (Mycobacteria Other Than Tuberculosis) or NTM (non-tuberculous mycobacteria) –cause opportunistic infections



Strict aerobes

Virulence factors

No spore, no flagellum, no exotoxin,no endotoxin, no invasive enzyme

- **Capsule:**polysaccharide;CR3;enzyme; protect
- **Lipid**/Lipo arabinomannan
- **Heat-shock protein/Tuberculin protein**: antigenicity,

-Heat-shock prot: a protein induced in a living cell in response to a rise in temperature above the normal level.
-Resistant to dessication, but sensitive to UV light
-M. TB is facultative intracellular pathogen unlike M.leprae, therefore can be cultured

Lipid

a. **Phospholipid**

monocytes proliferate,cause tubercles

b. **Wax D**

c. **Sulfatide**

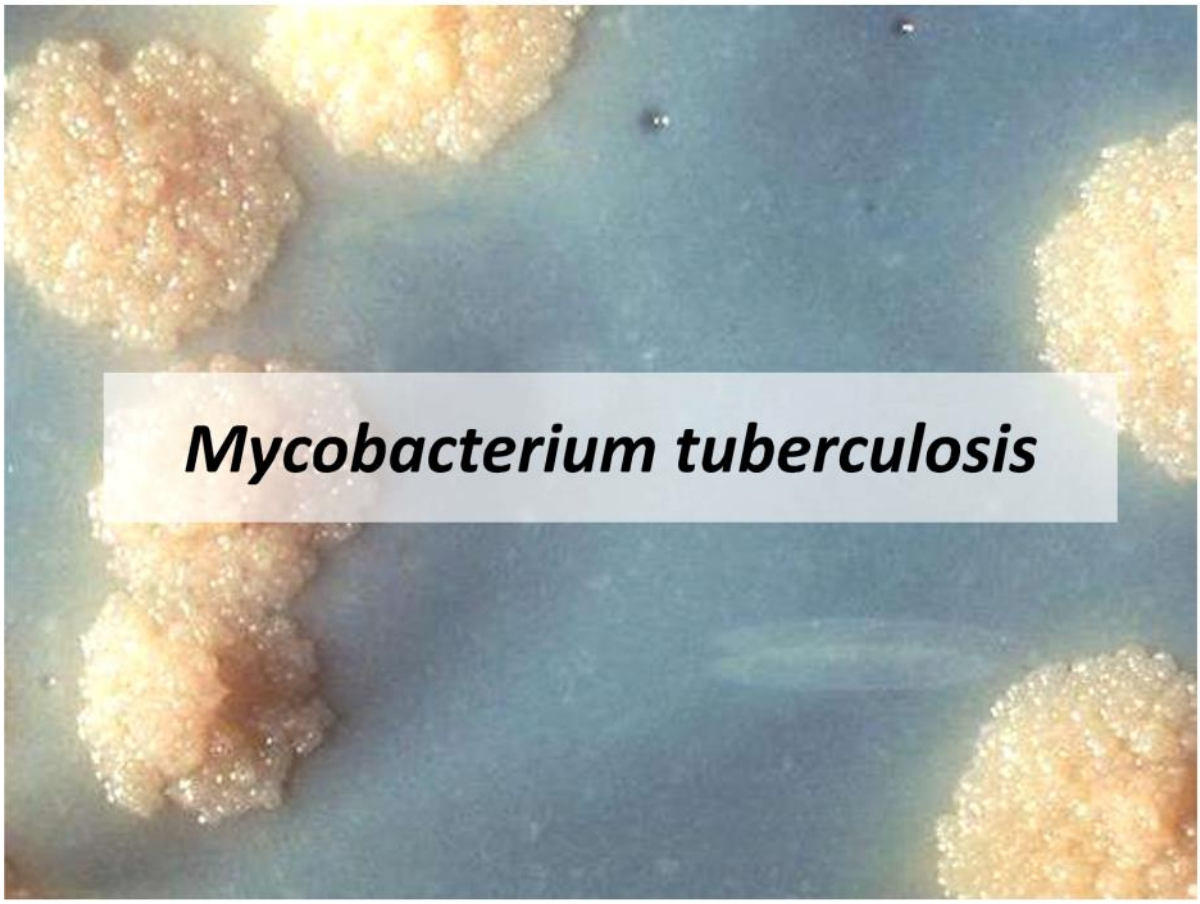
suppress phagosome

d. **Cord factor (trehalose-6,6-dimycolate)**

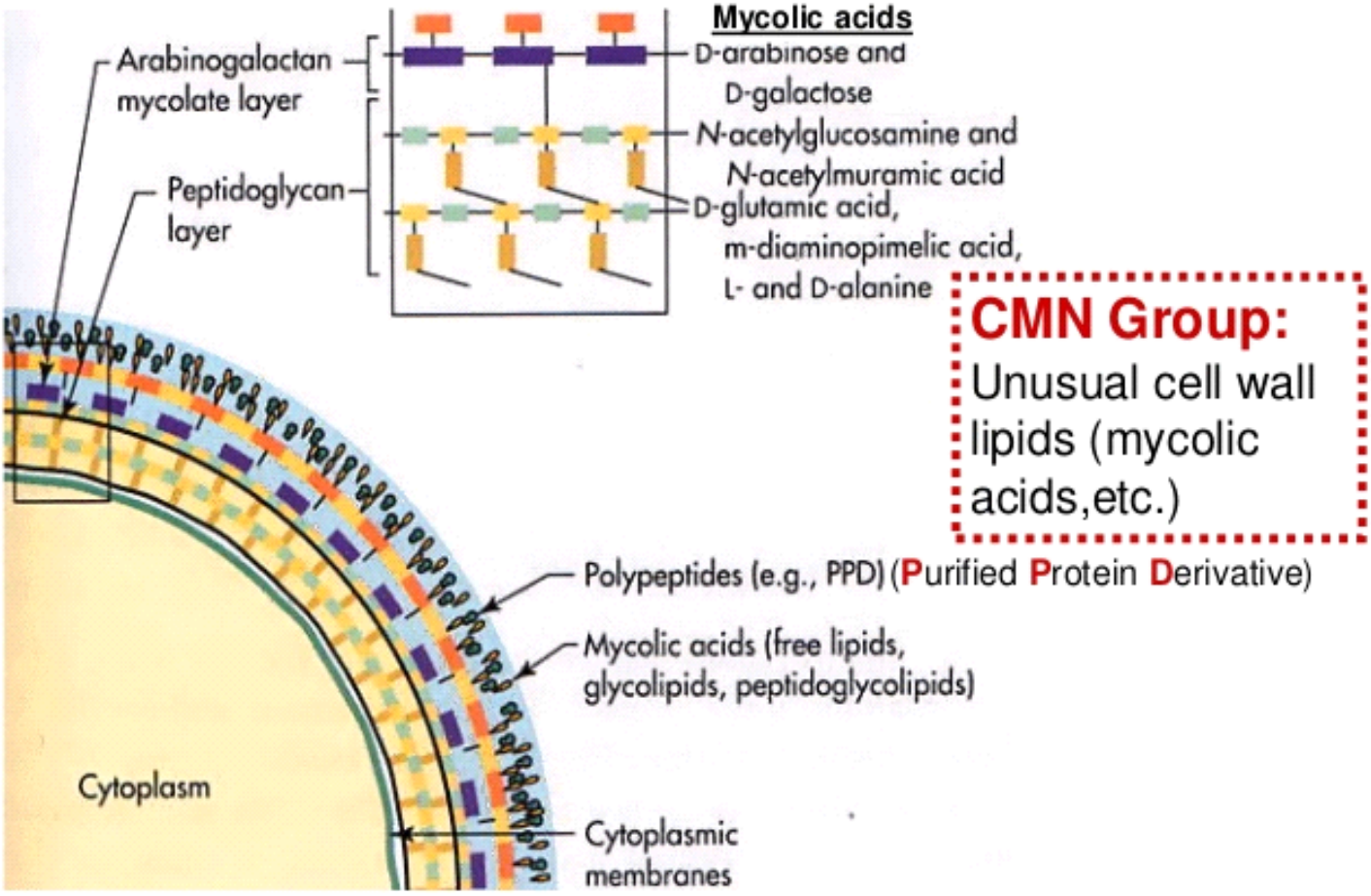
destroy mitochondria, cause chronic granulomatosis, suppress WBC

Cell Wall

- Complex
- Contains Mycolic Acid
  - Lipids account for 60% of Cell Wall Weight
- Responsible for Many Characteristics
  - Acid Fastness
  - Slow Growth
  - Antibiotic Resistance
  - Antigenicity
  - Clumping

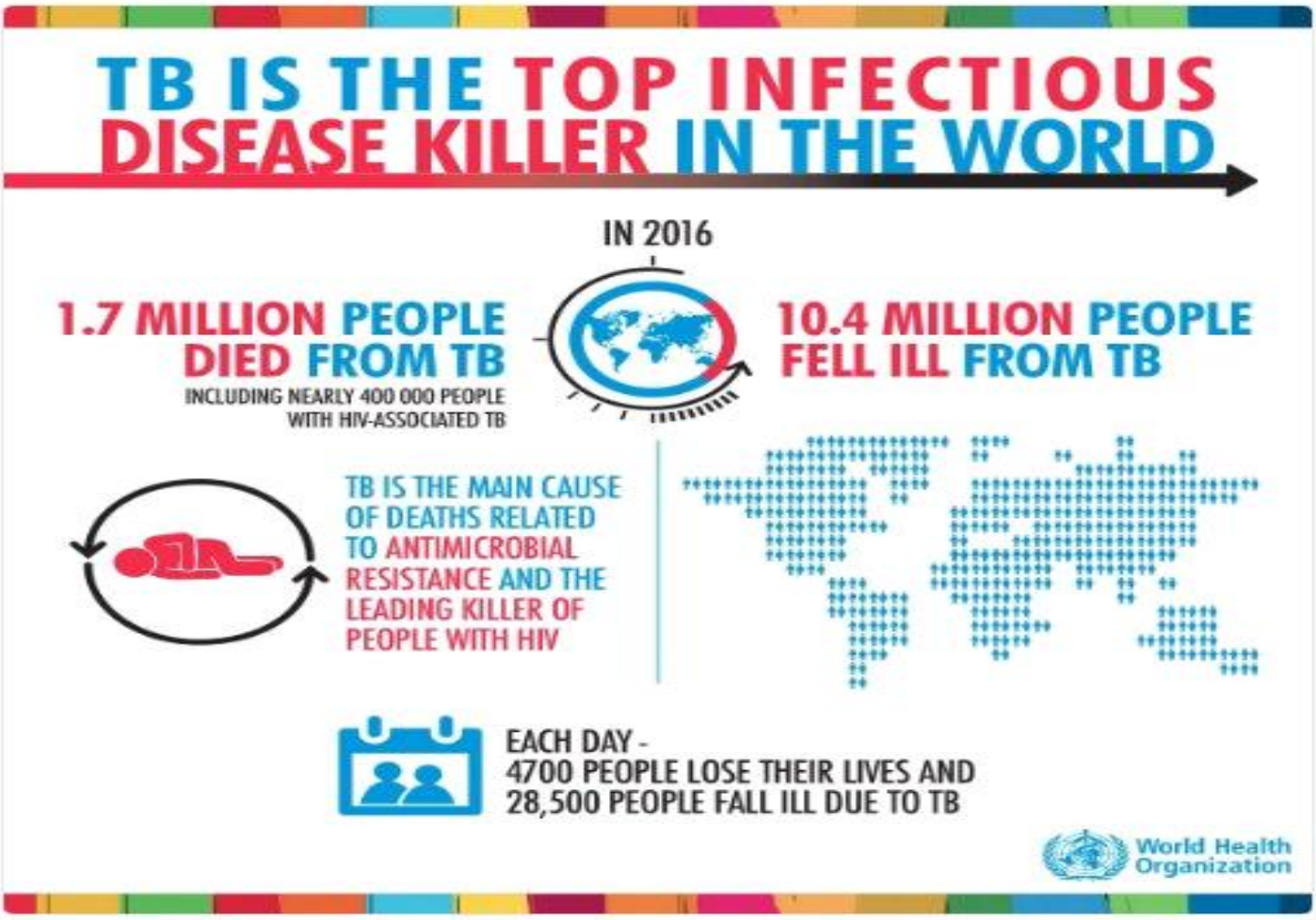

Mycobacterium tuberculosis

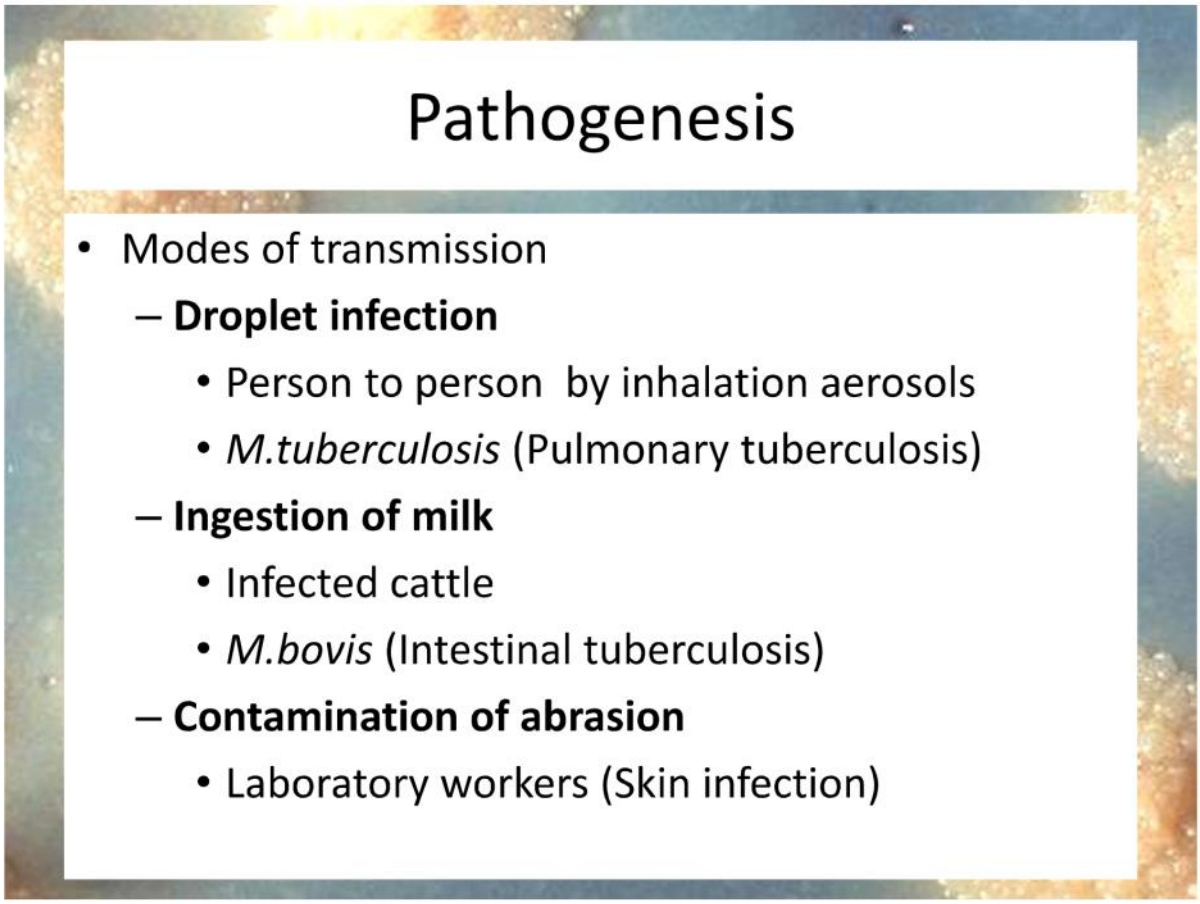
Lipid-Rich Cell Wall of Mycobacterium



CMN:

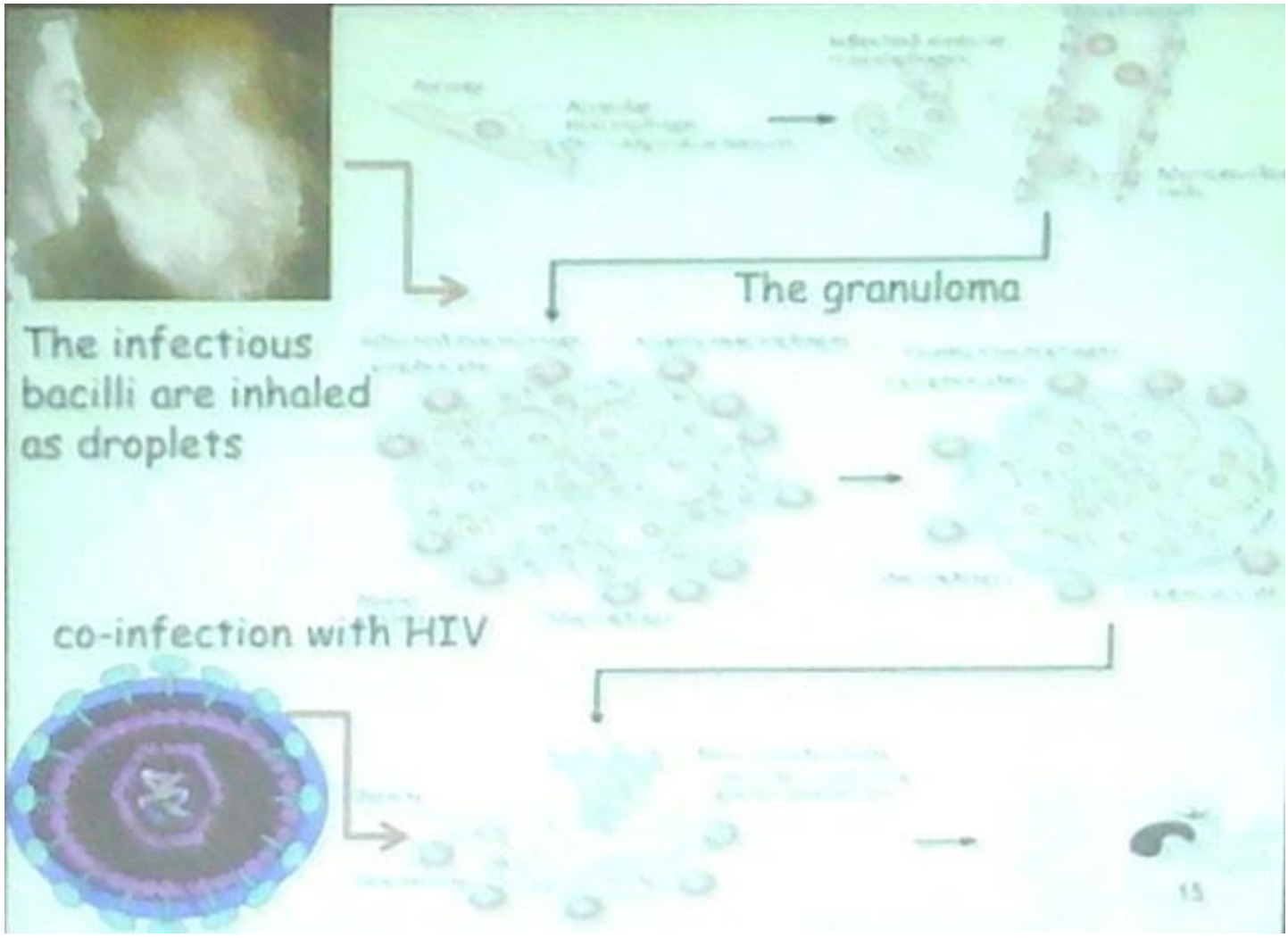
- Corynebacterium
- Mycobacterium
- Nocardia

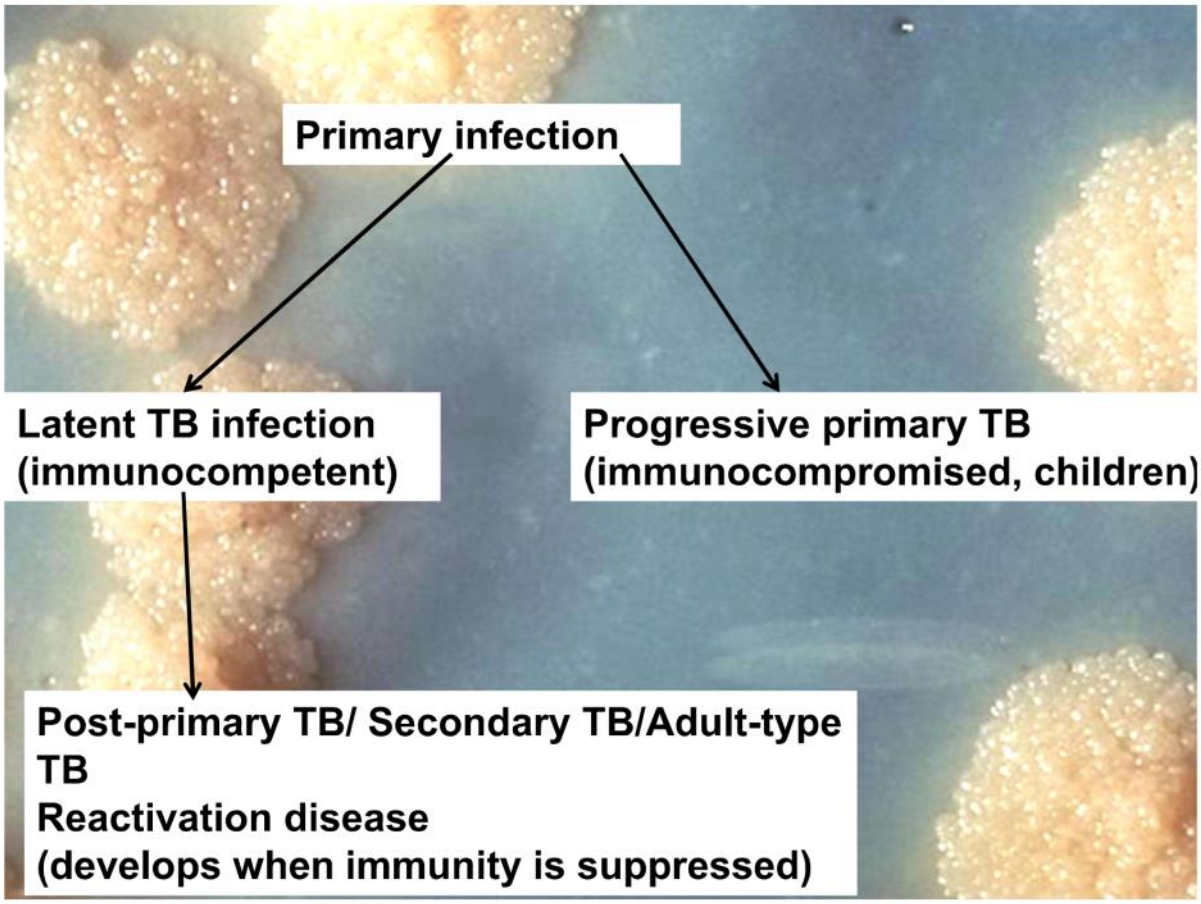

TB IS THE TOP INFECTIOUS DISEASE KILLER IN THE WORLD
IN 2016
1.7 MILLION PEOPLE DIED FROM TB
INCLUDING NEARLY 400 000 PEOPLE WITH HIV-ASSOCIATED TB
10.4 MILLION PEOPLE FELL ILL FROM TB
TB IS THE MAIN CAUSE OF DEATHS RELATED TO ANTIMICROBIAL RESISTANCE AND THE LEADING KILLER OF PEOPLE WITH HIV
EACH DAY -
4700 PEOPLE LOSE THEIR LIVES AND
28,500 PEOPLE FALL ILL DUE TO TB
World Health Organization



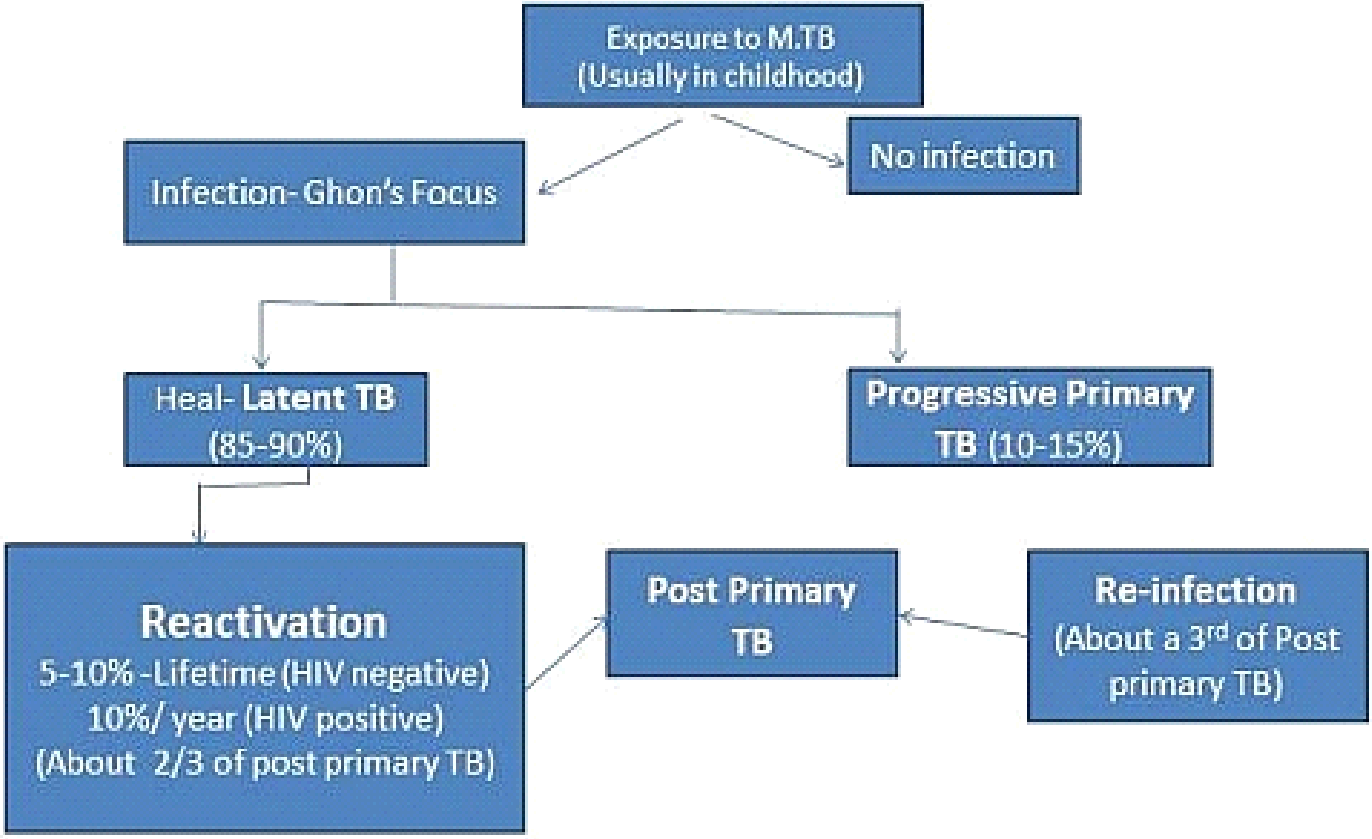
Spread of the organism within the body occurs by two mechanisms:
(1) A tubercle can erode into a bronchus, empty its caseous contents, and thereby spread the organism to other parts of the lungs, to the gastrointestinal tract if swallowed (e.g. M.bovis in milk), and to other persons if expectorated.
(2) It can disseminate via the bloodstream to many internal organs. Dissemination can occur at an early stage if cell-mediated immunity fails to contain the initial infection or at a late stage if a person becomes immunocompromised.

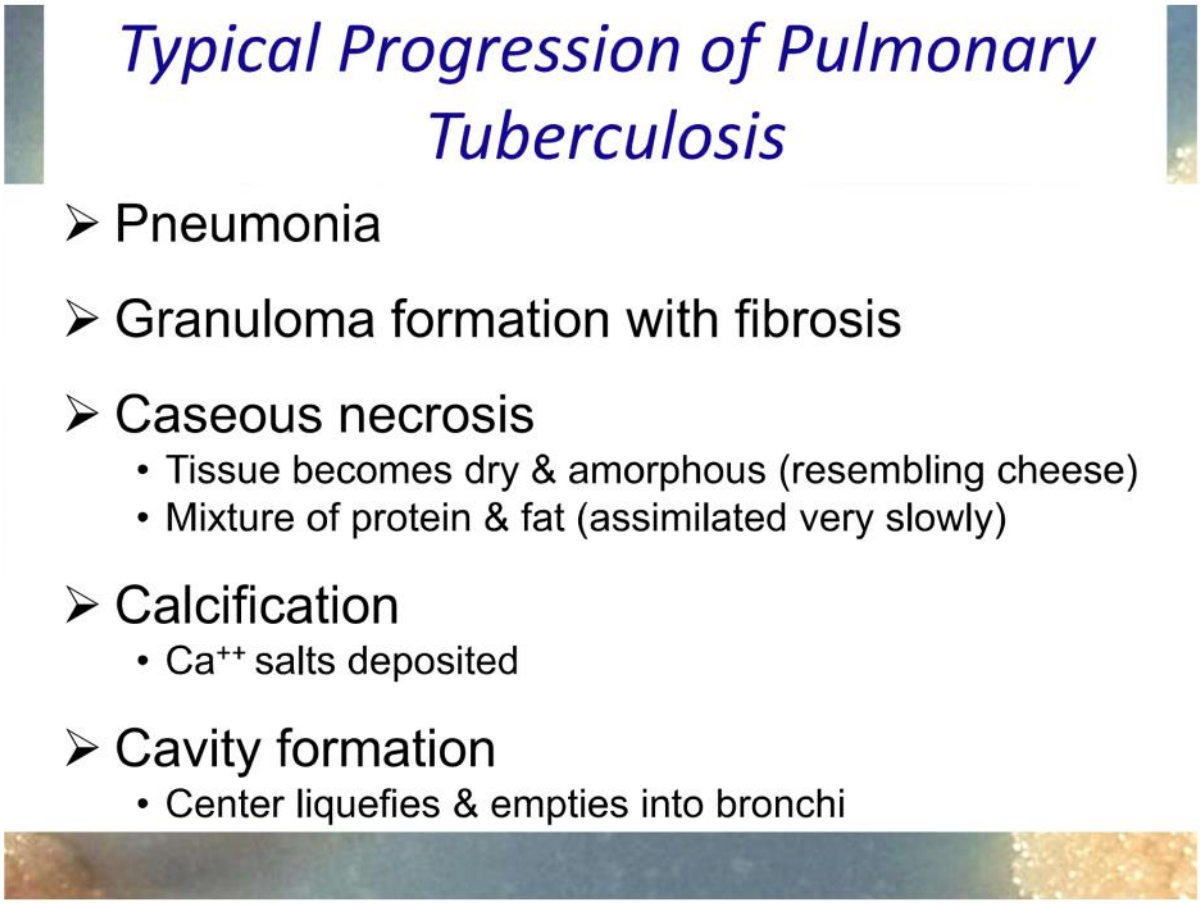

Epidemiology
• 2 Billion People Infected World Wide
• 8.8 Million New Cases / Year
• 2 Million Deaths / Year
• Kenya is one of the 22 countries most affected by TB in the world


The infectious bacilli are inhaled as droplets
The granuloma
co-infection with HIV


Primary infection
Latent TB infection
(immunocompetent)
Progressive primary TB
(immunocompromised, children)
Post-primary TB/ Secondary TB/Adult-type TB
Reactivation disease
(develops when immunity is suppressed)

Natural History of TB

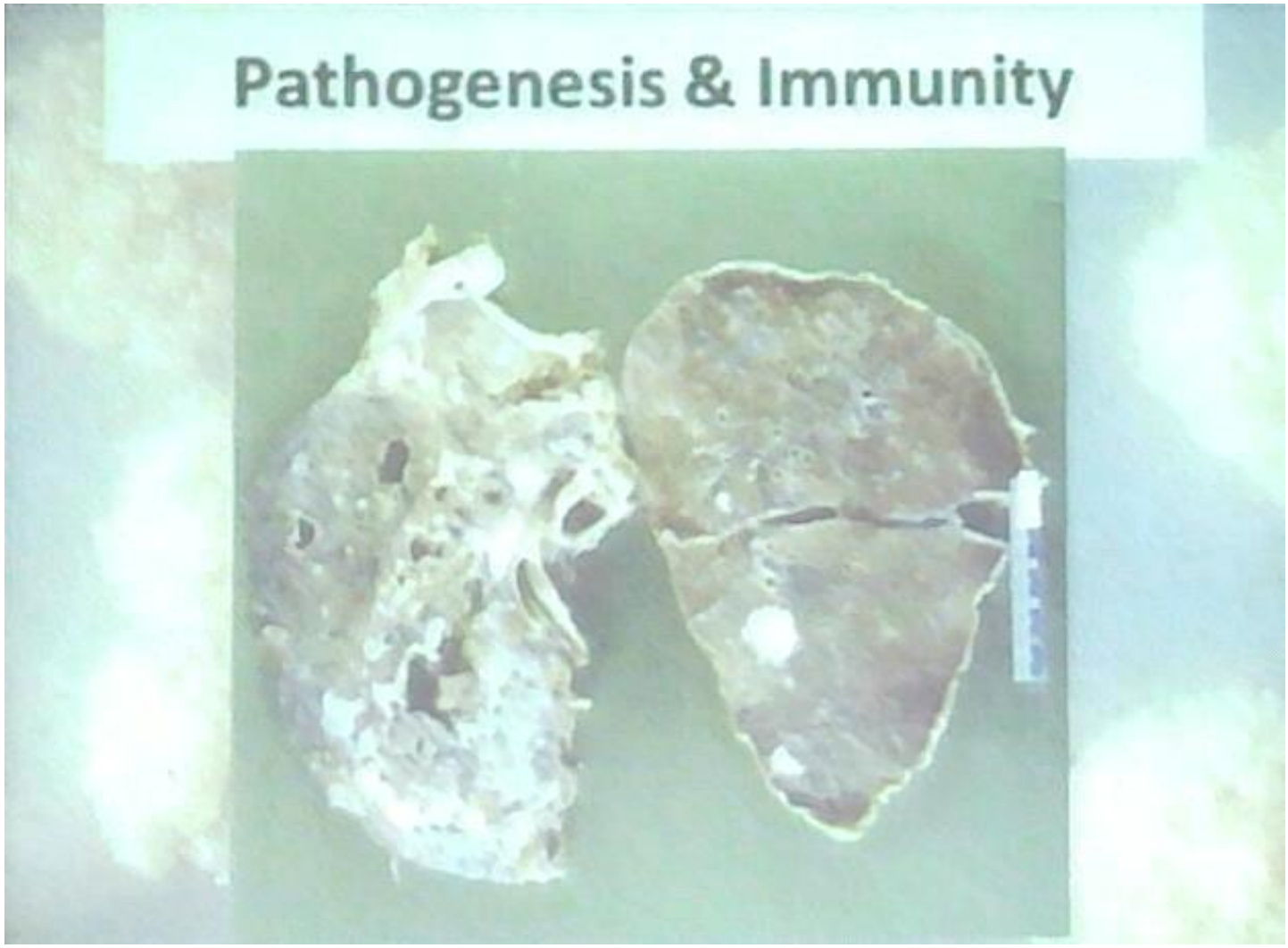


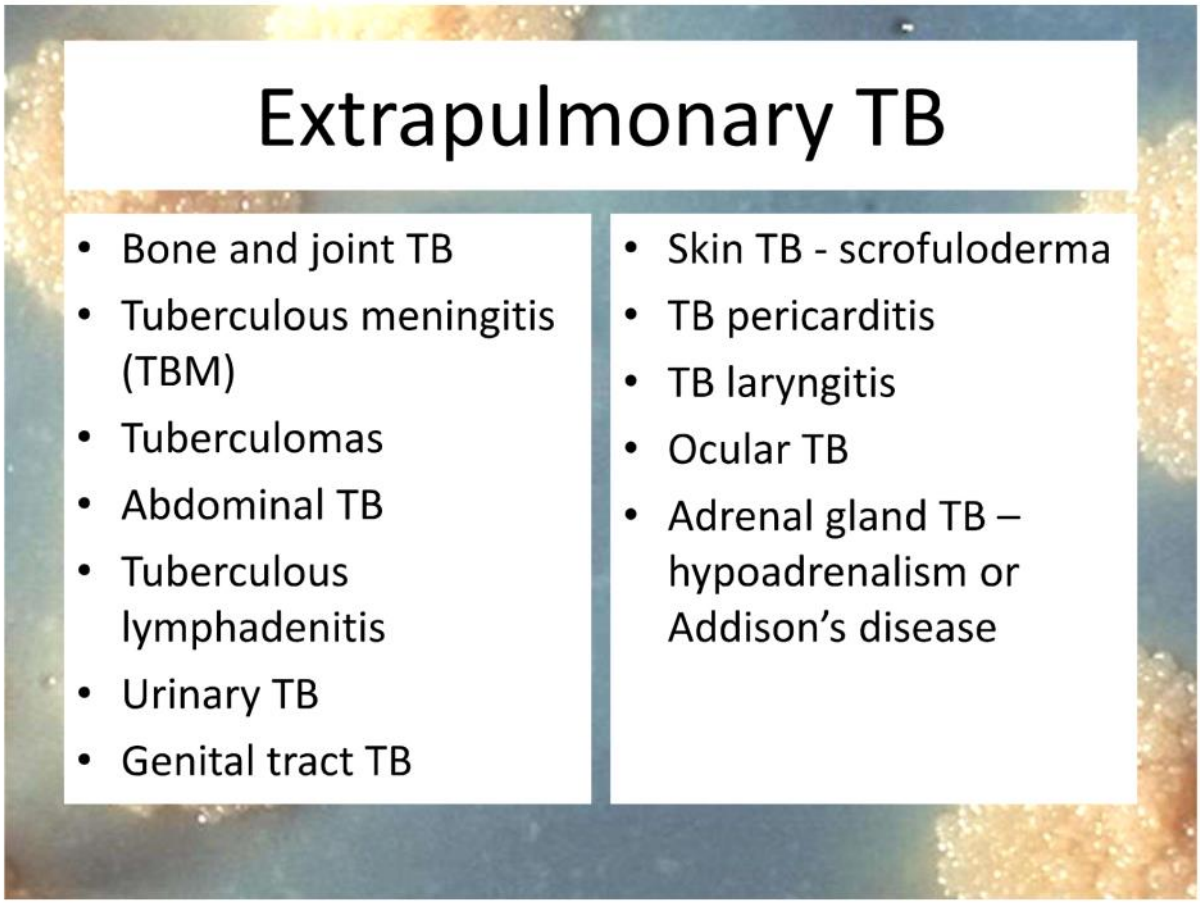


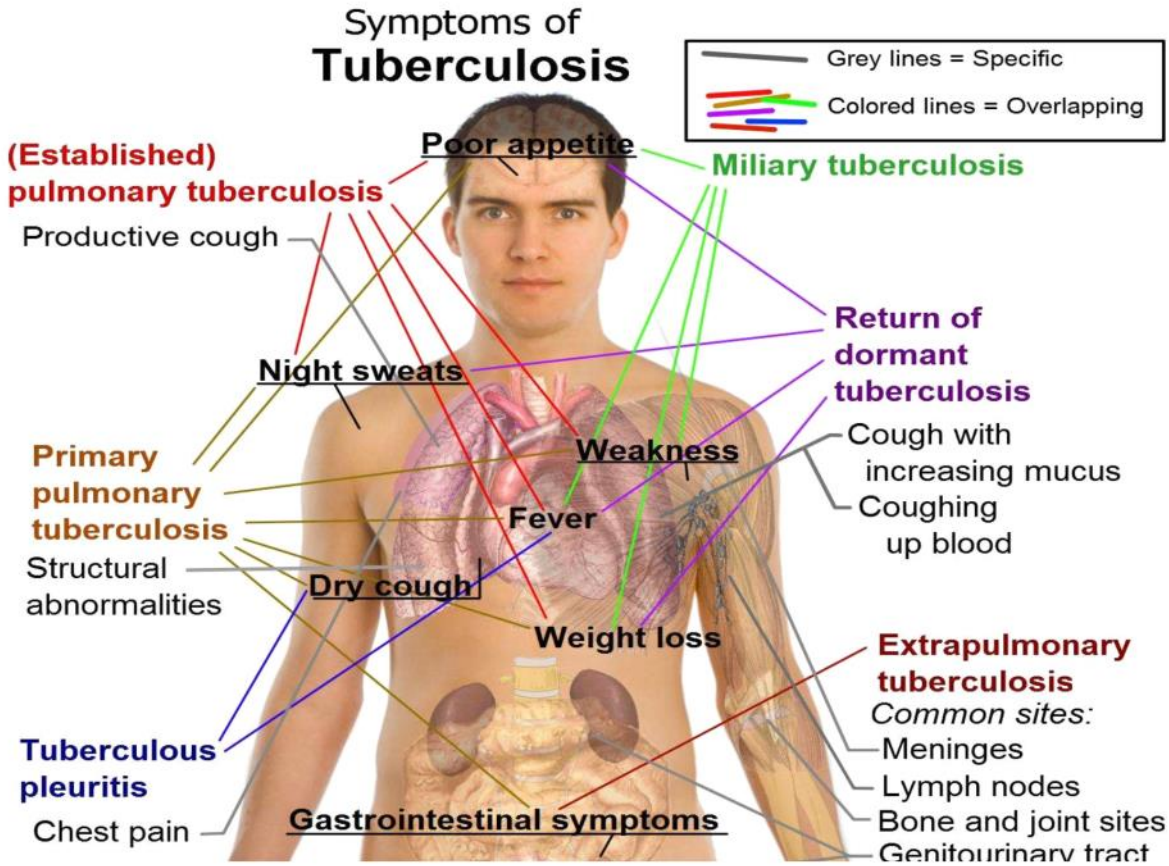
-There are two types of lesions:
(1) ***Exudative lesions***, which consist of an acute inflammatory response and occur chiefly in the lungs at the initial site of infection.
(2) ***Granulomatous lesions***, which consist of a central area of giant cells containing tubercle bacilli surrounded by a zone of epithelioid cells. These giant cells, called ***Langhans' giant cells***, are an important pathologic finding in tuberculous lesions. A ***tubercle*** is a granuloma surrounded by fibrous tissue that has undergone central caseation necrosis. Tubercles heal by fibrosis and calcification.
-The primary lesion of tuberculosis usually occurs in the lungs. The parenchymal exudative lesion and the draining lymph nodes together are called a ***Ghon complex***

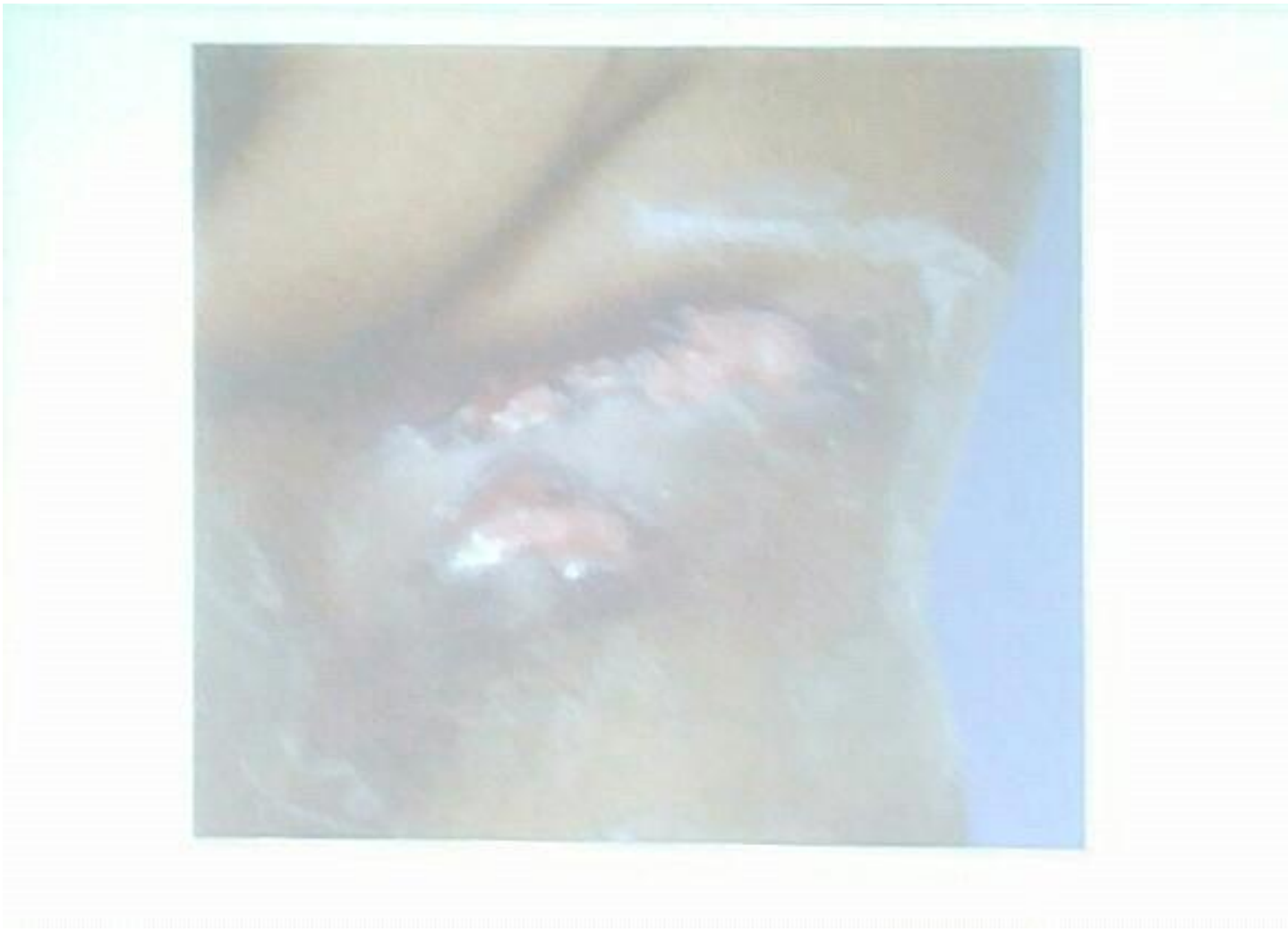
Ghon complex

- Nodules in lung tissue and lymph nodes
- Caseous necrosis inside nodules
- Calcium may deposit in the fatty area of necrosis
- Visible on x-rays

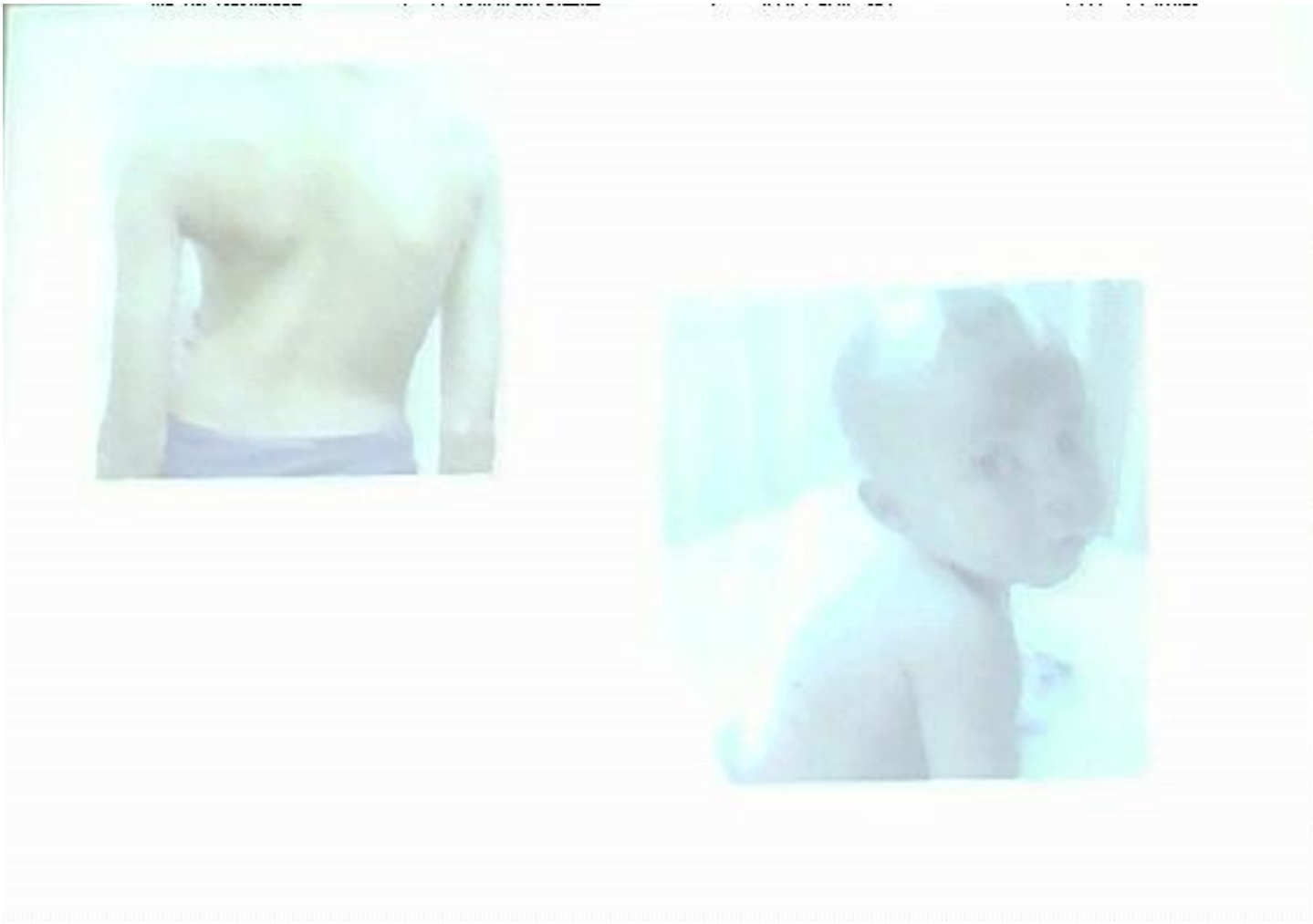

Pathogenesis & Immunity


Extrapulmonary TB
Bone and joint TB
Tuberculous meningitis (TBM)
Tuberculomas
Abdominal TB
Tuberculous lymphadenitis
Urinary TB
Genital tract TB
Skin TB - scrofuloderma
TB pericarditis
TB laryngitis
Ocular TB
Adrenal gland TB – hypoadrenalism or Addison's disease

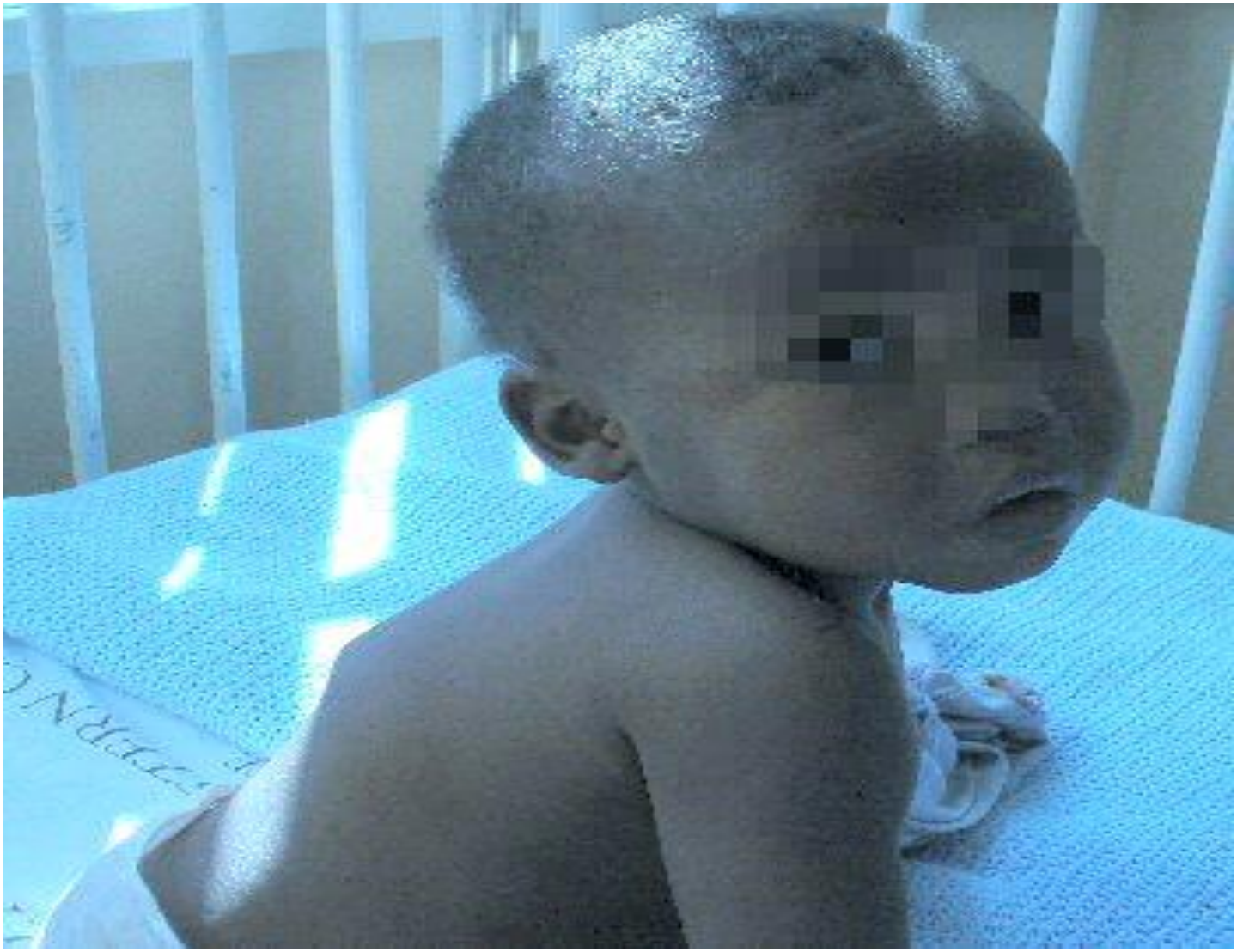

Symptoms of
Tuberculosis
Grey lines = Specific
Colored lines = Overlapping
(Established) pulmonary tuberculosis
Productive cough
Poor appetite
Miliary tuberculosis
Return of dormant tuberculosis
Night sweats
Cough with increasing mucus
Coughing up blood
Primary pulmonary tuberculosis
Weakness
Fever
Structural abnormalities
Dry cough
Weight loss
Extrapulmonary tuberculosis
Common sites:
Meninges
Lymph nodes
Bone and joint sites
Genitourinary tract
Tuberculous pleuritis
Chest pain
Gastrointestinal symptoms



Skin TB



Bone TB



Laboratory diagnosis

- Specimen
  - Sputum (expectorated or induced)
  - Pleural fluid
  - Gastric washings
  - Urine
  - Aspirates
  - CSF
  - Tissue biopsies

- Staining of specimen using
  - Ziehl Neelsen (ZN) stain –acid-fast bacilli (AFBs)
  - Kinyoun staining
  - Fluorescence microscopy using auramine O or rhodamine stain

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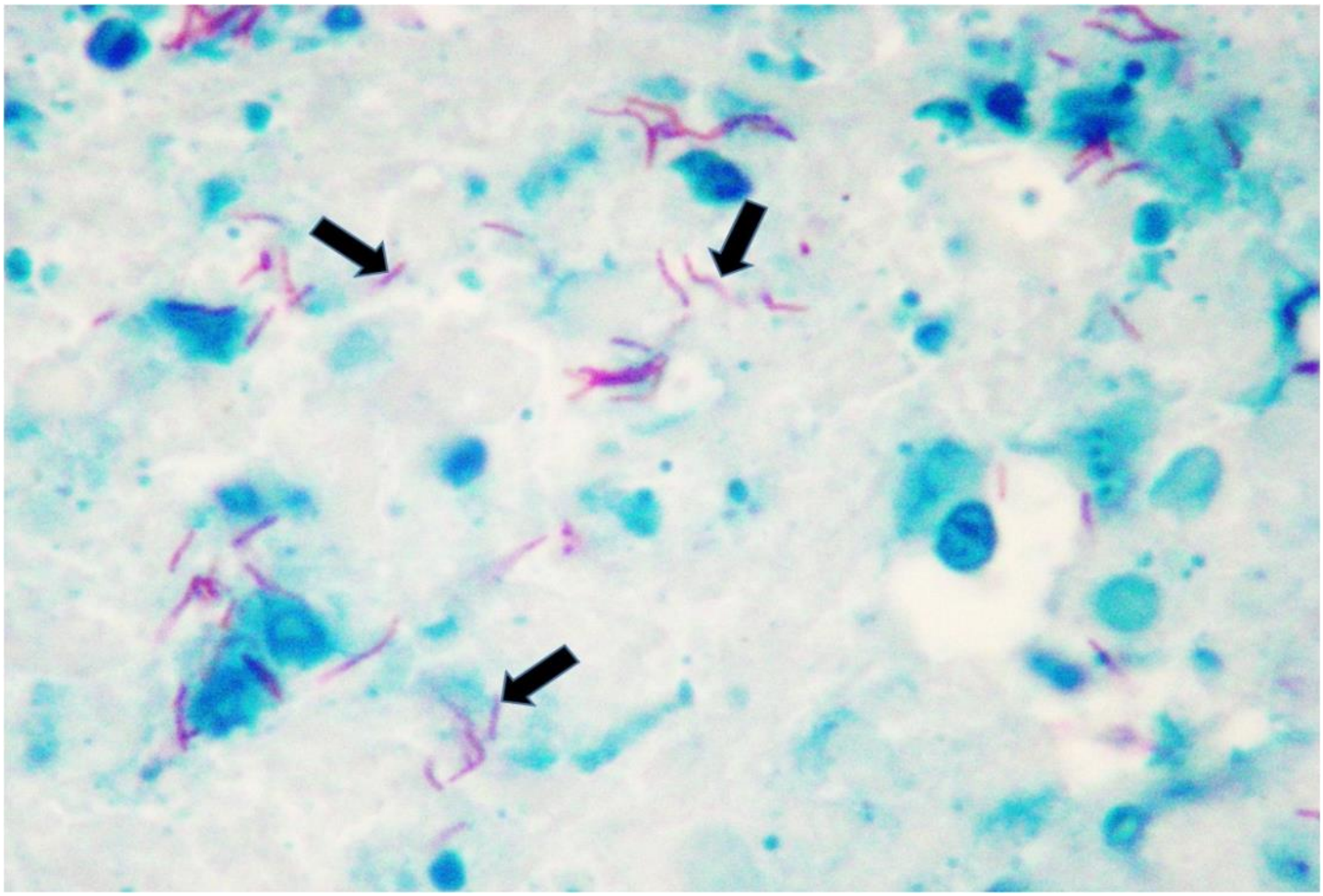
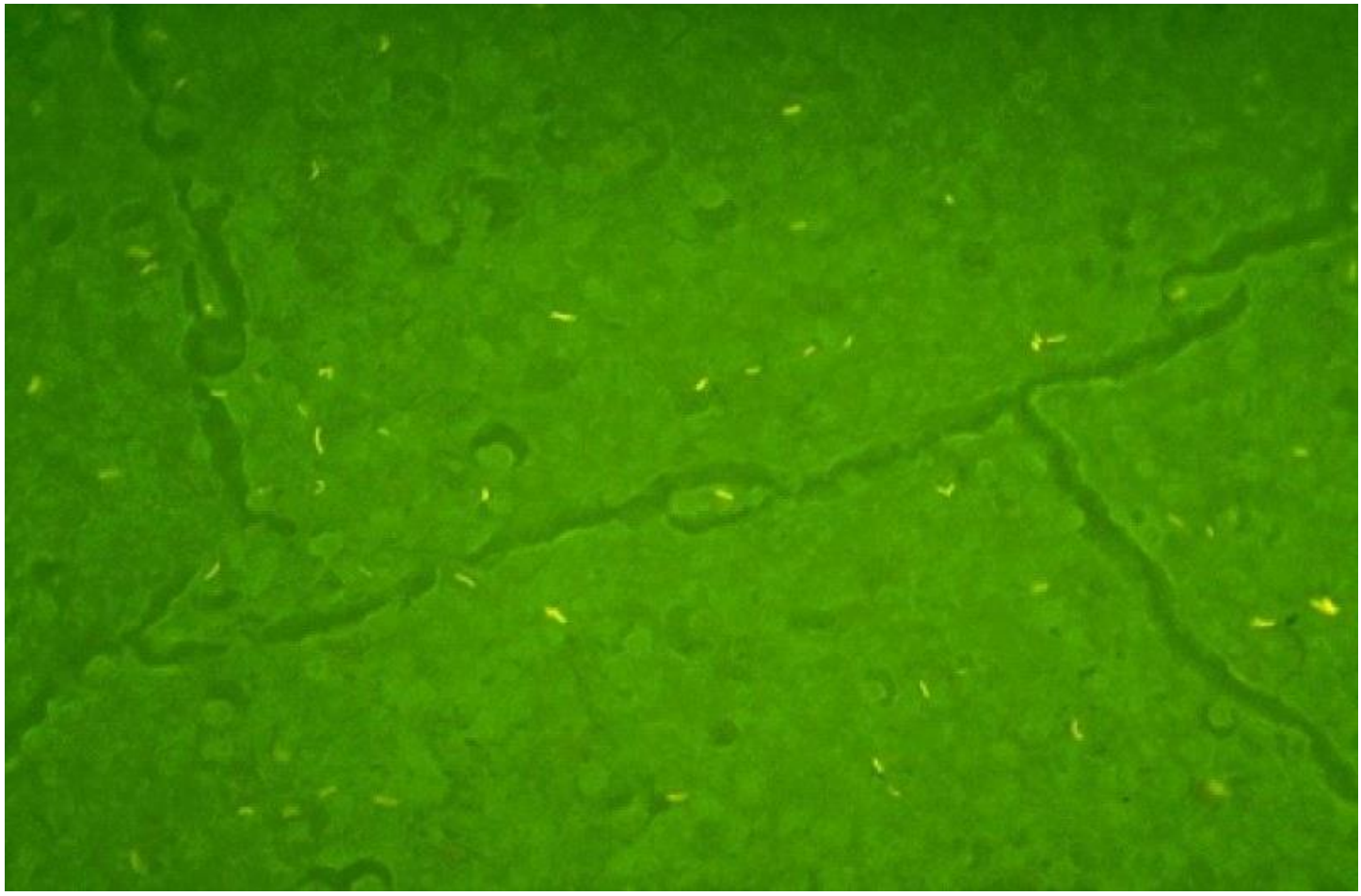
Auramine-rhodamine: a fluorescent stain for screening
Acid fast: for confirming


ZN stained smear



Auramine stain



- Culture – Gold standard in TB diagnosis - require incubation for 6 – 8 weeks before declaring negative
  - Solid culture (Lowenstein Jensen, Middlebrook)
  - Semi automated Liquid culture Bactec 460
  - Automated Liquid culture system (MGIT – mycobacterial growth indicator tube)
- No gold standard for diagnosis of LTBI

Culture methods

- Solid – LJ

- Liquid Broth (BD)

- To confirm *M.tuberculosis* from culture:
  - Growth rate
  - Colonial morphology
  - Ziehl Neelsen staining results
  - Molecular – PCR – from culture; some direct from sputum
  - Gene/Xpert - is a nucleic acid amplification test, that can identify (MTB) DNA and resistance to rifampicin (RIF)

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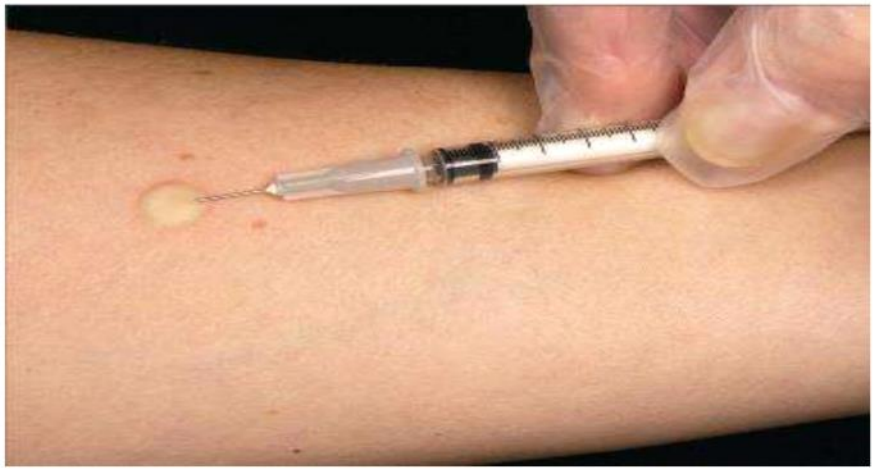
- Immunological diagnostic tests
  - Tuberculin skin test – does not distinguish between vaccination and disease. Usually negative in patients with advanced AIDS
  - QuantiFERON , T-SPOT TB – Detect interferon γ. For active & latent TB



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Treatment

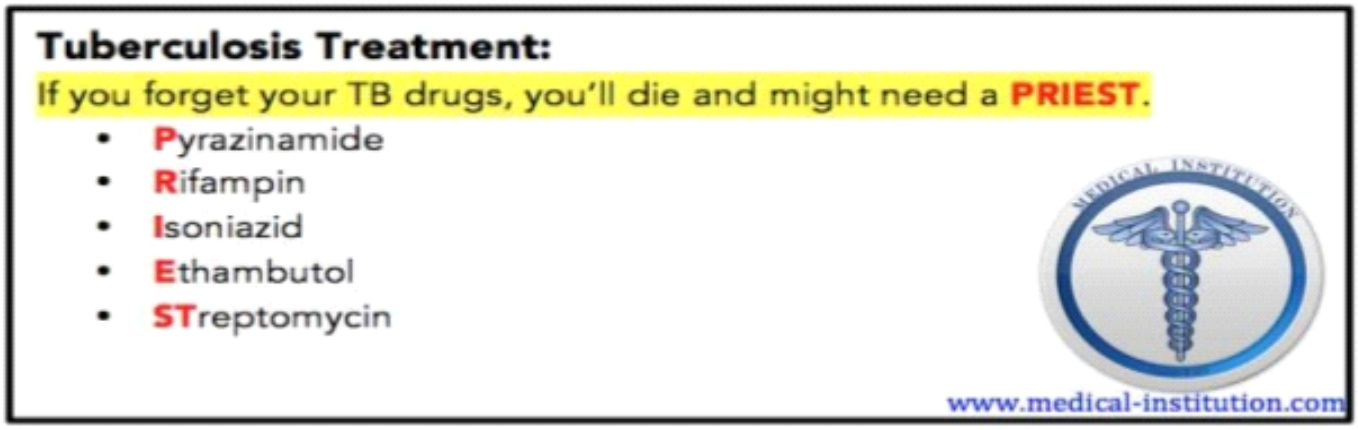
- 1st line: isoniazid, rifampicin/ rifabutin, ethambutol, pyrazinamide, streptomycin

- 2nd line: para-amino salicylic acid, cycloserine, quinolones (ofloxacin/ ciprofloxacin/ levofloxacin/ etc), amikacin, kanamycin, capreomycin, ethionamide

Treatment for TB

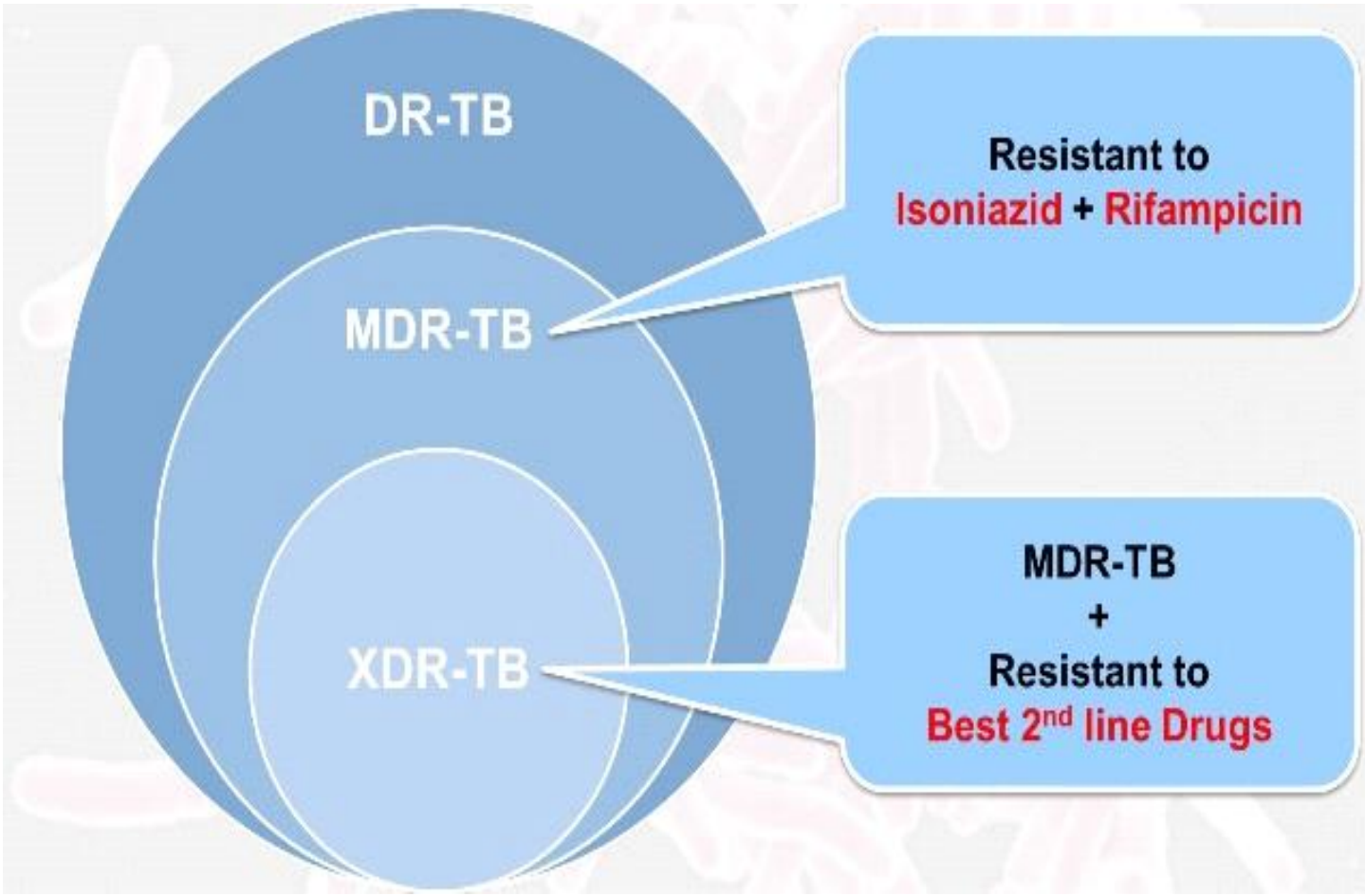
- There are two phase of anti tuberculous therapy

1. **Initial phase**: Bactericidal phase, in which bacilli is killed symptoms resolves and patient become non infectious. Duration is 2 months.
2. **Continuation phase:** Sterilization phase in which remaining tubercle bacilli is eliminated and organ is sterilized. Duration is 7 months.

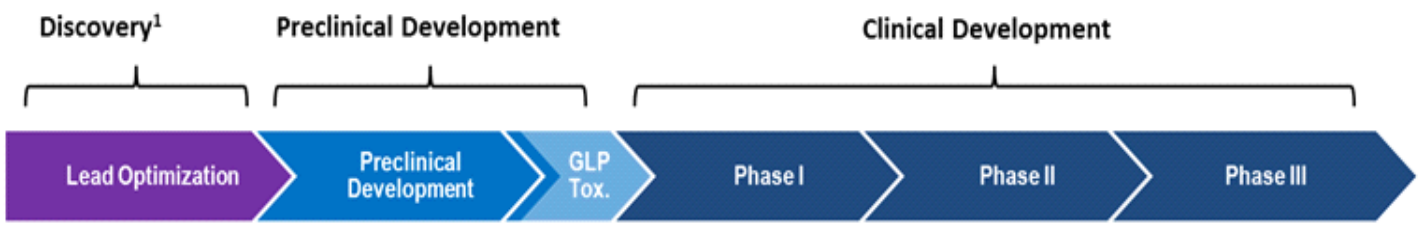


1. **Initial pahse:isoniazid,rifampin & pyrazinamide (add streptomycin in case of MDR)**
2. **Continuation pahse: isoniazid and rifampin**

- Drug resistance
  - **Multidrug resistant TB (MDR TB):** TB that is resistant to at least rifampicin & isoniazid
  - **Extensively drug resistant TB (XDR TB):** TB which is resistant to isoniazid and rifampin, plus resistant to any fluoroquinolone and at least one of three injectable second-line drugs (i.e., amikacin, kanamycin, or capreomycin)


DR-TB
MDR-TB
XDR-TB
Resistant to
Isoniazid + Rifampicin
MDR-TB
+
Resistant to
Best 2nd line Drugs

Global TB Drug Pipeline



Lead Optimization	Preclinical Development	GLP Tox.	Phase I	Phase II	Phase III
Diarylquinolines	CPZEN-45	BTZ043		AZD5847	Delamanid (OPC-67683)
InhA Inhibitors	DC-159a	TBA-354		Bedaquiline (TMC-207)	Gatifloxacin
LeuRS Inhibitors	Q201			Linezolid	Moxifloxacin
Mycobacterial Gyrase Inhibitors	SPR-10199			Novel Regimens[2]	Rifapentine
Pyrazinamide Analogs	SQ609			PA-824	
Riminophenazines	SQ641			Rifapentine	
Ruthenium (II) complexes				SQ-109	
Spectinamides				Sutezolid (PNU-100480)	
Translocase-1 Inhibitors					

Chemical classes: fluoroquinolone, rifamycin, oxazolidinone, nitroimidazole, diarylquinoline, benzothiazinone

[1] Ongoing projects without a lead compound series can be viewed at http://www.newtbdrugs.org/pipeline-discovery.php.

[2] Combination regimens: first clinical trial (NC001) of a novel TB drug regimen testing the three drug combination of PA-824,

WORKING GROUP ON NEW TB DRUGS

Prevention and control

- BCG vaccine
- Respiratory isolation of persons with suspected TB till noninfectious
- Ventilation of household
- Contact tracing
- Nutrition
- Chemoprophylaxis
- Vit D??

- **Using UV lights in the ventilation sys of quarantine facilities**

Need for a New TB Vaccine

- Developed in the early 1900s, the current TB vaccine, BCG, has been ineffective in curbing the global TB epidemic - 1.8 million TB-related deaths & 9.3 million new cases of TB annually
- TB is the number one killer of people living with HIV/AIDS
- Drug resistance and TB/HIV co-infection are key barriers in bringing the epidemic under control
- Nearly half a million died from TB/HIV in 2007; more than 80 countries have reported multidrug-resistant TB
- TB primarily affects adults of working age and exacts a vast economic toll in treatment costs and in lost productivity (approx. $16 billion)
- The World Bank estimates the loss of 4% to 7% of GDP in some countries

AERAS

Mycobacteria: Leprosy & MOTTs

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M.leprae

- Reservoir – infected humans; Low infectivity
- Transmission: Skin-to-skin contact
- Grows best in cooler part of the body - the skin, peripheral nerves, anterior chamber of the eye, upper respiratory tract, and testes
- Incubation period – years or decades

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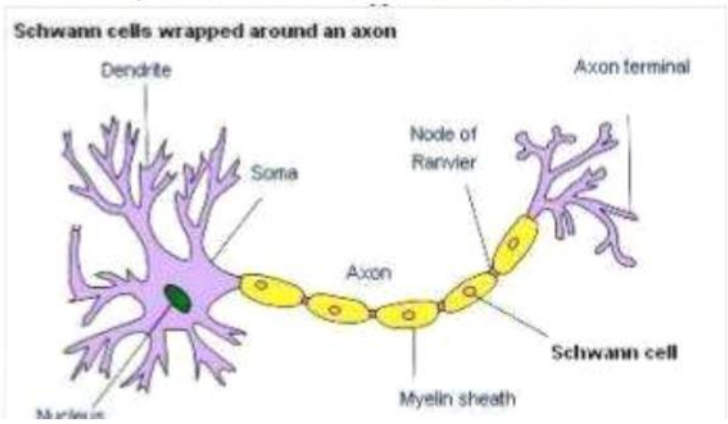
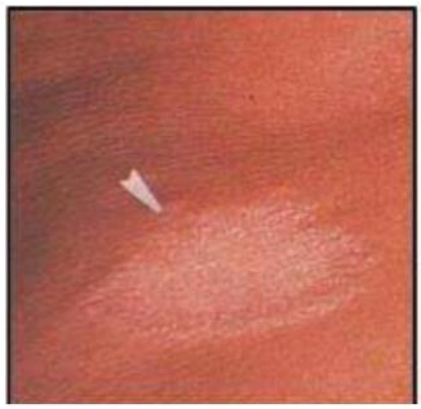
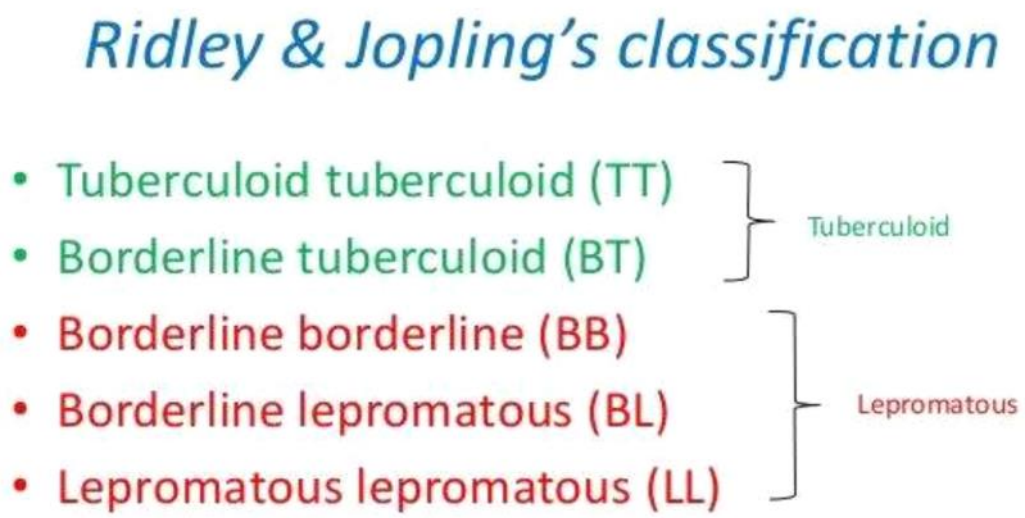
Leprosy= Hansen's disease

Pathogenesis

- Leprosy is a chronic granulomatous disease that usually involves skin, peripheral nerves and nasal mucosa.
- Incubation period is long and varies from 3-15 years.
- Prolonged close contact with infective patient is necessary for transmission of the disease.
- The principal target cell of lepra bacilli are Schwann cell and the resulting nerve damage causes manifestation of leprosy, which include anesthesia and muscle paralysis.
- A non-specific or Indeterminate skin lesion is the **First sign of disease.**







Tuberculoid leprosy: paucibacillary leprosy

Tuberculoid leprosy

- Relatively few or no bacilli because of adequate cell mediated immunity
  - One or a few hypopigmented macules or plaques - sharply demarcated and hypesthetic
  - Devoid of normal skin organs (sweat glands and hair follicles) - are dry, scaly
  - Nerves may be destroyed with loss of sensation and perspiration (Arthur's phenomenon)
  - **Lepromin test positive**

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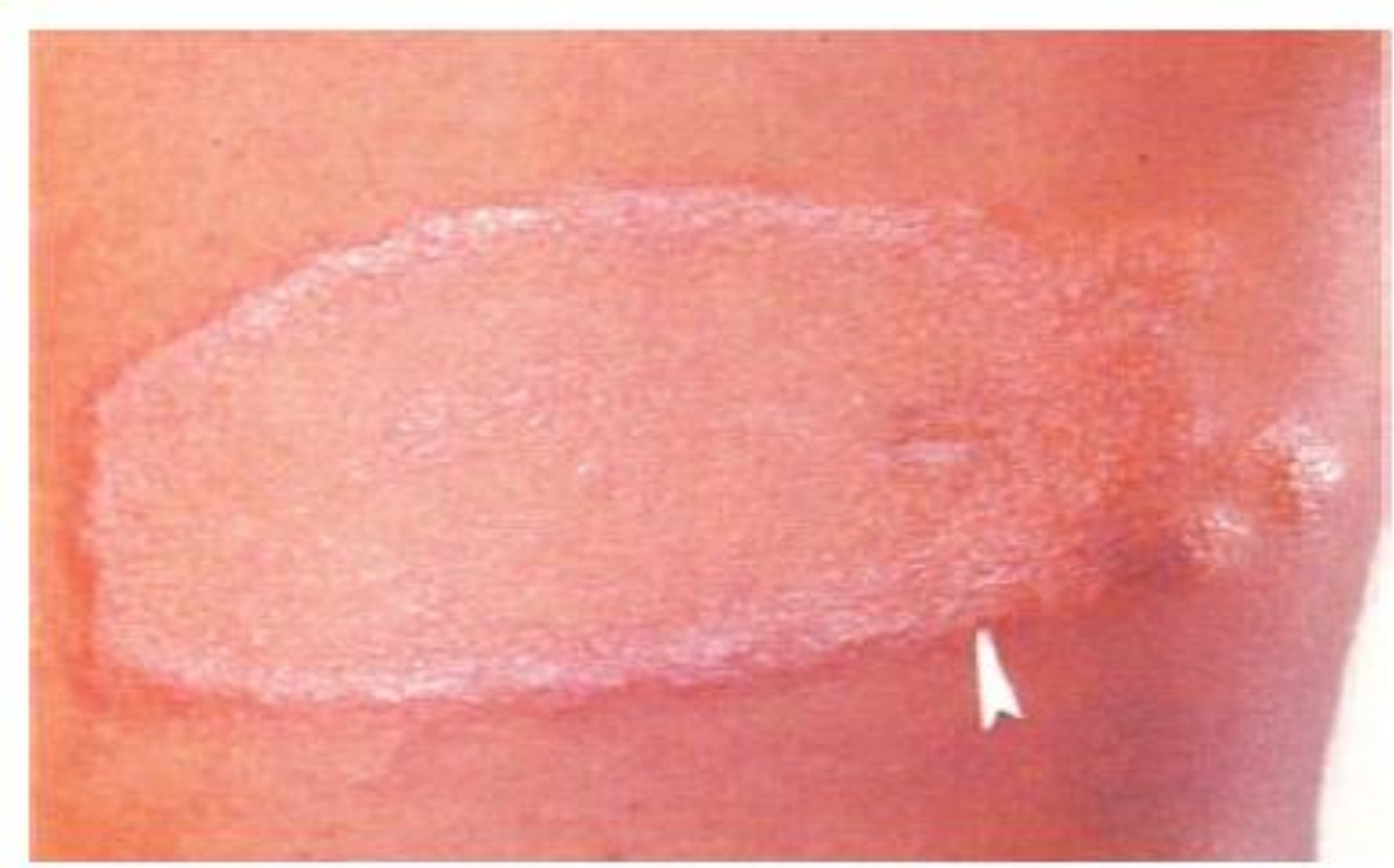
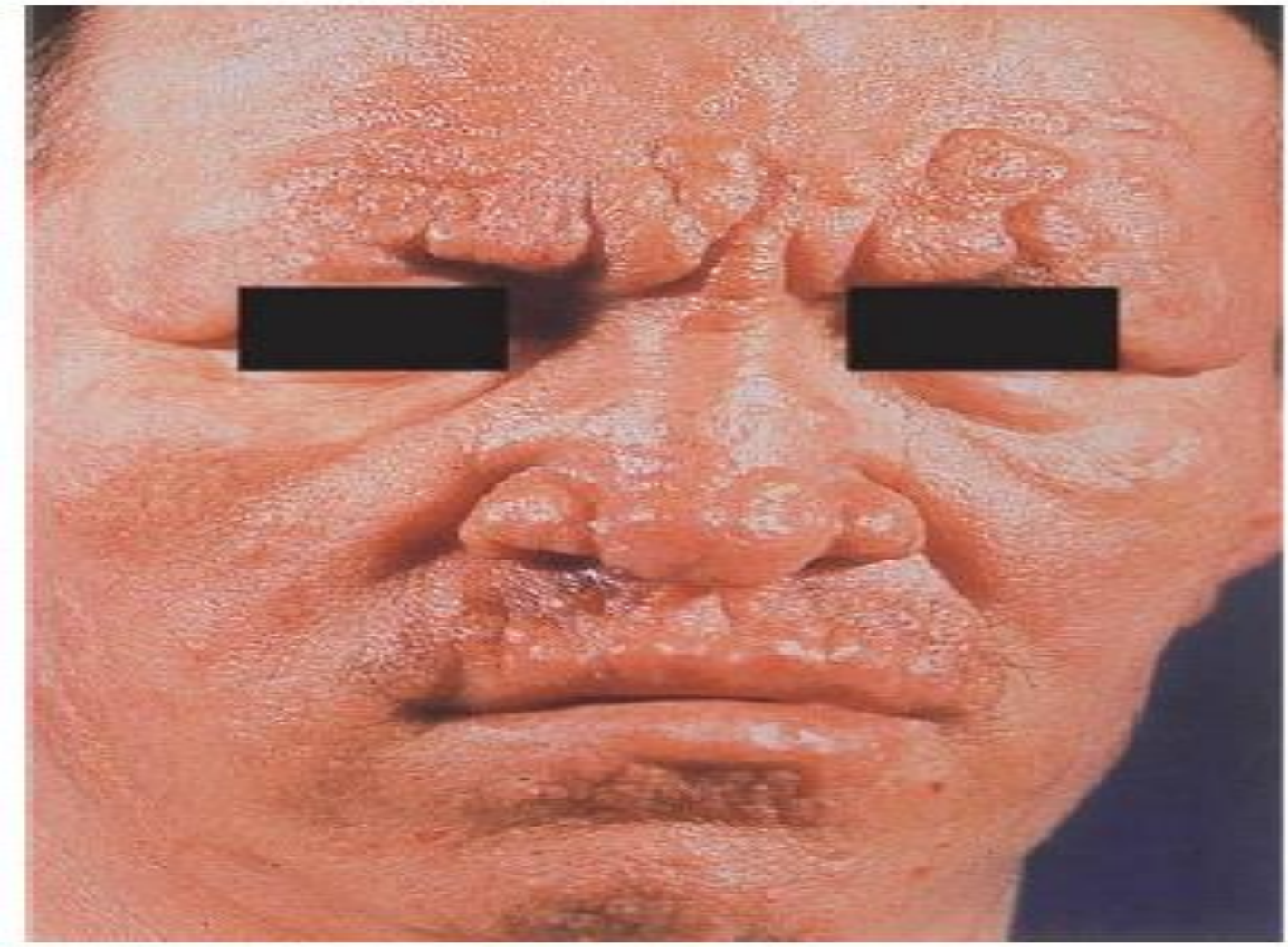


-Arthur's phenomenon: a form of immune complex-mediated hypersensitivity
-The CMI response consists primarily of CD4-positive cells and a Th-1 profile of cytokines, namely, interferon-γ, interleukin-2, and interleukin-12. It is the CMI response that causes the nerve damage seen in tuberculoid leprosy.

Lepromatous leprosy

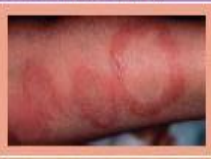
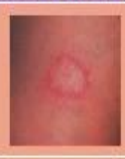
- Lesions have large numbers of bacilli even on skin that appears normal – poor CMI
  - Symmetrically distributed skin nodules with poorly defined margins
  - Nerve damage leads to loss of digits
  - Late manifestations include loss of eyebrows (initially the lateral margins only) and eyelashes, and dry scaling skin, particularly on the feet
  - **Lepromin test negative**



-Lepromatous leprosy is also known as multibacillary leprosy
-The nerve damage seems to be caused by direct contact as there are many organisms

Feature	Tuberculoid Leprosy	Lepromatous Leprosy
Type of lesion	One or few lesions with little tissue destruction	Many lesions with marked tissue destruction
Number of acid-fast bacilli	Few	Many
Likelihood of transmitting leprosy	Low	High
Cell-mediated response to *M. leprae*	Present	Reduced or absent
Lepromin skin test	Positive	Negative

People with LL produce INF-β whereas those with TL produce INF-γ. INF-β inhibits synthesis of INF-γ thereby reducing the CMI response needed to contain the infection

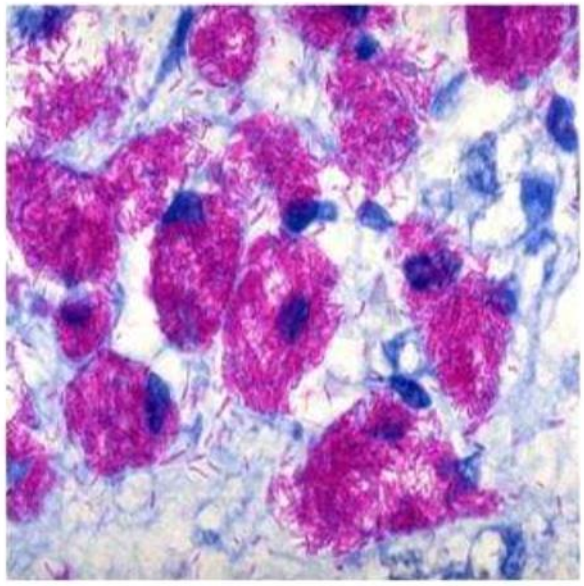
Operational	Multibacillary, >5 skin lesions		Paucibacillary, 1–5 skin lesions	
Ridley–Jopling*	Lepromatous leprosy (LL)	Borderline leprosy (BL)	Tuberculoid leprosy (TT)	Indeterminate (I)
Clinical findings				
Cellular immunity	Least (Th2 CD4⁺ T-cell response) →		Greatest (Th1 CD4⁺ T-cell response)	
Type of lesions	Macules, papules, and plaques and sometimes diffuse infiltration of the skin	Macules, papules, and plaques with variable induration	Infiltrated thin plaques with raised edges, often hypopigmented	Macules, often hypopigmented
Distribution	Symmetric; favors face, buttocks, lower extremities	Tendency to symmetry	Localized, asymmetric	Variable
Definition	Vague, difficult to distinguish normal versus affected skin	Less well-defined borders	Well-defined, sharp borders	Not always defined
Sensation	Not affected	Diminished	Absent	Impaired
Bacilli in skin lesions	←			Usually none detected

Note that in LL, only the cell-mediated response to M. leprae is defective (i.e., the patient is anergic to M. leprae). The cell-mediated response to other organisms is unaffected, and the humoral response to M. leprae is intact. However, these antibodies are not protective.

Mycobacterium leprae
- Laboratory diagnosis -

- Collection of specimens:
  - skin lesion biopsy, skin scrapping
  - Nasal exudate
- Microscopy:
  - Ziehl-Neelsen stained smear: acid fast bacilli, accumulated in intracellular, encapsulated globular masses - "leprosy globi" - in lepromatous leprosy

- (Cultivation – not applicable)



Treatment & Management

- Chemotherapy
- First line drugs are rifampicin, dapsone, and clofazimine
- The patients bacterial load decides length of treatment (6-24 months)
- Second line drugs are ofloxacin and minocycline
- Triple –drug combinations have been used in cases where a patient has only a single lesion

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The atypical mycobacteria are classified into four groups according to their rate of growth and whether they produce pigment under certain conditions. The atypical mycobacteria in groups I, II, and III grow slowly, at a rate similar to that of M. tuberculosis, whereas those in group IV are "rapid growers," producing colonies in fewer than 7 days. Group I organisms e.g. M. marinum produce a yellow-orange–pigmented colony only when exposed to light (photochromogens), whereas group II organisms e.g. M.scrofulaceum produce pigments in the dark (scotochromogens). Group III mycobacteria e.g. M. avium produce little or no yellow-orange pigment, irrespective of the presence or absence of light (nonchromogens).

Scrofula

- A cervical lymphadenitis
- Source: Environmental H_2O sources, human respiratory tract
- Chronic, painless mass in the neck – known as a cold abscess
- In children – agent - *M.scrofulaceum*
  – Surgery, usually resistant to antibiotics
- In adults – agent - *M.tuberculosis* – antiTB drugs.

33

M.marinum

- Causes swimming pool or **fish tank granuloma**

- Lesions usually localized but may form secondary lesions
- Self-limiting; can use minocycline, cotrimoxazole or rifampicin with ethambutol

34

M.ulcerans

- Causes Buruli ulcer
- Found in low-lying marshy areas subject to periodic flooding
- Treatment
  - Early, pre-ulcerative lesion –excision and primary closure
  - Ulcerated lesions – excision & grafting
  - Antimicrobial agents – variable results

35

CONCLUSION

 Describe the structure and main pathogenic features of M. tuberculosis

What is extra-pulmonary TB?

 What is Latent M. tuberculosis and Active TB

 MDR and XDR TB: what are they, how have they come about, and how have they spread? Can they be treated? If so, how, and how is this different from treatment of traditional TB infections?

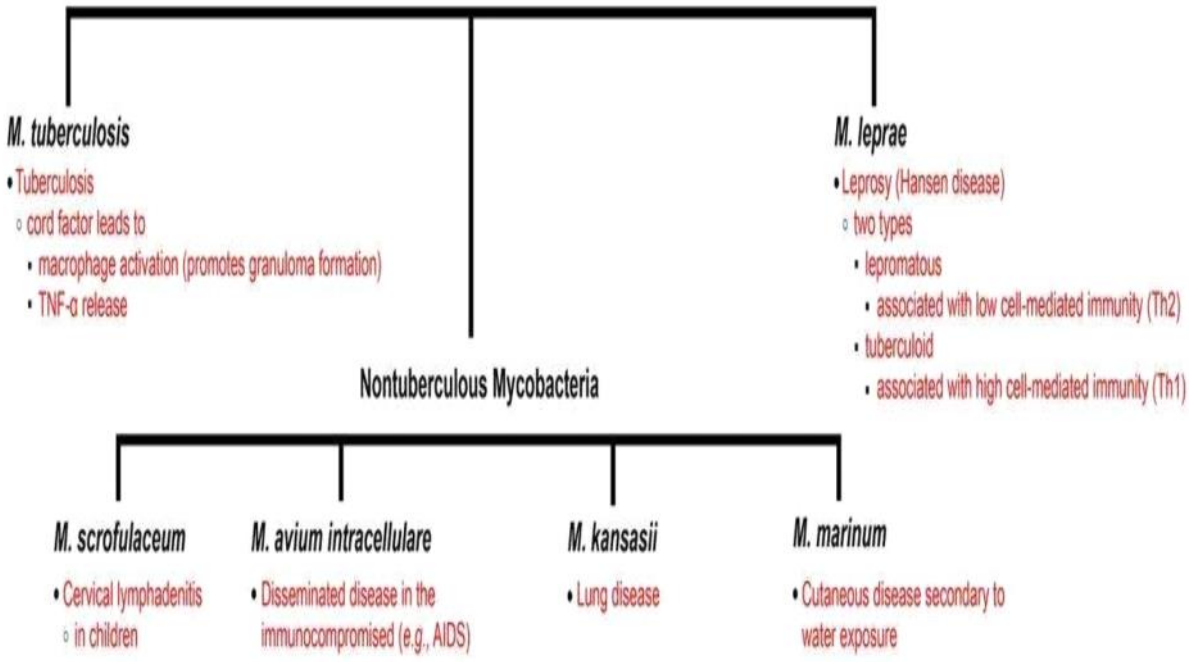
 What is the connection between TB and AIDS?

. Different classifications of Leprosy

? Non-Tubercular Mycobacteria infections

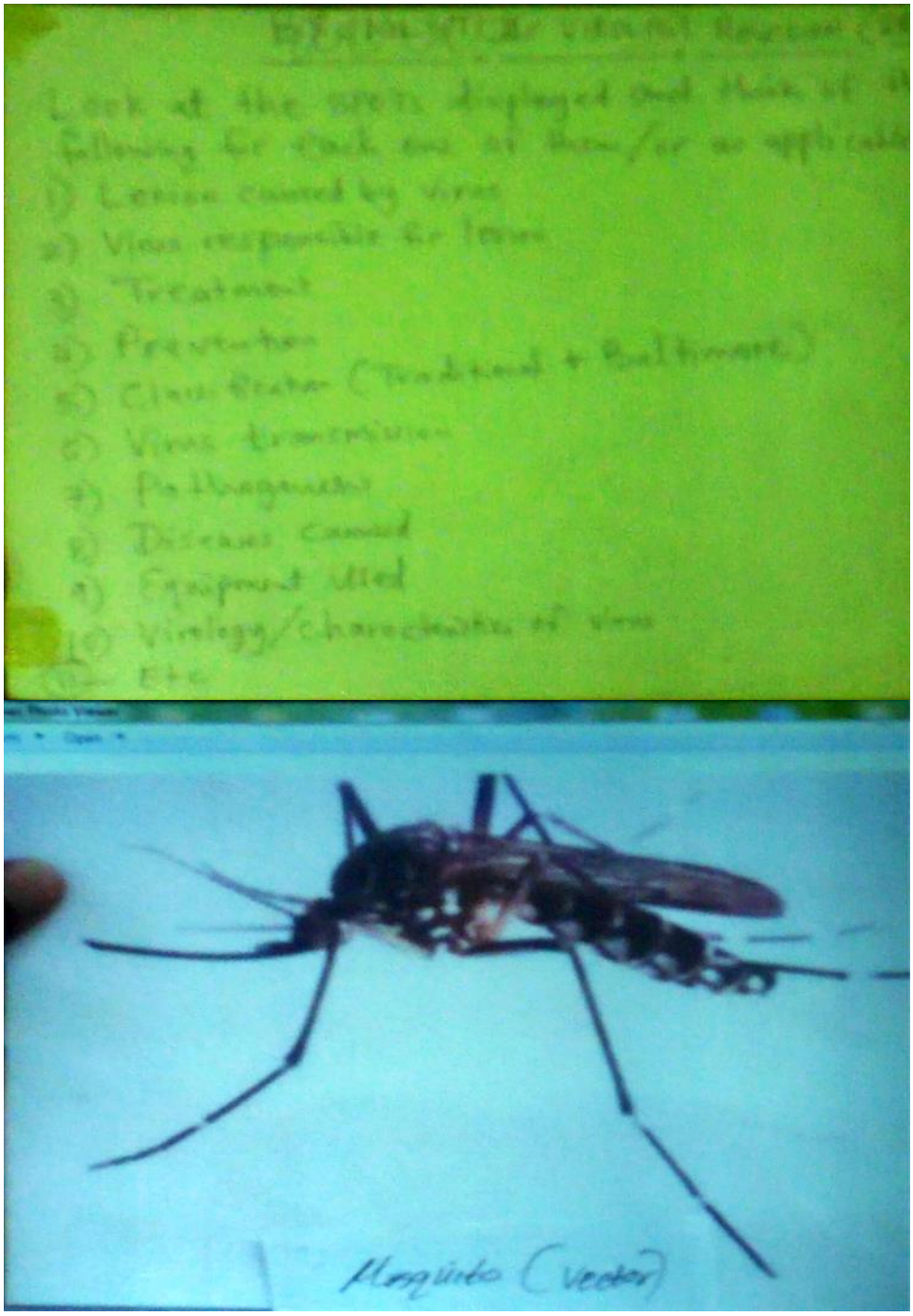
Mycobacterium

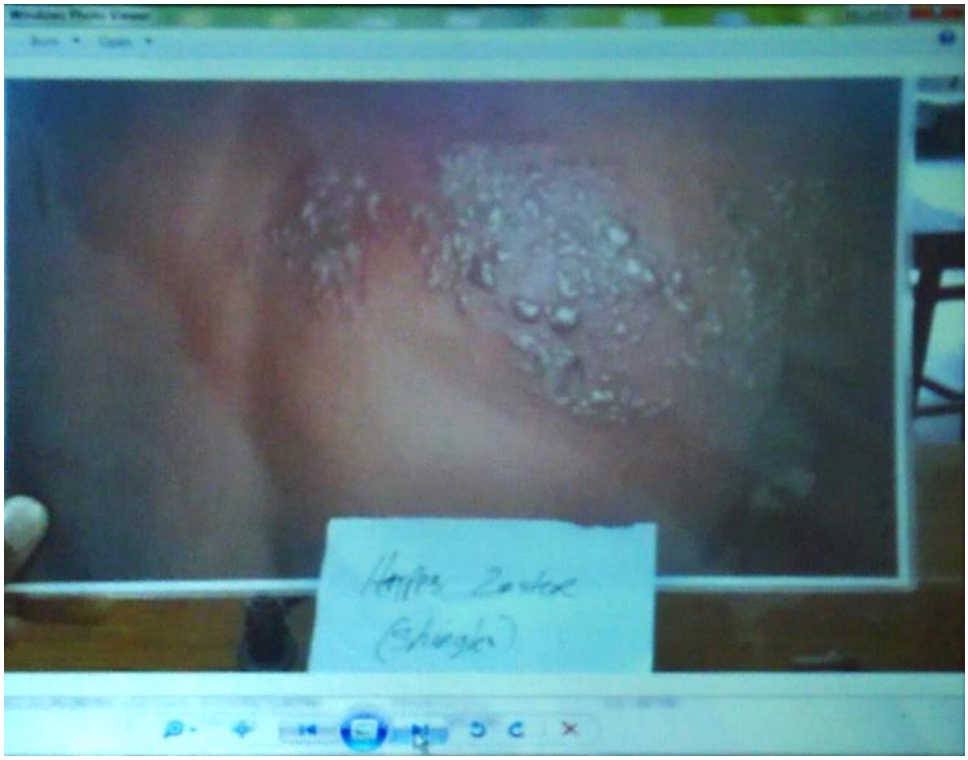
All are acid-fast

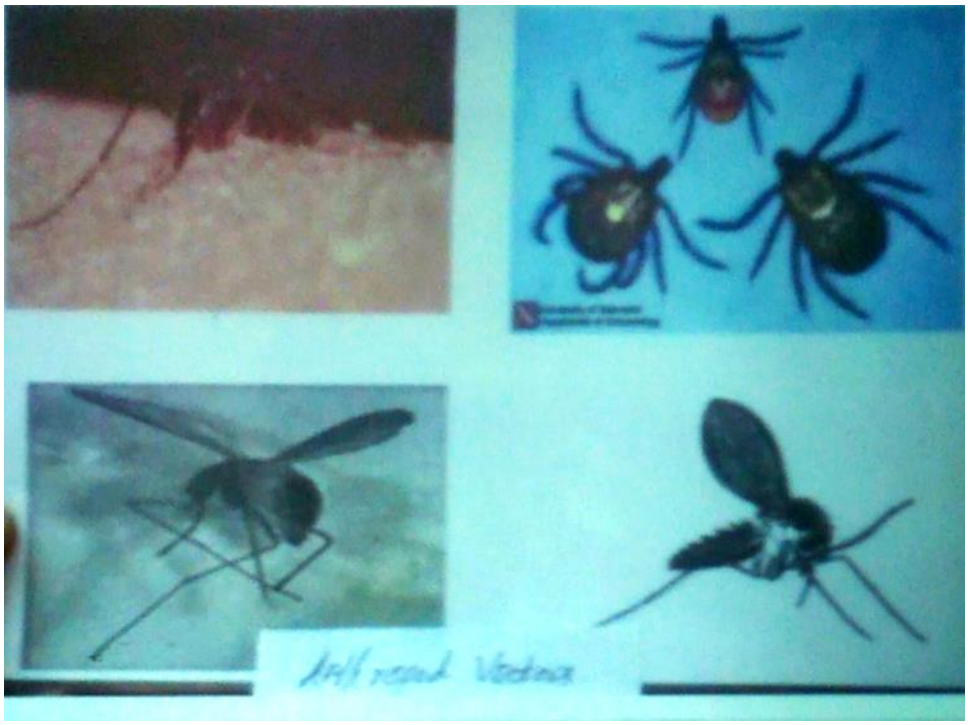


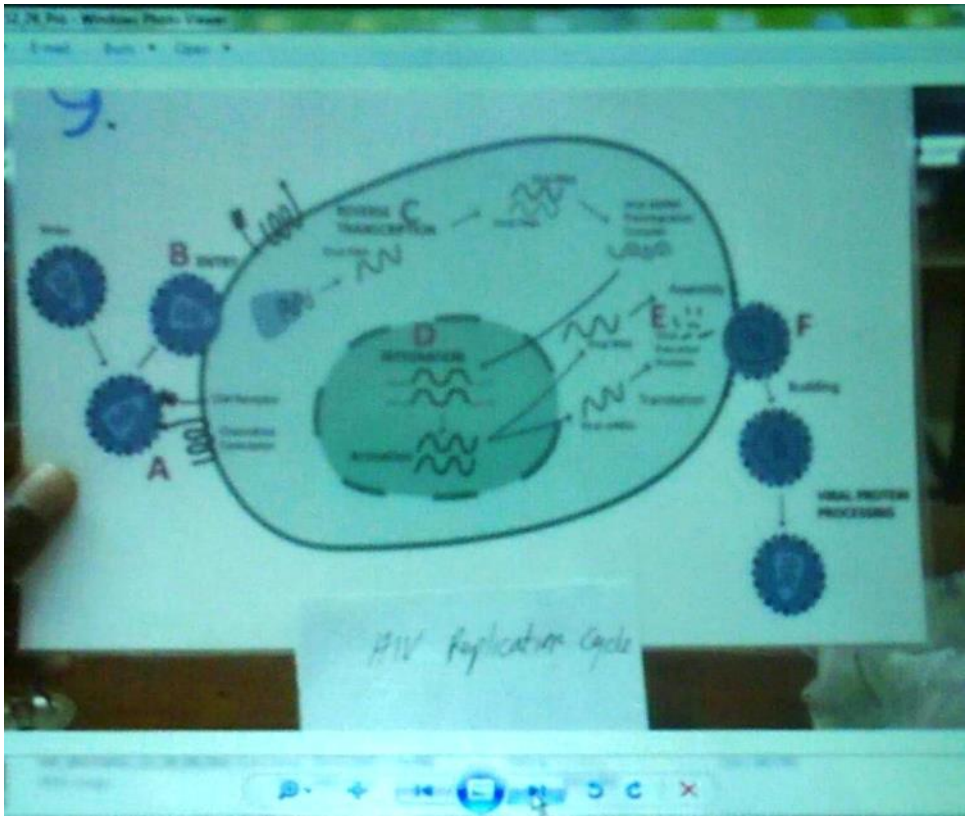
Spot Exam Revision

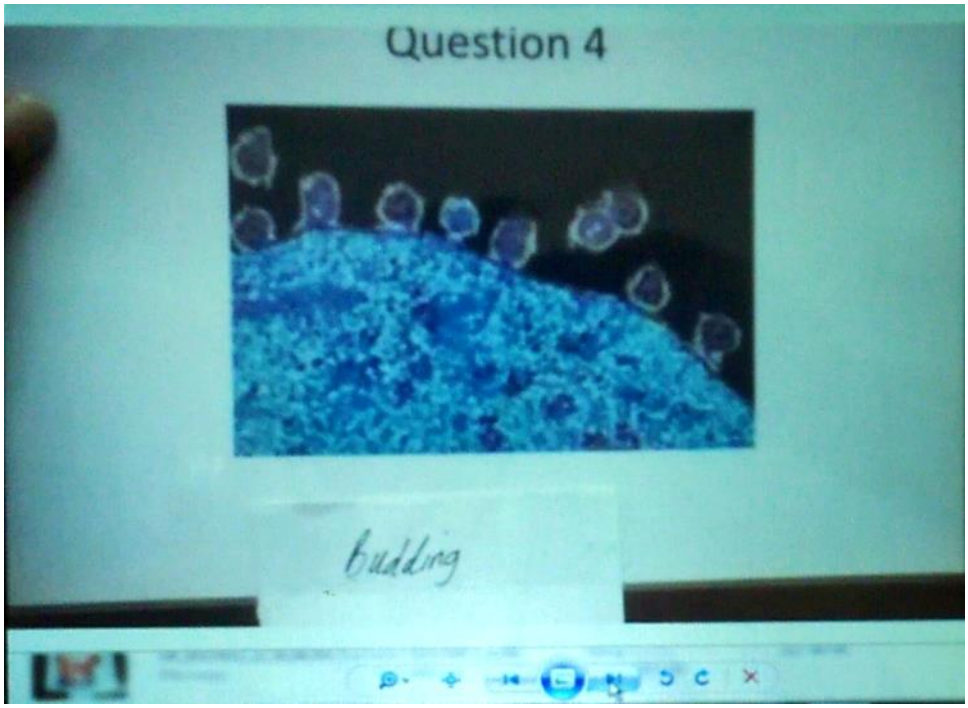
Wednesday, August 1, 2018 2:20 PM

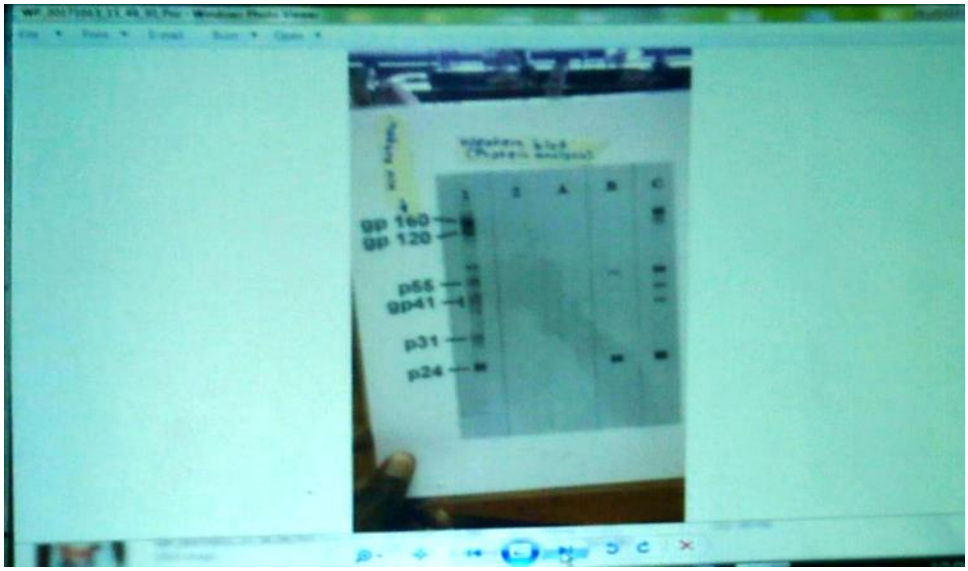


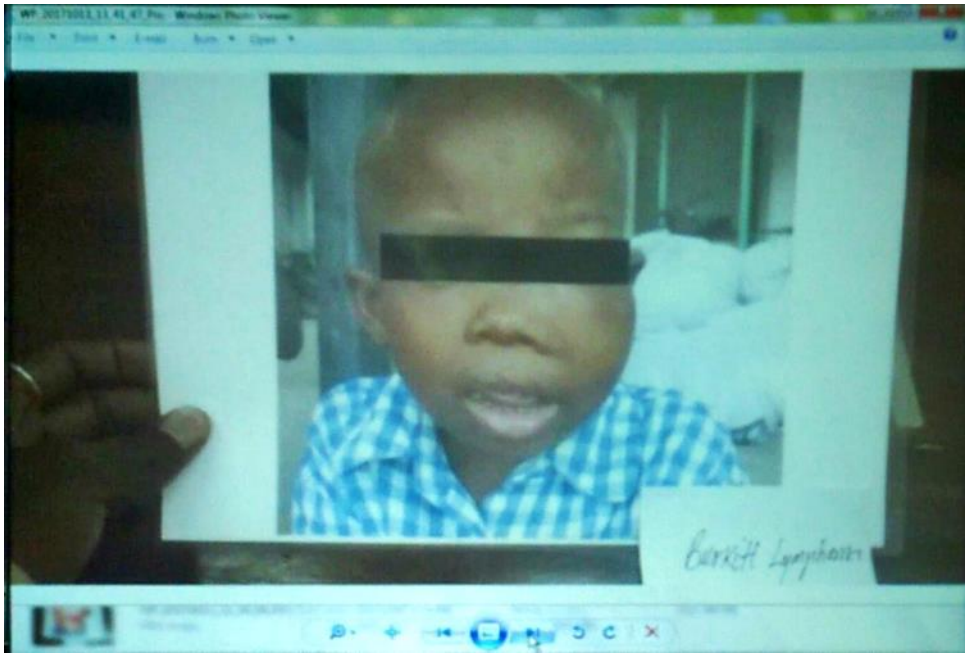


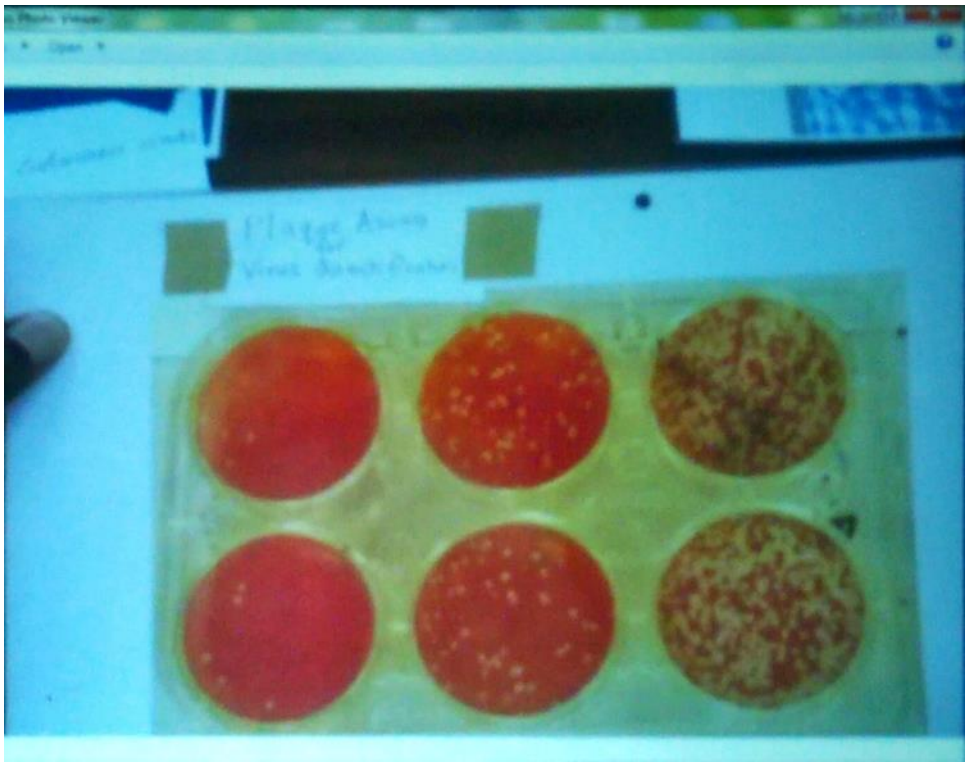


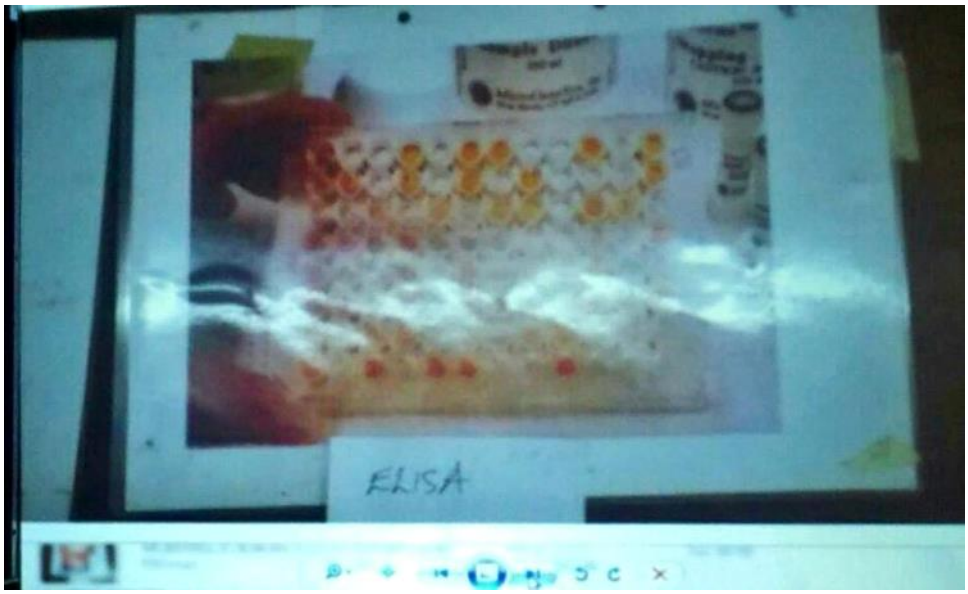

HIV Replication Cycle

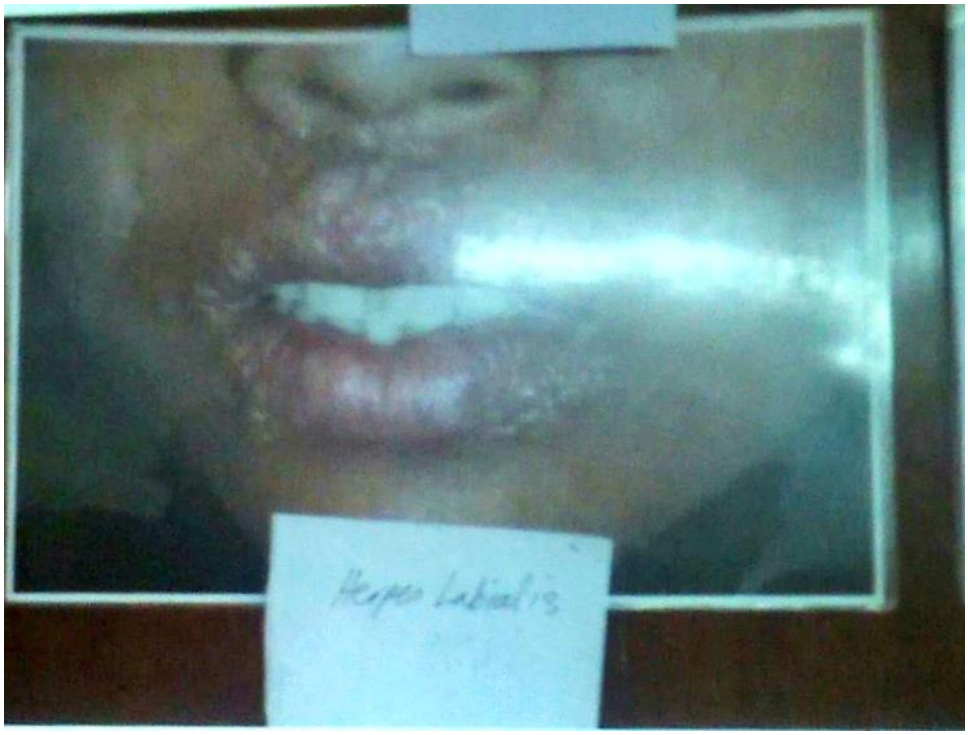

Question 4
budding

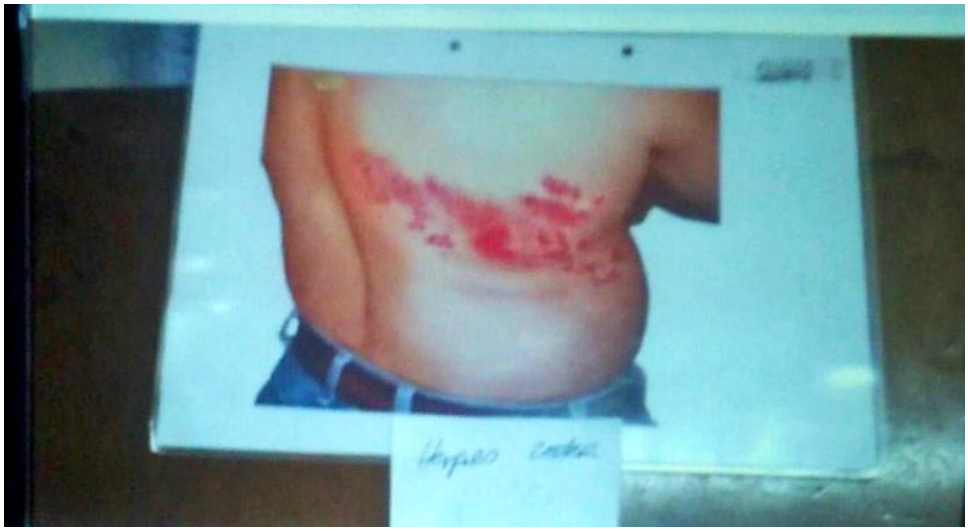

gp 160
gp 120
p55
gp41
p31
p24

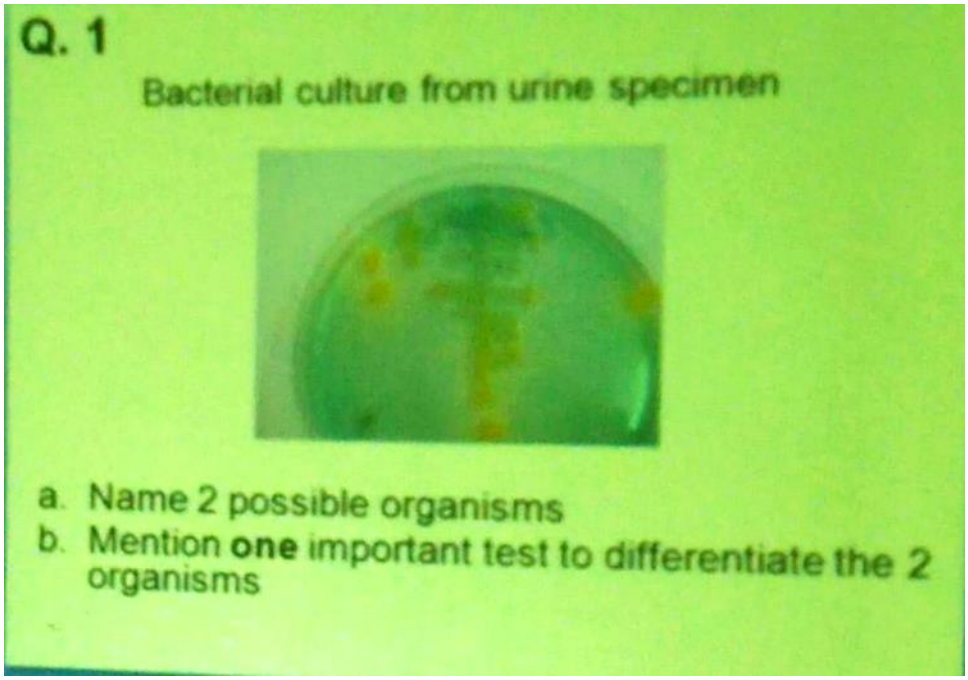

Burkitt Lymphoma



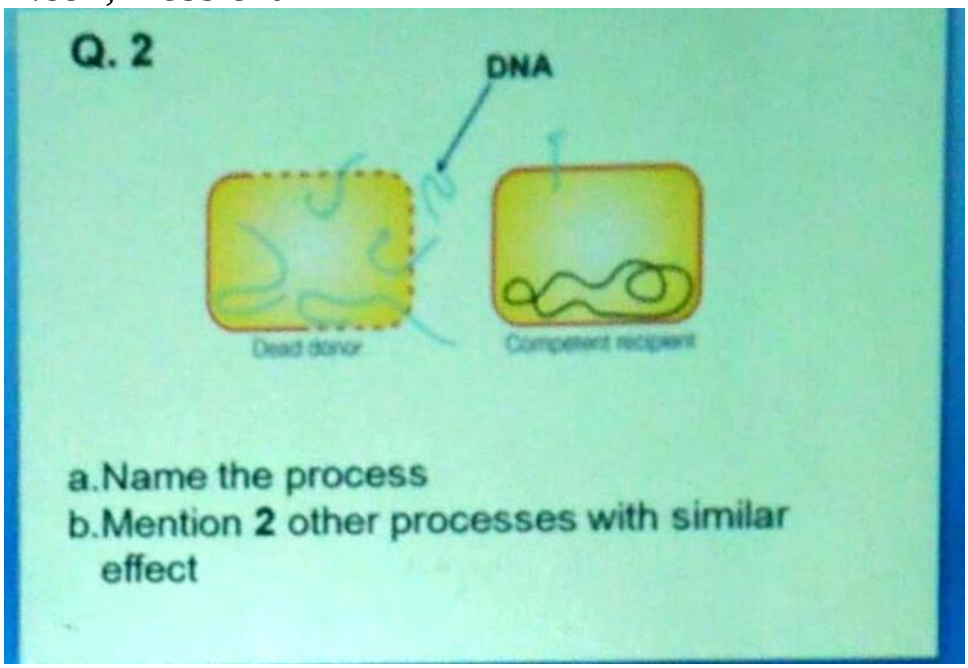

ELISA

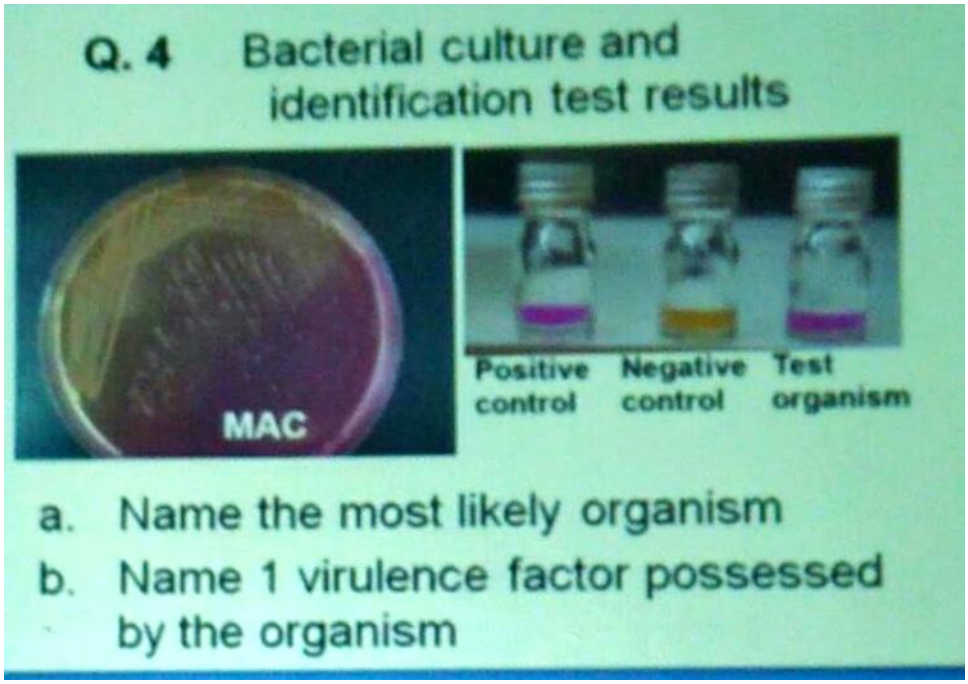

Herpes Labialis


Herpes Zoster

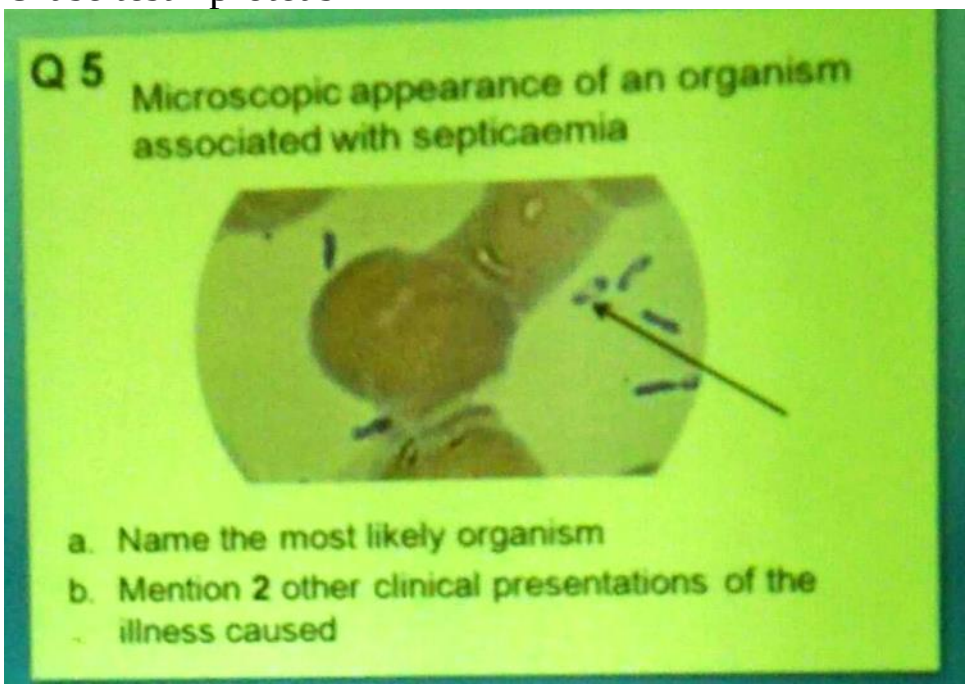


E.coli, klebsiella

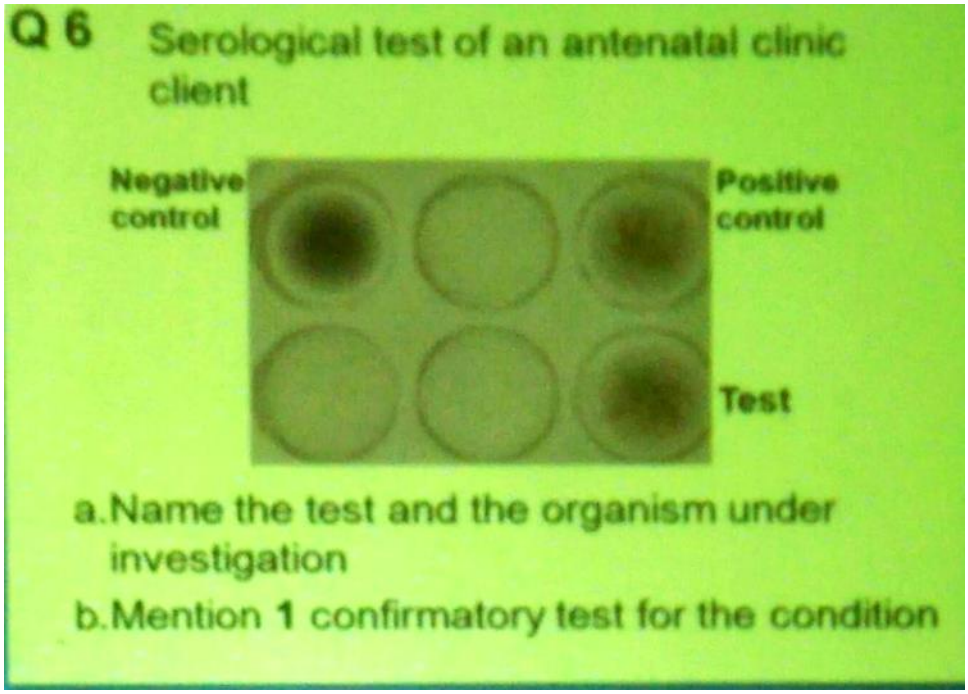




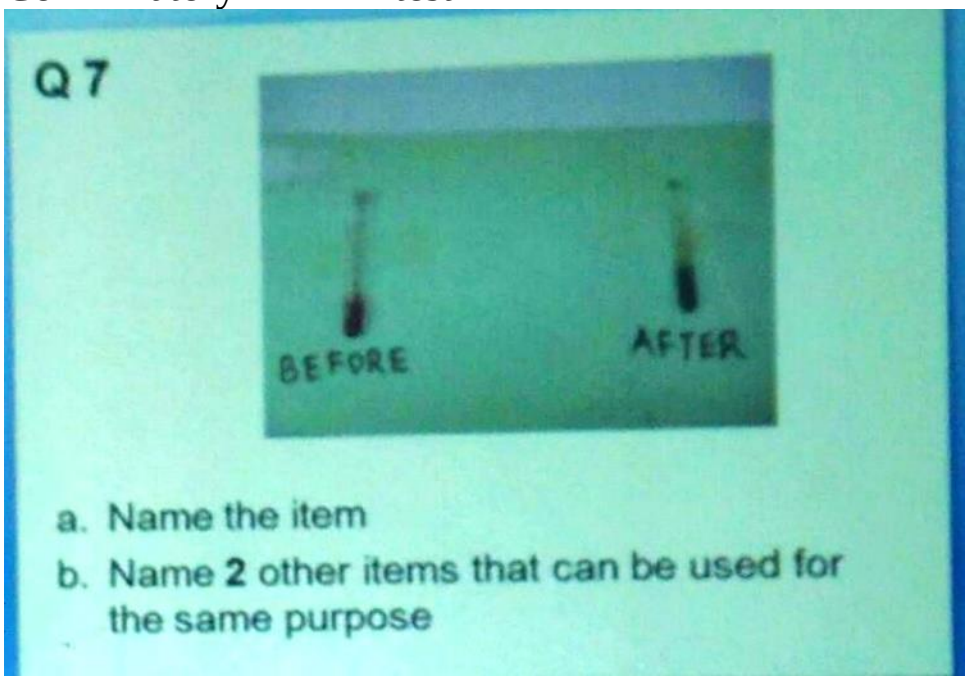
Urase test - proteus



Safety pin- yersinia Pestis
Bipolar staining
Bubonic

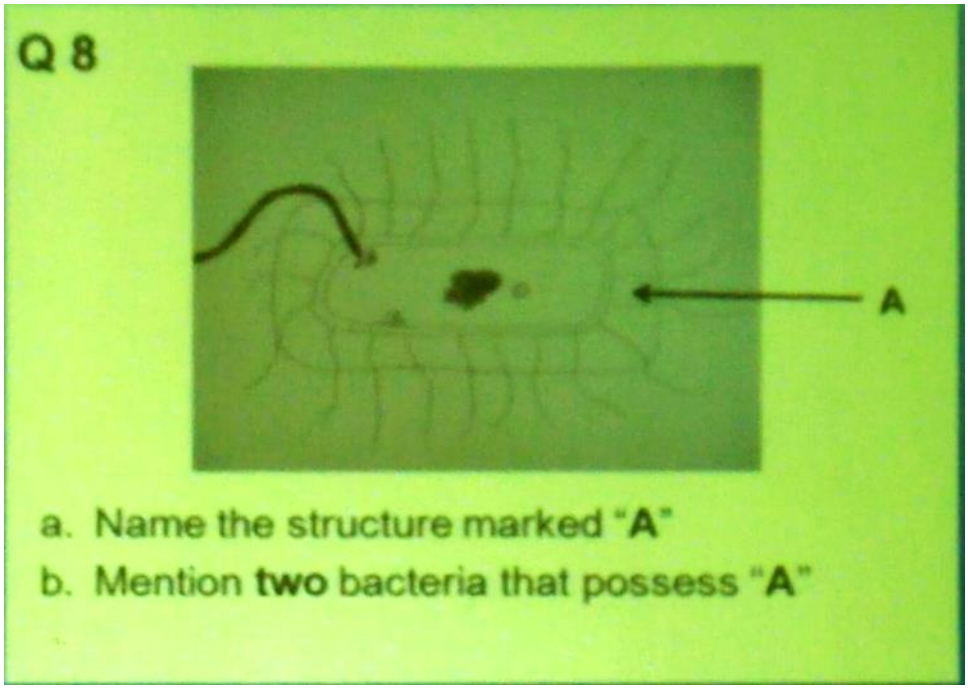


Syphilis RPR
Confirmatory - TPHA test



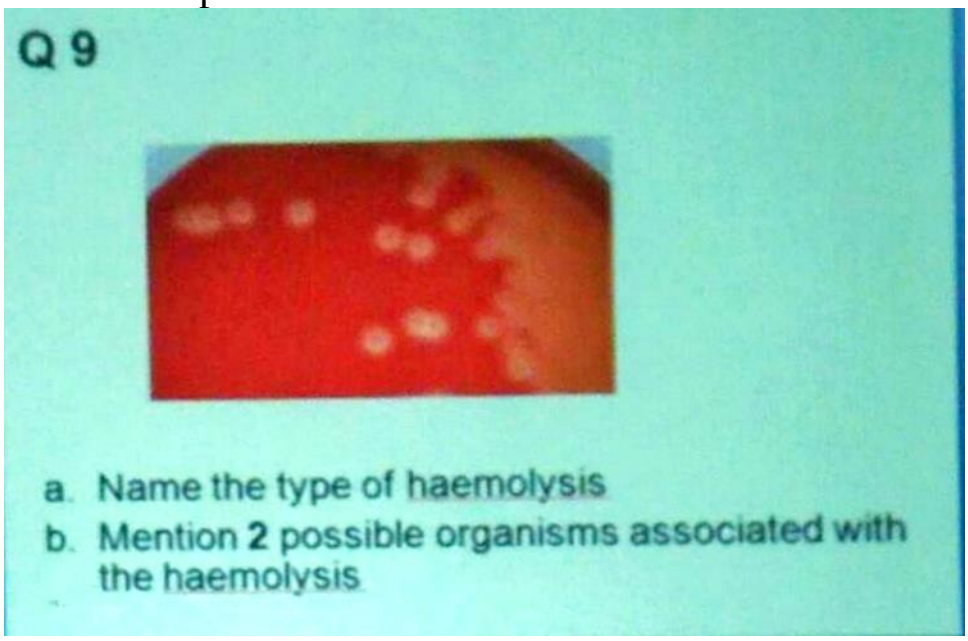
Browne's tubes- sterilization
Sterilization- changes to green
For chemical control of sterilization

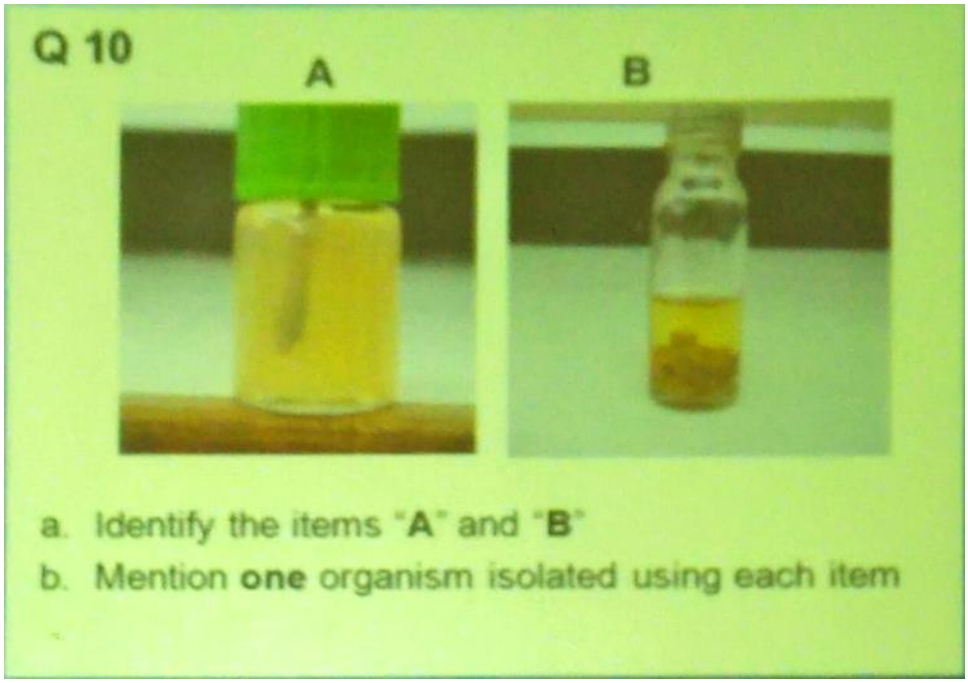
- Autoclave tape



Capsule.

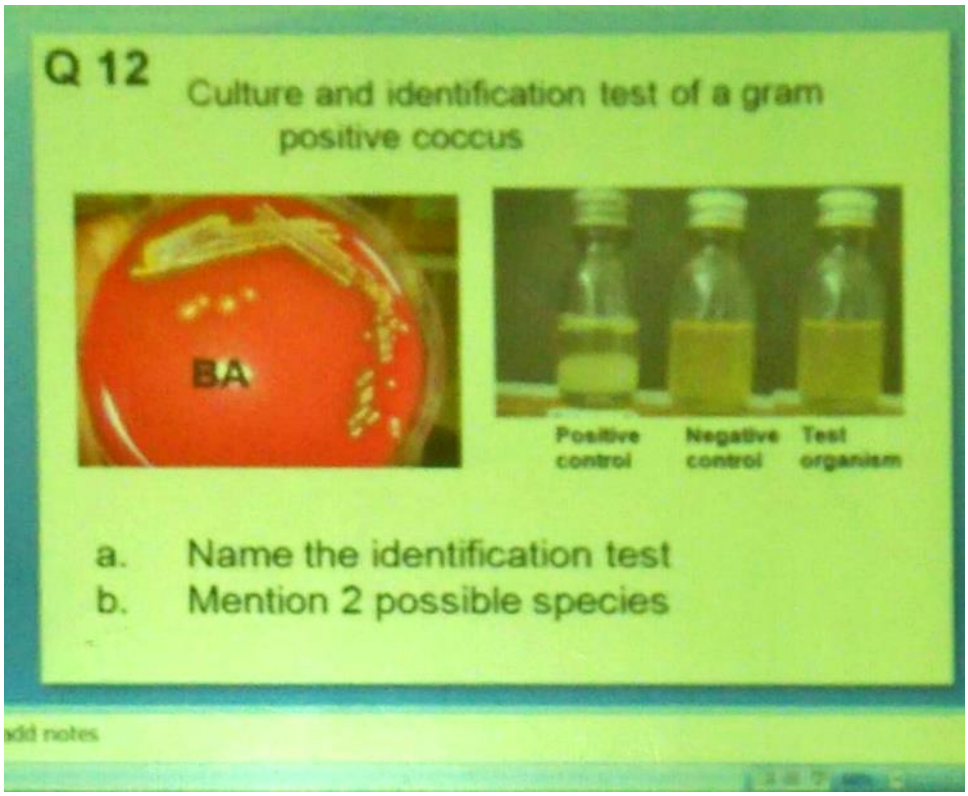
- Strep pneumonia
- Haemophilus



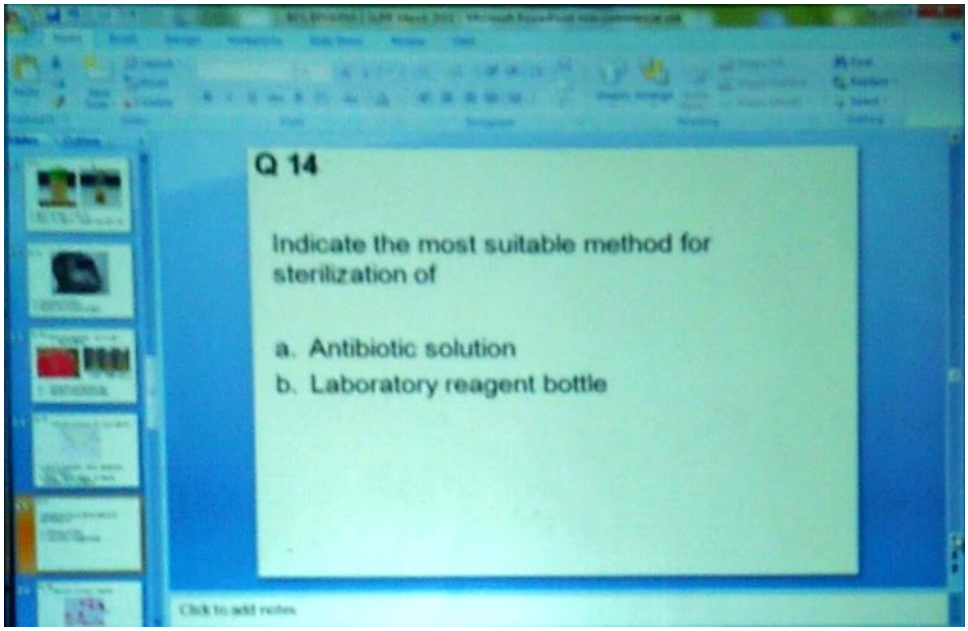


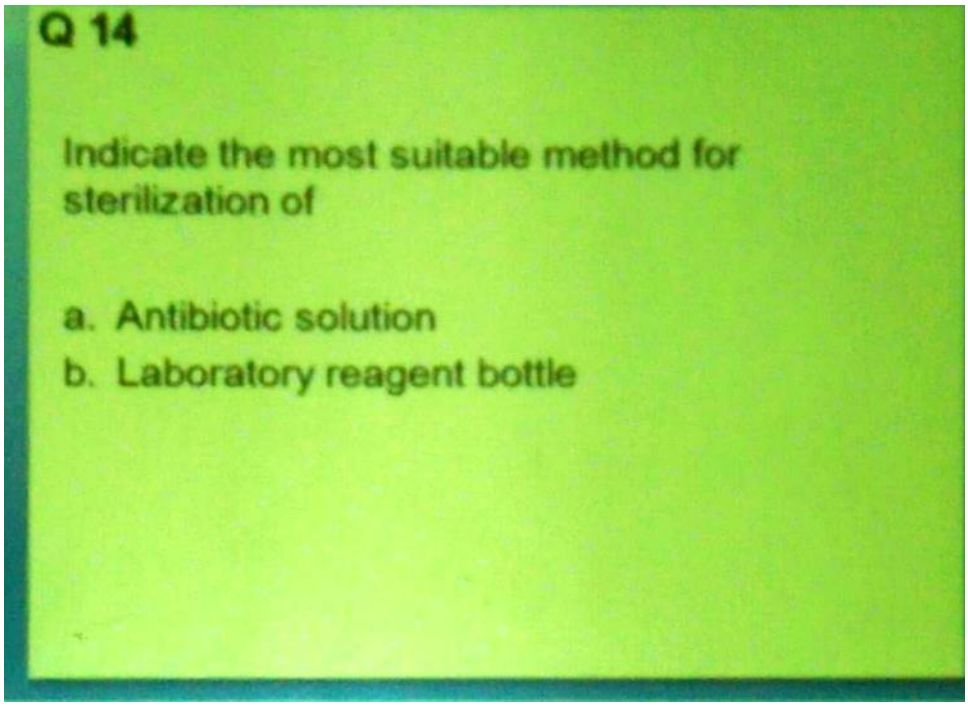
A- Stuart. Neiseria gonorrhea

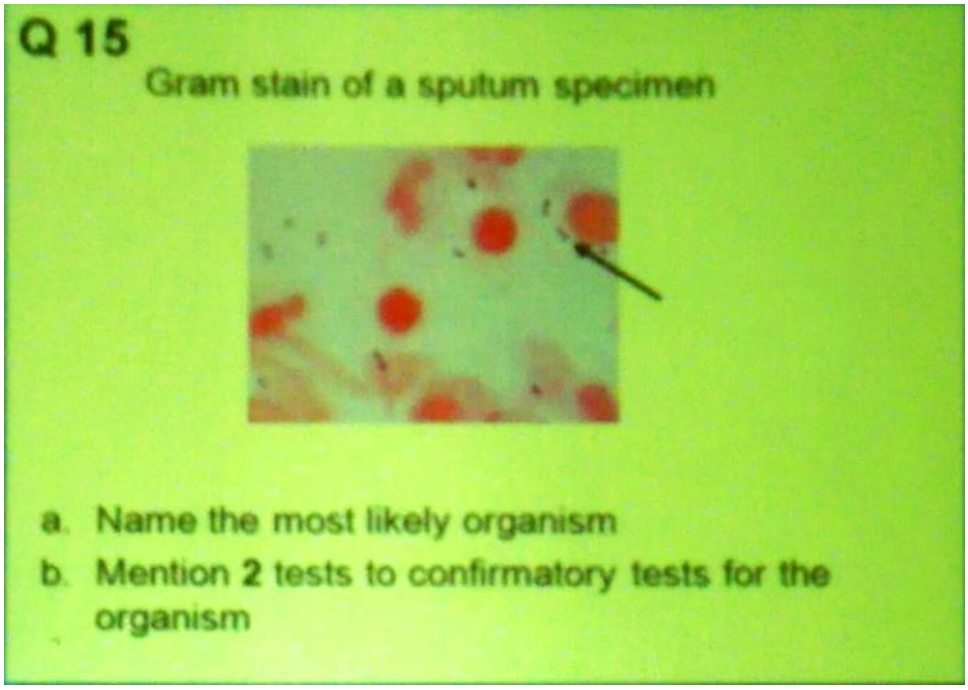
B-RCM



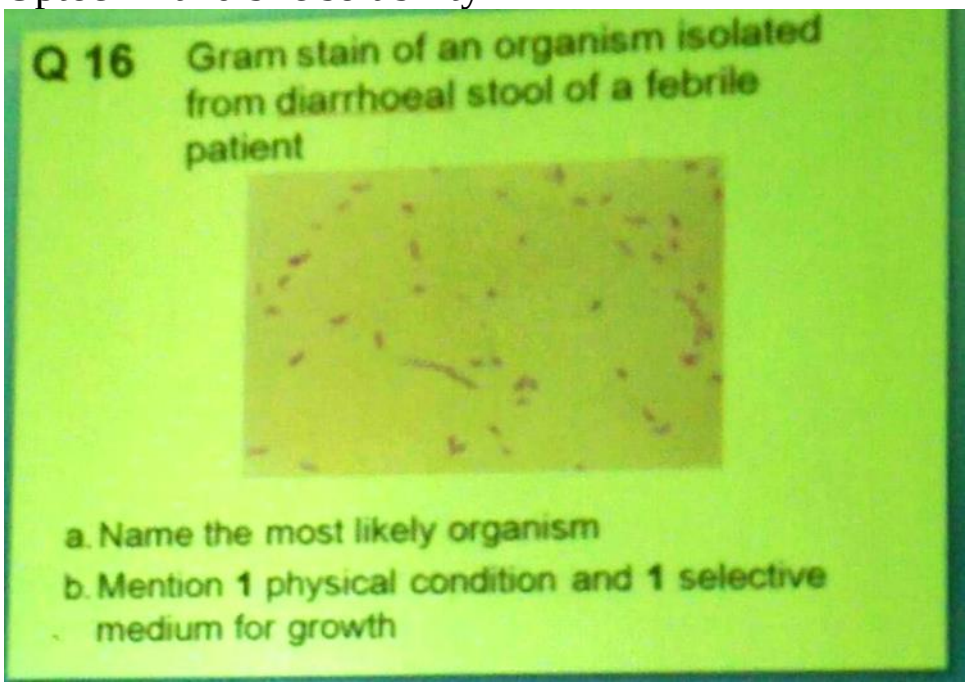
Tube coagulase test
Coagulase negative staphylococcus


Q 14
Indicate the most suitable method for sterilization of
a. Antibiotic solution
b. Laboratory reagent bottle
Click to add notes


Q 14
Indicate the most suitable method for sterilization of
a. Antibiotic solution
b. Laboratory reagent bottle



Gram negative - strep pneumoniae
Optochin and bile solubility



Campylobacter- wings

Q 17

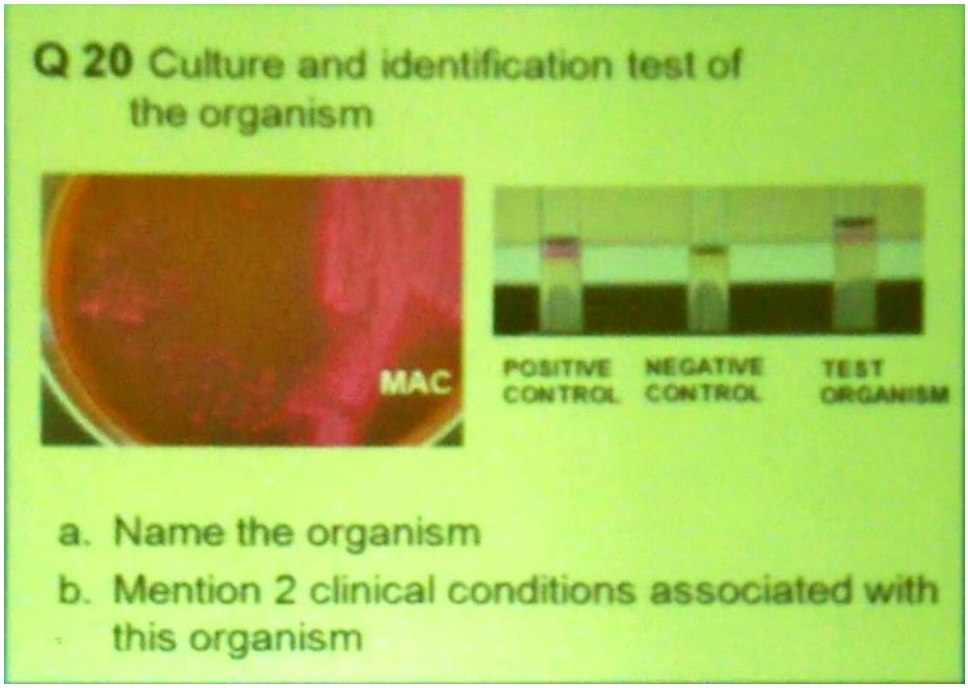
Indicate the most suitable method of disinfection for

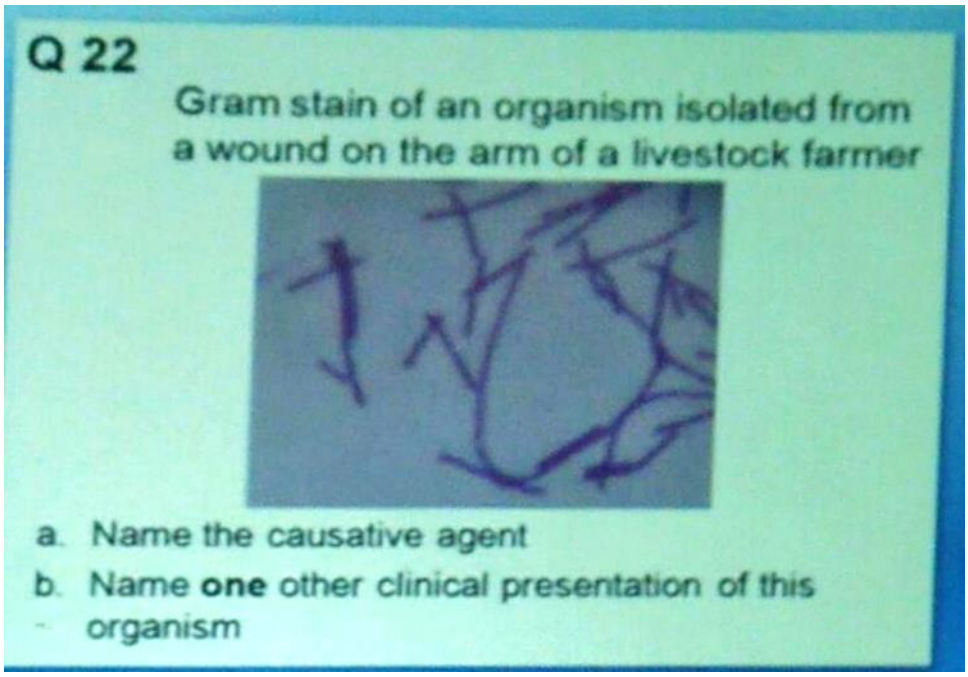
a. Skin before venipuncture

b. Laboratory bench top

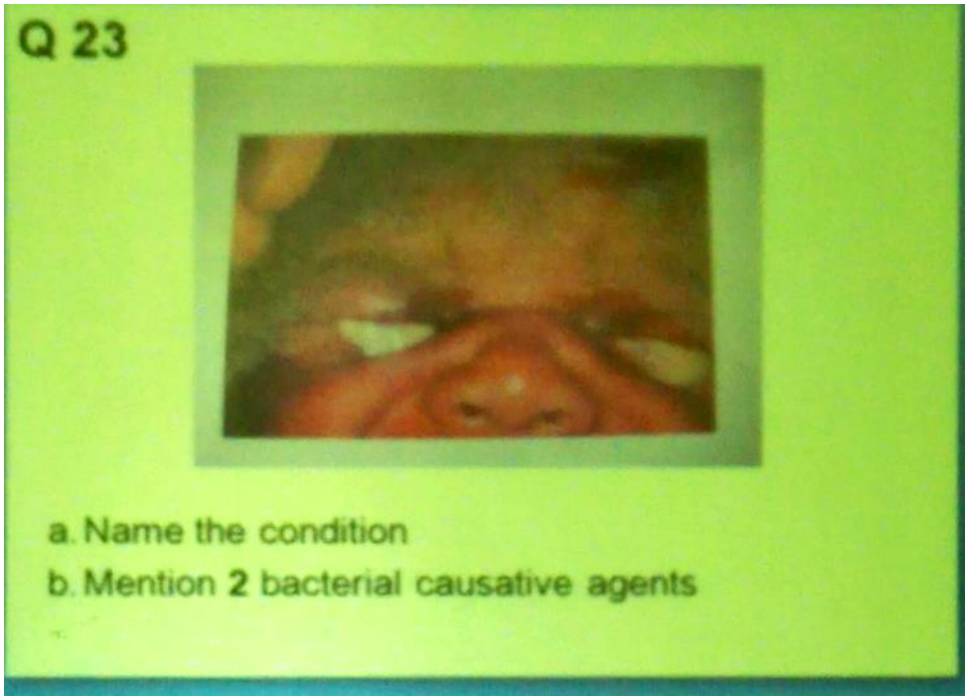
Q 19 Skin manifestation of a chronic bacterial infection

a. Name the causative agent and the clinical condition
b. Mention one antimicrobial agent for treatment

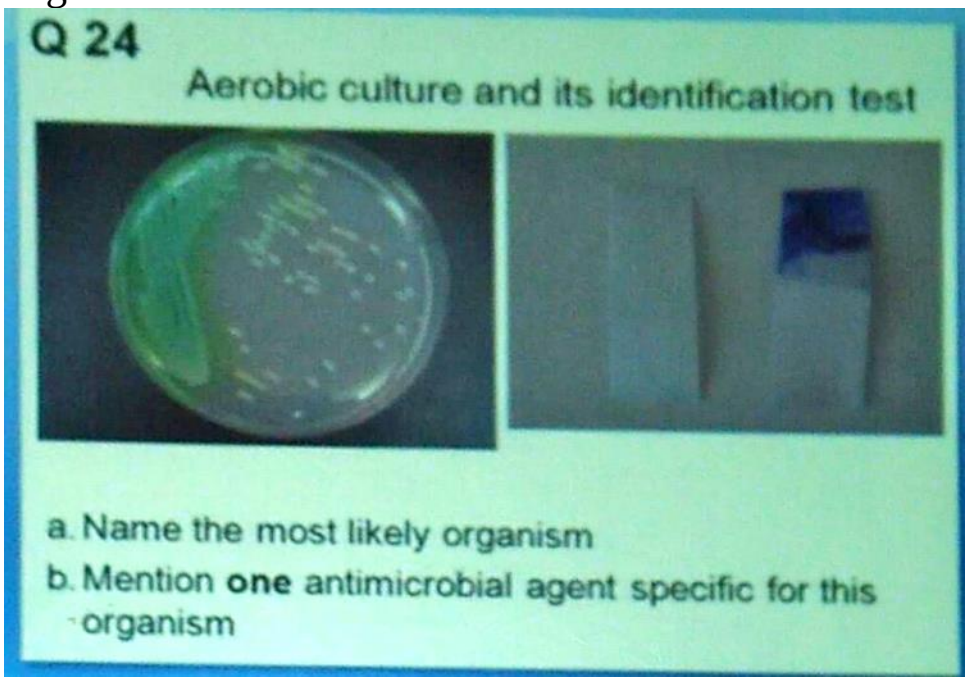




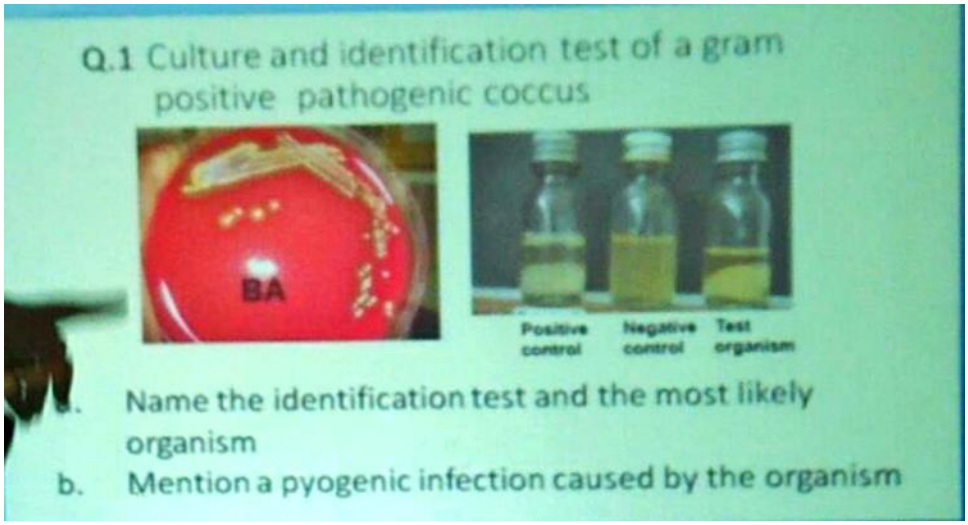
Bacillus anthracis
Septicemia



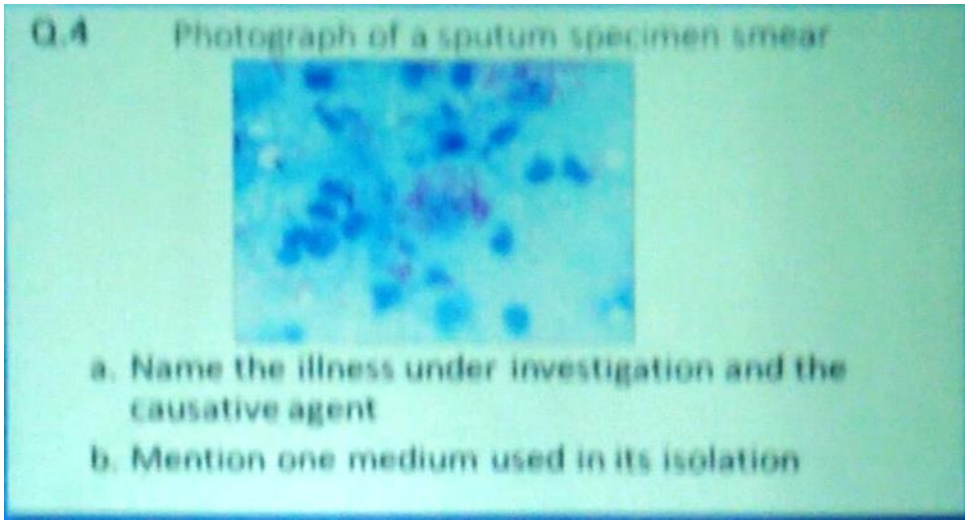
N.gonorrhea

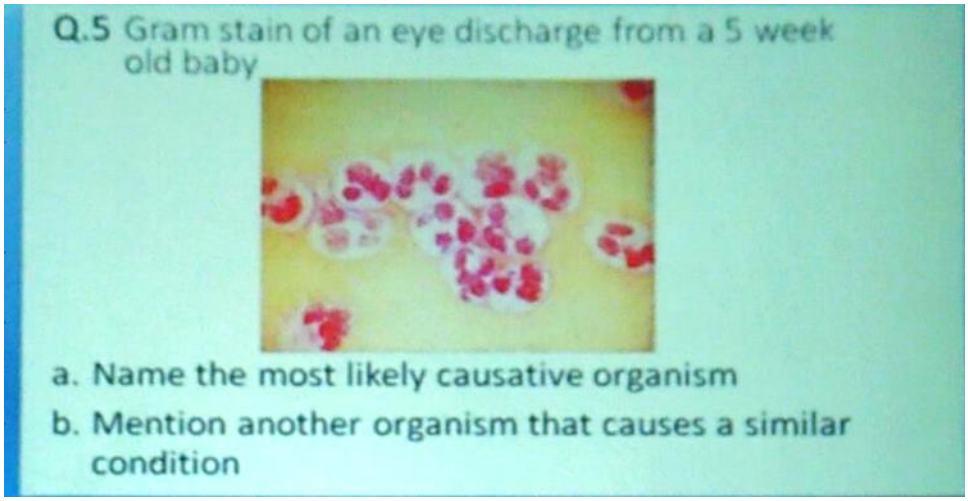


Pseudomonas

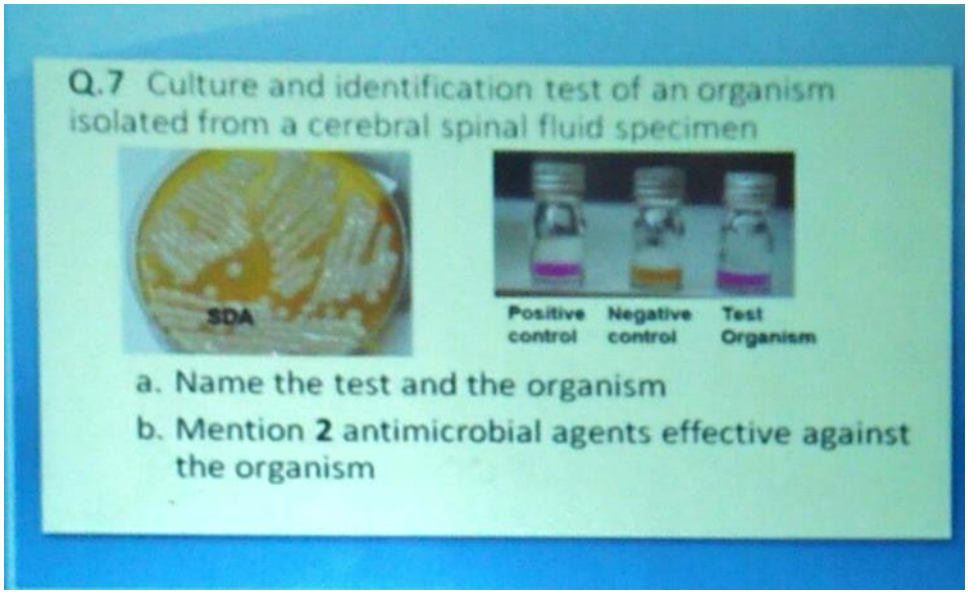


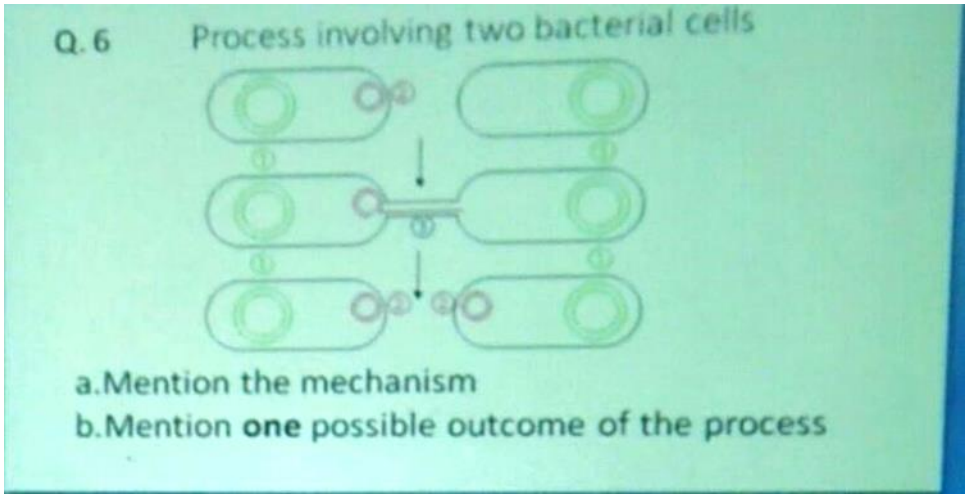
S.aureus

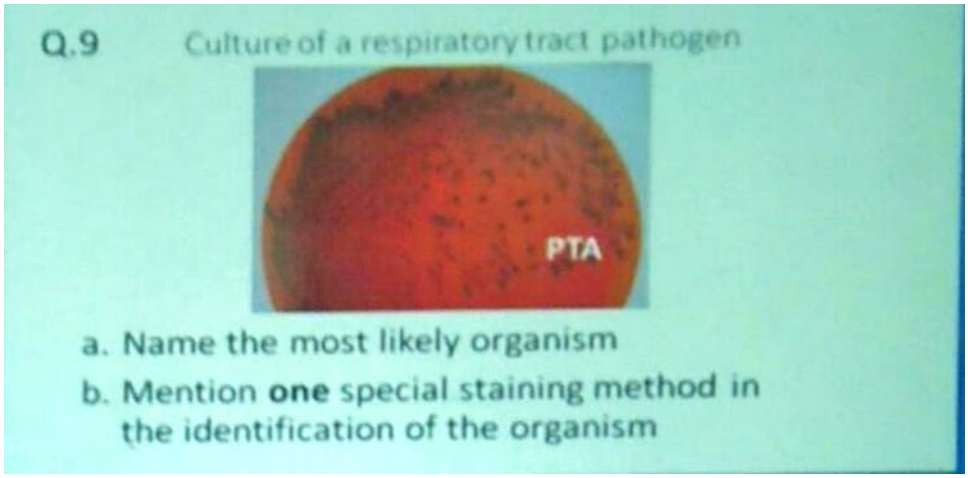




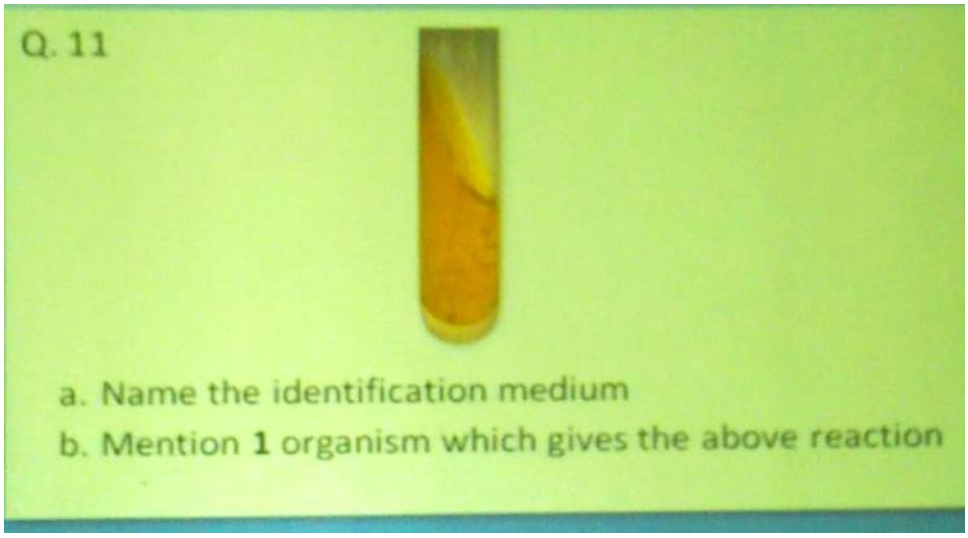
Gram negative diplococci . N.gonorrhea
Clamydiatricho



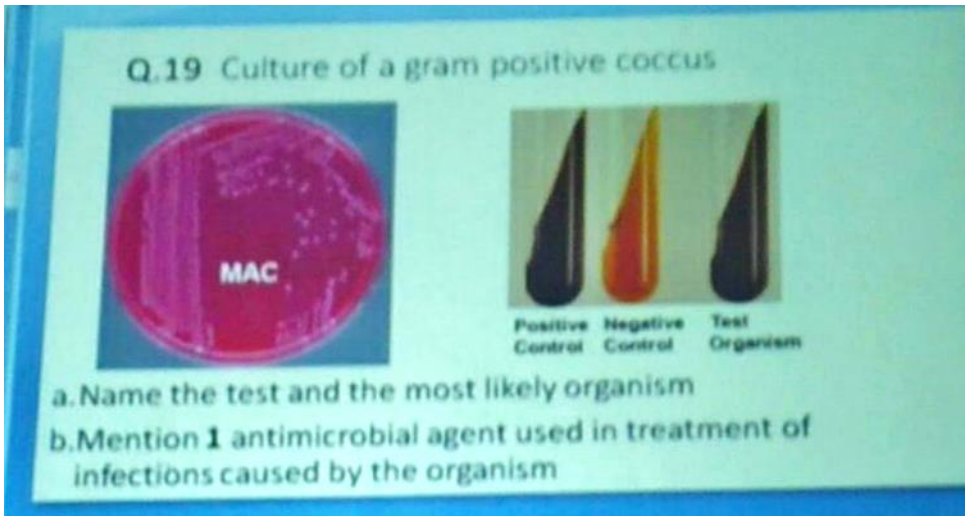




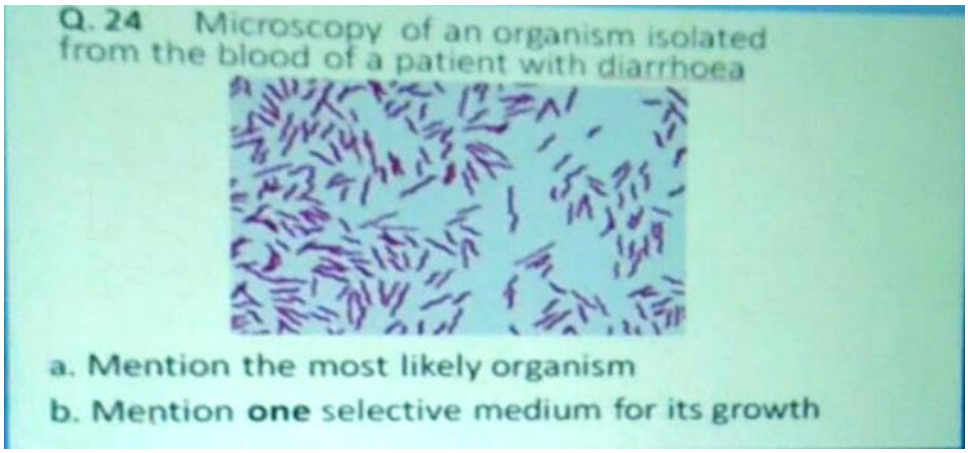
Dark grey colonies- corynobacterium diphtheria
Albertstaun



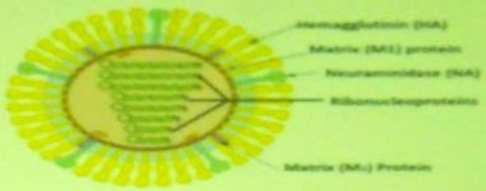
E.coli klebsiella-



Bile esculin test for e.fecalis



25.



a) Name the family of this virus (1 mark)

b) List two antiviral drugs for this virus (1 mark)

26. **Serology results for Hepatitis B infection**

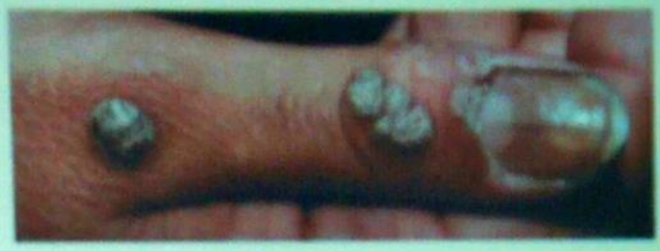
	HBsAg	Anti-HBs	Anti-HBc (Total)
A	Negative	Negative	Negative
B	Negative	Positive	Negative
	Negative	Positive	Positive
	Positive	Negative	Positive

a. Match the letters **A & B** with the corresponding interpretation (2mks)

i. Immunized after vaccination

ii. Susceptible

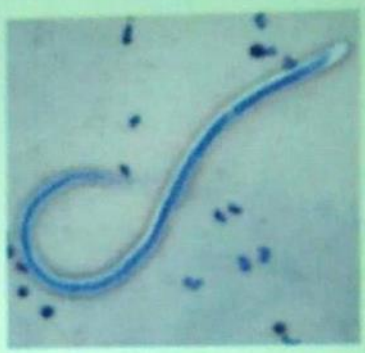
27.



a. Name the condition and the causative virus (1 mark)

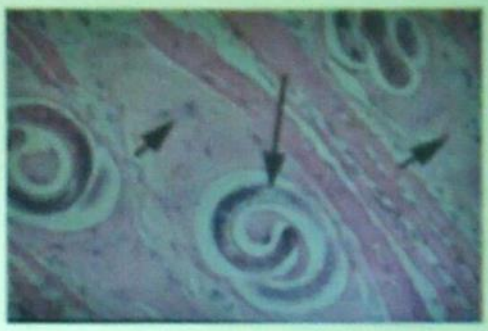
b. List two cancers associated with the virus (1 mark)

Q31



a. Identify the stage, genus and species of this parasite
b. Name one drug used to treat its infection in Man

Q35

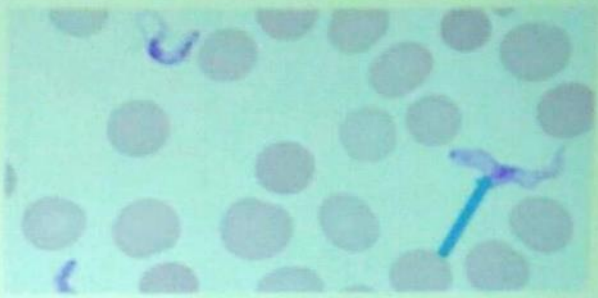


a. Identify the parasite in a muscle biopsy (long arrow)
b. Name one clinical presentation of infection with it

Q37

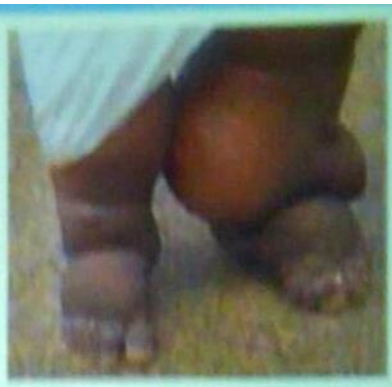
a. Identify stage, genus & species of these parasites
b. List two drugs used to treat its infection

Q39



a. Identify the stage and parasite shown by the arrow
b. Name one specimen useful in its diagnosis

Q45



a. Name the condition shown in the picture
b. Name one drug used to treat this condition

Q46

a. Name the stage, genus and species of the parasite shown
b. Give one reason for your identification

Q48

a. Identify the insect shown in the picture
b. Name one parasite transmitted by the insect

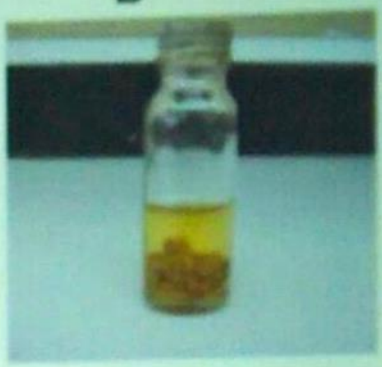
Q50

a. Name the stage, genus & species of this parasite
b. Name two methods of prevention of infection by it

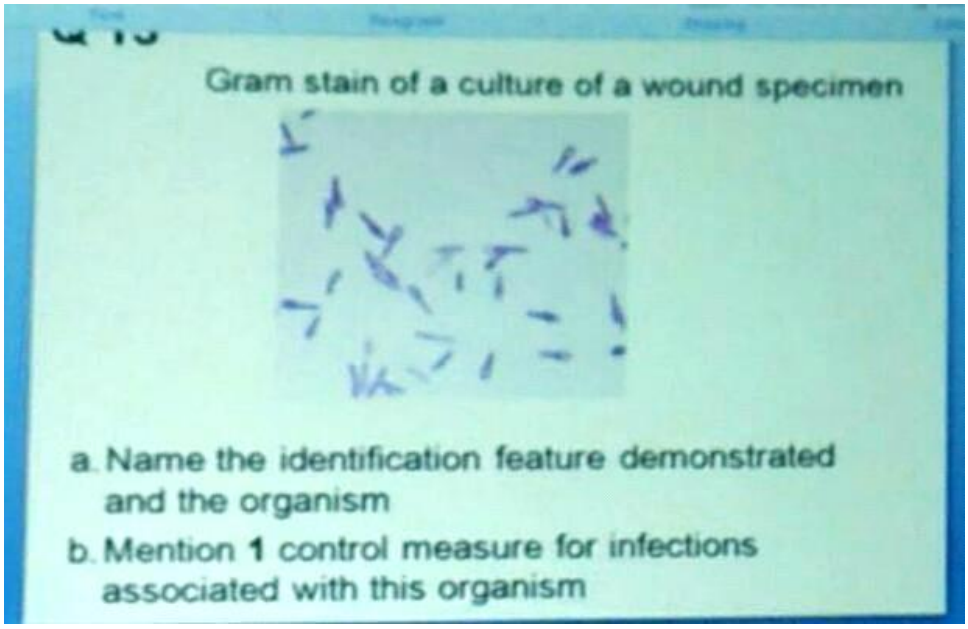
Q 10

A

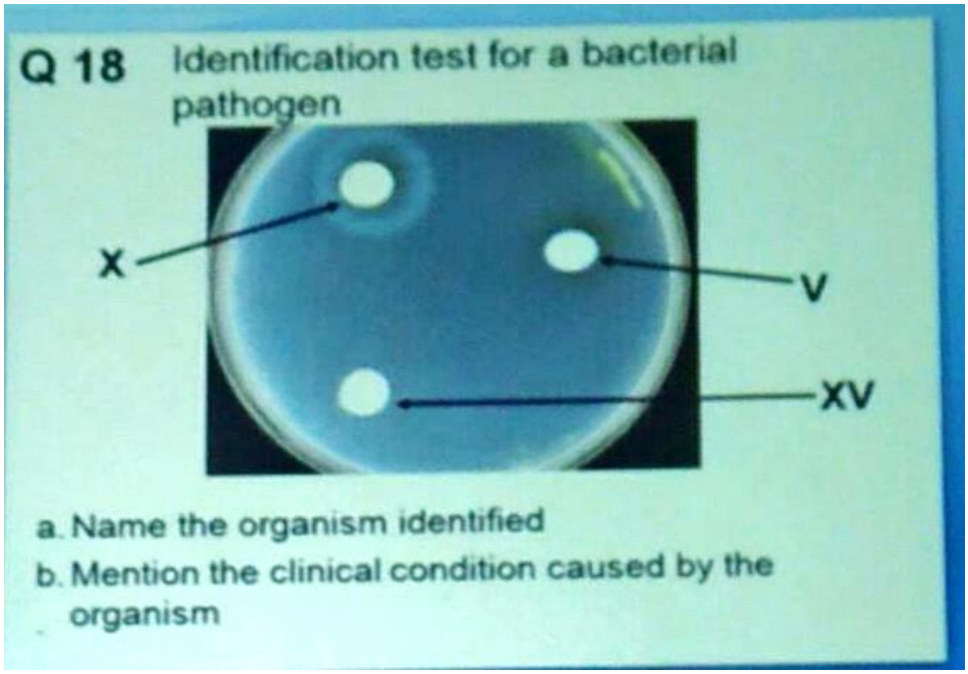
B

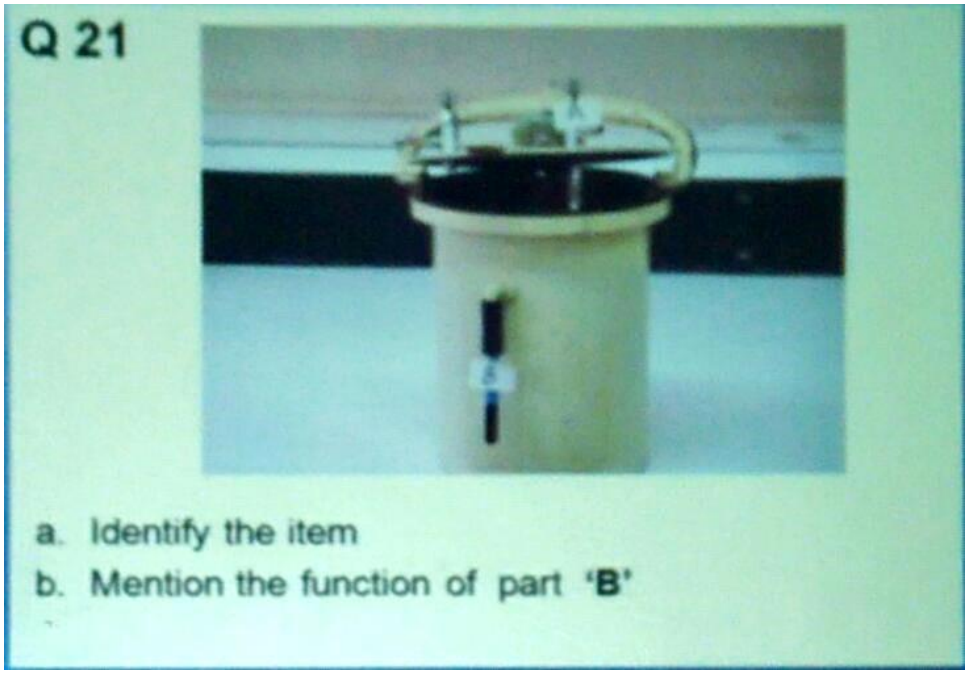


a. Identify the items "**A**" and "**B**"
b. Mention **one** organism isolated using each item

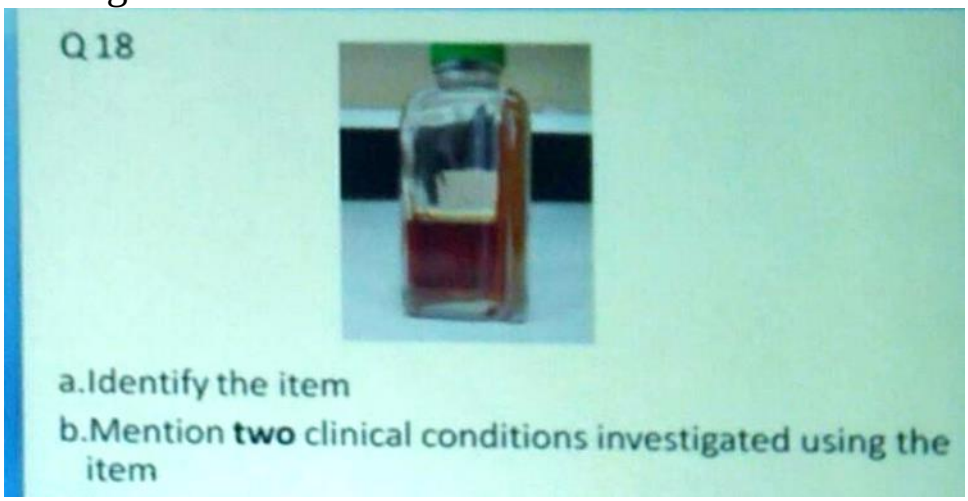

Gram stain of a culture of a wound specimen
a. Name the identification feature demonstrated and the organism
b. Mention 1 control measure for infections associated with this organism

Drumsticks

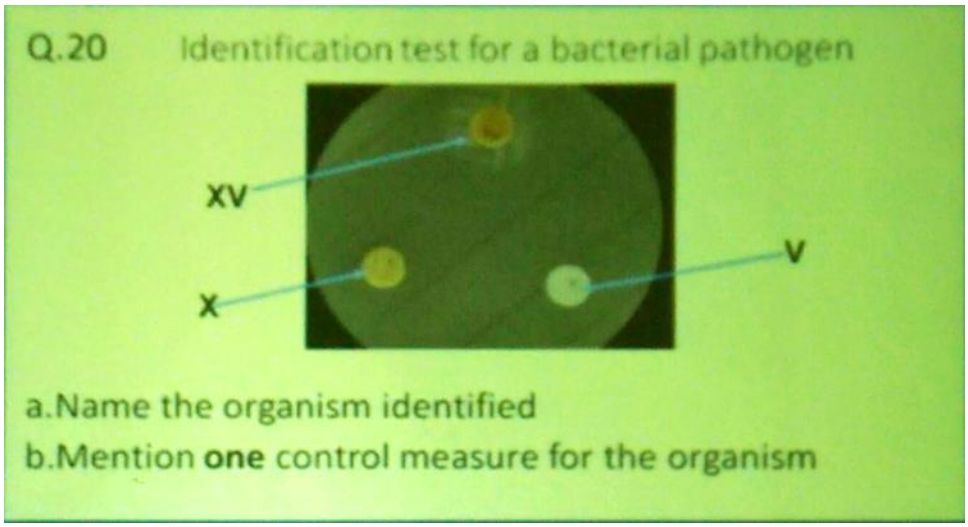

Q 18 Identification test for a bacterial pathogen
X
V
XV
a. Name the organism identified
b. Mention the clinical condition caused by the organism

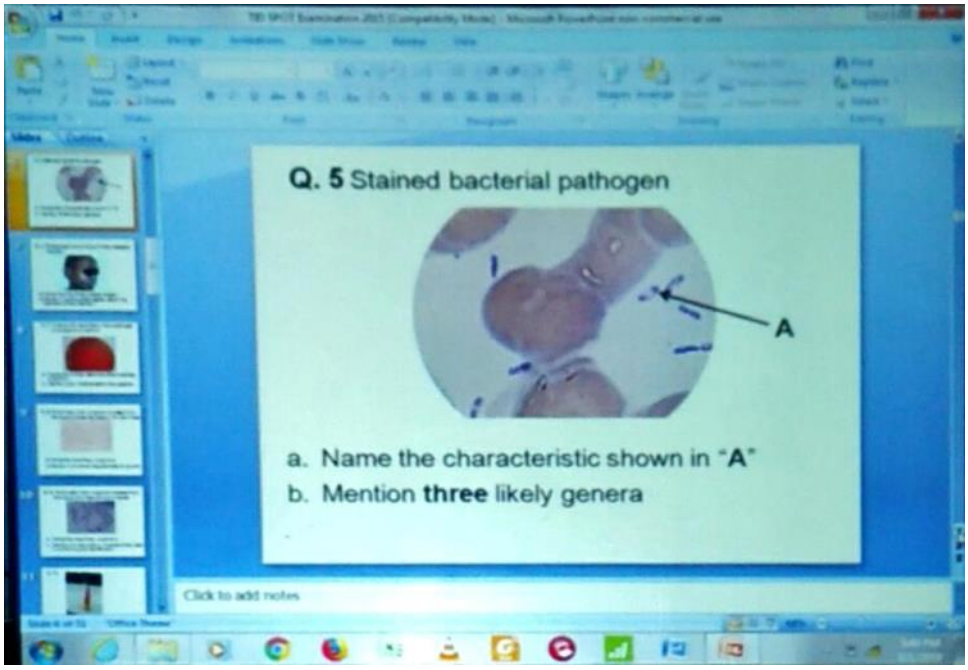


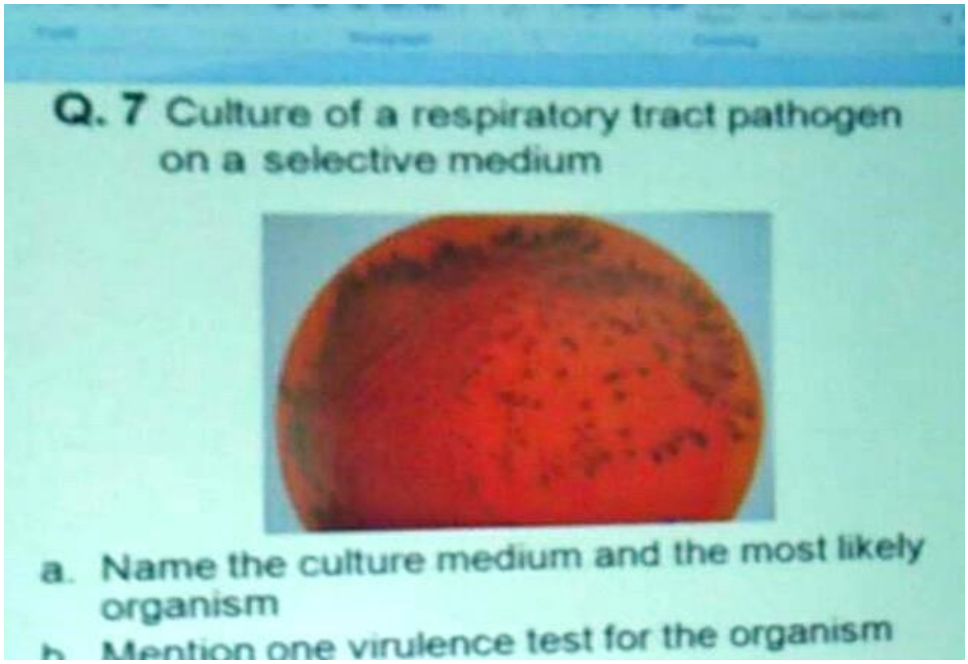
Fields mackintosh
B- anaerobiasis tube indicator
Changes to colourless



Brucellosis
Salmonellosis




Q. 5 Stained bacterial pathogen
A
a. Name the characteristic shown in "A"
b. Mention three likely genera
Click to add notes

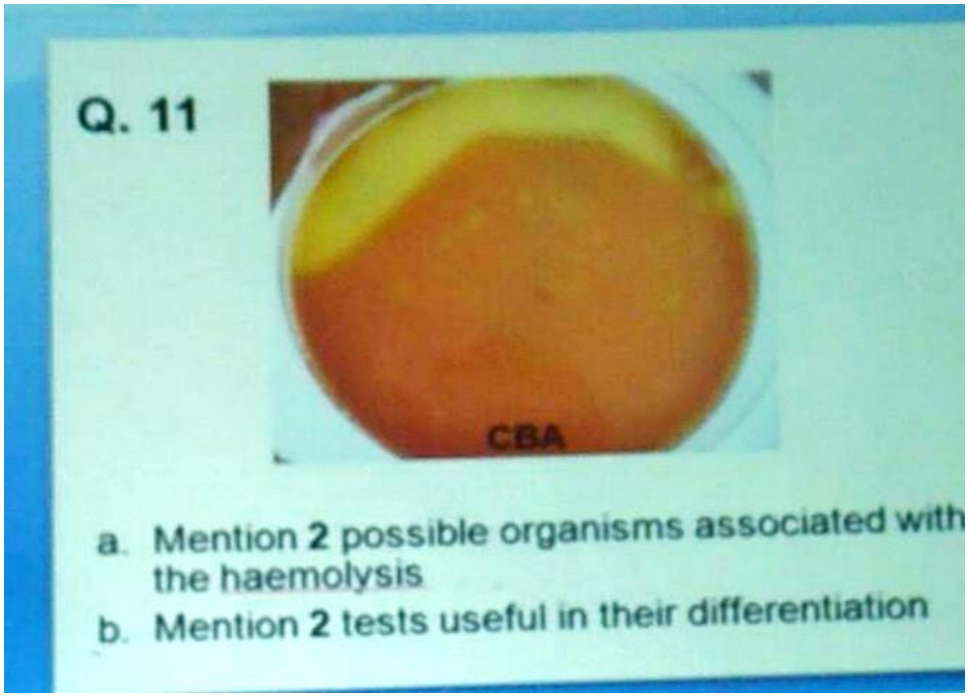

Q. 7 Culture of a respiratory tract pathogen on a selective medium
a. Name the culture medium and the most likely organism
b. Mention one virulence test for the organism

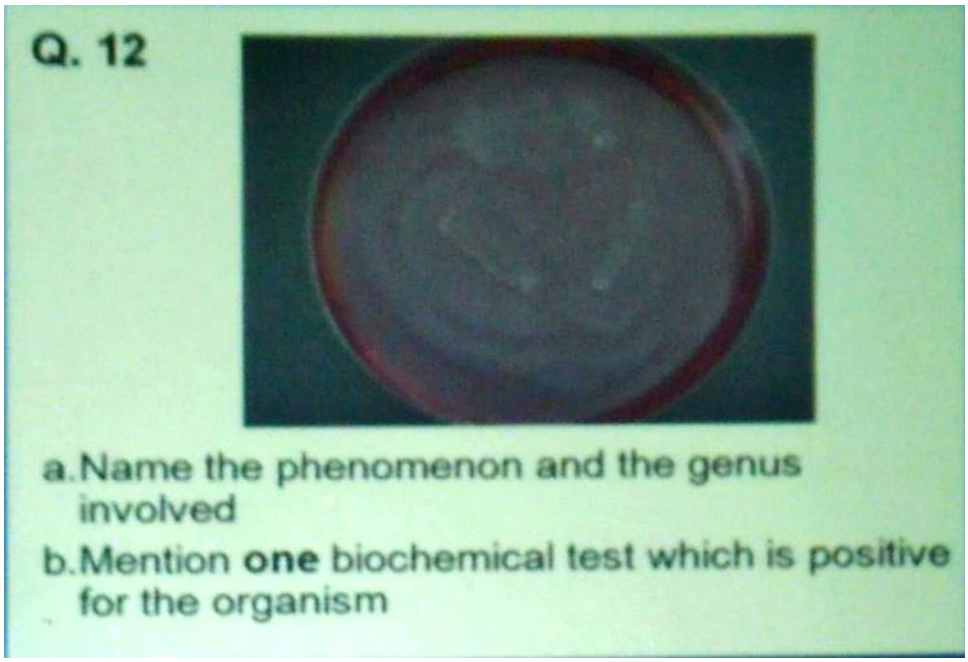
Q.9 Gram stain of an organism isolated from the blood of a hides and skin dealer

a. Name the most likely organism
b. Mention two laboratory characteristics used in confirming the identification

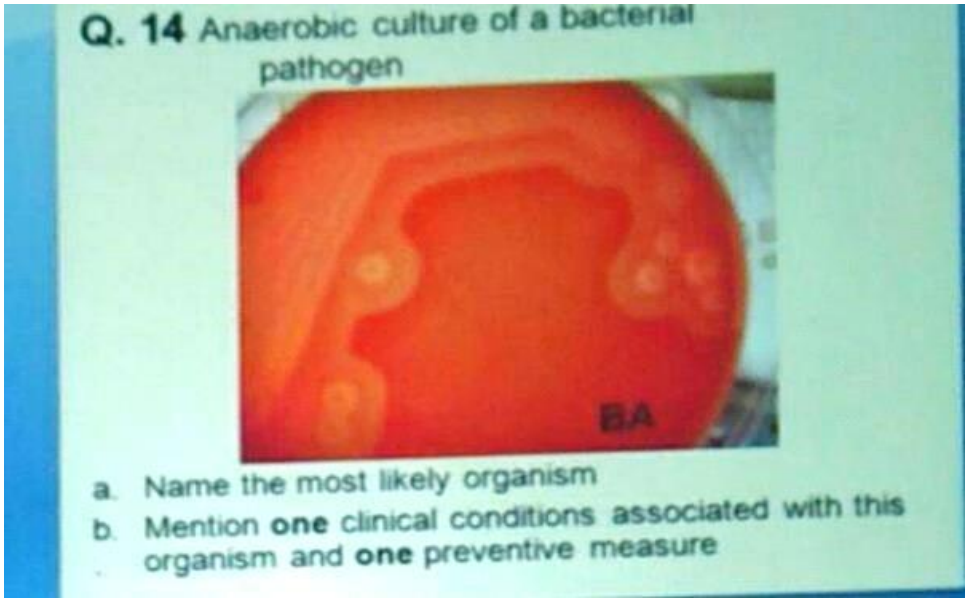
Q. 10

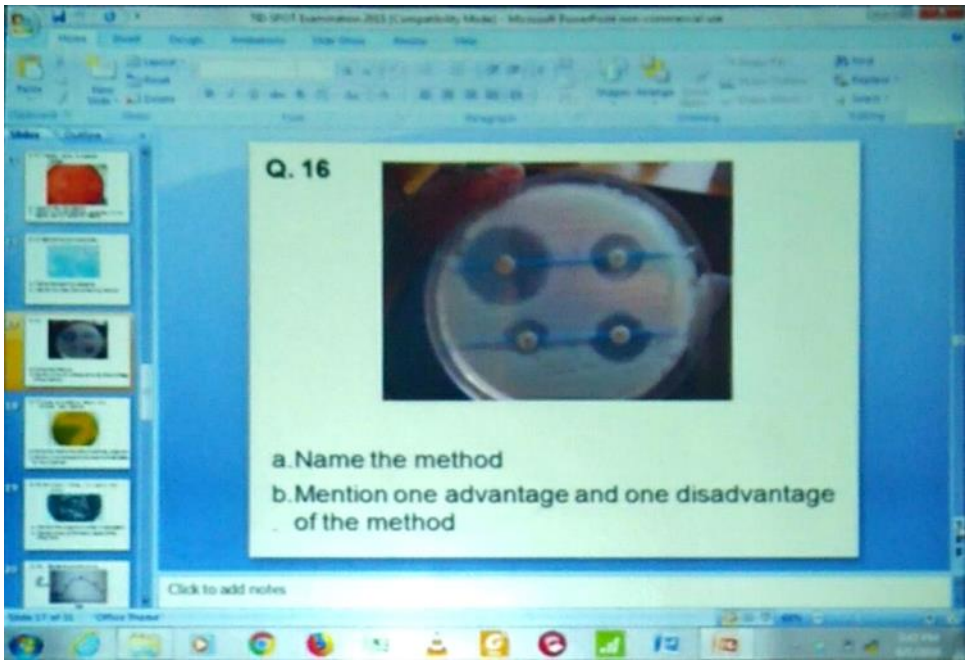
a. Name the medium and the most likely organism
b. Mention **2** antimicrobial agents effective against the organism



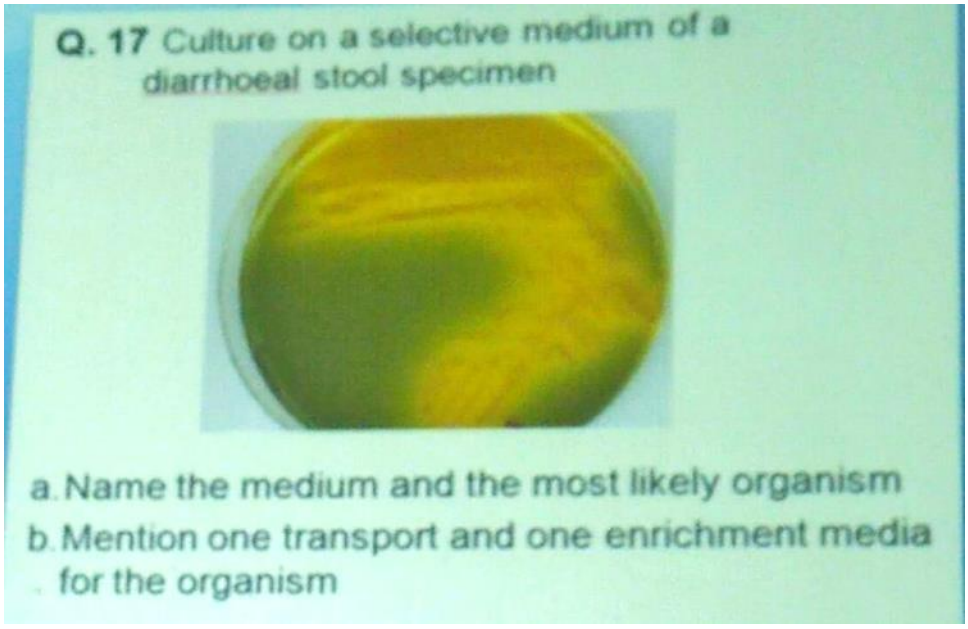


Dienes phenomenon

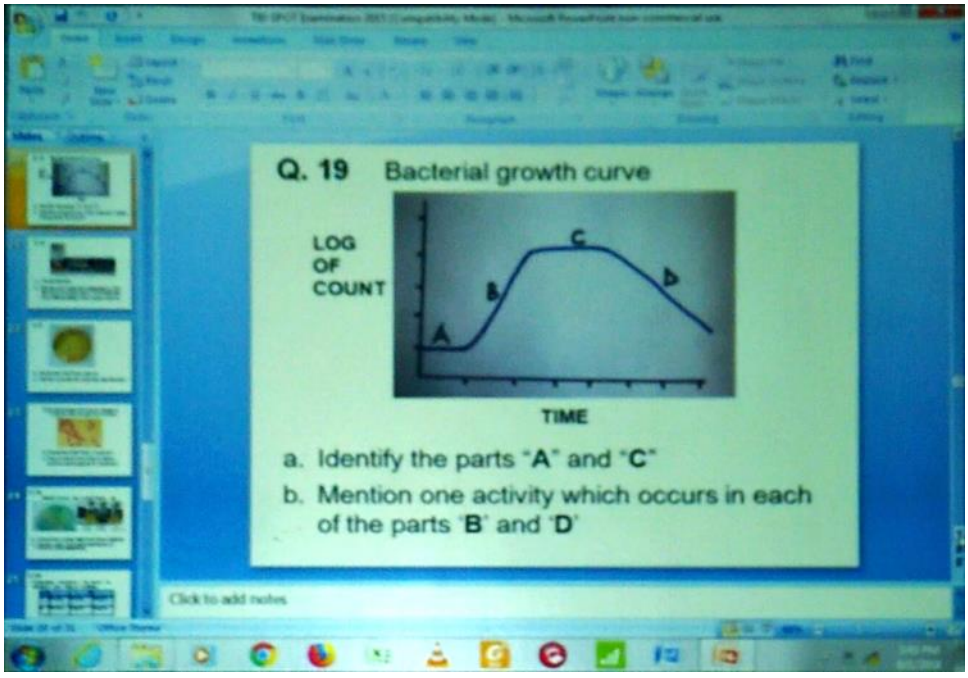

Q. 14 Anaerobic culture of a bacterial pathogen
BA
a. Name the most likely organism
b. Mention one clinical conditions associated with this organism and one preventive measure

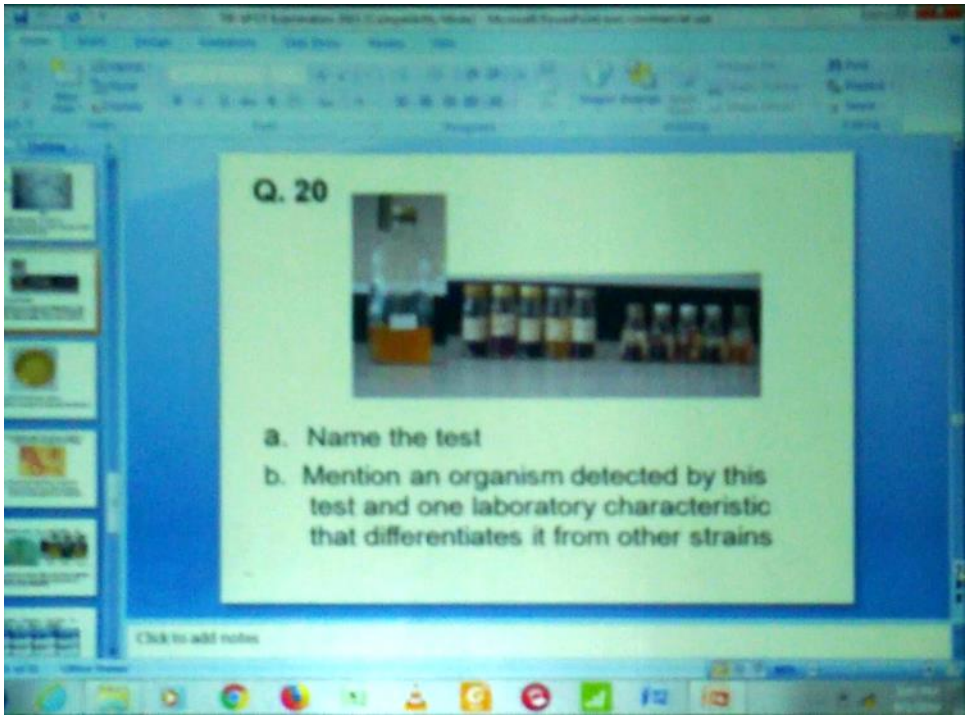

Q. 16
a. Name the method
b. Mention one advantage and one disadvantage of the method
Click to add notes

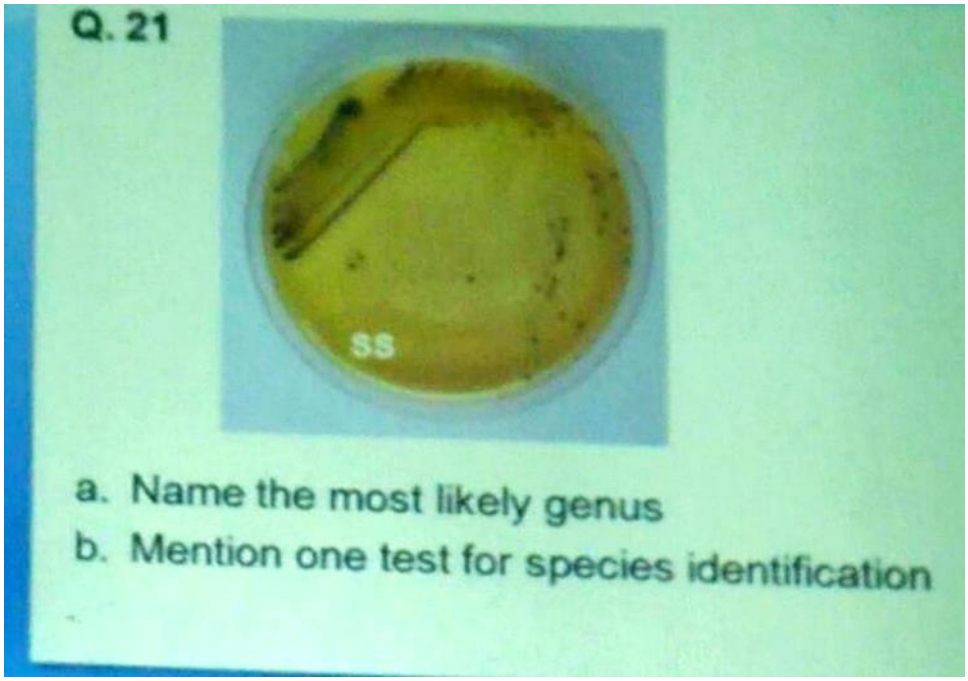
Storks



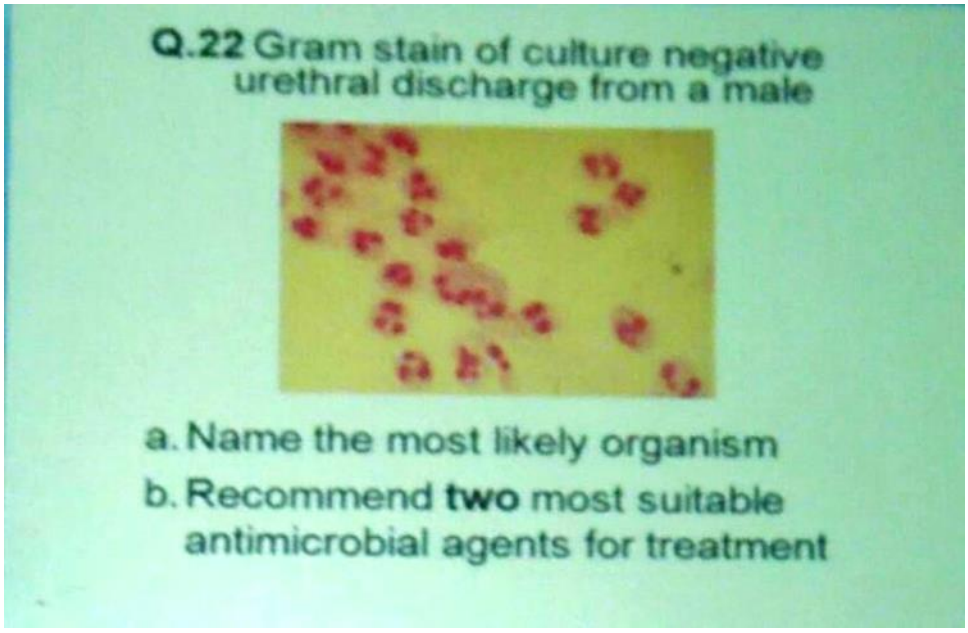
TCBS
Caryblair
Selenite F



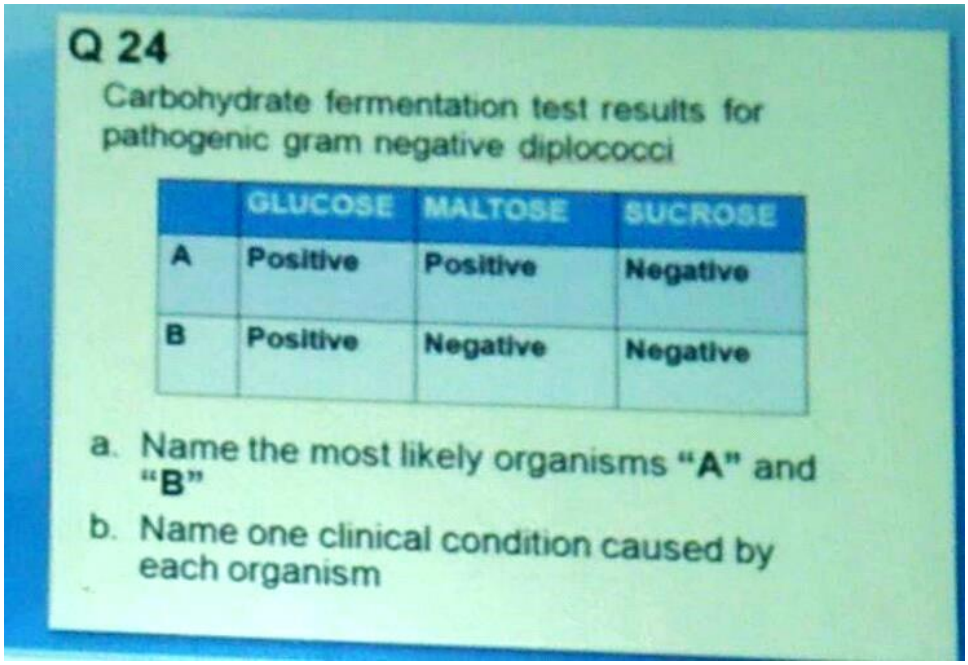




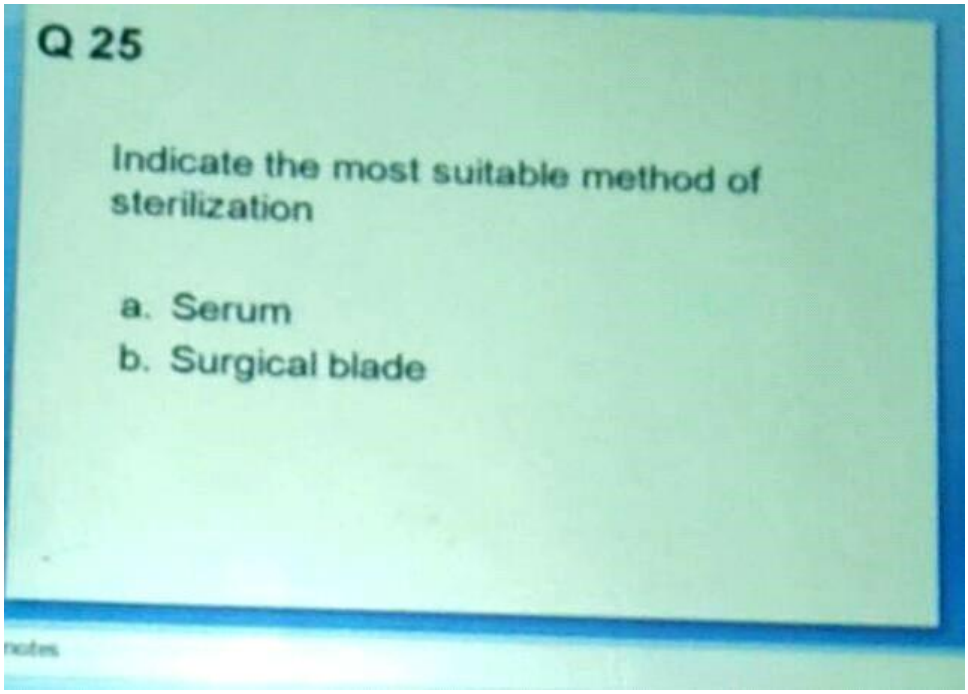
Ss media. Salmonella



N.gonorrhea
If specimen is csf- meningitidis

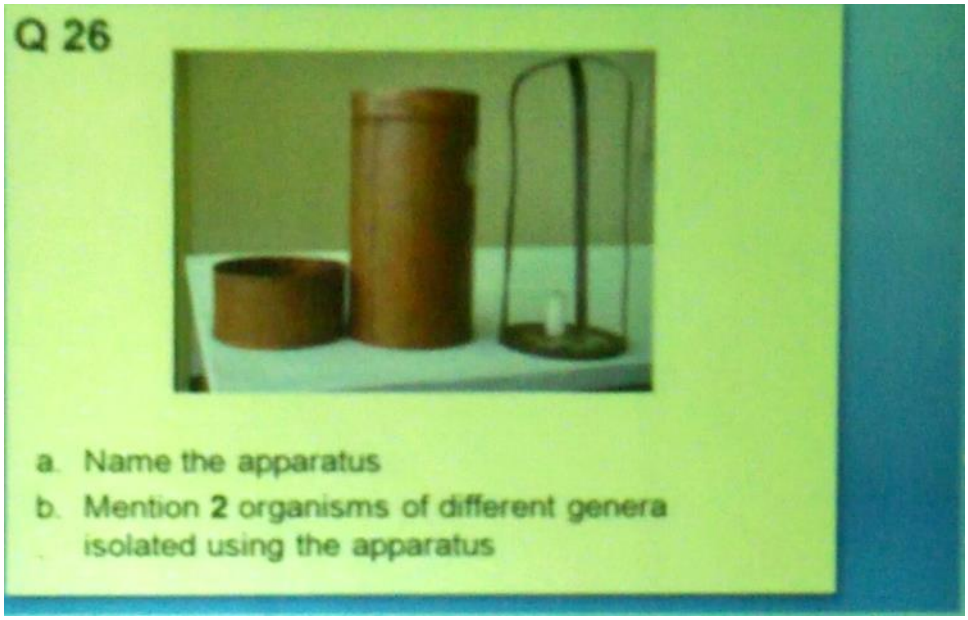


A-Neiseria meningitis
B-gonorrhea

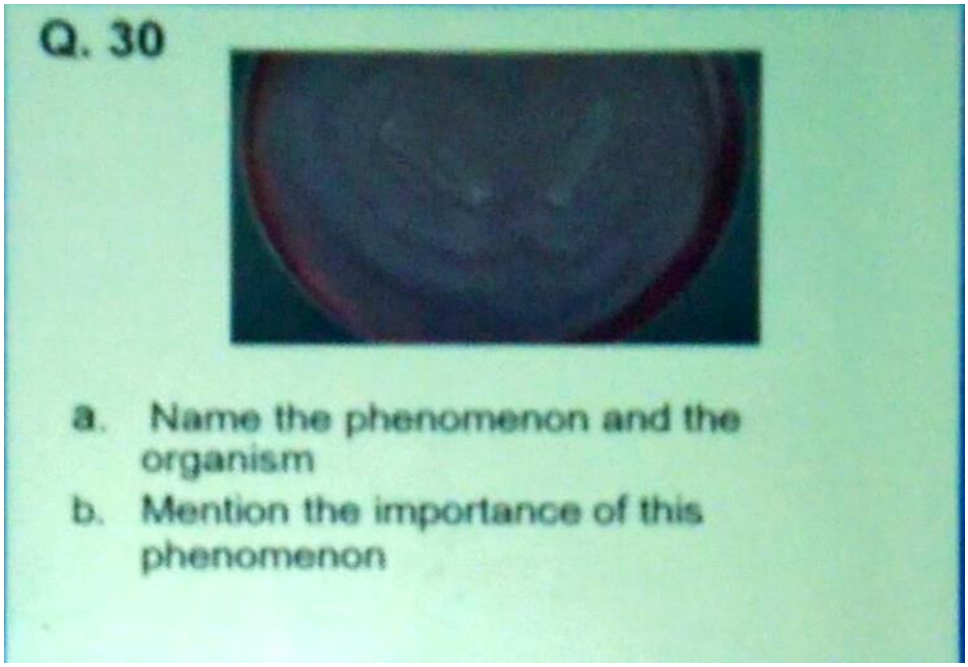


Serum- microfilter,

Blade-radiation



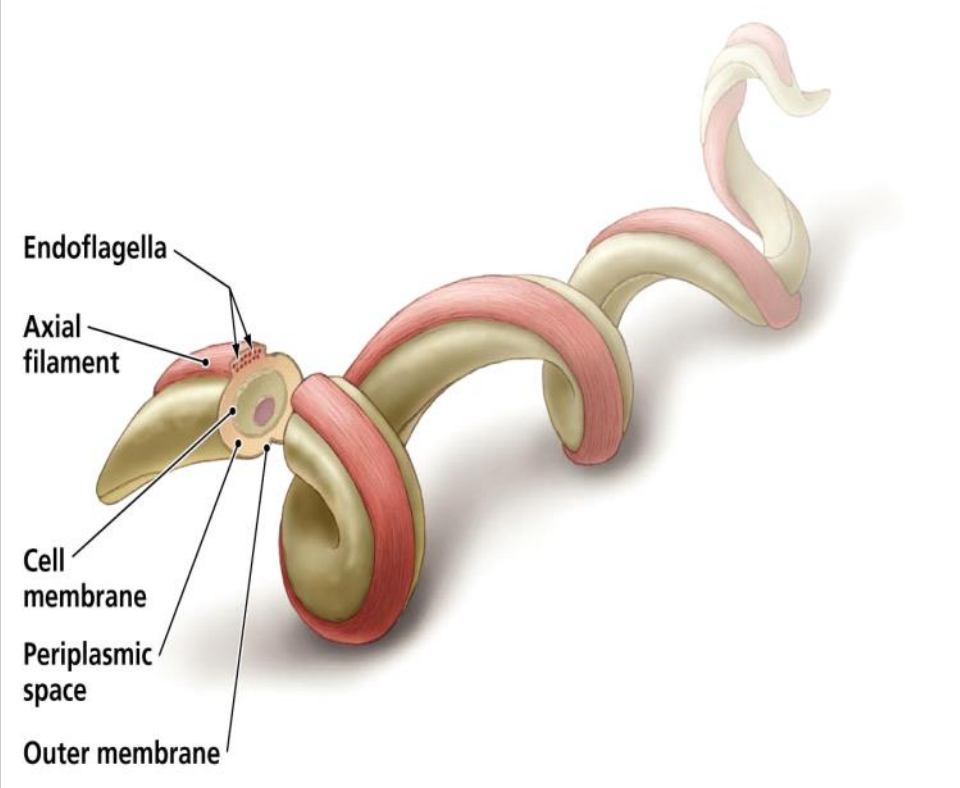
Strep pneumonia
H.influenzae

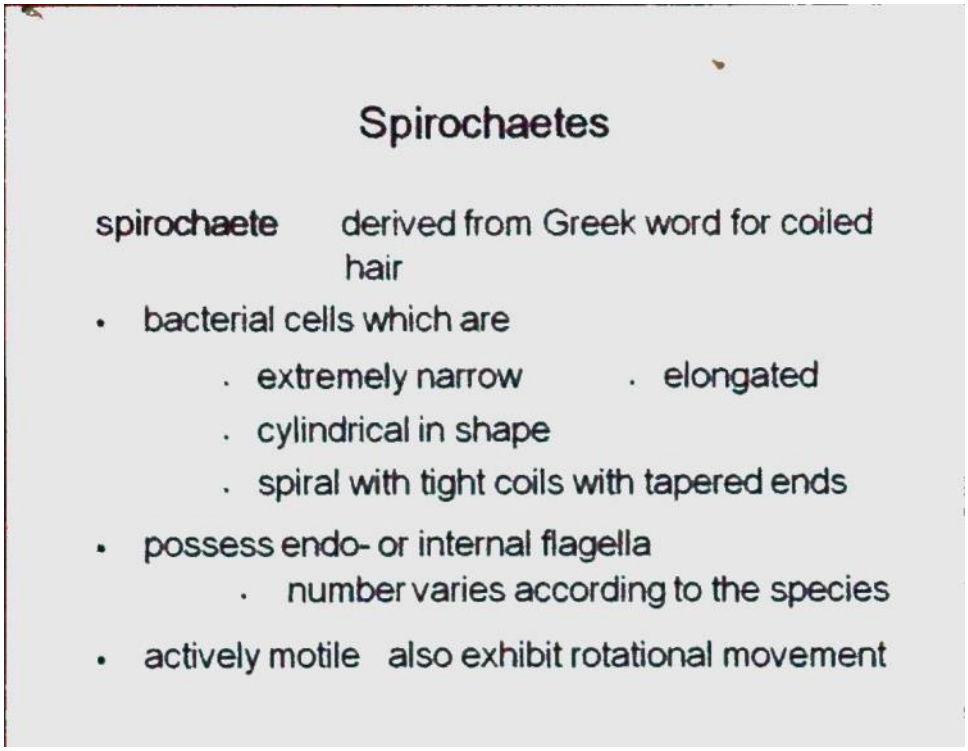


Importance- same species

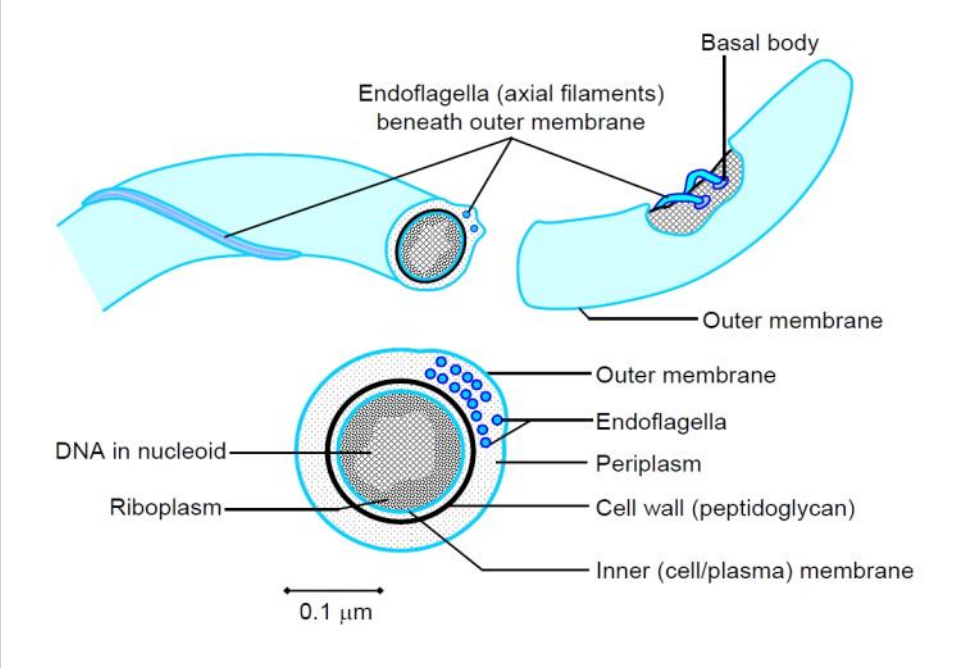
Spirochaetes: Treponema

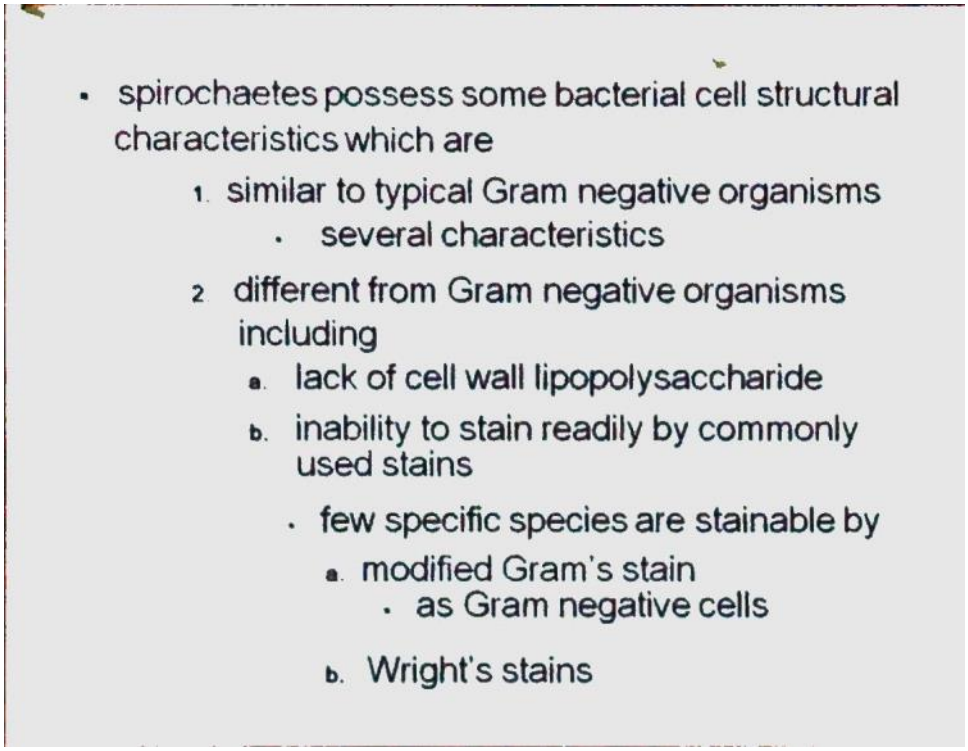
Tuesday, August 7, 2018 3:14 PM





Axial filaments contain endoflagella = periplasmic flagella





Cant be cultured bcoz it is an obligate (but not intracellular) pathogen. Unlike treponemes and leptospitrae, borreliae are larger, accept Giemsa and other blood stains, and can be seen in the standard light microscope

Genera of spirochaetes associated with human infections

mainly

1. Treponema
2. Borrelia
3. Leptospira

Treponema

- composed of pathogenic and non-pathogenic organisms

Non-pathogenic species

1. human bacterial normal flora mainly in the mouth and genital tract

2. saprophytic species
   a. Reiter's strain of *Treponema pallidum*
      - antigenically related to pathogenic *T. pallidum*
      - can be grown in artificial media
        - requires anaerobic incubation
   b. Nichol's strain of *T. pallidum*
      - both Reiter's and Nichol's strains are used in laboratory studies

Main pathogenic species of Treponema

- previously 1. *Treponema pallidum*
  2. *T. pertenue* 3. *T. carateum*
- re-classified as sub-species of *T. pallidum*
- other species associated with human disease include *T. denticola* as causative agent of infections in the mouth
- all Treponema species or sub-species are similar in morphology and antigenic composition
  - cause cross reactions in serological tests
- differentiated by a. geographical location
  b. clinical manifestations c. genetic characteristics

Treponema pallidum pallidum

- not visualized in specimens by Gram's stain and light microscope
- may be visualized by special staining methods and microscopes
  1. dark field microscope
  2. fluorescence staining and microscopy
  3. special staining in infected tissues and microscopy
  4. electron microscope

Growth of *T. pallidum pallidum* in cultures

- does not grow in artificial culture media
- live organisms can be inoculated in various parts of laboratory animals for propagation
    - spectrum of manifestations of disease observed in infected humans rarely develops in the animal

Physical properties

- delicate organism
    - loses viability rapidly when exposed to
        a. dry conditions
        b. heat
        c. low temperatures including 0° to 4° c for more than 2 days

Antigenic properties and antibodies of *T. pallidum pallidum*

- exact antigenic components are not clearly identified
- immune system is stimulated during infection
- distinct antibodies are produced in response to infection including
    1. antibody which reacts with **cardiolipin**
        - cardiolipin is a lipid compound in beef heart muscle
            - extracted and prepared for use in laboratory tests
        - antibody is referred to as
            a. Wasserman's
            b. reagin
            c. lipoidophil
            d. anticardiolipin antibody

2. antibody formed in response to a specific antigen contained within the treponemes referred to as **antitreponemal antibody**

Clinical implications of *T. pallidum pallidum*

- natural infection is limited to humans
- causative agent of syphilis
  - illness characterized by severe manifestations and long term complications in the absence of adequate treatment

Transmission of *T. pallidum pallidum*

- transmission depends on the presence of organisms in the blood and syphilitic lesions
  1. **sexual** transmission
     - as venereal disease or STD or STI
     - transmission rate depends on the stage of the illness
  2. **vertical** transmission from infected pregnant female to the expected baby
  3. **blood transfusion**
     - transfusion of blood containing spirochaetes into a susceptible recipient

Sexually transmitted *T. pallidum pallidum*

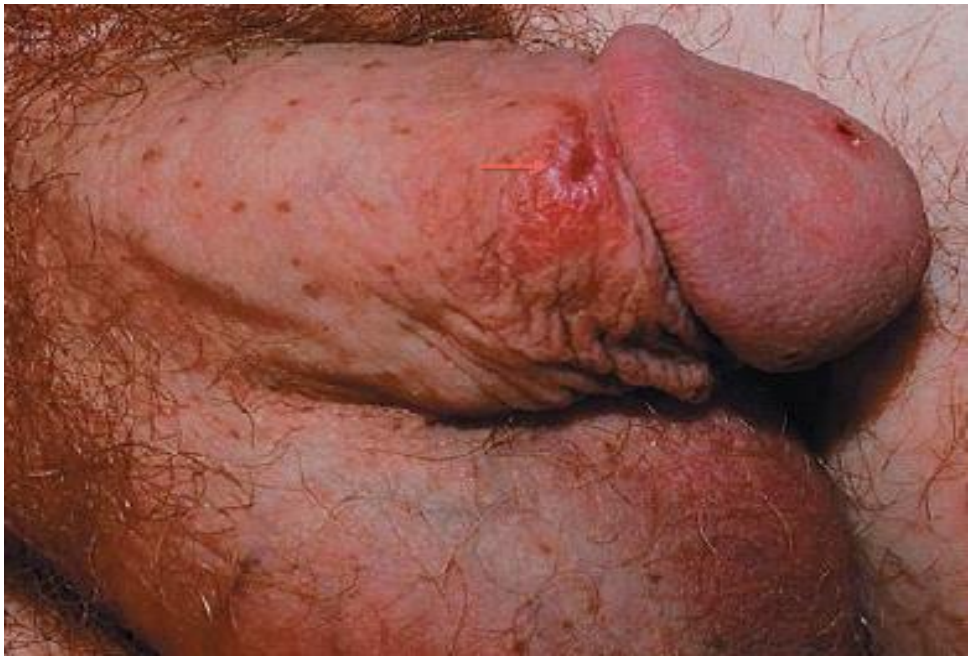
- infectious lesion in the majority is on the skin or mucosal surface of the external genital organs
- entry into a susceptible person is through broken skin or mucous membrane
- multiplication occurs at the site of entry
- incubation period follows during which the person is not infectious

manifestations

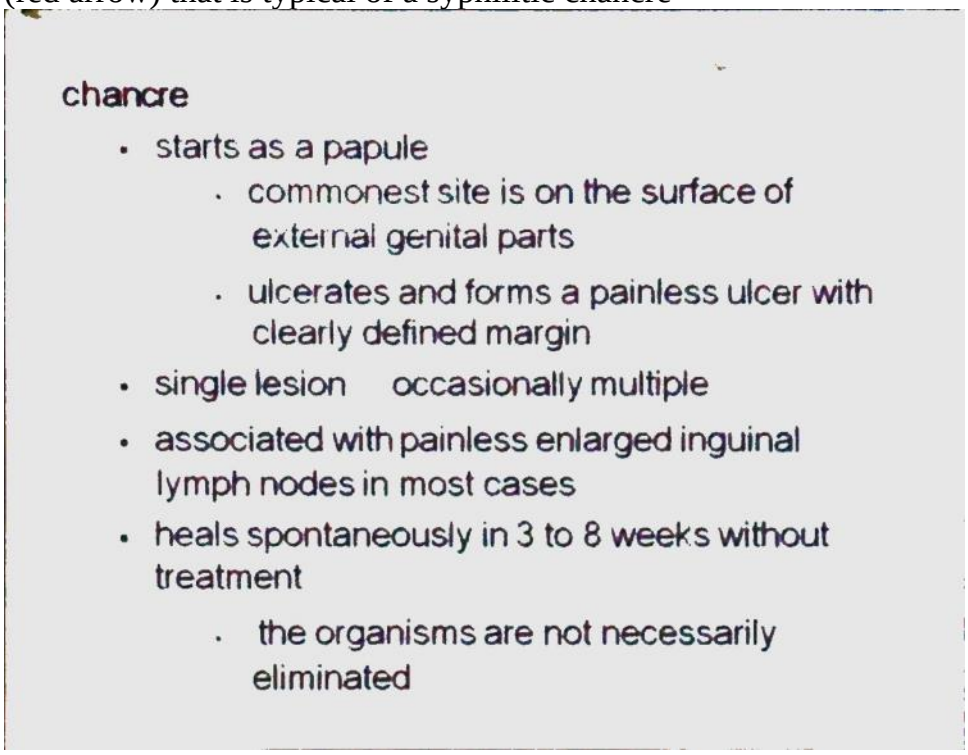
- change as the disease progresses
- basis for classification of syphilis into
  1. primary 2. secondary 3. tertiary
  4. late syphilis

Primary syphilis

- characterized by
  a. localized invasion of mucus membranes
  b. relatively rapid multiplication of the organism
  c. initial dissemination through lymphatics and blood circulation
- manifestations occur within 10 to 90 days after exposure
- main lesion is an ulcer referred to as the **primary sore** or **chancre** or **hard chancre**
  - exudate contains *T. pallidum pallidum*



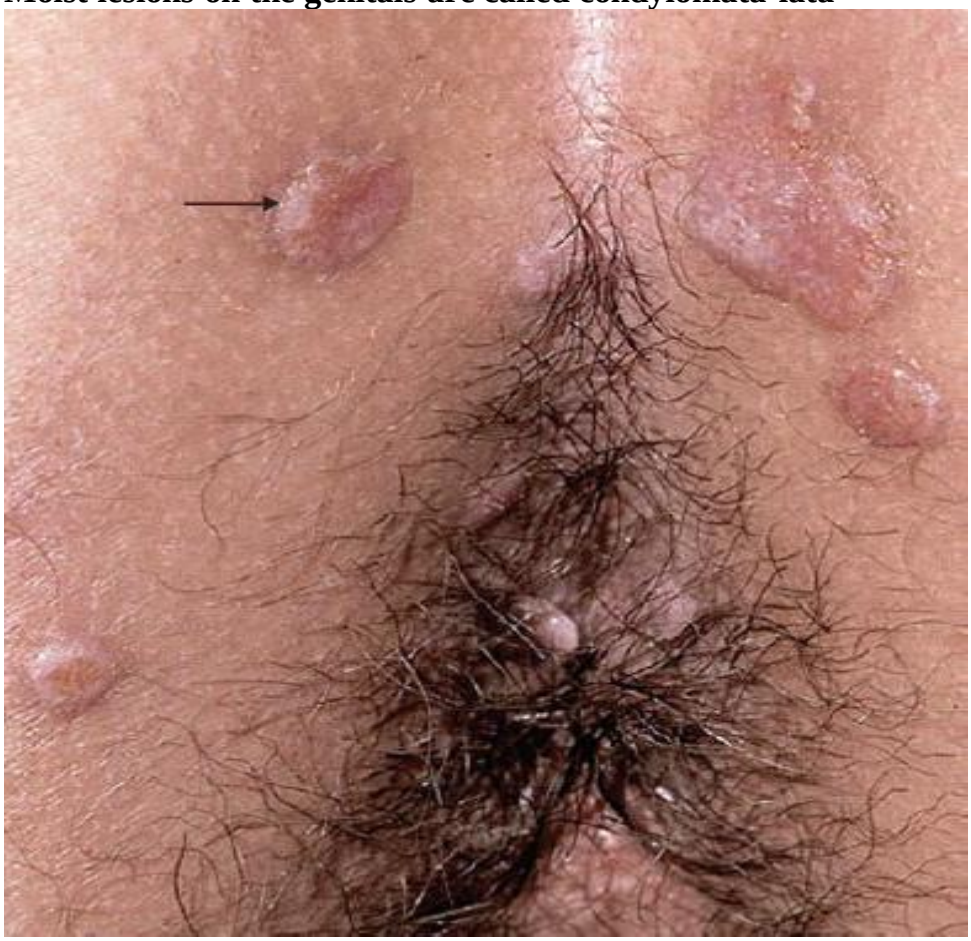
Chancre of primary syphilis. Note the shallow ulcer with a rolled edge (red arrow) that is typical of a syphilitic chancre



Secondary syphilis

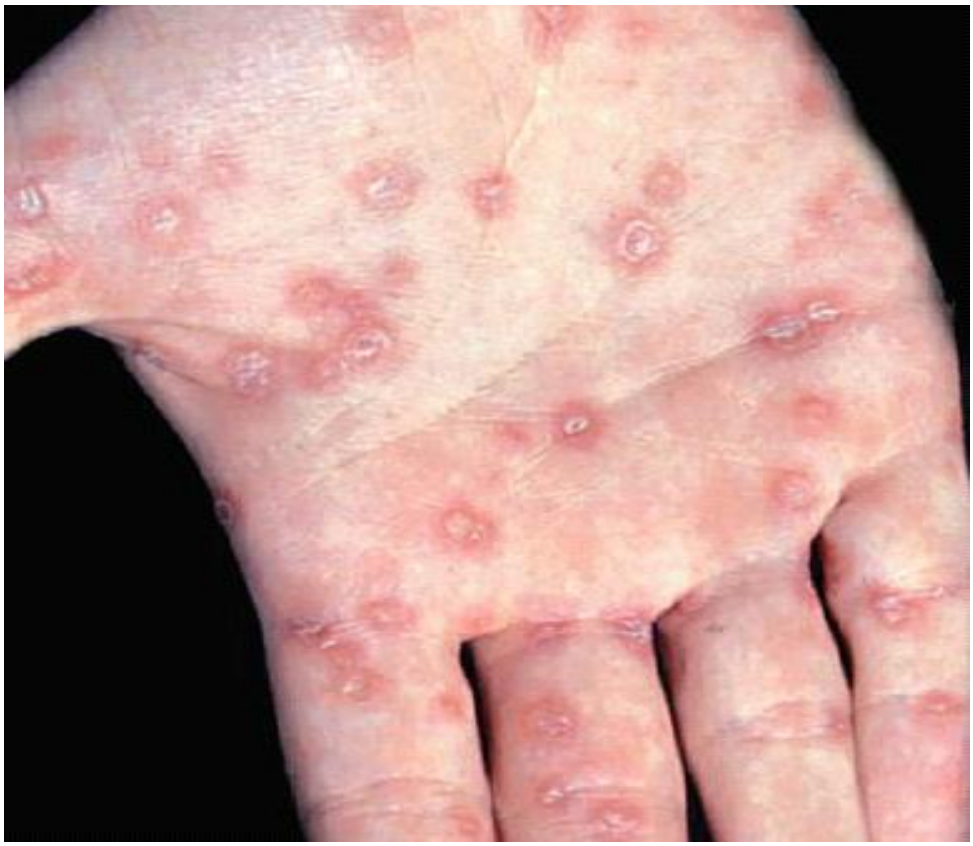
- characterized by invasion of the blood circulation and widespread dissemination
- generalized infection with varied manifestations including
  1. skin rash
  2. lesions on the mucous membranes
  3. ulcers in the mouth
  4. generalized lymph node enlargement
  5. small swellings described as plaques on various parts including the skin and mucosal surfaces
     - can develop into wart-like lesions referred to as *condylomata lata*
- uncommon manifestations include inflammatory processes involving bones joints possibly eyes

Moist lesions on the genitals are called condylomata lata



Condylomata lata

- lesions of secondary syphilis contain numerous *T. pallidum pallidum*
- possible outcome
  a. healing in the absence of treatment
  b. development of asymptomatic state referred to as **latent syphilis**
  c. progression to tertiary syphilis

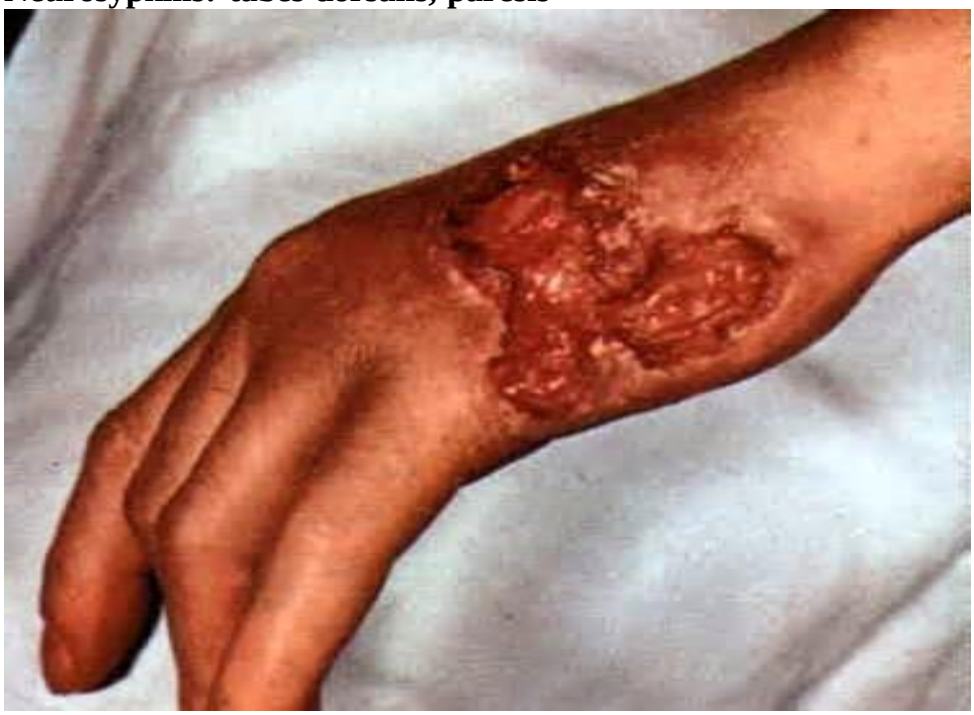


Secondary syph: papulosquamous lesions on the right palm.Palmar lesions are typically bilateral

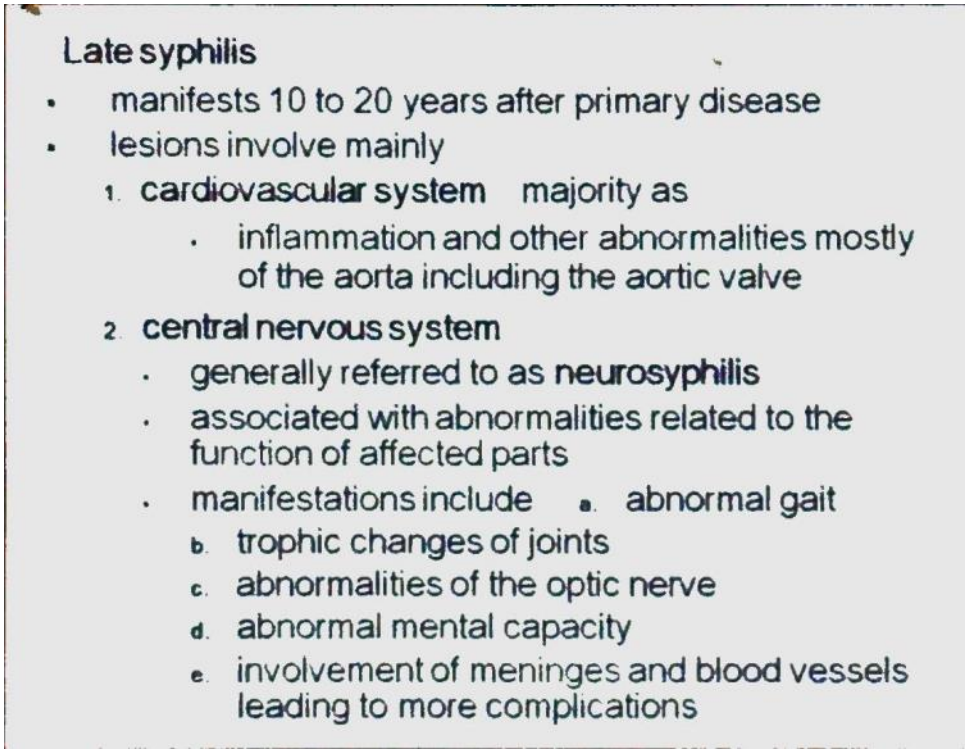
Tertiary syphilis

- develops approximately 3 to10 years after the primary lesion
- *T. pallidum pallidum* is rarely detected in lesions
- manifestations include small swellings on various parts due to chronic inflammatory process on various tissues and organs including the a. skin
  b. mucous membranes c. bones
  . lesions referred to as **gummas**
- some of the skin gummatous lesions undergo ulceration

Neurosyphilis: tabes dorsalis, paresis



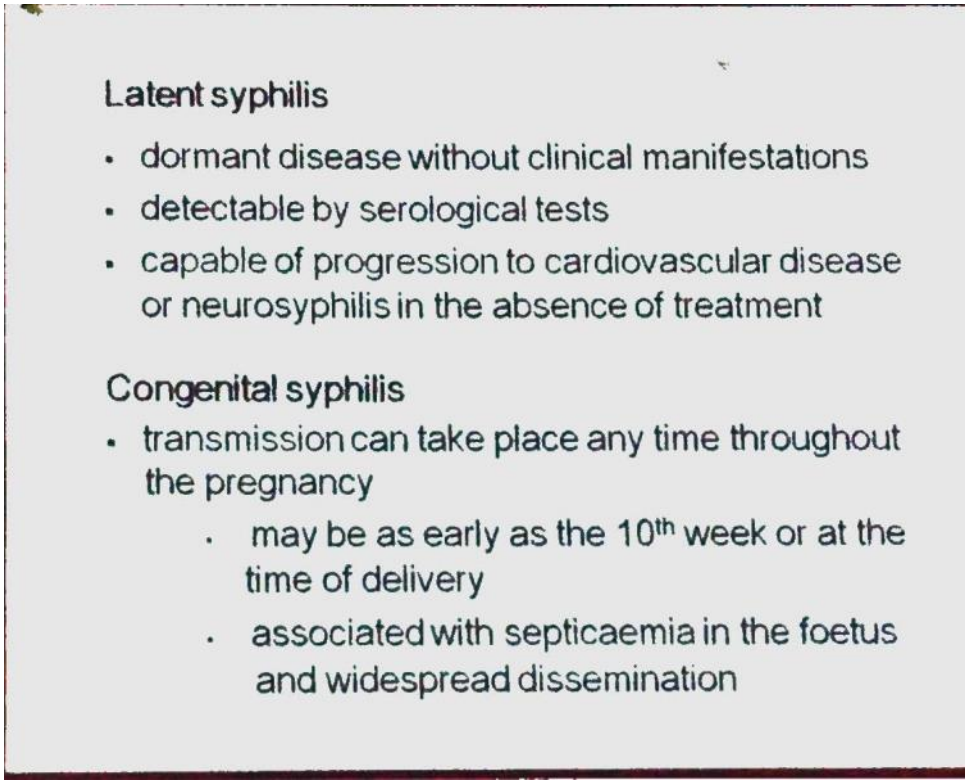
-Gumma: syphilitic granuloma
-In tertiary syphilis, it infects the endothelium of small blood vessels, causing endarteritis

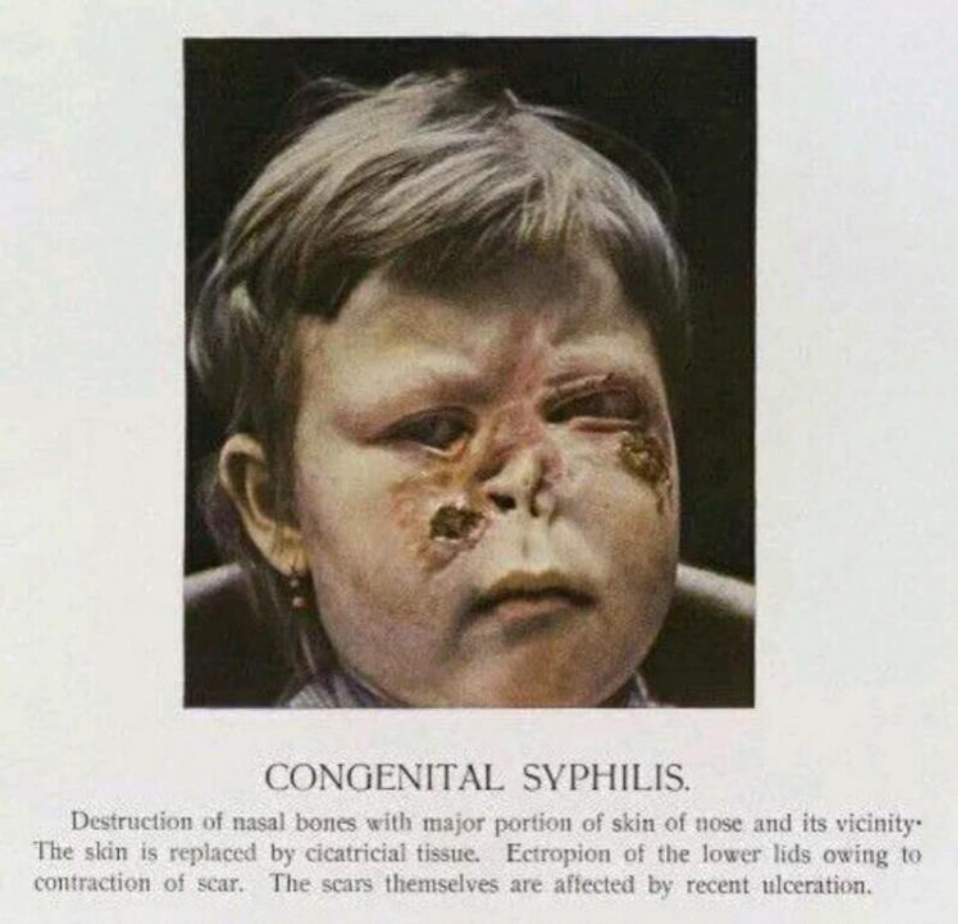


Aneurysm of the ascending aorta

The latent period can be divided into:

1. **early stage where symptoms of secondary syphilis can reappear and patients can infect others**
2. **late stage where no symptoms occur and patients are not infectious**

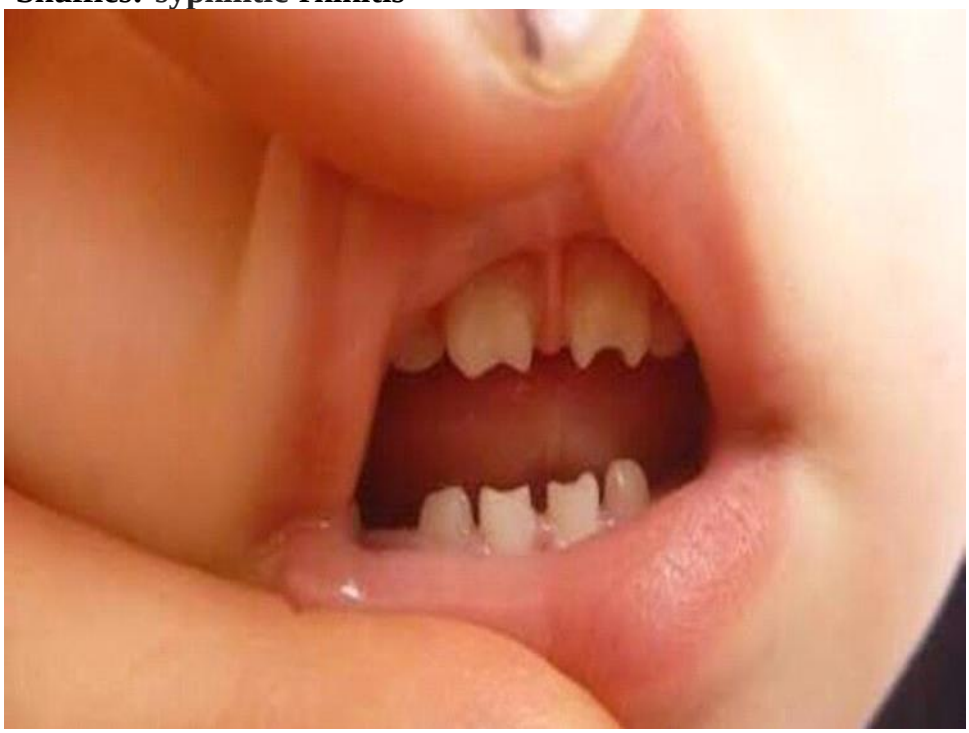




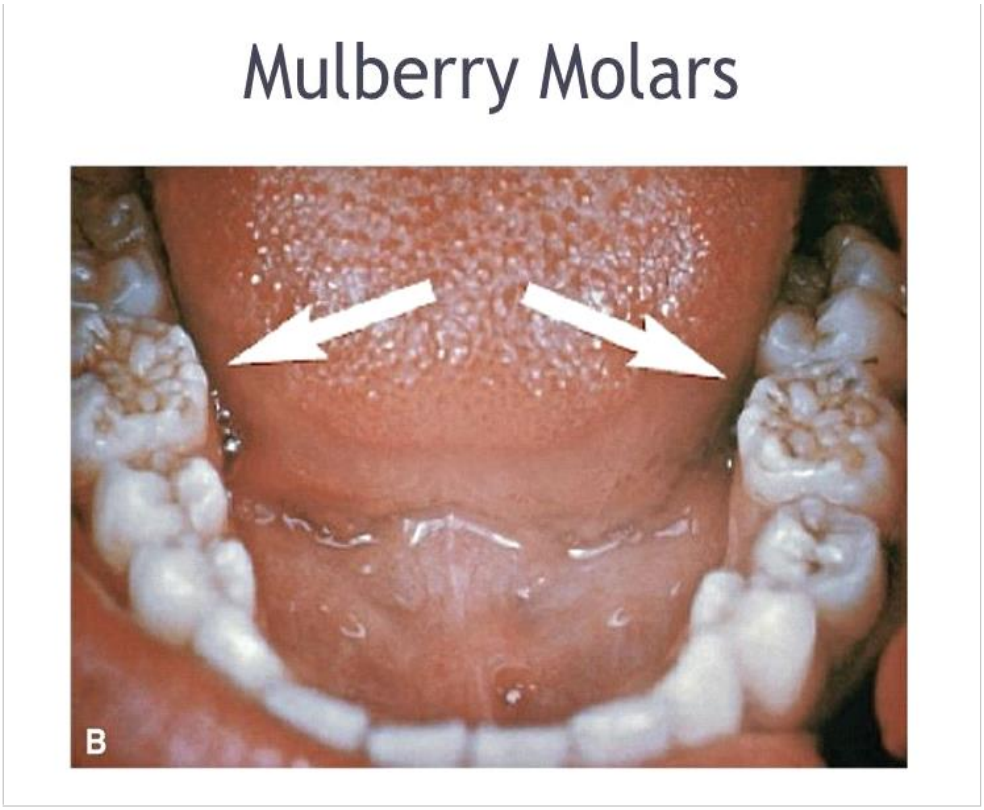
CONGENITAL SYPHILIS.

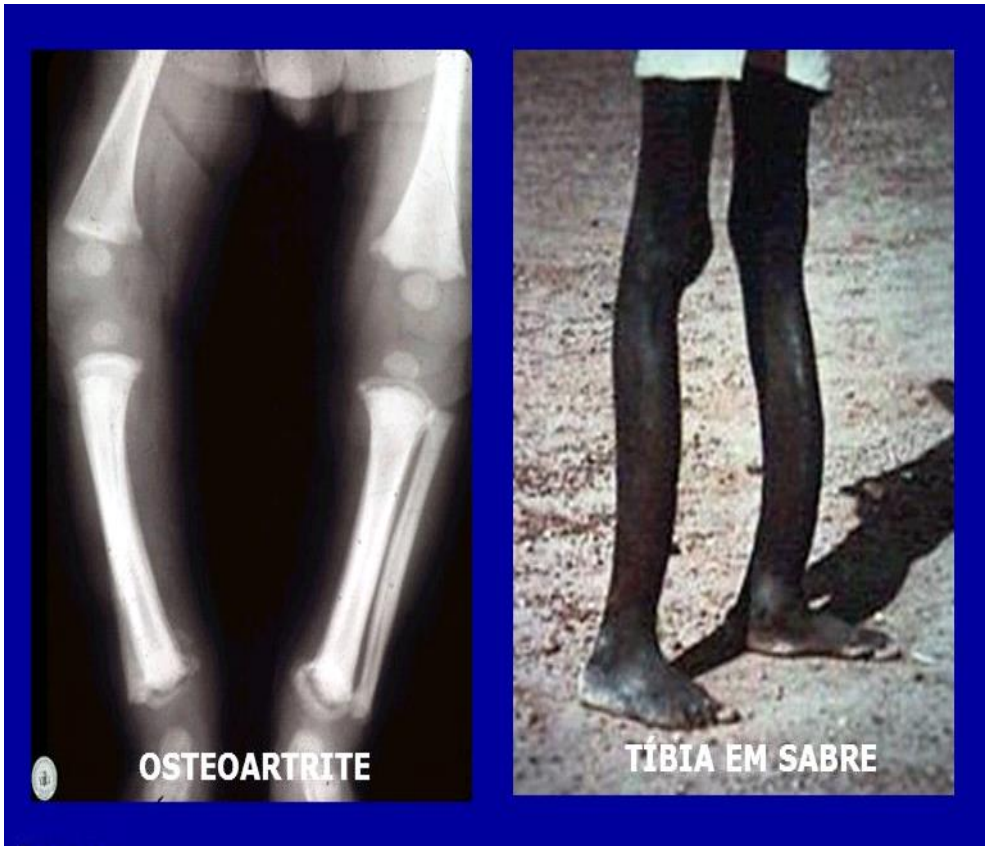
Destruction of nasal bones with major portion of skin of nose and its vicinity. The skin is replaced by cicatricial tissue. Ectropion of the lower lids owing to contraction of scar. The scars themselves are affected by recent ulceration.

-Congenital syphilis: 8th nerve damage, notched teeth (hutchison's), tabes dorsalis
-Skin and bone lesions, such as Hutchinson’s teeth,mulberry molars, saber shins, saddle nose, rhagades, snuffles, and frontal bossing, are common.
-Snuffles: syphilitic rhinitis

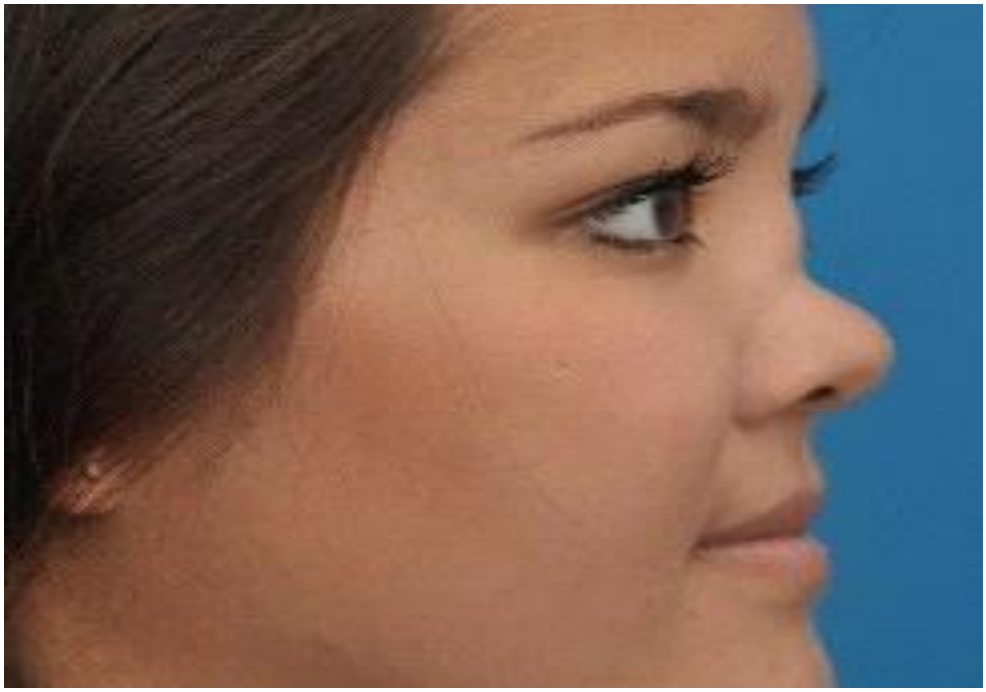


Hutchison's teeth

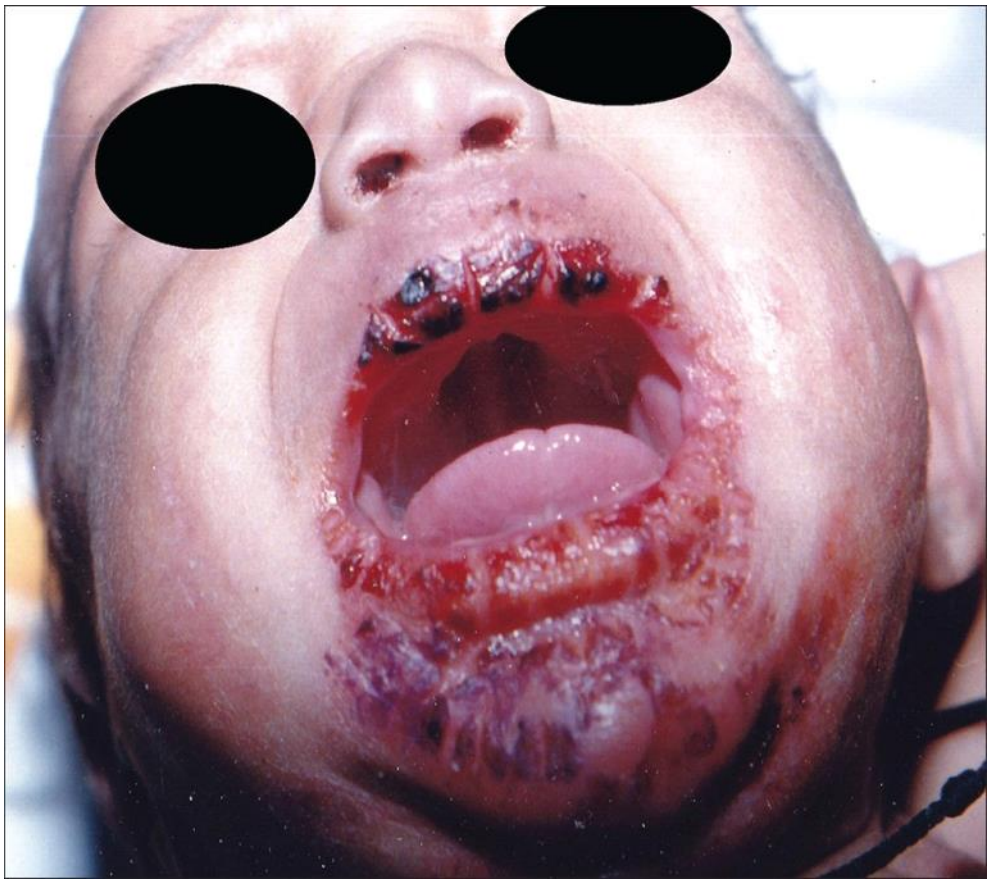




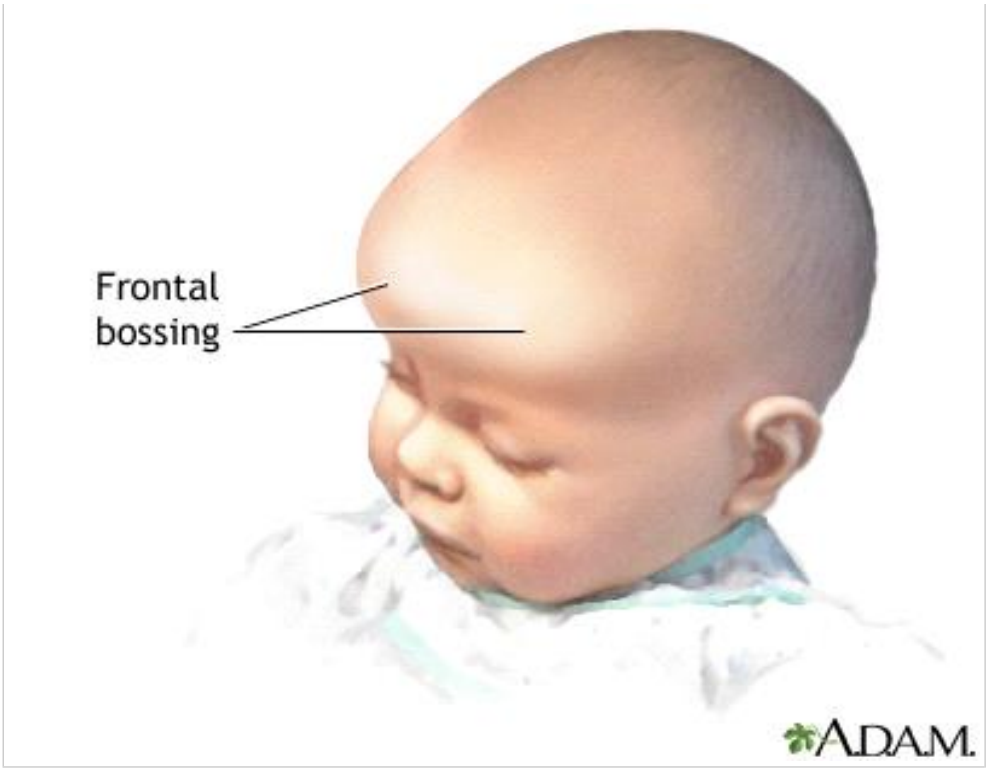
Saber shins



Saddle nose

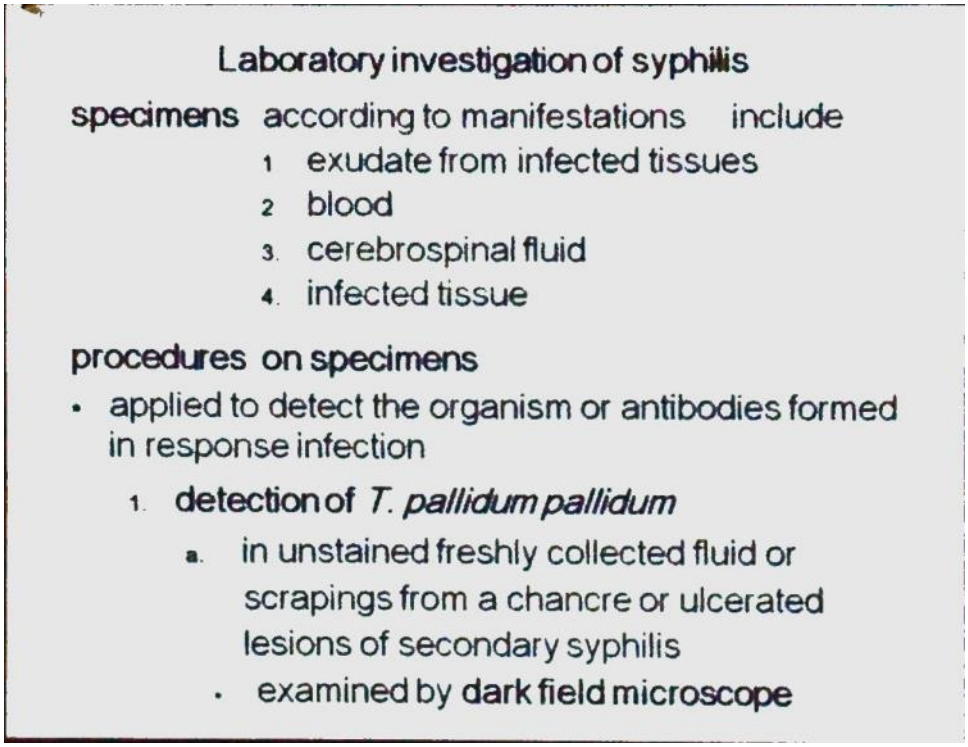


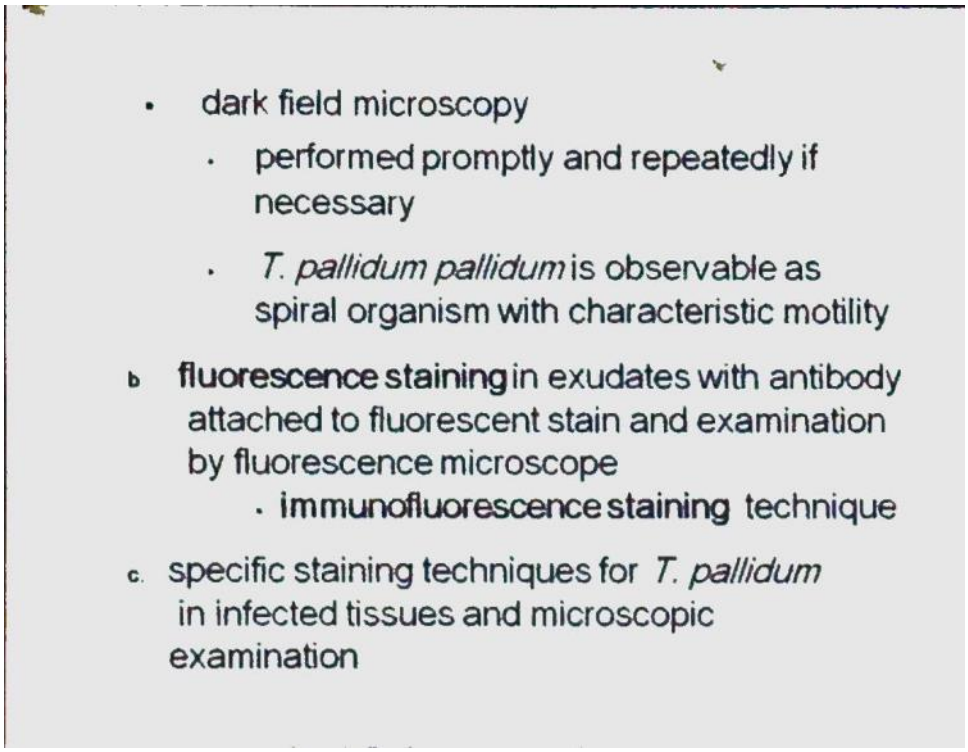
Rhagades



manifestations of congenital syphilis

- include
  a. death of fetus which may be associated with a miscarriage or still born at term
  b. developmental abnormalities
  c. baby born with latent infection or manifestations which develop anytime within the first two years including
     - failure to thrive
     - skin rash
     - nasal and other abnormalities



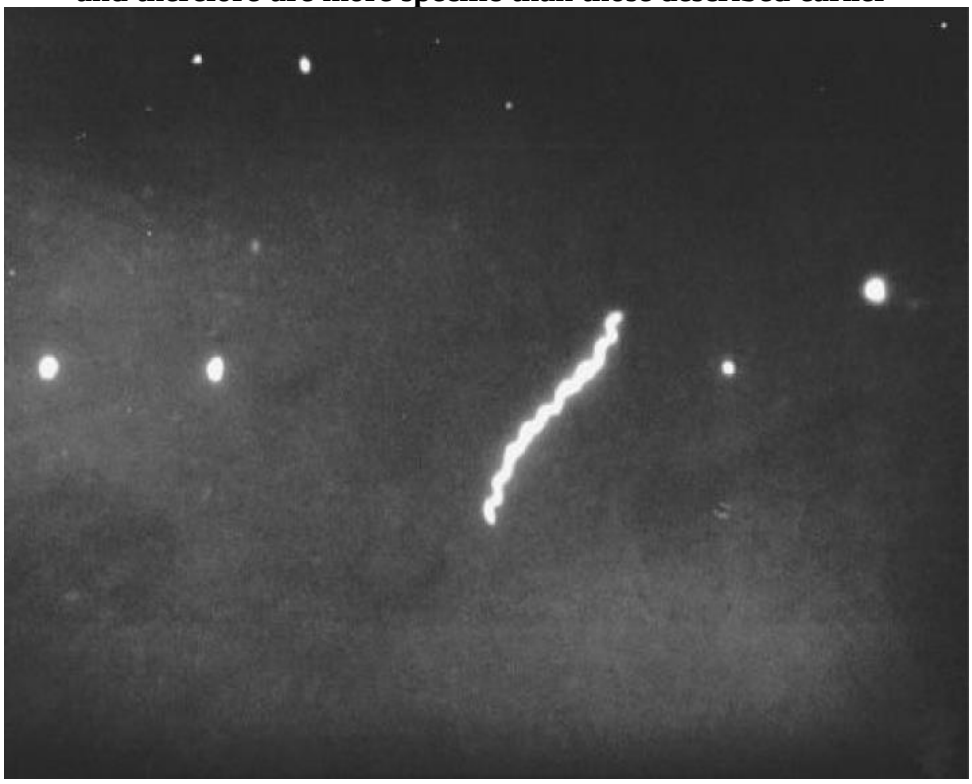


3 important approaches in lab diagnoses:

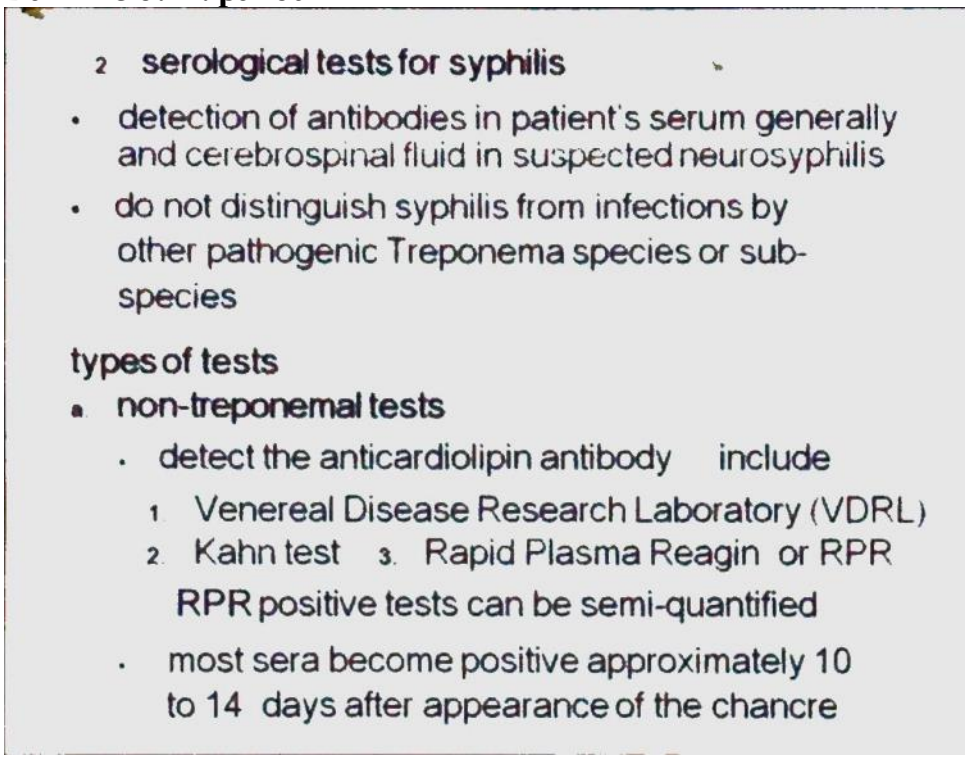
1. **Microscopy**
   a. **Dark field**
   b. **DFA - direct fluorescent antibody**
2. **Nonspecific serologic tests by use of nontreponemal anitigens eg cardiolipin which react with antibodies in serum samples from patients with syphilis. These antibodies, which are a mixture of IgG and IgM, are called "reagin" antibodies. Flocculation tests (e.g. VDRL and RPR tests) detect the presence of these antibodies. False-positive reactions occur in infections such as leprosy, hepatitis B, and infectious mononucleosis and in various autoimmune diseases.**

Therefore, positive results have to be confirmed by specific tests. These tests can also be falsely negative as a result of the prozone phenomenon. In the prozone phenomenon, the titer of antibody is too high (antibody excess), and no flocculation will occur. On dilution of the serum, however, the test result becomes positive

3. **Specific tests: These tests involve the use of treponemal antigens and therefore are more specific than those described earlier**



Dark-field: T. palidum



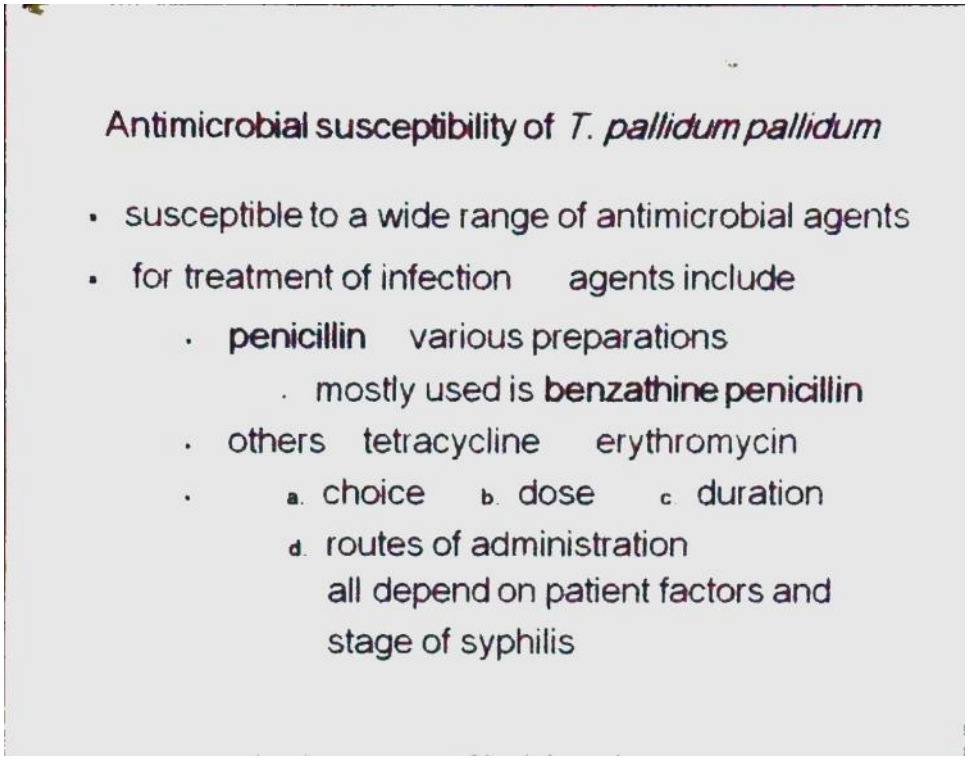
- associated with
  - a. false negative results
    - may occur in early primary and late stages of syphilis
  - b false positive results
    - may be due to other infectious and non infectious diseases
- positive in all patients with secondary syphilis
- used as screening tests
  - positive results are subjected to confirmatory tests
- sera of patients testing positive and are confirmed positive become negative after successful treatment
  - may be used to monitor response to treatment

-False positive reactions occur in infections such as leprosy, hepatitis B, and infectious mononucleosis and in various autoimmune diseases
-Falsely negative as a result of the *prozone phenomenon*. In the prozone phenomenon, the titer of antibody is too high (antibody excess), and no flocculation will occur. On dilution of the serum, however, the test result becomes positive
-Congenital syphilis is based on the finding that the infant has a higher titer of antibody in the VDRL test than has the mother

- b Treponemal tests for syphilis
  - detect specific antibody to treponemal antigen
  - associated with fewer false positive reactions
  - majority remains positive after completion of treatment tests include
    1. *T. pallidum* haemagglutination assay (TPHA)
    2. Fluorescent Treponemal antibody absorption test (FTA-ABS)
    3. ELISA
    4. *T. pallidum* immobilization test or TPI
       - has several disadvantages including use of live treponemes
       - used less frequently
- c. other tests include gene detection methods

These tests remain positive for life after effective treatment and cannot be used to determine the response to treatment or

reinfection



-Benzathine pen: long acting penicillin for prim and sec syphilis
-Pen G for congenital and late syph
-Syphilis Rx is associated with Jarisch–Herxheimer reaction
-Jarisch–Herxheimer reaction: is a reaction to endotoxin-like products released by the death of harmful microorganisms within the body during antibiotic treatment. Efficacious antimicrobial therapy results in lysis of bacterial cell membranes, and consequently releases bacterial toxins into the bloodstream , resulting in a systemic inflammatory response or systemmic shock. This reaction occurs after treatment of spirochetal diseases such as syphillis, Lyme disease, leptospirosis, and relapsing fever

Prevention of *T. pallidum pallidum* infection

1. **sexually transmitted infection**
   - methods of prevention of STI and STD in general are applied
   - screening clients with other STDs for syphilis and giving appropriate treatment if infected
2. **congenital syphilis**
   - antenatal screening of expectant females
   - prompt diagnosis
   - adequate treatment of infected expectant females
3. **blood transfusion**
   - screening all donated blood for *T. pallidum* before use and discarding if infected

Non-venereal diseases due to Treponema

- transmitted through person to person contact or via contaminated articles

1. **bejel** or **non-venereal** or **endemic syphilis**
   - caused by *T. pallidum* subspecies *endemicum*
   - usually begins in childhood in the mucous membranes as a small patch which can start in the mouth
   - progresses gradually associated with raised eroding small swellings on the limbs and trunk
   - later lesions include gummas which may occur on the skin bones and nasopharynx
   - encountered in tropical and subtropical areas of Africa and other continents

-Bejel: in Africa
-Yaws: tropical countries (caused by T. pallidum subspecies pertenue)
-Pinta: Central and S. America (caused by Treponema carateum)

2. **yaws**

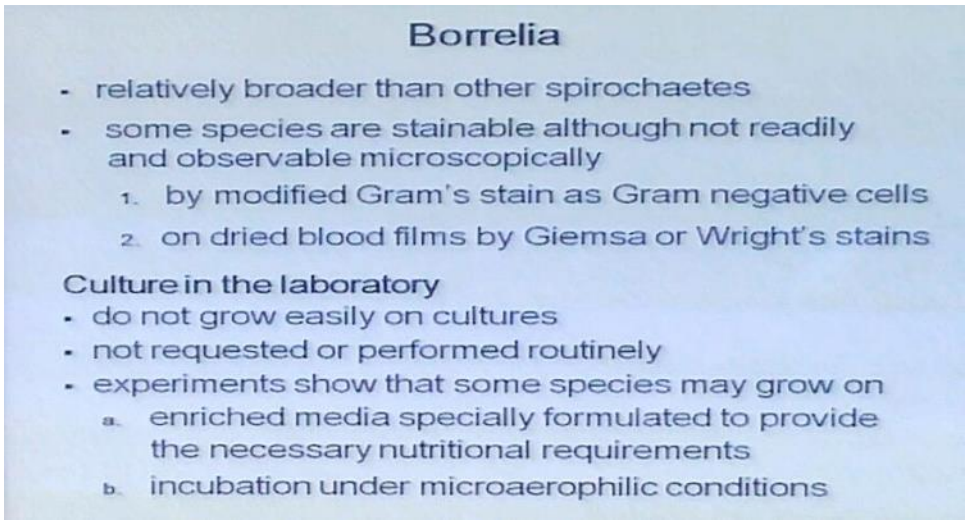
- causative agent is *T. pallidum pertenue*
  - infects through broken skin
- numerous manifestations which vary according to the stage of the illness include
  - painless papular nodules initially
  - later develops into destructive lesions involving
    a. skin may form ulcers
    b. lymph nodes c. bones and joints
    d. other destructive lesions on soft tissues
- encountered mostly in various areas of S. America Central Africa SE Asia

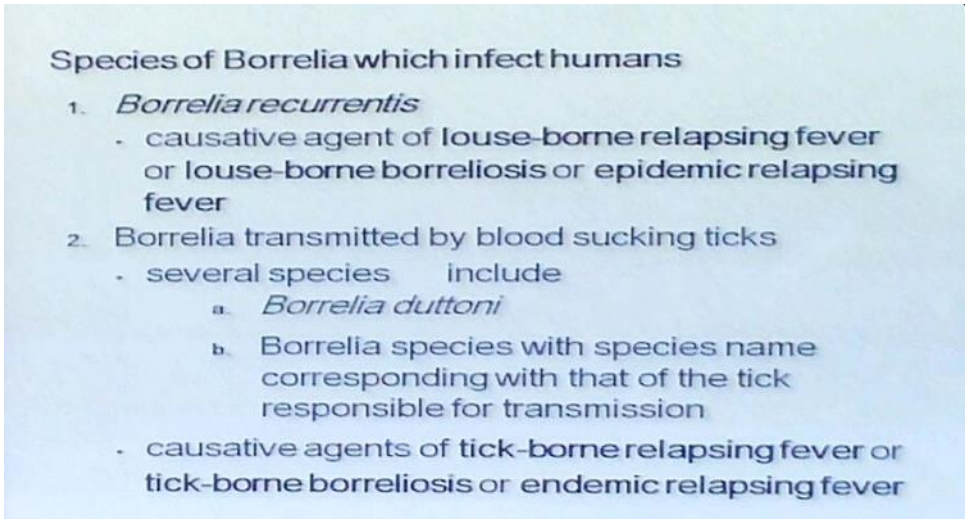
3. **pinta**

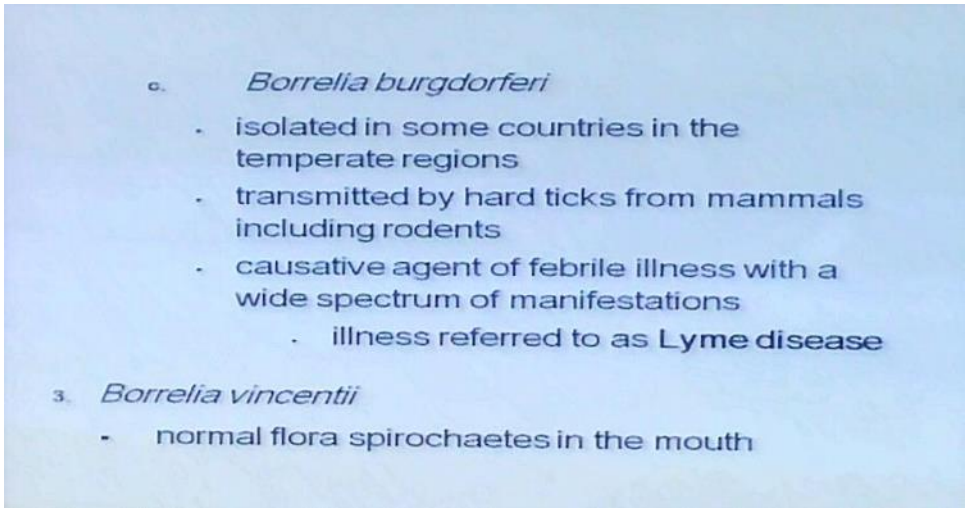
- causative agent is *Treponema carateum* or *T. pallidum carateum*
- primarily restricted to skin
- clinically characterized by
  - initial lesions as small pruritic papules
  - later lesions consist of enlarged plaques which persist for months to years
  - disseminated illness is characterized by recurrent hypopigmentation or depigmentation of skin lesions and marked scar formation

Spirochetes: Borrelia & Leptospira

Thursday, August 9, 2018 11:15 AM







Lyme disease can cause Bells palsy

Transmission of Borrelia species associated with relapsing fever

Borrelia recurrentis

- transmitted by lice from person to person
- infected humans with the organisms in the blood form the reservoir
  - lice acquire the organisms while feeding on infected human blood
- enters susceptible person through broken skin
- rubbing or crushing the infected lice releases fluid containing spirochaetes and facilitates entry
- over-crowding in places with scarce facilities for cleanliness favours transmission

Borrelia duttoni and related tick-borne species

- humans acquire infection through broken skin
  - from a tick bite or from crushed infected tick
- ticks
  - transmit the borreliae between animals and from animals to humans
  - infected animals involved in transmission include
    a. rodents b. pigs c. armadillos d. porcupines
    - together with infected ticks constitute the reservoir
  - infection in ticks
    a. persists throughout its life
    b. is passed on via the ova to next generations

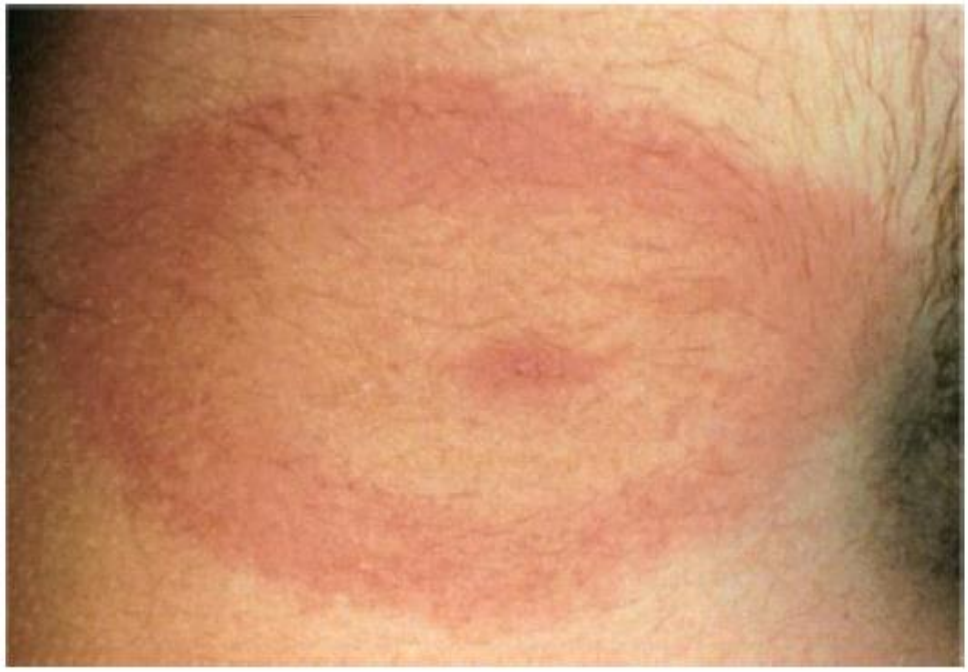
Manifestations of relapsing fever

- louse-borne or tick-borne similar manifestations
  - characterized by febrile and afebrile periods
- febrile period
  - lasts approximately 3 to 5 days
  - spirochaetes are abundant in the blood
  - immune system responds by production of antibodies to specific antigenic components
  - together with other immune defense mechanisms antibodies recognize and act to eliminate the spirochaetes in the circulation at the time
  - overall effects
    a. marked reduction of borreliae in the blood
    b. fever to subsides

- fever recurs after 4 to10 days and spirochaetes reappear in the blood causing a relapse
- several **recurrences** or **relapses** occur
- during each febrile episode
  - a few borreliae undergo mutation
    - acquire new antigenic determinants which differ structurally from the previous ones
    - phenomenon of antigenic variation
  - organisms with new antigenic determinants
    - constitute a new strain
    - are not recognized by the circulating antibodies at the time and therefore are not eliminated
    - multiply and cause the subsequent relapse

Clinical Findings

The clinical findings have been divided into three stages; In stage 1 (early localized stage), the most common finding is **erythema chronicum migrans** (also called **erythema migrans**), an expanding, erythematous, macular rash that often has a "target" or "bull's eye" appearance



-In stage 2 (early disseminated stage), which occurs weeks to months later, cardiac and neurologic involvement predominates. Myocarditis, accompanied by various forms of heart block, occurs. Acute (aseptic) meningitis and cranial neuropathies, such as facial nerve palsy (Bell's palsy), are prominent during this stage. Bilateral facial nerve palsy is highly suggestive of Lyme disease

-In stage 3 (late disseminated stage), arthritis, usually of the large joints (e.g., knees), is a characteristic finding. Lyme arthritis is thought to be autoimmune in origin. Encephalopathy also occurs in stage 3

Laboratory investigation of relapsing fever

1. detection of Borrelia species in peripheral blood
   - chances of detection are high during the febrile periods by
   a. direct microscopic examination for motile spiral organisms
   b. examination of dry smears stained by Giemsa or Wright's stain
   c. dark field or phase contrast microscopic examination for motile spiral organisms
      - more reliable procedure
2. other methods of investigation

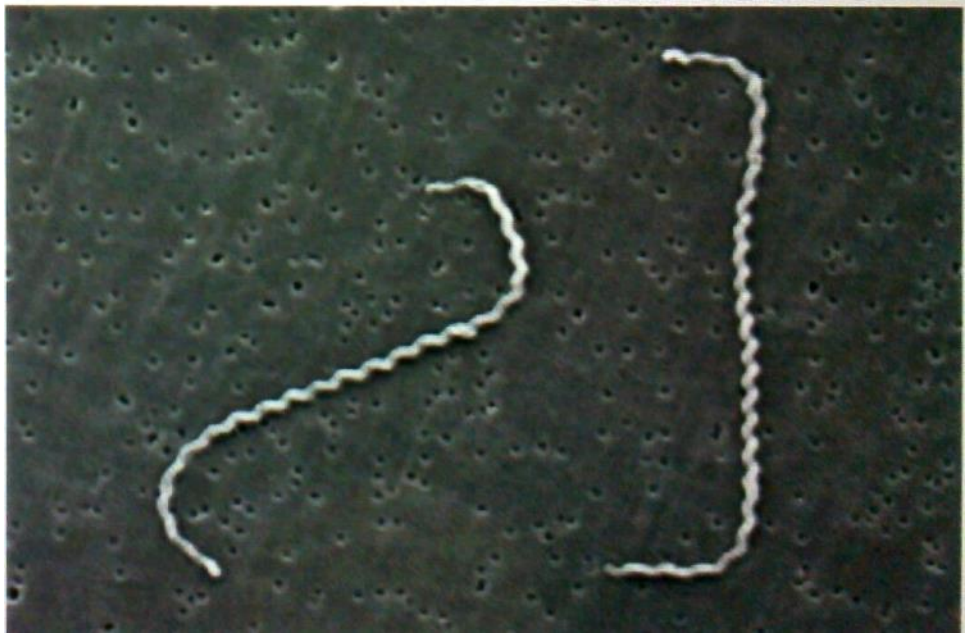
Antibiotic susceptibility of Borrelia

- sensitive to several agents including penicillin

Borrelia vincentii

- relatively longer and broader actively motile
- fastidious nutritional requirements for growth
  - possibility of growth on specially formulated enriched medium under anaerobic incubation
- significant as one of the causative agents of **ulcerative gingivostomatitis** and **ulcerative oropharyngitis** also referred to as **trench mouth**
  - in association with
    1. other abnormalities including
       a. trauma b. vitamin deficiency
    2. other organisms in the mouth

Leptospira



Leptospira

- narrower than other spirochaetes
  - possesses numerous closely set coils
- recognized by its characteristic vigorous motility
- visualized by dark field or phase contrast or electron microscopes
- stainable by special methods including fluorescent staining methods
- culturable in specifically formulated enriched media
  - liquid or semi-solid preparations as obligate aerobes
  - slow growth especially in primary isolation
    - may take 6 to 14 days or longer
- also capable of growing on embryonated eggs

Species of genus Leptospira

- composed of saprophytic organisms and potential pathogens
- two species morphologically indistinguishable
  - each species is composed of numerous serotypes

1. *L. interrogans*
   - hundreds of serotypes
   - includes a serotype associated with rodents which is pathogenic to humans *L. interrogans icterohaemorrhagiae*
2. *L. biflexa*
   - saprophytes in the environment

Leptospira interrogans serotype associated with human disease

- parasitic to small animals including rodents
  - found in their kidneys
- no disease manifestations in the animals
  - can also infect other animals including domestic animals
  - the infected small animals provide the reservoir
- passed out in the urine and contaminates the environment
- saprophytes in water or damp soil
- **transmission to humans** is by accidental exposure through contact with infected urine of the animal

- directly or through contaminated soil or water

Clinical implication

- causative agent of human leptospirosis
  - entry is through broken skin or mucous membranes
  - infection is associated with invasion into the blood circulation and septicaemia
  - associated with haematogenous spread to various internal organs including the kidneys
    - associated with excretion in urine
  - increased risk of exposure for people who work in damp places populated by rodents

Manifestations of human leptospirosis

- vary from asymptomatic to severe illness
- symptomatic leptospirosis
  - initially characterized by septicaemia constituting the septicaemic phase
    - manifestations include mild non-specific signs and symptoms including fever
  - may progress severe illness characterized by an internal organ damage
    - with manifestations due to abnormal functions of the organ

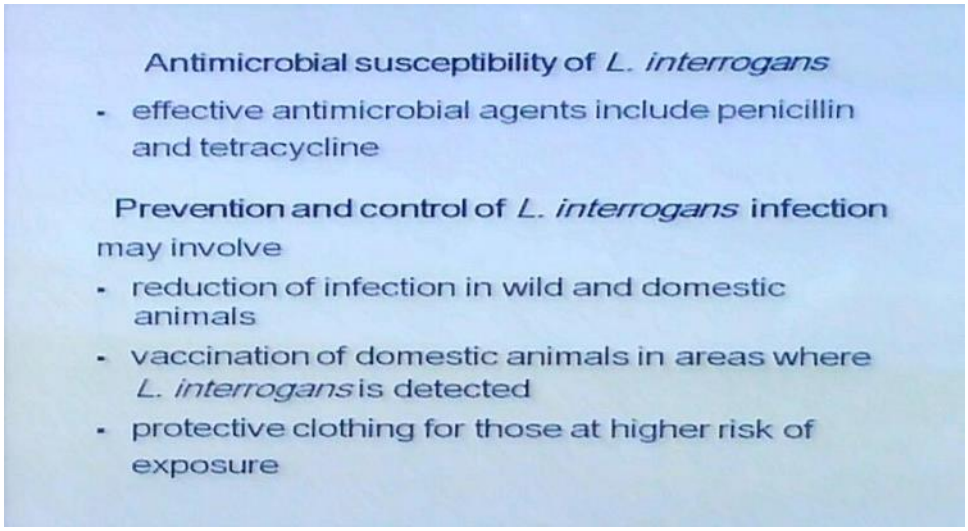
The illness is typically biphasic, with fever, chills, intense headache, and conjunctival suffusion (diffuse reddening of the conjunctivae) appearing early in the disease, followed by a short period of resolution of these symptoms as the organisms are cleared from the blood.

Laboratory investigation of leptospirosis

- involves detection of spirochaetes in specimens and serological tests for antibodies
- specimens include 1. blood 2. urine 3. tissue

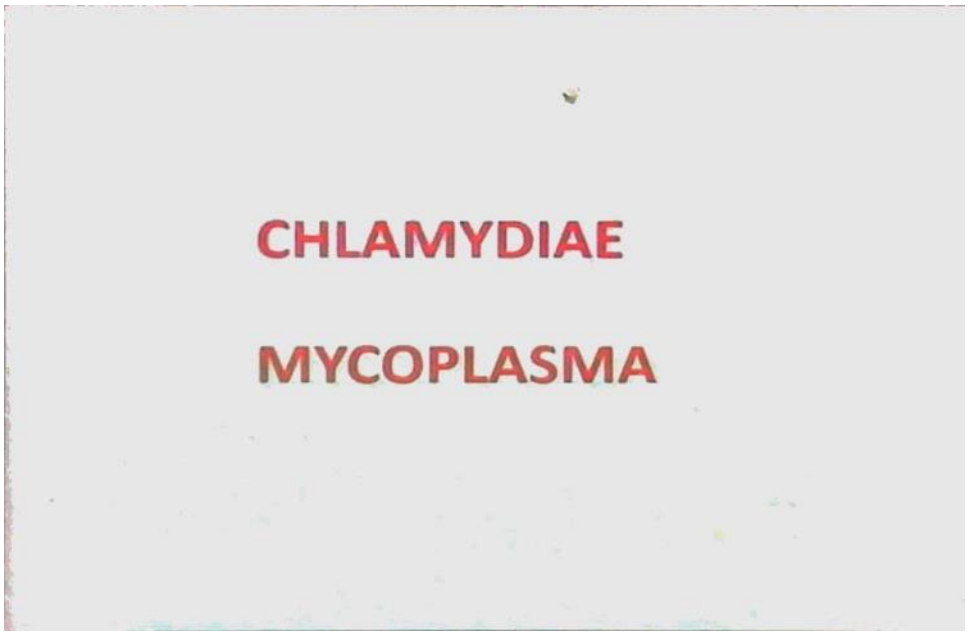
procedures

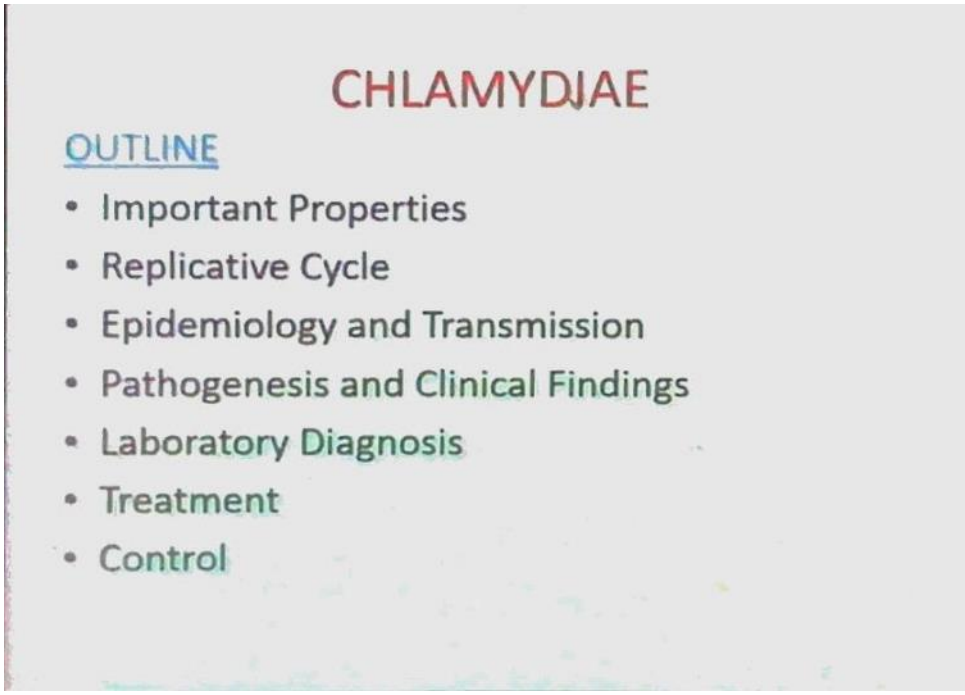
1. culture
2. dark field microscopy
   - chances for positive results on blood are higher during the septicaemic phase
3. serology
   - detection and demonstration of rising antibody titre in serum
4. DNA detection and amplification in specimen


Antimicrobial susceptibility of L. interrogans
- effective antimicrobial agents include penicillin and tetracycline
Prevention and control of L. interrogans infection may involve
- reduction of infection in wild and domestic animals
- vaccination of domestic animals in areas where L. interrogans is detected
- protective clothing for those at higher risk of exposure

Chlamydia & Mycoplasma

Tuesday, August 14, 2018 3:10 PM





CURRENTLY 2 GENERA:

- Chlamydia
- Chlamydophila

IMPORTANT PROPERTIES

- obligate intracellular organisms.
  - Cannot synthesize own ATP
- parasites of humans, animals & birds

- Share some characteristics with viruses:
  - –Very small
  - –Don't synthesize ATP (get ATP from host cell)
  - –Don't replicate extracellularly

- Unlike Viruses:
  - -Contain both DNA &RNA
  - -Have ribosomes
  - -Replicate by binary fission
  - -Respond to antibacterial agents

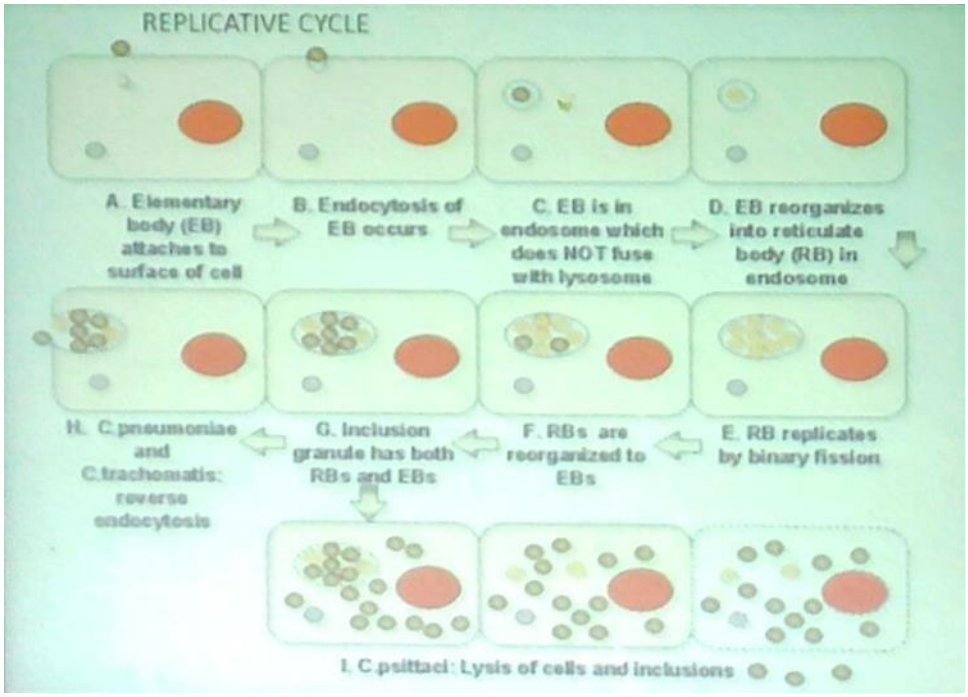
REPLICATIVE CYCLE

1. The cycle begins when the metabolically inert spore-like **elementary** body enters the cell.

2. It then reorganizes into a larger metabolically active **reticulate** body.

3. The reticulate body undergoes **repeated binary fission** to form daughter elementary bodies.

4. Formed elementary bodies are released from the cell.



- Pathogenic Species

Chlamydia trachomatis

Chlamydophila pneumoniae

Chlamydophila psittaci

C. trachomitis

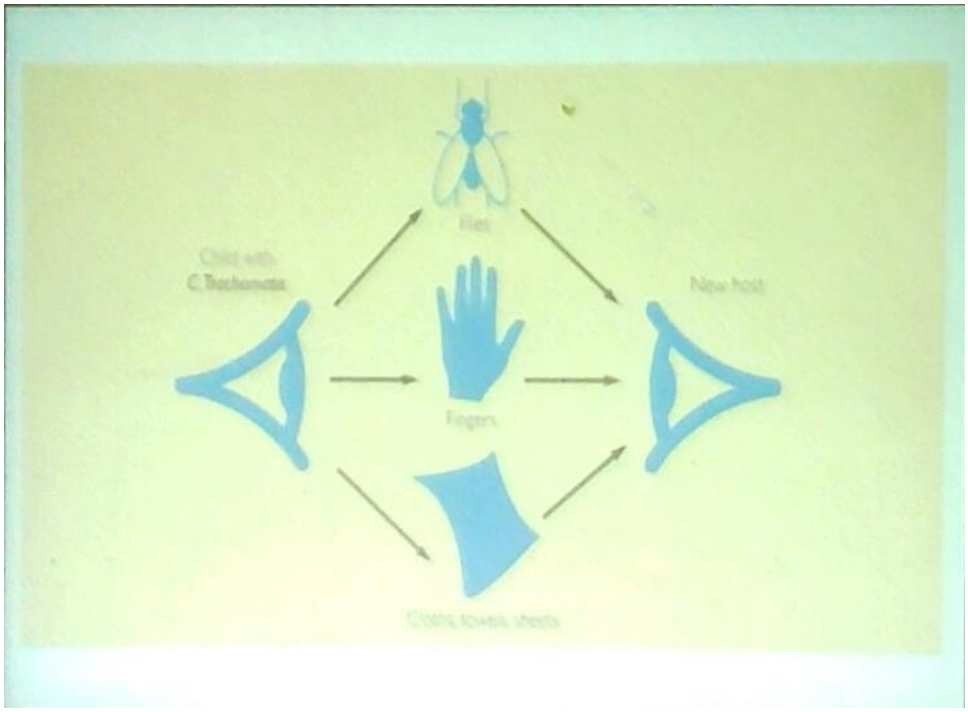
- Occurs worldwide.
- Infects only humans .
- Transmitted sexually, passage through the birth canal, flies, contaminated fingers.

Clinical manifestations

1. **Trachoma** chronic follicular keratoconjuctivits

- Leading cause of preventable blindness in the developing world
  - Eye disease of conjunctiva & cornea
  - Caused by Serotypes A, B1, B2 , and C
  - Infections result in scarring & corneal damage

- .....Trachoma
- Spread by transfer of infected discharge from eye of infected person by hands, clothing, towels
- Flies important carriers
- Poverty, overcrowding, poor personal hygiene, inadequate water.... enhance spread



WHO STAGES

1.Trachomatous inflammation, follicular (TF)—Five or more follicles of >0.5 mm on the upper tarsal conjunctiva

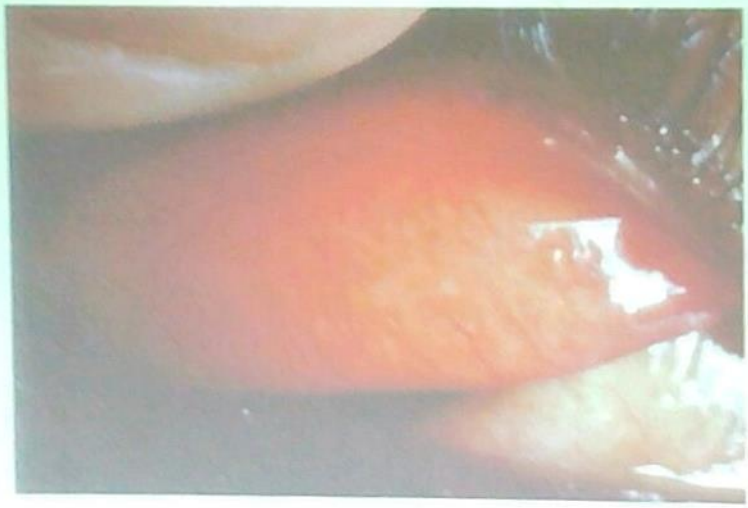
2.Trachomatous inflammation, intense (TI)—Papillary hypertrophy and inflammatory thickening of the upper tarsal conjunctiva obscuring more than half the deep tarsal vessels

3.Trachomatous scarring (TS)—Presence of scarring in tarsal conjunctiva.

4.Trachomatous trichiasis (TT)—At least one ingrown eyelash touching the globe, or evidence of epilation (eyelash removal)

5.Corneal opacity (CO)—Corneal opacity blurring part of the pupil margin

Stage 1: Trachoma infection: small bumps under the eye lid



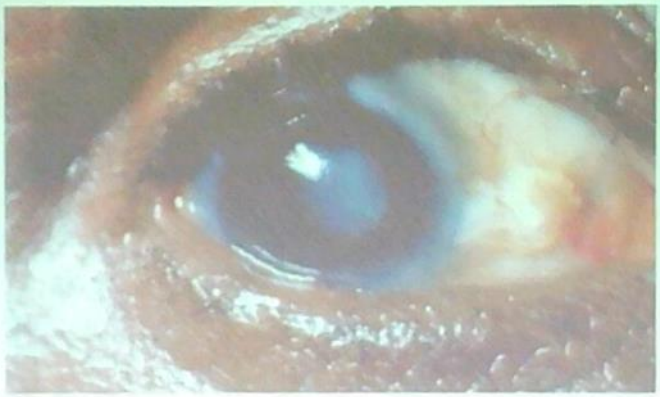
Follicles Under the eyelid.

Stage 2: Follicles, inflammation,

Stage 3: Trachoma with scarring

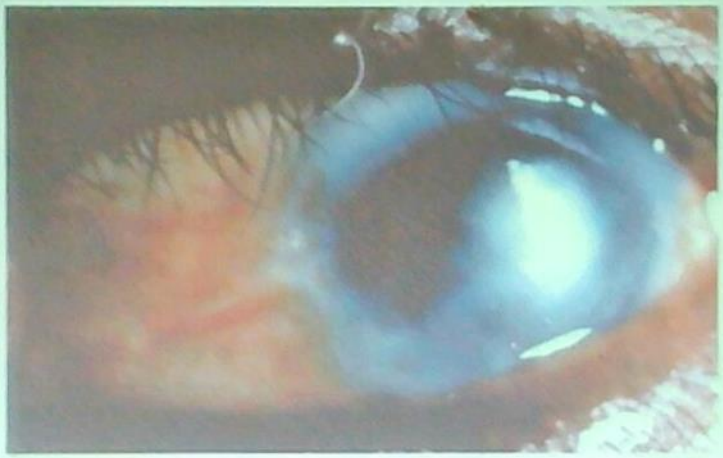
- Scar tissue forms.
- Eyelid is difficult to turn for examination

Stage 4: Trachoma with trichiasis

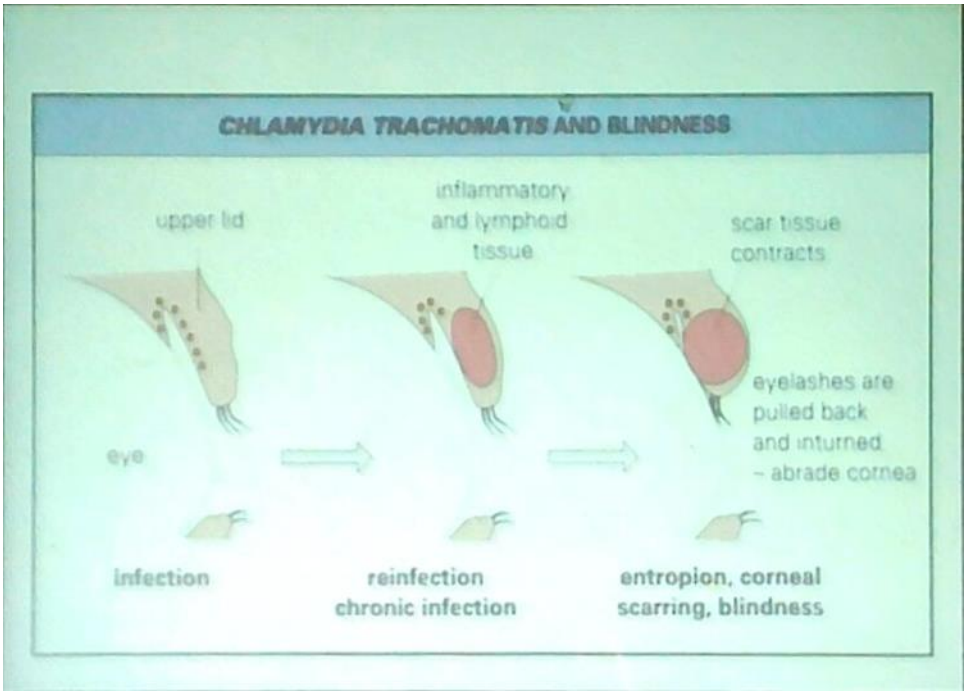


Eyelids turn in towards the cornea

Stage 5: Corneal Opacity



- Corneal Scarring
- Bacteria/Virus enters damaged cornea



2. **Inclusion conjunctivitis**:

- Associated with serotypes D-K
- Half of infected adults have concurrent genital tract infection
- Can affect neonates born of mothers with genital infection
- Presents with mucopurulent discharge in the eye (Ophthalmia neonatorum)
- No corneal scarring

3. **Neonatal pneumonia**:

- Associated with serotypes D-K
- Most acquired from mothers genital tract
- Often preceded by inclusion conjunctivitis
- Presents with cough & wheezing; fever

4. Lymphogranuloma venereum (LGV)

- Associated with serotypes L1, L2, and L3
- Sexually transmitted- enters thru skin abrasions
- Primary lesion: small painless papule or ulcer, at infection site
- Secondary symptoms, weeks later- Fever, headache, Lymphadenopathy (inguinal buboes), Abscesses
- Chronic infxn.: scarring, lymphatic obstruction; may resemble elephantiasis

Epididymitis, Salpingitis, Cervicitis, PID

- Caused by Serotypes D-K

LABORATORY DIAGNOSIS

- Microscopy: Cytoplasmic inclusions

- *C. trachomitis* inclusion bodies contain glycogen, can visualize by staining with iodine.
- visualized with giemsa, fluorescent antibody staining or hybridization with a DNA probe.

...Laboratory Diagnosis

- Antigens can be detected in exudates or urine by ELISA.

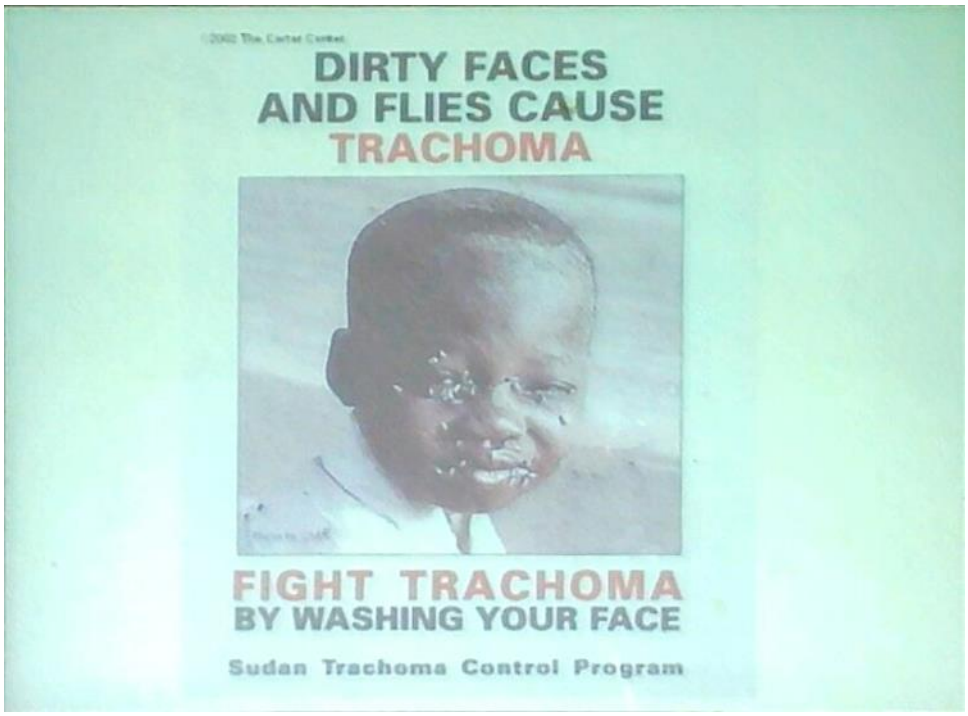
- Pathogen can be grown in cell cultures eg
  - —Chicken embryo yolk sac
  - —McCoy cell lines

TREATMENT

- Trachoma – erythromycin, doxycycline
- LGV – doxycycline; aspirate buboes
- Genital & ocular – azithromycin, doxycycline

CONTROL

- Antibiotic prophylaxis- oral azithromycin
- Public education: hygiene
- Tracing and treating partners in genital tract infections.



C.psittaci

- infects wild & domestic birds
- Human infection: inhalation of organism in dried infected bird droppings
- Influenza-like illness, pneumonitis
- Diagnosis – serology: ELISA
- Rx – tetracycline/ doxycycline/ erythromycin

❖ Proper control of importation or handling of psittacine birds.

C.pneumoniae

- inflammatory process in respiratory tract atypical pneumonia, bronchitis, sinusitis
- Person-to-person spread via respiratory droplets
- Diagnosis – serology, PCR, cell cultures
- Rx – doxycycline/ erythromycin

MYCOPLSAMAS

OUTLINE

- Important Properties
- Antigenic Properties
- Pathogenesis and Epidemiology
- Laboratory Diagnosis
- Treatment

MYCOPLSAMAS

Important Properties

- Family Mycoplasmaceatea
- Genera: *Mycoplasma, Ureaplsama*.
- can grow in cell free culture media.
- multiply by binary fission.
- They lack a cell wall
- Only bacteria that contain cholesterol in the cell membrane

Colonial morphology: fried egg-appearance

Antigenic Properties

- Mycoplasmas have glycolipids- can account for the neurological manifestations of *M. pneumoniae* infection.

- Alter the I antigens on RBCs: stimulate anti-I antibodies (cold agglutinins)- autoimmune response and damage to erythrocytes.

...Antigenic Properties

- Variable membrane lipoproteins form an antigenic variation system - escaping the host immune response.

MYCOPLSAMAS

PATHOGENESIS AND EPIDEMIOLOGY

Respiratory and Urogenital

- Respiratory Infections

M. pneumoniae

- Common cause of atypical pneumonia.
-Transmitted by respiratory droplets.
-Ciliary motion is inhibited and necrosis of the epithelium occurs.

It produces hydrogen peroxide which contributes to damage by respiratory tract cells.

MYCOPLSAMAS

....Respiratory Infections

- *M. hominis* - respiratory disease in newborns
- *M. fermentans* –throat, associated with adult respiratory distress syndrome.

❖Extrapulmonary

- due to production of autoantibodies.
-Include: meningitis, hemolytic anaemia, mycarditis, pericarditis.

MYCOPLSAMAS

Urogenital Infections

- *M. hominis:* pelvic inflammatory disease, acute pyelonephritis.
- *Ureaplasma urealyticum:* nongonoccocal urethritis.

MYCOPLSAMAS

LABORATORY DIAGNOSIS

- Serologic testing
- Culture of specimen for primary isolation.
- Use of specific DNA probes.

Colonial morphology: fried egg

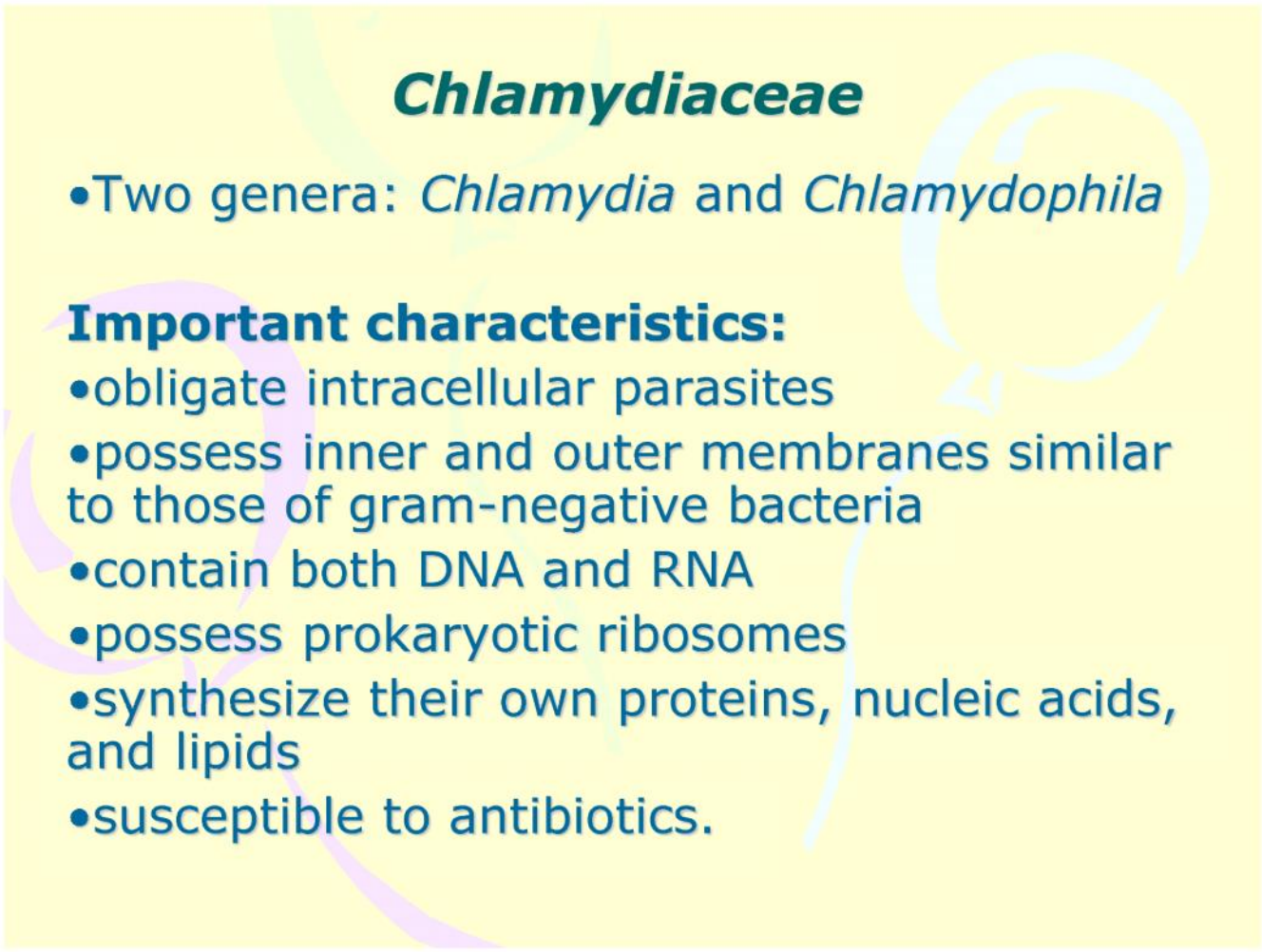
MYCOPLSAMAS

TREATMENT

- ** **Resistant to antibiotics which interfere with bacterial cell wall synthesis** **
- *M.pneumoniae* – tetracyclines/ quinolones/ macrolides
- *U.urealyticum* – less susceptible to quinoloes; use erythromycin

Chlamydia & Mycoplasma

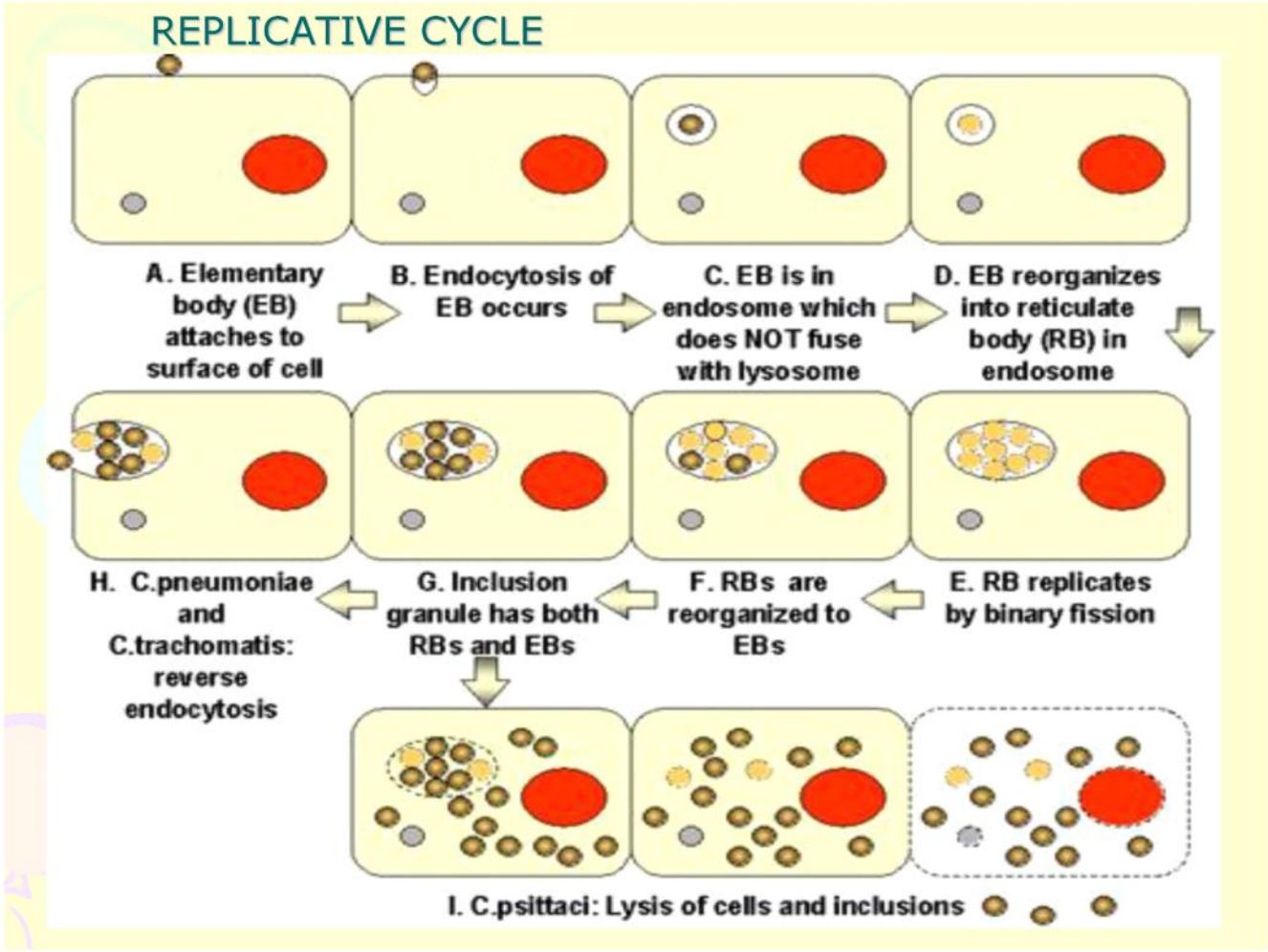
Monday, September 3, 2018 11:06 PM



Chlamydiaceae

.....

- metabolically inactive infectious forms **(elementary bodies [EBs])**
- metabolically active, noninfectious forms **(reticulate bodies [RBs])**
- EBs are resistant to many harsh environmental factors


REPLICATIVE CYCLE
A. Elementary body (EB) attaches to surface of cell
B. Endocytosis of EB occurs
C. EB is in endosome which does NOT fuse with lysosome
D. EB reorganizes into reticulate body (RB) in endosome
E. RB replicates by binary fission
F. RBs are reorganized to EBs
G. Inclusion granule has both RBs and EBs
H. C.pneumoniae and C.trachomatis: reverse endocytosis
I. C.psittaci: Lysis of cells and inclusions

Chlamydia trachomatis

- Serovars (antigenic difference-major outer membrane protein)

- A, B, C……Primarily conjunctiva
- D-K……Primarily urogenital tract
- L1, L2, L3 ……Inguinal lymph nodes

Trachoma:

- Chronic, inflammatory granulomatous process of the eye surface, leading to corneal ulceration, scarring, and blindness.
- Active trachoma, characterized by the presence of lymphoid follicles on the conjunctiva and intermittent shedding of chlamydiae
- Is primarily a disease of children.
- Blindness can occur as a complication

- …..Trachoma

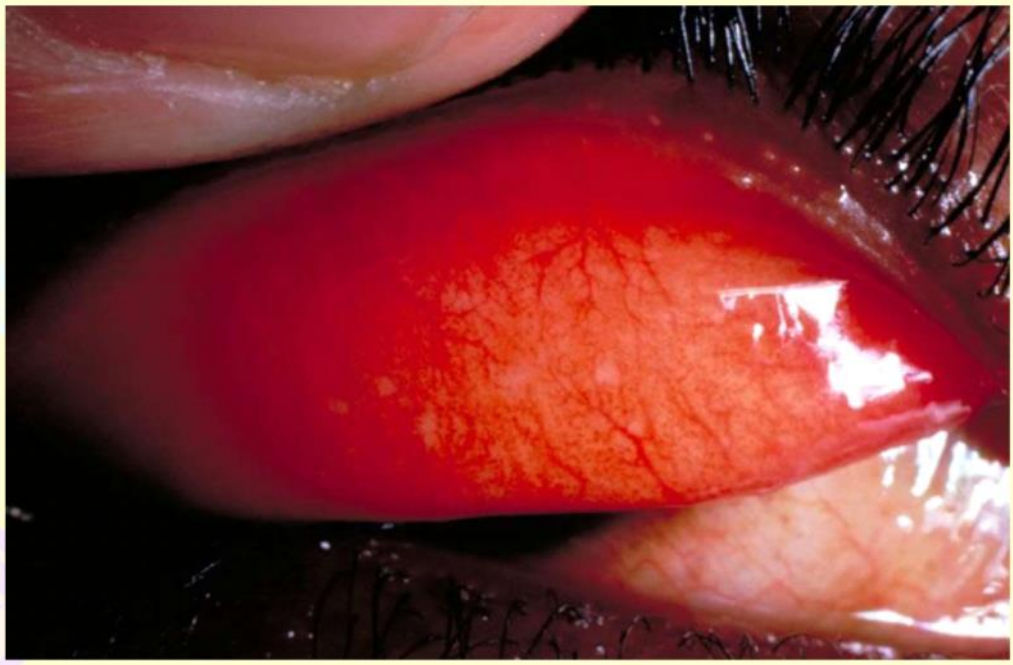
- Spread by transfer of infected discharge from eye of infected person by hands, clothing, towels

- Flies important carriers

- Poverty, overcrowding, poor personal hygiene, inadequate water…. enhance spread

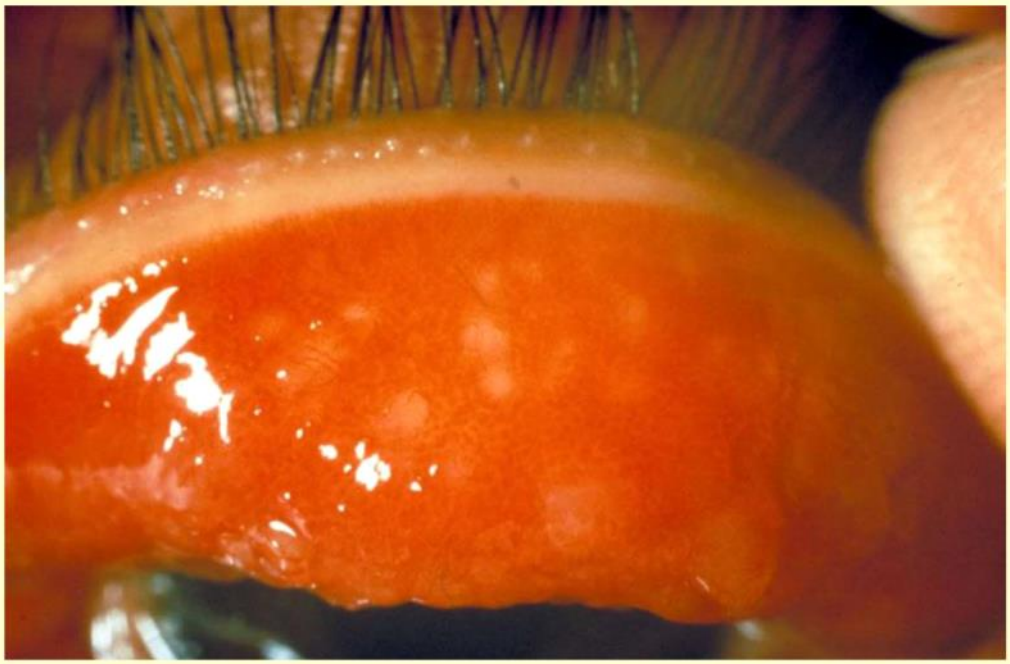
What are the stages of Trachoma Disease?

Stage 1: Trachoma infection: small bumps under the eye lid

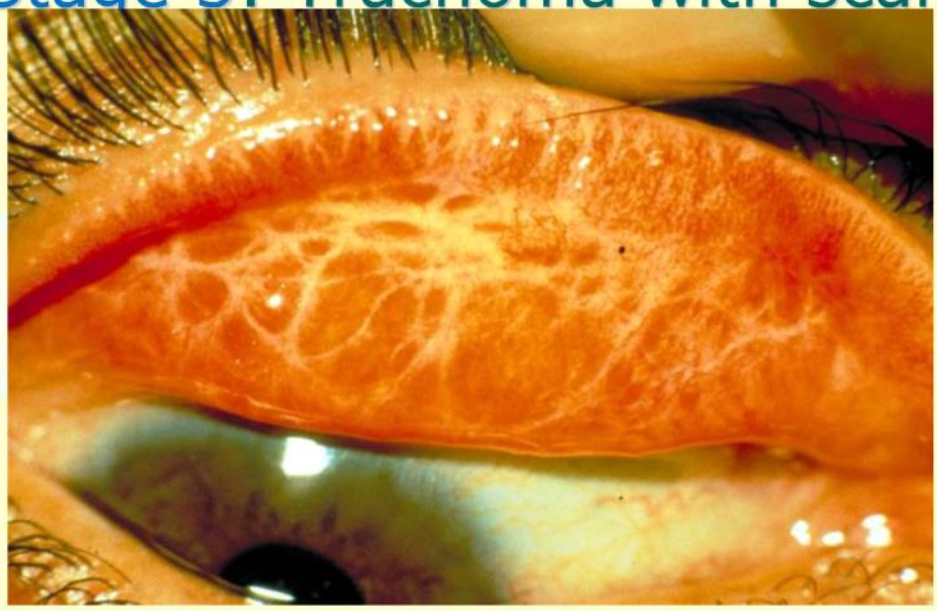


Follicles Under the eyelid.

Stage 2: Follicles, inflammation,

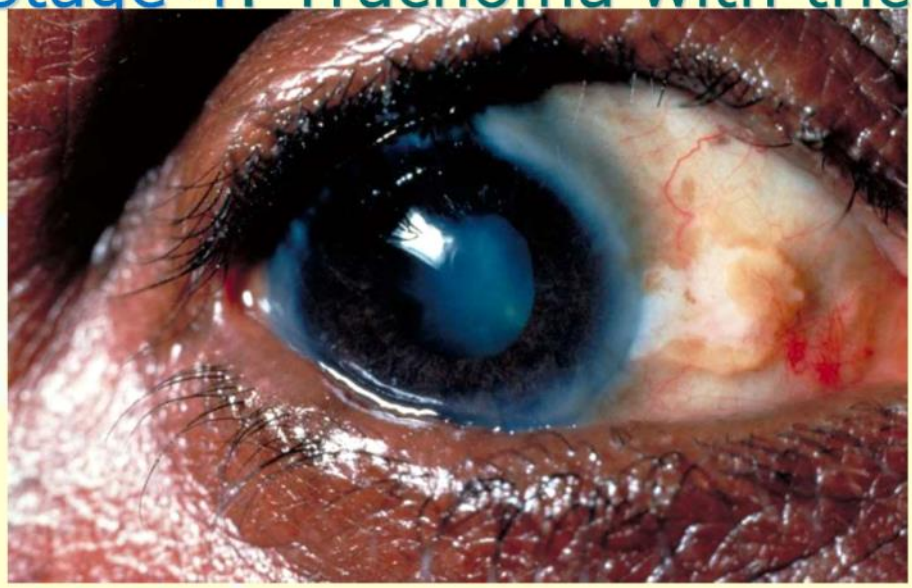


Stage 3: Trachoma with scarring



- Scar tissue forms.
- Eyelid is difficult to turn for examination

Stage 4: Trachoma with trichiasis



Eyelids turn in towards the cornea

Stage 5: Corneal Opacity

- Corneal Scarring
- Bacteria/Virus enters damaged cornea

Adult inclusion conjunctivitis:

- Acute process with mucopurulent discharge, dermatitis, corneal infiltrates, and corneal vascularization in chronic disease.
- Most prevalent in sexually active young people, being spread from genitalia to the eye….*poor hygiene

Neonatal conjunctivitis

- Acute process characterized by a mucopurulent discharge.
- Develops in infants around 14 days after birth.
- Presents as a swelling of the eyelids and orbit and a purulent infiltration of the conjunctiva.
- Acquired from the mother during birth.
- If untreated the infection usually resolves, but a substantial proportion of these infants develop chlamydial pneumonia about 6 weeks after birth

Genital infection: *Infection in men*

- *C. trachomatis* serovars D-K are responsible for about 30% of cases of non-specific urethritis in men.
- The infection can be asymptomatic, with infected men serving as a reservoir of infection.
- In symptomatic patients, varying amounts of mucopurulent discharge are produced.
- Occasionally this progresses to epididymitis or prostatitis
- It is likely that chronic chlamydial epididymitis may eventually lead to occlusion of the tube and infertility due to azoospermia.

Genital infection: *Infection in women*

- In symptomatic women, *C. trachomatis* serovars D-K cause mucopurulent cervicitis and urethritis.
- However, many women harbour the organism asymptomatically in their cervix.
- Not only a risk to their sexual partners or offspring, but also to themselves, as ascending infection frequently occurs.
- This results first in an endometritis, in which chlamydiae survive monthly menstrual shedding of the uterine lining, followed by infection of the fallopian tubes to cause acute salpingitis.

…genital tract infection in women

- Collectively, endometritis and salpingitis are known as *pelvic inflammatory disease*, which is largely caused by *C. trachomatis*.
- Chlamydial pelvic infection may lead to further abdominal involvement and the formation of pelvic adhesions. Perihepatitis (*Fitz-Hugh-Curtis syndrome*) and even peri-appendicitis may result.

Lymphogranuloma venereum

- Genital tract infection with *C. trachomatis* serovars L1-L3
- Usually begins with a genital ulcer followed by lymphadenopathy of the regional lymph nodes.
- Buboes are seen if infection persists, can spread to the gastrointestinal and genito-urinary tracts, causing strictures and, in rare cases, peno-scrotal elephantiasis.

Site of infection	Disease	Organism (serovars)
Eye	Trachoma	*C. trachomatis* (A, B, Ba, C)
	Inclusion conjunctivitis	*C. trachomatis* (D-K)
	Ophthalmia neonatorum	*C. trachomatis* (D-K)
Genital tract		
Male	Non-specific urethritis, proctitis, epididymitis	*C. trachomatis* (D-K)
Female	Cervicitis, urethritis, endometritis, salpingitis, PID, perihepatitis, peri-appendicitis, infertility with tubal occlusion	*C. trachomatis* (D-K)
	Abortion, premature birth	*C. trachomatis* (D-K)[a]
Male and female	Lymphogranuloma venereum	*C. trachomatis* (L1-L3)
Respiratory tract	Neonatal atypical pneumonia	*C. trachomatis* (D-K)
	Pharyngitis, bronchitis, pneumonia	*Ch. pneumoniae*
	Psittacosis	*Ch. psittaci*
Chronic diseases	Atherosclerosis, coronary disease	*Ch. pneumoniae*[a]
	Stroke, Alzheimer's disease	*Ch. pneumoniae*[b]

LABORATORY DIAGNOSIS

- Cytoplasmic inclusions

-Microscopic examination of clinical specimen

- *C. trachomitis* inclusion bodies contain glycogen, can visualize by staining with iodine, giemsa, fluorescent antibody staining or hybridization with a DNA probe.

…Laboratory Diagnosis

- Antigens can be detected in exudates or urine by ELISA.

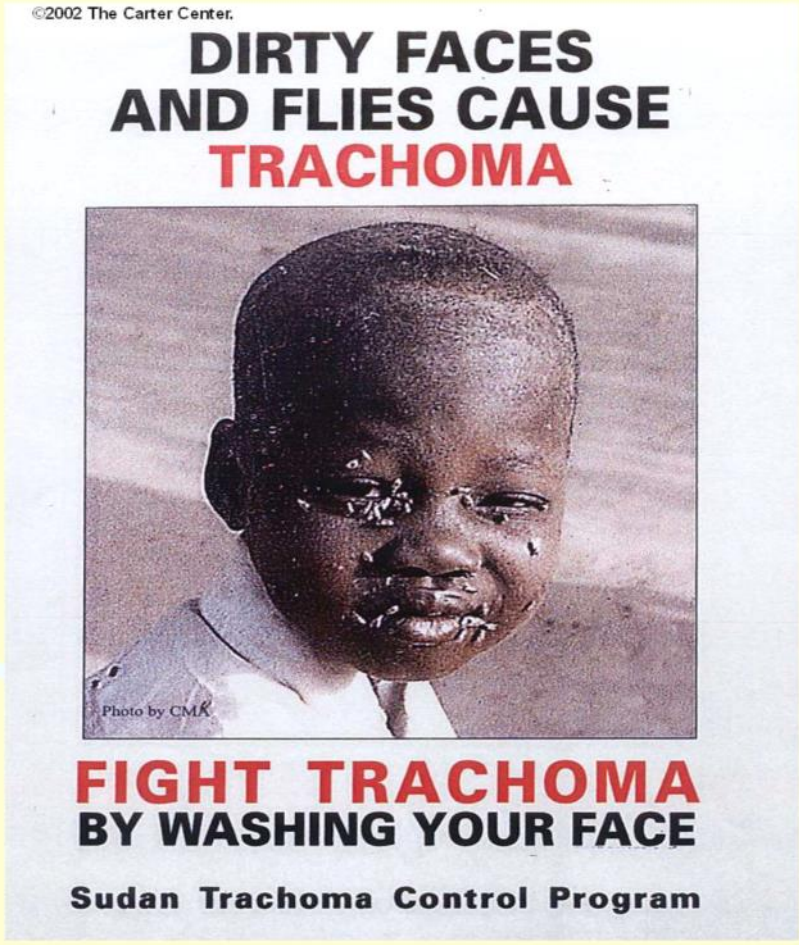
- Pathogen can be grown in cell cultures eg
  - –Chicken embryo yolk sac
  - –McCoy cell lines

TREATMENT

- LGV – doxycycline; aspirate buboes
- Genital & ocular – azithromycin, doxycycline
- Newborn conjunctivitis and pneumonia should be treated with erythromycin for 10 to 14 days

CONTROL

- Antibiotic prophylaxis- oral azithromycin
- Public education: hygiene
- Tracing and treating partners in genital tract infections.


©2002 The Carter Center.
DIRTY FACES
AND FLIES CAUSE
TRACHOMA
Photo by CMK
FIGHT TRACHOMA
BY WASHING YOUR FACE
Sudan Trachoma Control Program

Chlamydophila pneumoniae

- Spread via respiratory secretions
- Human pathogen, No animal reservoir
- Causes bronchitis, pneumonia, sinusitis, atypical pneumonias
- 50% of people have serologic evidence
- A significant cause of acute exacerbations of asthma

- Diagnosis – serology, PCR, cell cultures
- Macrolides (erythromycin, azithromycin , clarithromycin), tetracyclines (tetracycline, doxycycline), or levofloxacin administered for 10 to 14 days

Chlamydophila psittaci

- Infects wild & domestic birds
- Human infection: inhalation of organism in dried infected bird droppings
- The incubation period is about 10 days
- Ranges from an 'influenza-like' syndrome, with general malaise, fever, anorexia, sore throat, headache and photophobia, to a severe illness with delirium and pneumonia.
- Diagnosis – serology (ELISA)
- Rx – tetracycline/ doxycycline/ erythromycin
  - ❖ Proper control of importation or handling of psittacine birds
  - ❖ Occupational hazard-use PPE

MYCOPLSAMAS

OUTLINE

- Important Properties
- Antigenic Properties
- Pathogenesis and Epidemiology
- Laboratory Diagnosis
- Treatment

MYCOPLSAMAS

Important Properties

- Family Mycoplasmaceatea
- Genera: *Mycoplasma, Ureaplsama*.
- can grow in cell free culture media.
- multiply by binary fission.
- They lack a cell wall
- Only bacteria that contain cholesterol in the cell membrane

Antigenic Properties

- Mycoplasmas have glycolipids- can account for the neurological manifestations of *M. pneumoniae* infection.

- Alter the I antigens on RBCs: stimulate anti-I antibodies (cold agglutinins)- autoimmune response and damage to erythrocytes.

...Antigenic Properties

- Variable membrane lipoproteins form an antigenic variation system - escaping the host immune response.

MYCOPLSAMAS

PATHOGENESIS AND EPIDEMIOLOGY

Respiratory and Urogenital

- Respiratory Infections

M. pneumoniae

- Common cause of atypical pneumonia.

-Transmitted by respiratory droplets.

-Ciliary motion is inhibited and necrosis of the epithelium occurs.

It produces hydrogen peroxide which contributes to damage by respiratory tract cells.

MYCOPLSAMAS

….Respiratory Infections

- *M. hominis* - respiratory disease in newborns
- *M. fermentans* –throat, associated with adult respiratory distress syndrome.

❖Extrapulmonary

- due to production of autoantibodies.

-Include: meningitis, hemolytic anaemia, mycarditis, pericarditis.

MYCOPLSAMAS

Urogenital Infections

- *M. hominis:* pelvic inflammatory disease, acute pyelonephritis.
- *Ureaplasma urealyticum:* nongonoccocal urethritis.

MYCOPLSAMAS

LABORATORY DIAGNOSIS

- Serologic testing
- Culture of specimen for primary isolation.
- Use of specific DNA probes.

MYCOPLSAMAS

TREATMENT

- ** **Resistant to antibiotics which interfere with bacterial cell wall synthesis** **
- *M.pneumoniae* – tetracyclines/ quinolones/ macrolides
- *U.urealyticum* – less susceptible to quinoloes; use erythromycin

Actinomycetes,Streptomyces,Actinomadura

Wednesday, August 15, 2018 9:56 AM

General characteristics

- Gram-positive bacteria with branching filaments
- **fungal-like** organisms but they have a prokaryotic nuclei
- Gram positive
- Related to mycobacteria and corynebacteria
- Non-motile, Non-capsulated, Non-spore forming
- soil saprophytes but can cause chronic granulomatous infections in animals and man

Classification

- Family: Actinomycetaceae
- Based on the ability to grow aerobically or anaerobically
  1. **Anaerobic actinomycetes**
     - *Actinomyces*
     - *Bifidobacterium*
     - *Eubacterium*
  2. **Aerobic actinomycetes**
     - *Nocardia*
     - *Streptomyces*
     - *Actinomadura*

Actinomyces

- Anaerobic Gram-positive bacteria
- Branching filamentous rods
- Human commensal flora of the oropharynx, GIT, urogenital tract
- >30 species
- Cause **actinomycosis**- an infrequent invasive bacterial disease

Actinomyces species

A.israelii

A.meyeri

A.odontolyticus

A.neuii

A.radingae

A.viscosus

- *A. israelii* is an endogenous organism isolated from the mouths of healthy people
- However can cause suppurative infection in patients with tooth abscess or a tooth extraction

Pathogenesis

- The organisms have a low virulence potential
- Cause disease when the normal mucosal barriers are disrupted by trauma, surgery, or infection.
- Actinomycosis is characterized by;
  - multiple abscesses and granulomata,
  - tissue destruction,
  - formation of sinuses.

N/B Within diseased tissues, they form large masses of mycelia (sulfur granules)

Yellow sulfur granules

Clinical manifestations

1. **Cervicofacial actinomycosis**
   - Most frequent clinical form
   - The disease is endogenous in origin.
   - occurs mainly in cheek and submaxillary regions
   - Infection follows a tooth extractions or other dental procedures'
- Predisposing conditions
  - Poor oral hygiene
  - Oral mucosa trauma- Dental caries

- Initially xt by soft-tissue swelling of the perimandibular area (lumpy jaw)
- Followed by development of sinus tracts that discharge purulent material containing granules with a yellow sulfurlike appearance
- Invasion of the cranium or the bloodstream may occur if the disease is left untreated.

2. GUT actinomycosis

- 2nd most frequent clinical form
- Pelvic actinomycosis in women using an IUD

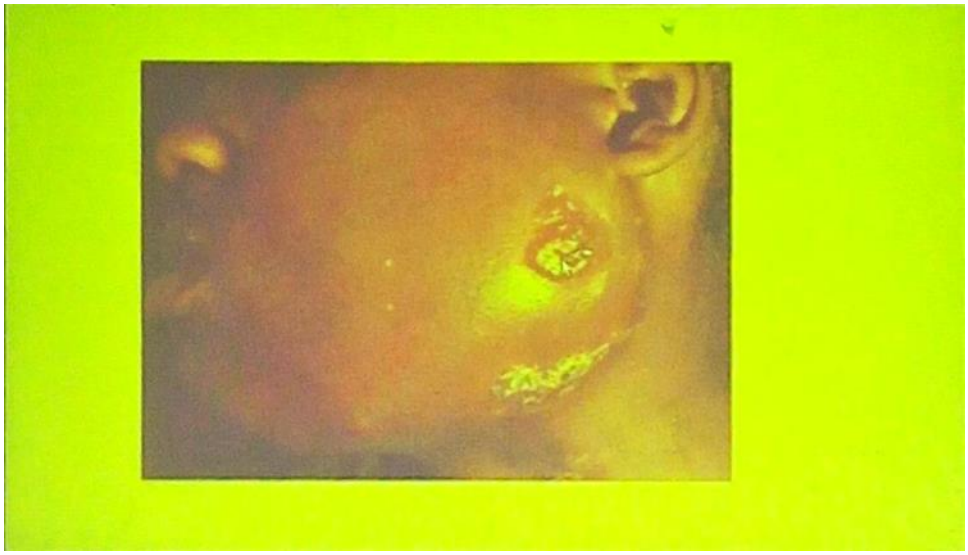
Presentation

- Genital mass +/- fever(fever not usually present unless peritonitis present)

3. Thoracic actinomycosis

- commences in the lung,
- usually secondary to aspiration of actinomyces from the mouth
- pneumonitis develops and spread outwards through the chest wall
- Pulmonary actinomycosis may disseminate hematogenously- brain abscess

4. Extrafacial bone and joint actinomycosis
5. GIT actinomycosis- A.israelii mostly involved
6. CNS actinomycosis- Brain abscess
    - haematogenously from the lungs
    - contiguously from cervicofacial actinomycosis
    - Following penetrating head injury



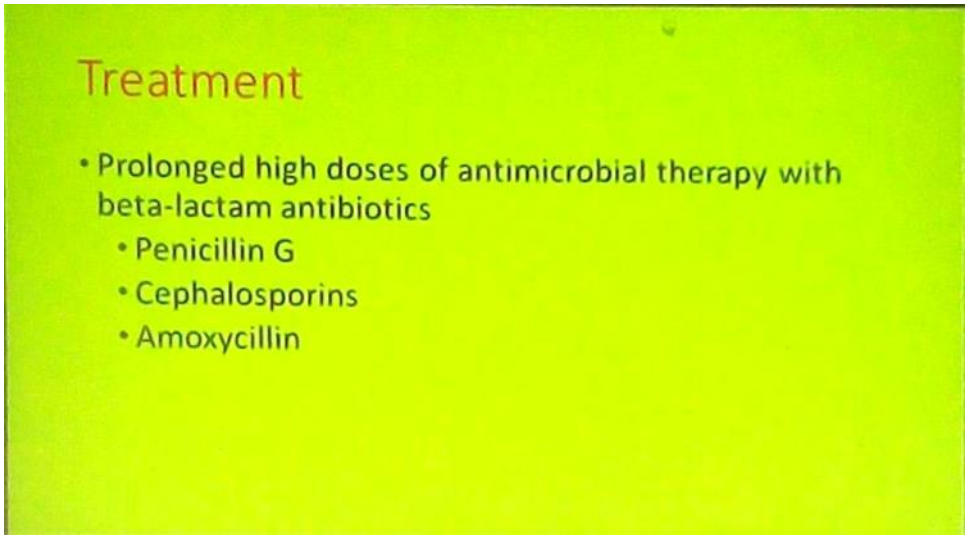
Laboratory diagnosis

- Specimen: abscess content, sinus discharge, bronchial secretions, biopsy material
- Culture: BA
  - Slow growing(produce growth on BA,CBA after 5-7 days-may take up to 15–20 days); incubation 35-37°C; **anaerobic conditions**
  - Colonies: small, cream or white, with a rough nodular surface
- Gram-stain- Gram-positive branching filametous rods except *A.meyeri* which is small and non-branching

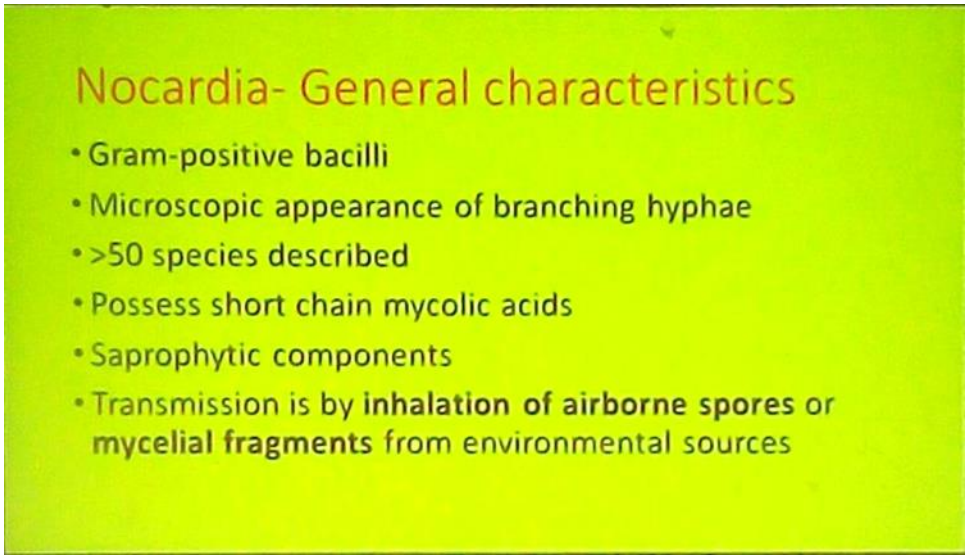
Branching diagram*

Other tests

- Serology
- PCR
- 16sRNA sequencing



AEROBIC ACTINOMYCETES



*first 4

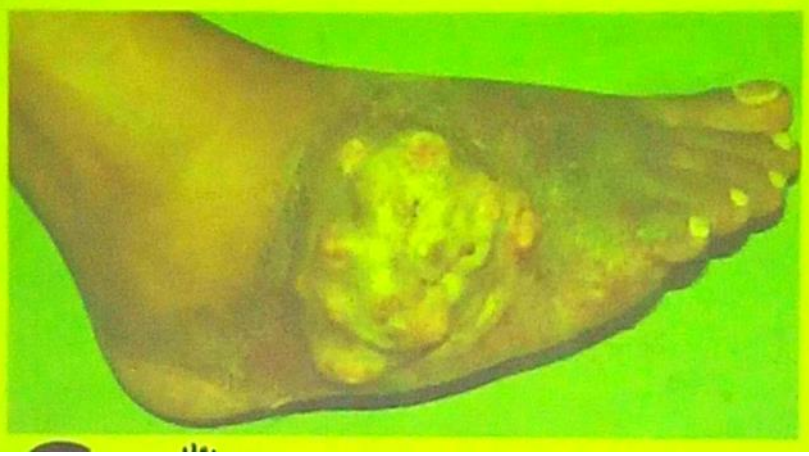
Clinical manifestations

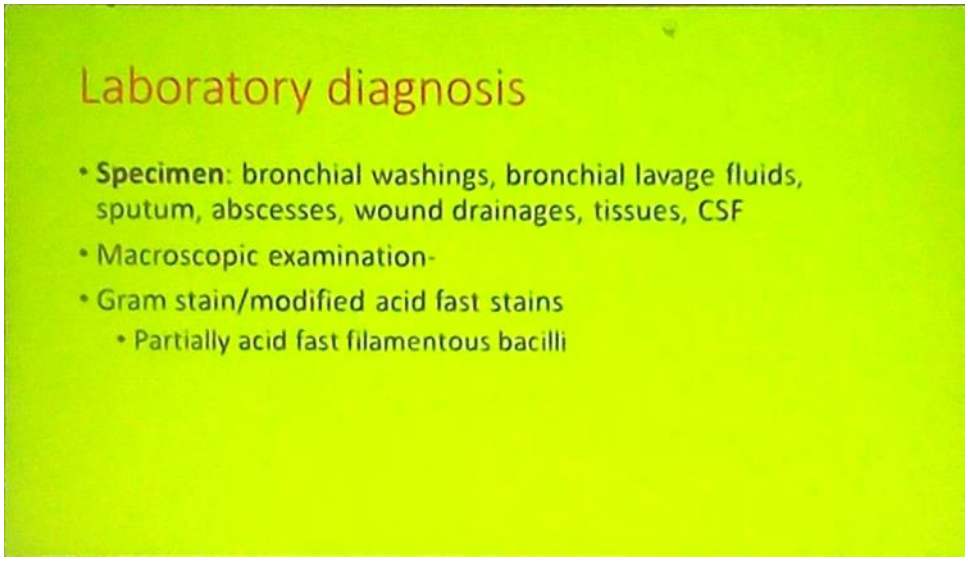
Predisposing factors

1. Underlying chronic lung disease e.g. COPD, asthma
2. Drug-induced systemic immunosuppression
3. Chronic granulomatous disease
4. Diabetes
5. HIV

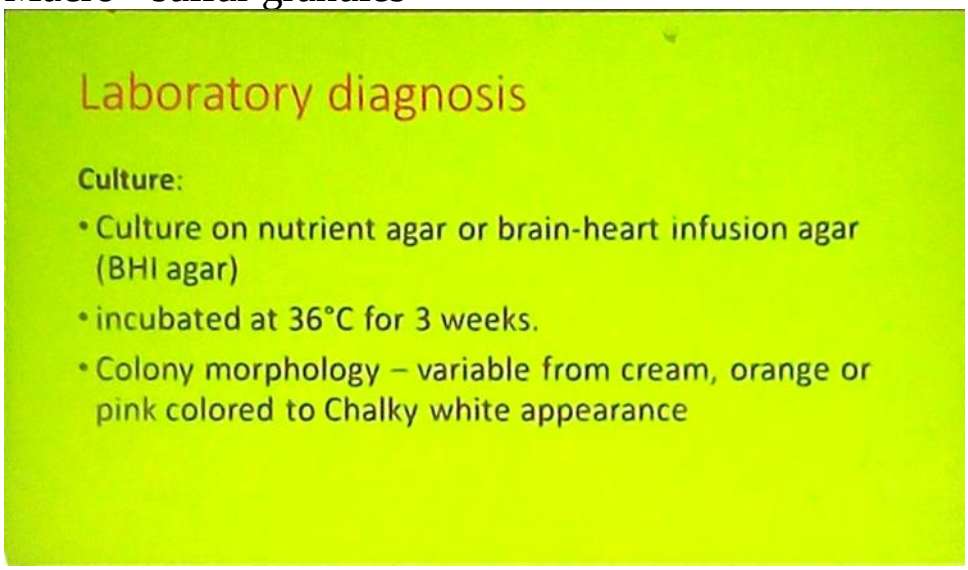
Clinical manifestations

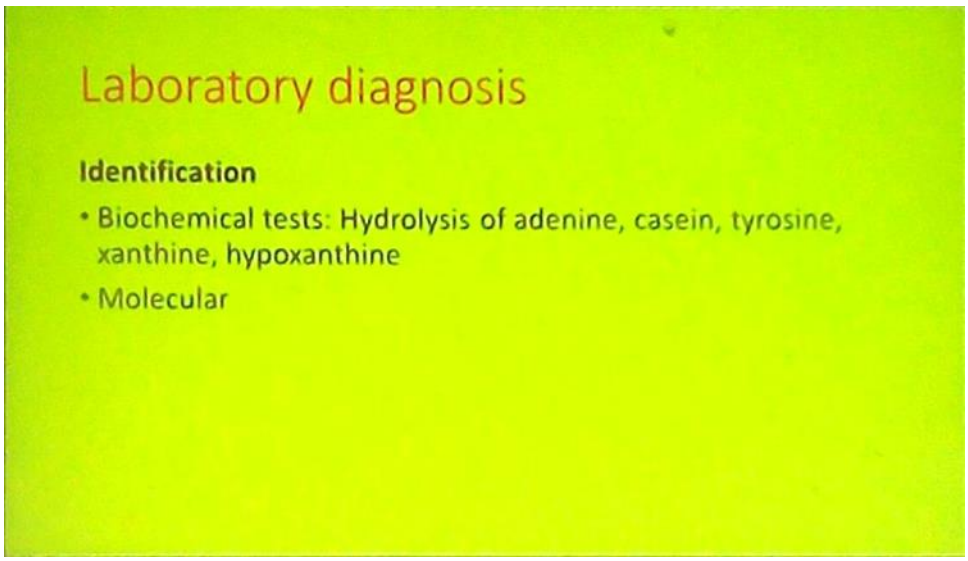
- Cutaneous Infection
  - mycetoma, lymphocutaneous infections, cellulitis, subcutaneous abscesses.
- Systemic nocardiosis
  - manifests primarily as pulmonary disease, pneumonia, lung abscess or other lesions resembling tuberculosis and endocarditis
  - occurs more often in immunodeficient persons.



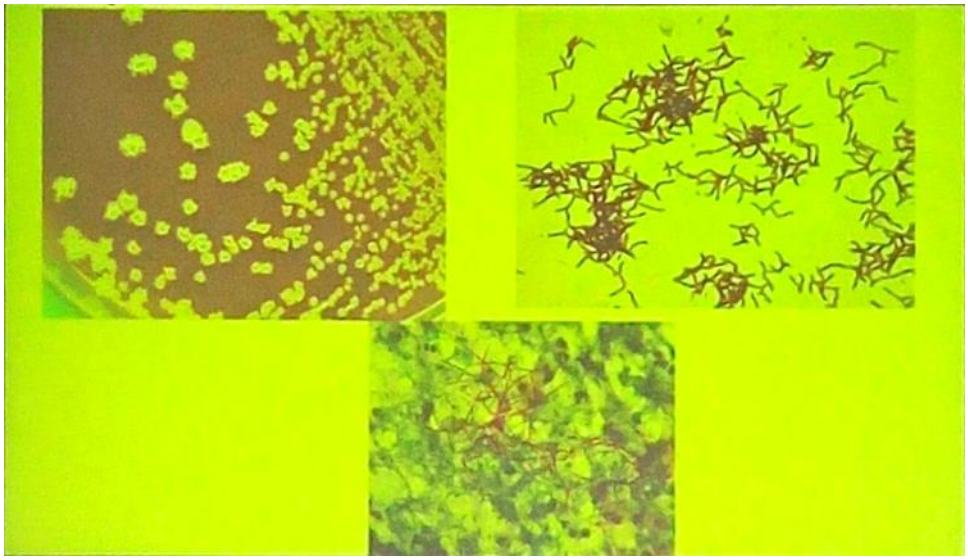


Macro - sulfur granules





PCR, 16s RNA Genetic Sequencing



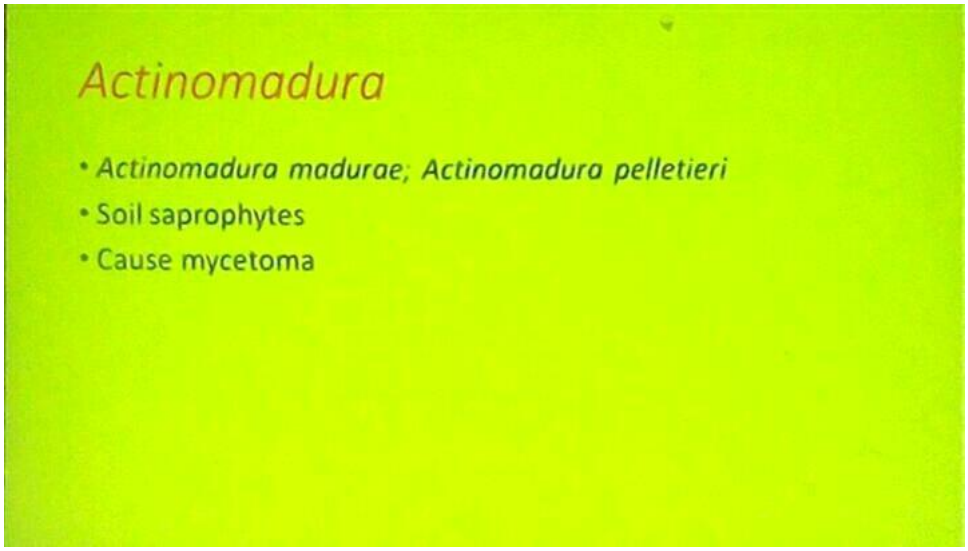
ZN stain- mycobacteria- no branching

Treatment

- Trimethoprim-Sulfamethoxazole
- Amikacin
- Ceftriaxone
- Imipenem
- Combination therapy in serious disease, CNS and dissemination

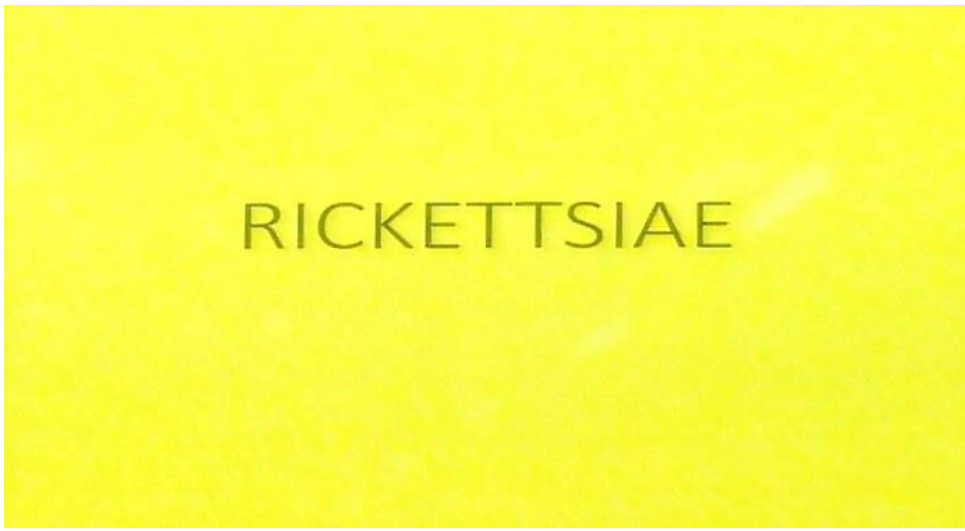
Streptomyces

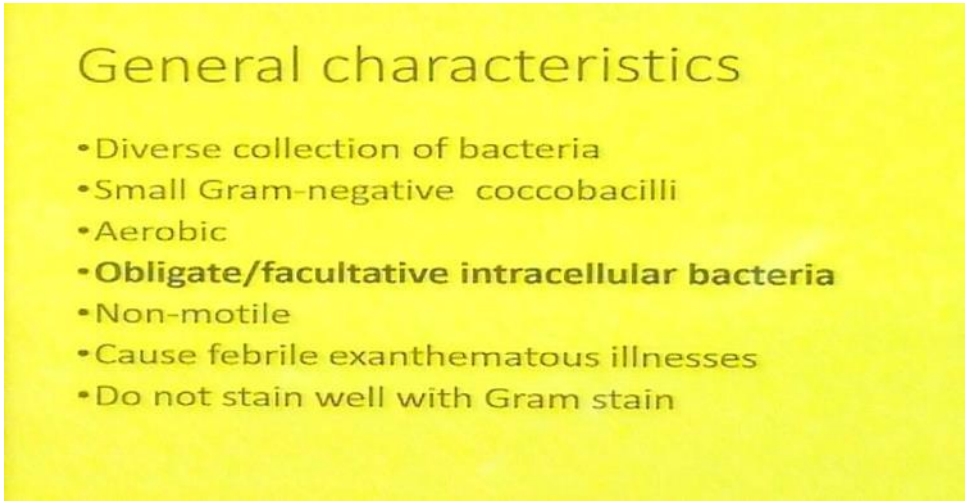
- *Streptomyces somaliensis*
- Saprophytic soil organisms
- Cause **mycetoma(actinomycetoma)**
- Few cases of invasive disease
  - Preexisting conditions: cancer, HIV, medical devices
- Diagnosis- requires microscopic and pathological correlation to rule out contamination

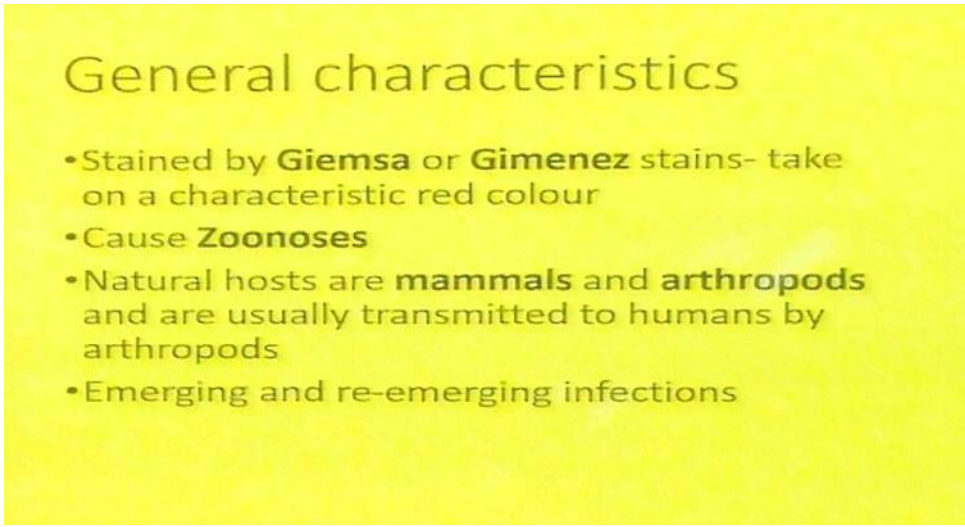

Actinomadura
• Actinomadura madurae; Actinomadura pelletieri
• Soil saprophytes
• Cause mycetoma

Rickettsiae

Thursday, August 16, 2018 11:06 AM







Genera

- Rickettsia
- Neorickettsia
- Orientia
- Ehrlichia
- Neoerlichia
- Anaplasma
- Coxiella
- *Bartonella

*Bartonella has been reclassified

Transmission

- Most transmitted by ectoparasites e.g **fleas, lice, mites, and ticks** during feeding
- Scratching **crushed** arthropods or infectious faeces into the **skin**
- **Inhaling** dust or **inoculating** conjunctiva with infectious material
- **Transfusion** or **organ transplantation** – rare but has been reported.

Epidemiology

- Widely distributed globally, in **endemic** foci,
- **Sporadic** and often **seasonal** outbreaks.
- All age groups at risk during **travel to endemic areas**
- Transmission increased during outdoor activities
- Infection can occur **throughout the year**
- **5- to 14-day** incubation period for most rickettsial diseases

Diseas pattern follows vector distribution

Rickettsia

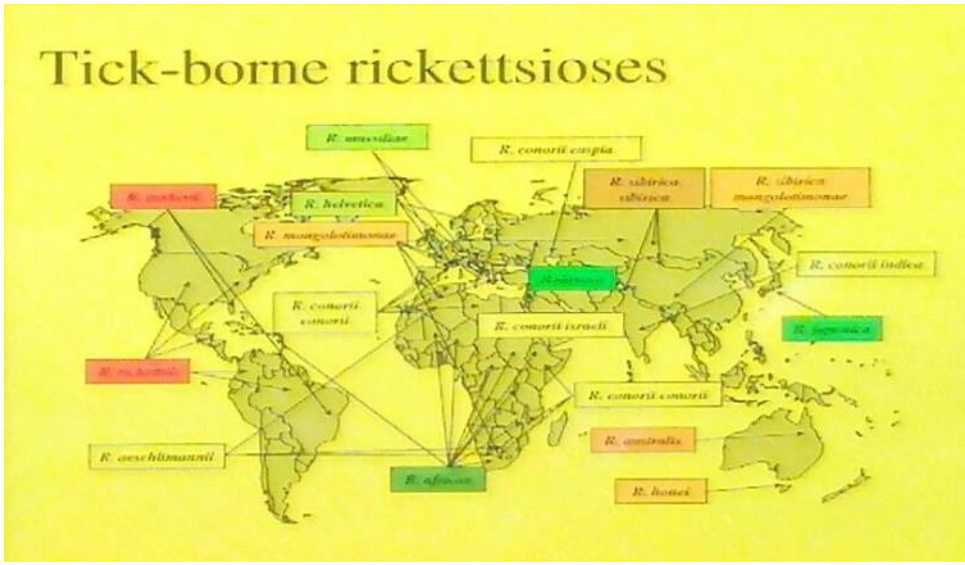
Classification

May be classified into

1. Spotted Fever Group(SFG) rickettsia
2. Typhus group(TG)rickettsia
3. *Rickettsia bellii* group
4. *Rickettsia canadensis* group

Spotted fever group

- Many species
- Transmitted by **Ixodid** ticks=Tick-borne rickettsioses
  - *R. africae*
  - *R. conori*
  - *R. rickettsii*
  - *R. akari*- mites
  - *R. felis*- flea



Spotted fever infections

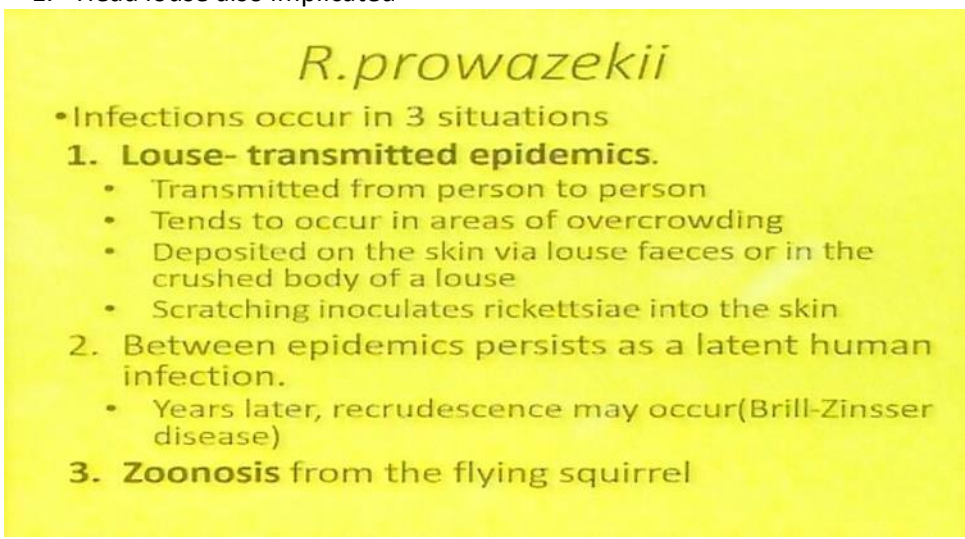
1. Rocky Mountain spotted fever(RMSF)
   - *R.rickettsii*
2. Mediterranean spotted fever or Bouteunneuse fever
   - *R.conorii*
3. African tick-bite fever(ATBF)
   - *R.africae*

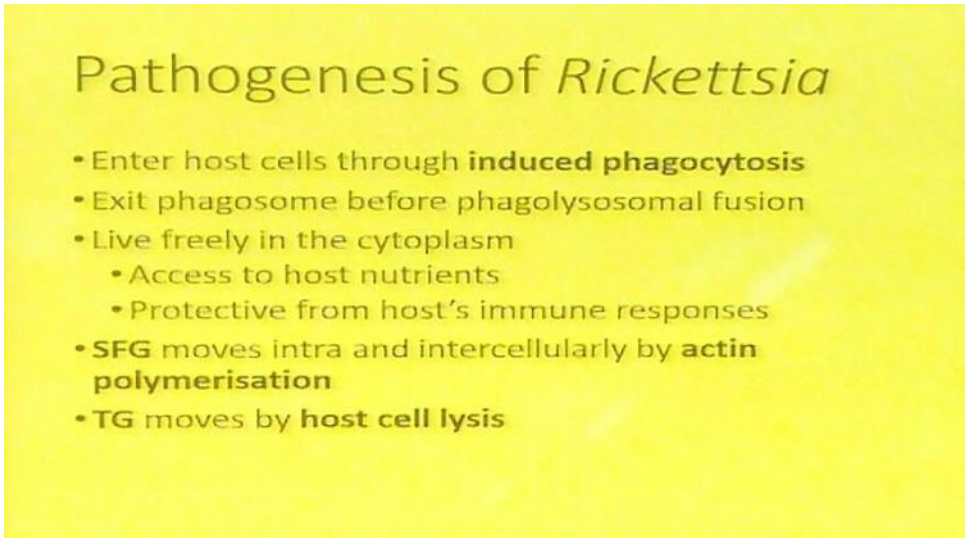
2. Also known as Kenya fever
3. Mostly isolated in tourists

Spotted fever infections

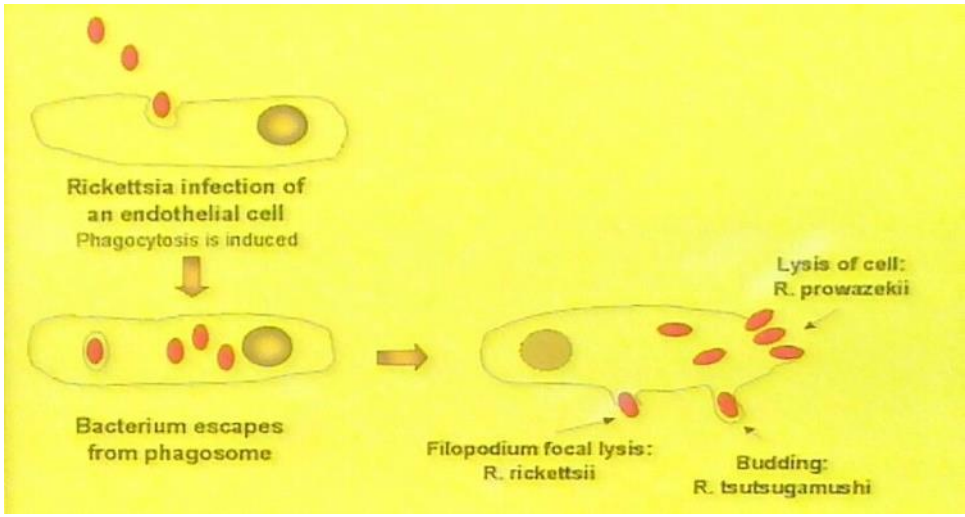
4. Rickettsialpox
   - *R. akari*
5. Cat flea rickettsiosis
   - *R. felis*
6. Tick-borne lymphadenopathy(TIBOLA), *Dermacentor-borne necrosis and lymphadenopathy(DEBONEL)*
   - *R.slovaka*

1. Head louse also implicated





SFG: spotted fever grp
TG: typhus grp



Clinical Manifestations

Spotted Fever

- Onset 2-4 days after infective bite
- Fever, severe headache, muscle pain and rash.
- Rash typically appears on ankles and wrists.
- Complications: partial paralysis of lower limbs; gangrene

Tissue tropism for small blood vessels

Clinical manifestations

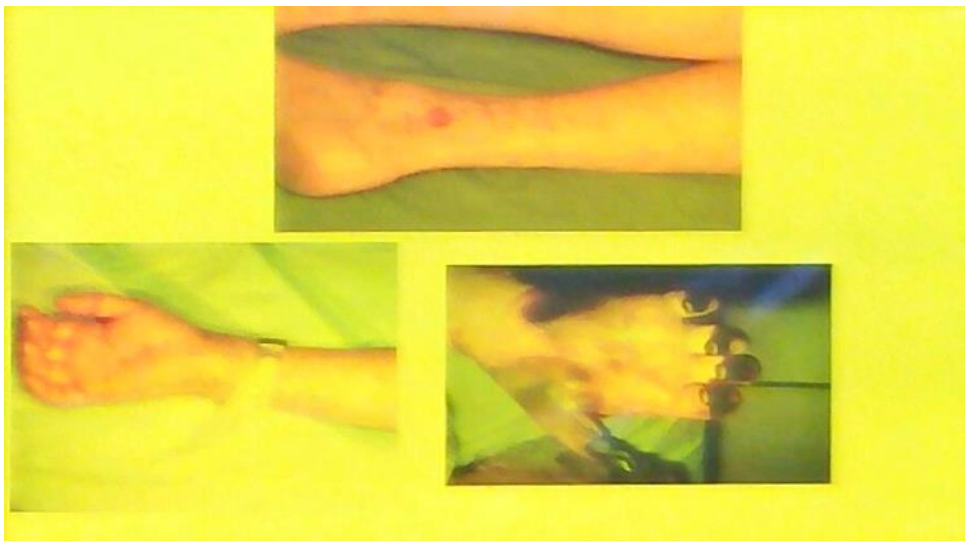
Typhus Fever

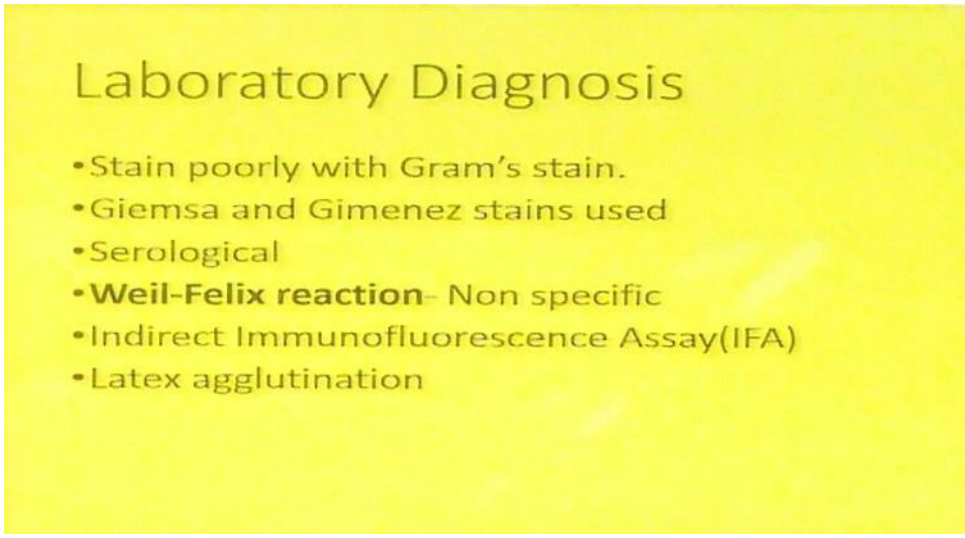
- Fever,
- Chills,
- Headache,
- Myalgia,
- Macules which appear on the trunk then to the extremities,
- Conjuctival injection
- Delirium

Clinical manifestations

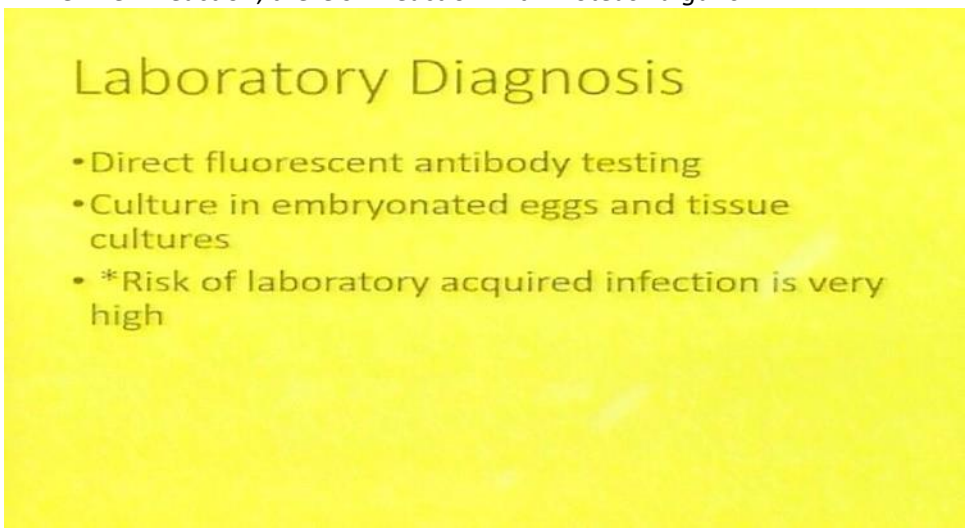
Murine typhus(endemic)

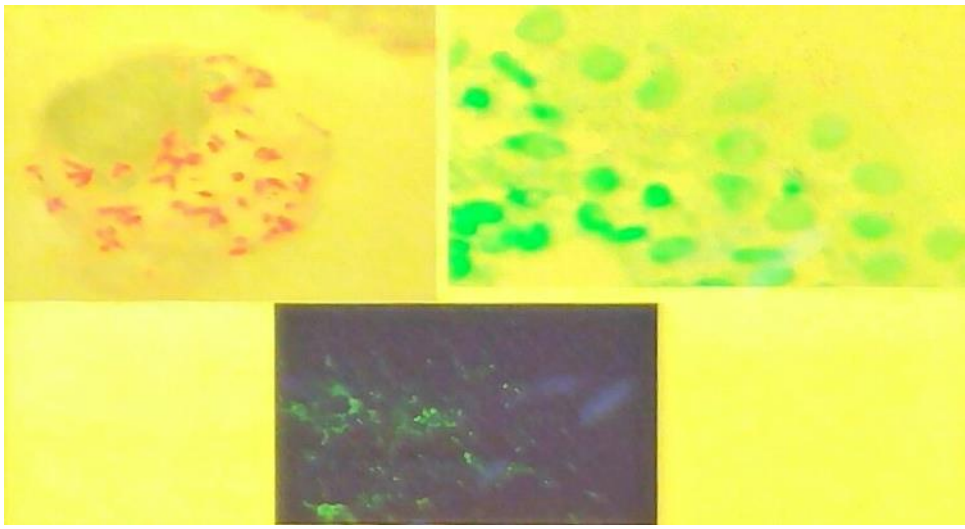
- Causes a milder form of fever
- Most infections being self limiting in chidren and young adults
- Pneumonitis
- Meningoencephalitis





In Weil-Felix reaction, there's X-reaction with *Proteus vulgaris*





Top right: geimsa showing intracellular pathogen
Top left: specimen from vector
Bottom: immuno

Treatment/Prevention/Control

- Doxycycline
- Chloramphenicol

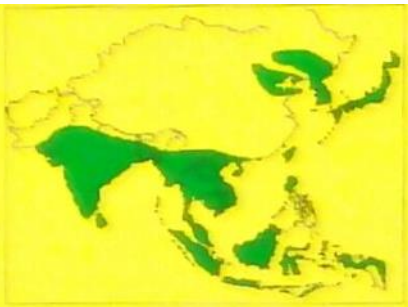
*Highly antimicrobial resistance

- Limiting exposure to
- Tick control: acaricides

ORIENTIA

Orientia tsutsugamushi

- Causes **scrub typhus,** an acute febrile illness
- Also known as tsutsugamushi disease
- Transmitted to humans by the bite of the larva of trombiculid mites(**chiggers**)
- Endemic to the "tsutsugamushi triangle".

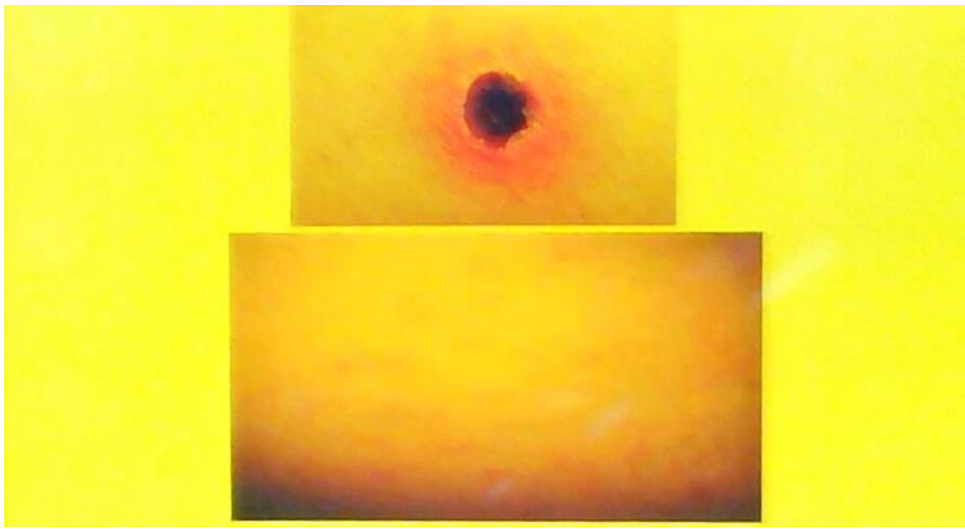


Clinical manifestations

- Illness varies from mild and self-limiting to fatal
- Incubation period of 6-21 days
- Fever, headache, myalgia, cough, and gastrointestinal symptoms
- Primary papular lesion → flat black eschar.
- Associated with regional and generalized lymphadenopathy

Clinical manifestations

- Symptoms gradually increase in severity
- A macular rash may appear on the trunk
- If untreated, meningoencephalitis develops
- Various cranial nerve deficits may occur



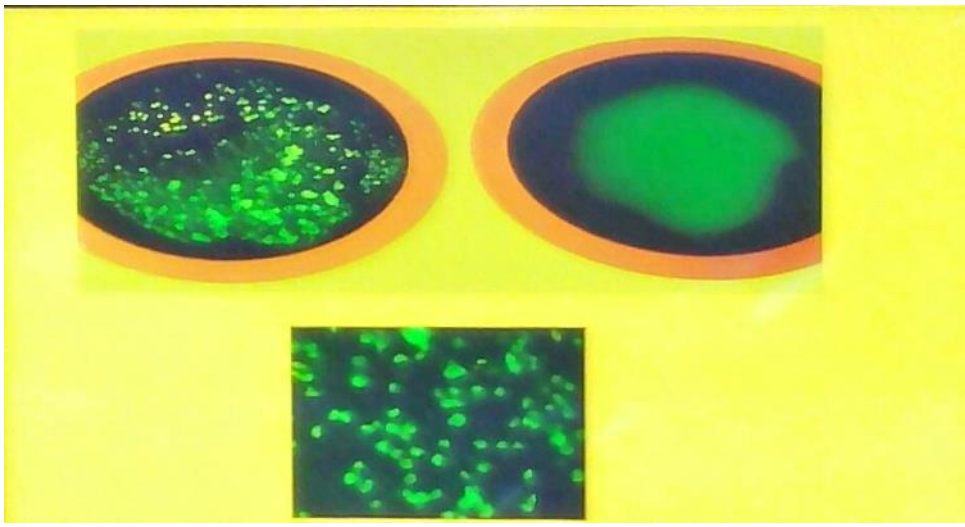
Top: black eschar

- Differential Dx: infection by aerobic gram-ve bacillus

Bottom: rash

Laboratory Diagnosis

Specimen: Skin or LN biopsy, blood, serum
- Serology e.g Weil-Felix agglutination test
- Complement-fixation test
- **IFA**- gold standard
- Indirect immunoperoxidase
- ELISA
- Rapid diagnostic tests
- Tissue culture
- PCR



Top right: +ve WF reaction, agglutination
Top left: -ve WF reaction
Bottom: +ve fluorescent

Treatment

- Doxycycline-DOC
- Chloramphenical
- Combination of Doxycycline and Rifampicin

*After infection there is non-sterile immunity

Prevention

- Protective clothing
- Insect repellants
- Avoid sitting or lying on bare ground or grass
- Clearing of vegetation and chemical treatment of soil

Control

- Case identification
- Public education
- Rodent control

Ehrlichia and Anaplasma

- *Anaplasma phagocytophilum*
- *Ehrlichia chaffeensis*
- *Ehrlichia ewingii*
- *Ehrlichia canis*
- Cause acute febrile tick-borne diseases

Ehrlichia and Anaplasma

1. Human monocytotropic ehrlichiosis (HME)
   - *Ehrlichia chaffeensis*
   - Primary vector is the Lone Star tick (*Amblyomma americanum)*
2. Human granulocytotropic anaplasmosis (HGA)
   - *Anaplasma phagocytophilum*
   - Transmitted by *Ixodes scapularis,*

General characteristics

- Exist intracellularly in two morphologically distinct forms
  - dense-cored cells (DC) and reticulate cells (RC)
- Lack important cell membrane components including LPS and peptidoglycan
- HME and HGA have similar clinical presentations
- fever,
- Headache
- leukopenia

Clinical manifestation

- HME more severe than HGA
- Fever, headache, myalgia, arthralgia,
- Skin eruptions
- Nausea, vomiting, abdominal pain,
- Cough
- GI symptoms

Diagnosis/Treatment/Prevention

Diagnosis
- Clinical suspicion
- Serology
- PCR

Treatment
- Tetracycline
- Doxycycline
- Rifampin

Prevention
- Avoid tick bites

Neorickettsia and Neoehrlichia

Neorickettsia

- Obligate intracellular bacteria
- *N.sennestu*
- Infect trematodes that parasitize fish
- Transmission to humans- eating raw fish
- In humans, infect mononuclear phagocytes
- Doxycycline

Neoehrlichiosis

- Candidatus *Neoehrlichia mikurensis*
- Emerging tick-borne pathogen
- Causes a systemic inflammatory syndrome
- Mostly in persons with underlying haematologic or autoimmune diseases.
- Transmitted by hard ticks (*Ixodes*)
- Closely associated with rodents in which transplacental transmission occurs

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- Candidatus *Neoehrlichia mikurensis*
- Emerging tick-borne pathogen
- Causes a systemic inflammatory syndrome
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- Closely associated with rodents in which transplacental transmission occurs

Coxiella

Coxiella burnetii

- Order: Legionellales
- Family: Coxiellaceae
- Genus: *Coxiella*
- Small, Pleomorphic, Gram negative coccobacilli
- Stain poorly with Gram's stain- Giemsa and Gimenez stains used

Coxiella burnetti

- Obligate intracellular bacteria that live inside acidic lysosomes
- Causes Q- fever
- 2 morphologic variants:
  1. **Small cell variant**(SCV) spore-like and can survive harsh environmental conditions
  2. **Large cell variant**(LCV) multiplies in the host monocytes and macrophages

Q-querry; previously, the cause not known

Epidemiology

- Various hosts:
  - mammals, birds, numerous different genera of ticks.
  - Farm animals are the primary reservoirs for human disease
- Excreted in urine, milk, faeces, and birth products
- Birth products containing high numbers of bacteria

Epidemiology

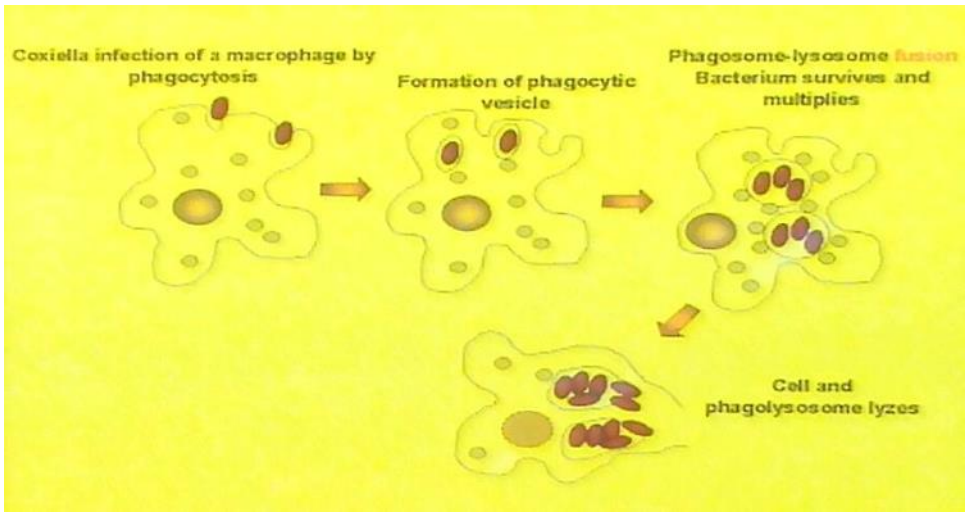
- Human infection occurs after
  - Inhalation or skin contact
  - Exposure to placenta of an infected woman
  - Blood transfusion.
- Due to its high infectivity and low infective dose, has been classified as an agent of bioterrorism

Pathogenesis

- **Attaches** to host macrophages using ankyrin
- **Passive** entry into the phagosome,
- **Delays fusion** of the phagosome with lysosomes to transform from SCV to LCV
- **Intracellular multiplication** is initialised in the phagolysosome
- **Proliferation** of organisms within phagolysosome
- **Rupture** of the host cell

Pathogenesis

- Infected macrophages transported systematically
- Reticuloendothelial system(liver, spleen, bone marrow) most heavily infected



Passive phagocytosis

Clinical Manifestations

- Can be acute or chronic

Acute disease:

- Long incubation period- average 20 days
- Sudden onset of severe headache, high fever, chills, myalgia.
- Respiratory symptoms are generally mild
- Hepatosplenomegaly present in ≃ half of cases

Clinical Manifestations

Chronic disease:

- Most common presentation is **infective endocarditis,** generally on a prosthetic or previously damaged heart valve

Laboratory Diagnosis

- Serology- most commonly used diagnostic test
  - Microagglutination test
  - Complement fixation test
  - Indirect immunofluorescent –antibody(IFA) test
    - Test of choice
  - Enzyme-linked immunosorbent assay(ELISA)
- Tissue culture
- PCR

Treatment

Treatment

- Acute infections:
  - Tetracyclines e.g doxycycline
- Chronic infections:
  - Treated for a prolonged period with a bactericidal combination of drugs e.g. Rifampin and either doxycycline or sulphamethoxazole-trimethoprim

Bartonella

General characteristics

- Facultative intracellular pathogens
- Infections with *Bartonella* are ubiquitous among mammals,
- Many species can infect humans either as their natural host or incidentally as zoonotic pathogens.

Bartonella

- ***Bartonella bacilliformis***:
  - Oroya fever, verruga peruana=Carrion's disease
  - Transmitted by phlebotomine sand flies.
- ***Bartonella henselae***
  - Cat scratch disease(CSD) and peliosis of the liver(bacillary peliosis)
- ***Bartonella quintana***
  - Trench fever
- Both *Bartonella henselae* and *Bartonella quintana*
  - Bacillary angiomatosis

Clinical manifestations

Bartonella bacilliformis

Oroya fever

- More common in children (>60% of cases)
- Acute bacteremia 60 days after bite of an infected sand fly.
- Colonizes the entire circulatory system
- Nearly every erythrocyte is infected

Clinical manifestations

- Severe reduction in hematocrit (>80% destruction)
  - Pallor
  - fever
  - anorexia
  - malaise
  - cardiac murmur
  - myalgia
  - headache
  - jaundice
  - tachycardia, and hepatomegaly

Clinical manifestations

- Complications:
  - high mortality in pregnant women and their unborn children,
  - cardiovascular and neurological problems, respiratory infections, and arthralgia
- Fatal in 40%–88% without antimicrobial intervention
- Secondary infections:
  - salmonellosis, toxoplasmosis, malaria, shigellosis, histoplasmosis

Clinical manifestations

Verruga peruana (VP)

- Blood-filled nodular hemangiomas of the skin=VP or Peruvian warts
- Occur on the head and extremities
- Persist for several weeks to months

Hemangioma pic

Clinical manifestations

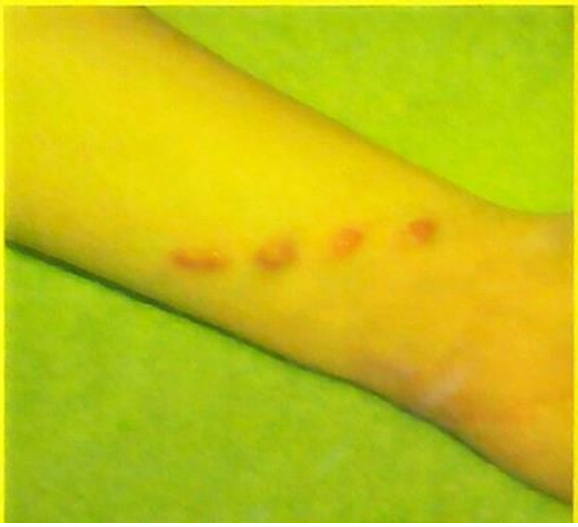
Bartonella quintana

- Trench fever, chronic bacteraemia, endocarditis
- Spread by *Pediculus humanus corporis*
- Trench fever- 1-3 days fever, recover every 4-6 days

Clinical manifestations

Bartonella henselae

- CSD
- Transmitted through the scratch or bite of infected cat
- Clinical manifestations
  - Inflammatory lymphadenopathy
  - Papular lesion of the skin which develops at the site of the injury



Laboratory diagnosis

- Special staining techniques
- Culture in enriched BA, prolonged incubation(1-6weeks) in a humid(37°C) atmosphere supplemented with CO_2
- Serology: IF, EIA, Western blot
- PCR

Treatment

- Tetracyclines,
- Macrolides,
- Aminoglycosides,
- Chloramphenical
- Control difficult: cats that transmit CSD are usually not sick

Practical

Wednesday, August 29, 2018 10:25 AM

Mycobacteria

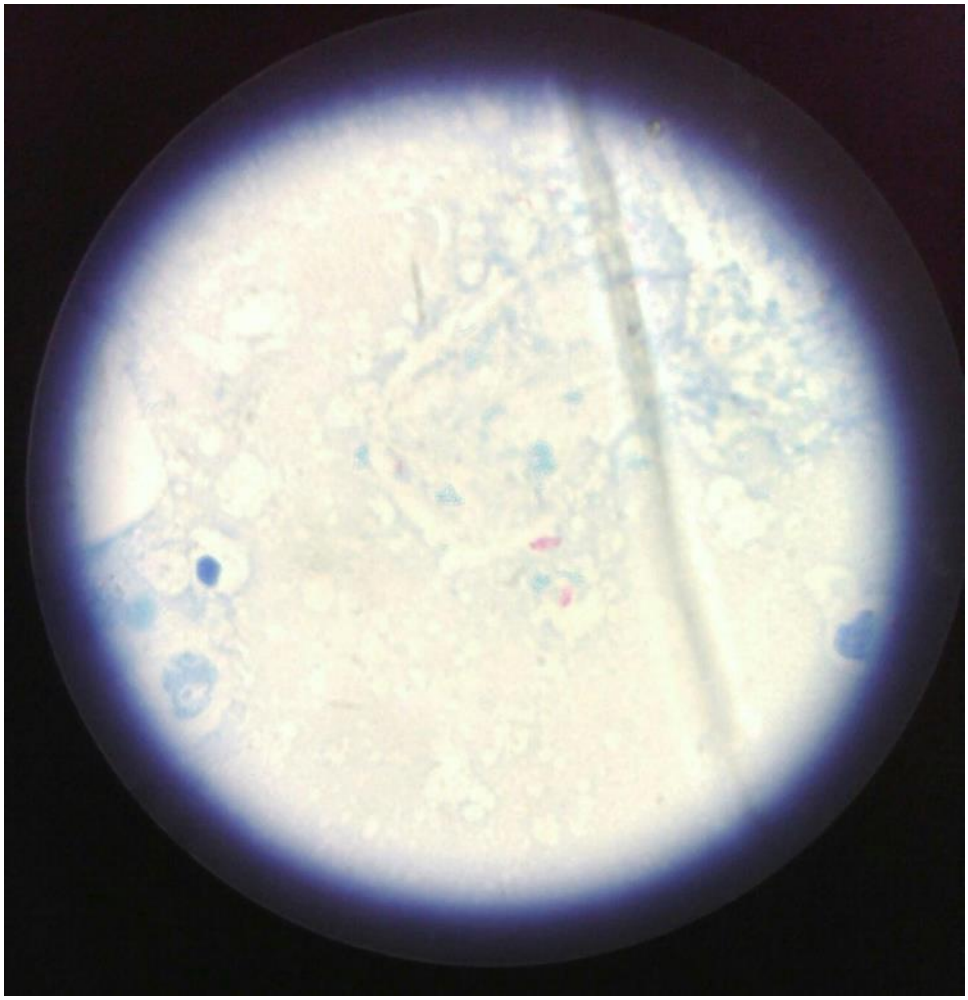
-ZN stain components:

- Carbol fuschin
- 3% acid alcohol for decolorisation
- 100ml methylene blue / malachite blue for counter staining

-4% NaOH for decontamination phenol

-L-J medium

-other selective media



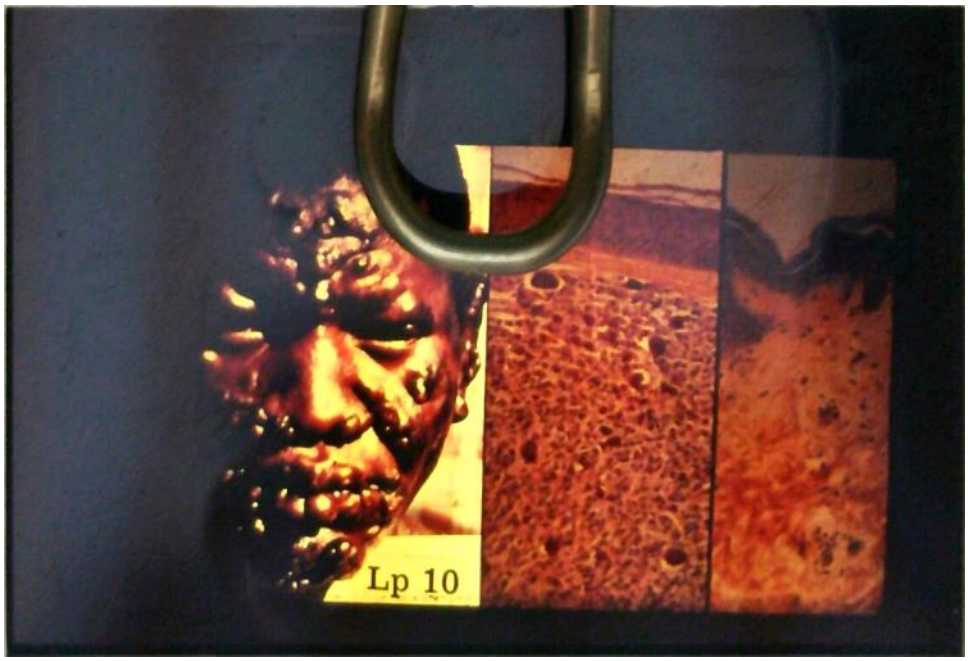
brigh red M.TB

MYCOBACTERIA 1

TROPHIC ULCER ON THE HAND OF A PATIENT

WITH TUBERCULOID LEPROSY.

-WHAT IS THE CAUSE OF THIS ULCERATION?



MYCOBACTERIA 2

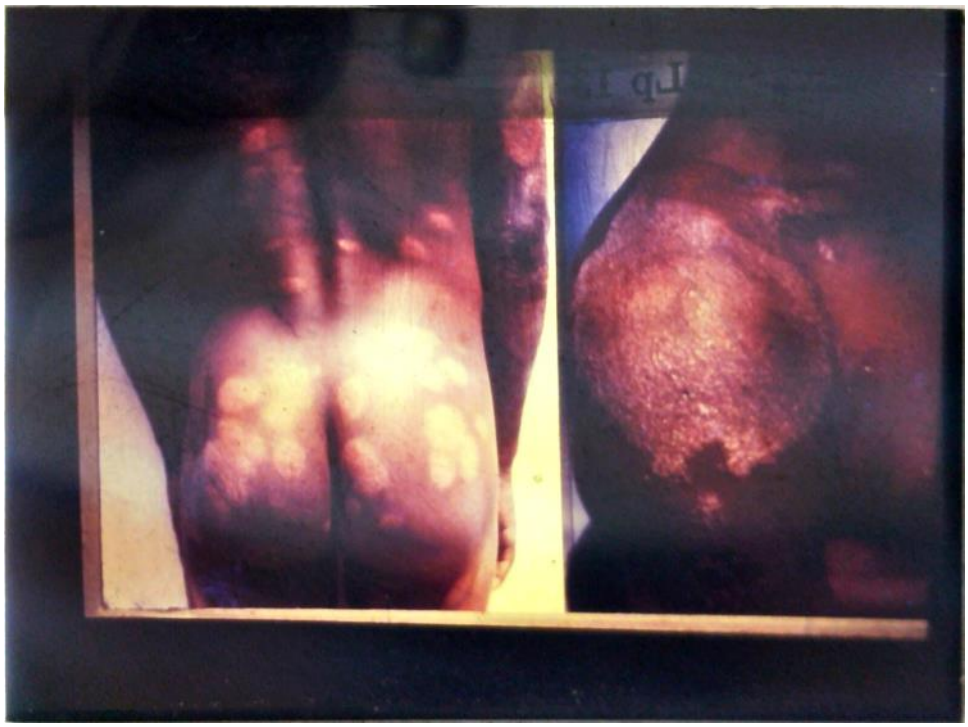
LEPROMATOUS LEPROSY

NOTE THE DESTRUCTIVE NODULES ON THE

FACIAL STUCTURES.

- LIST THE DIFFERENCES BETWEEN

LEPROMATOUS AND TUBERCULOID LEPROSY.

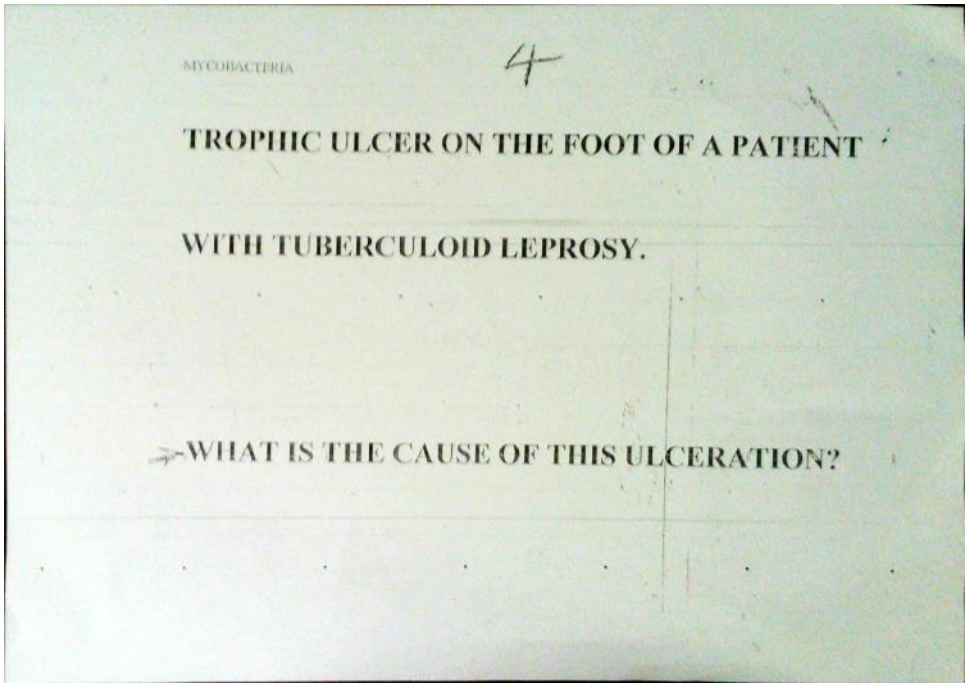


3

TUBERCULOID LEPROSY

NOTE THE DEPIGMENTED PATCHES.

WHAT ARE THE POSSIBLE COMPLICATIONS OF THIS FORM OF LEPROSY?



MYCOBACTERIA

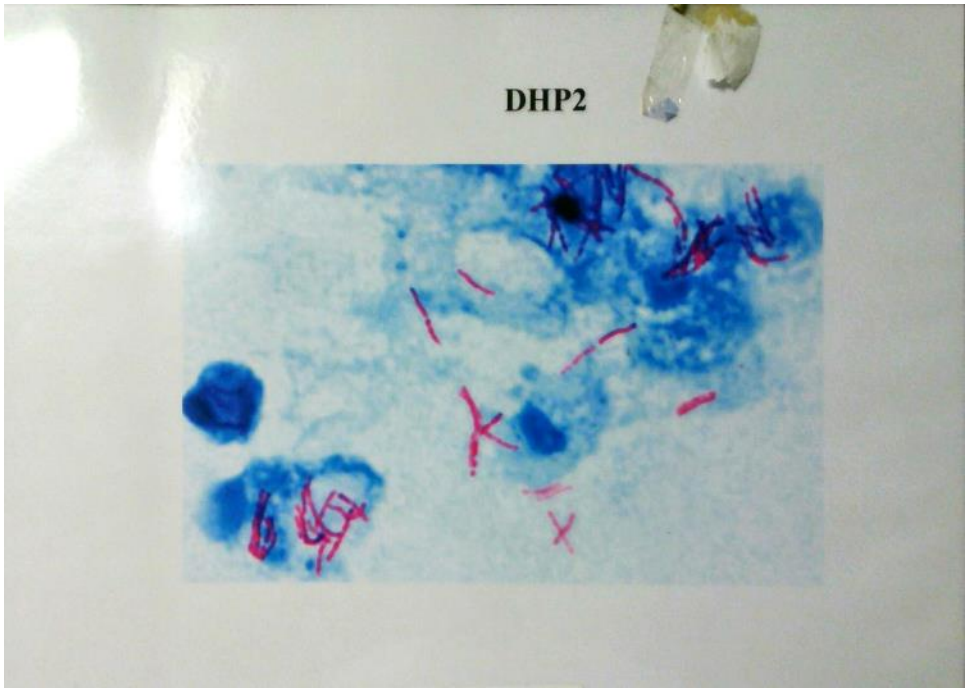
4

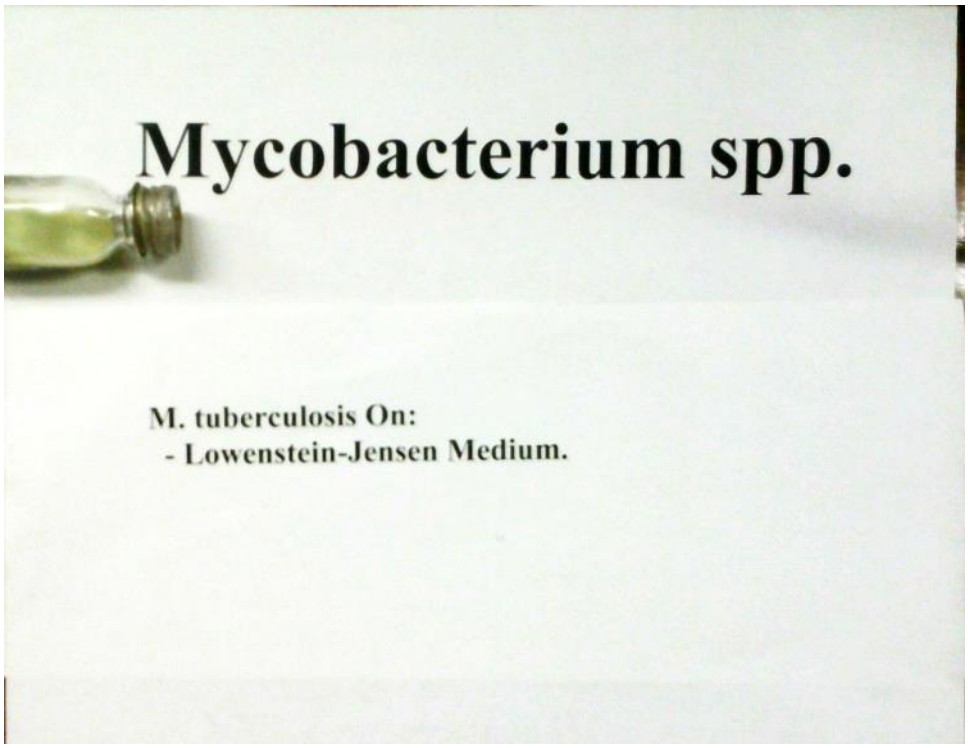
TROPHIC ULCER ON THE FOOT OF A PATIENT WITH TUBERCULOID LEPROSY.

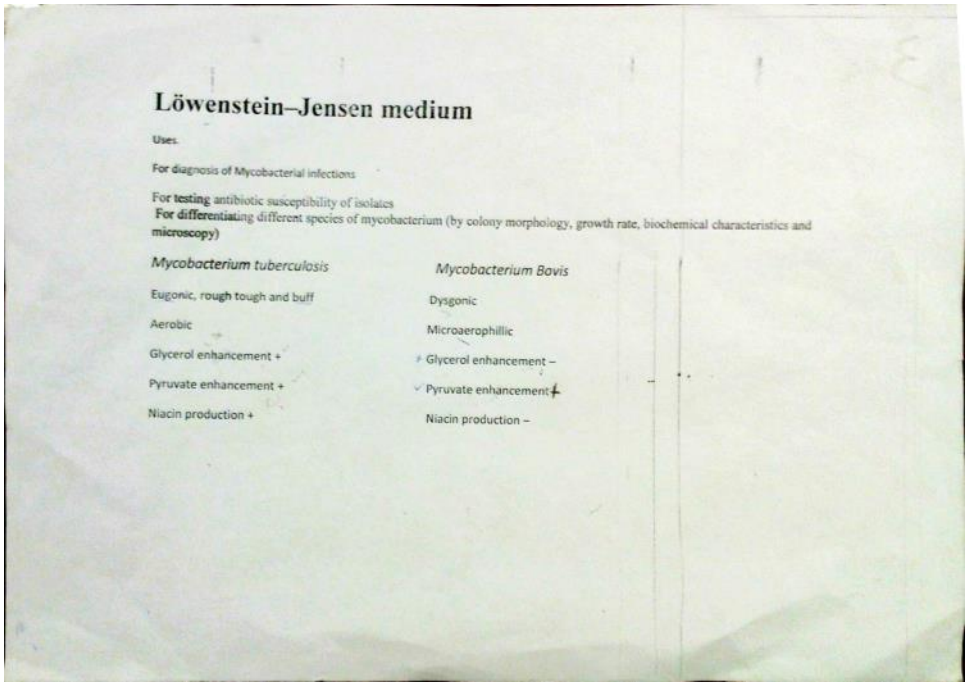
WHAT IS THE CAUSE OF THIS ULCERATION?

Ziehl–Neelsen stain

Mycobacterium tuberculosis




Mycobacterium spp.
M. tuberculosis On:
- Lowenstein-Jensen Medium.



Löwenstein–Jensen medium

Uses.

For diagnosis of Mycobacterial infections

For testing antibiotic susceptibility of isolates

For differentiating different species of mycobacterium (by colony morphology, growth rate, biochemical characteristics and microscopy)

Mycobacterium tuberculosis	*Mycobacterium Bovis*
Eugonic, rough tough and buff	Dysgonic
Aerobic	Microaerophillic
Glycerol enhancement +	Glycerol enhancement –
Pyruvate enhancement +	Pyruvate enhancement +
Niacin production +	Niacin production –

Spirochetes

-hard to grow, serological testing used more often
-T.palidum
-Treponemal test: confirmatory
-Non Treponemal test: for diagnosis eg RPR

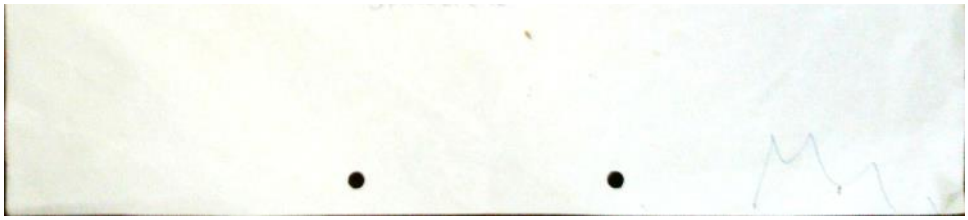
- Flocculation where positive
- No flocculation where negative
- Mononucleosis and Malaria Give positive results

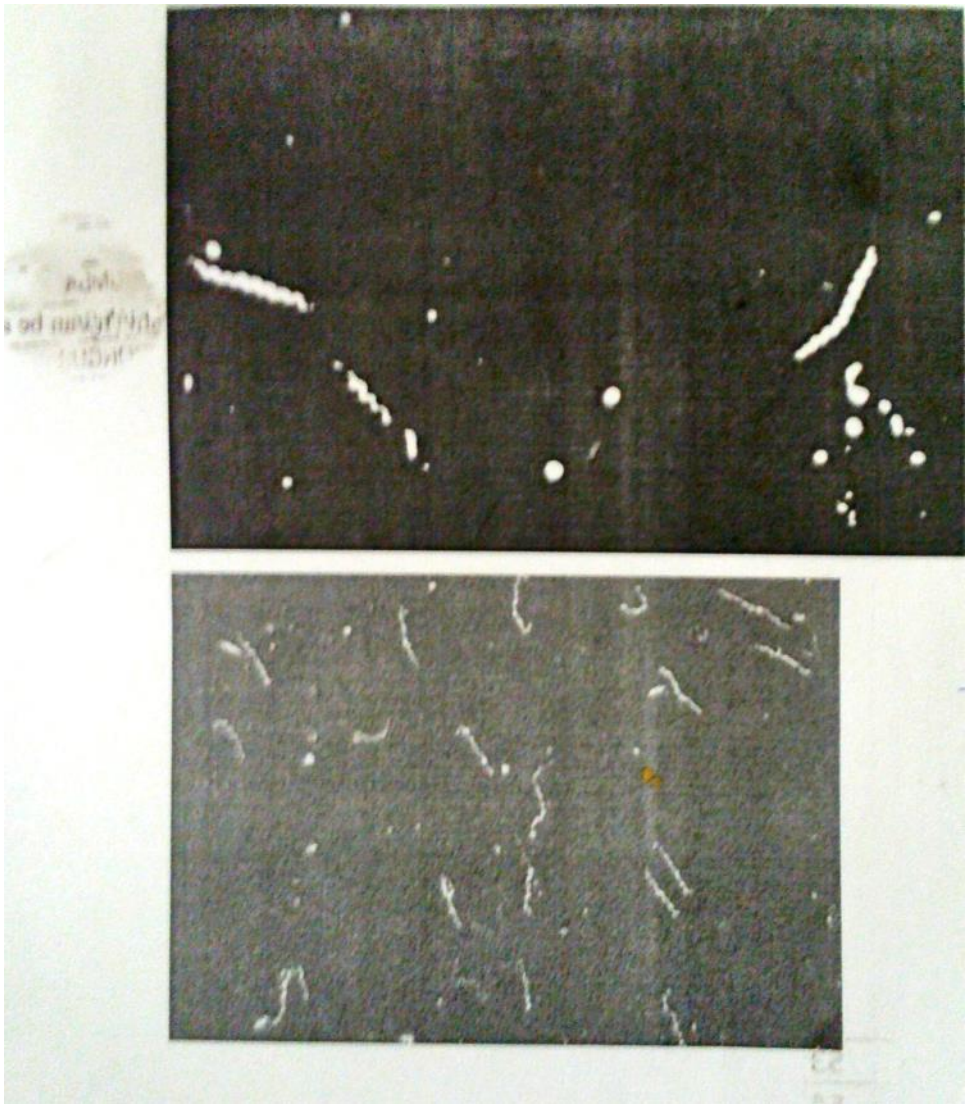
-Treponemal/Specific tests: TPHA

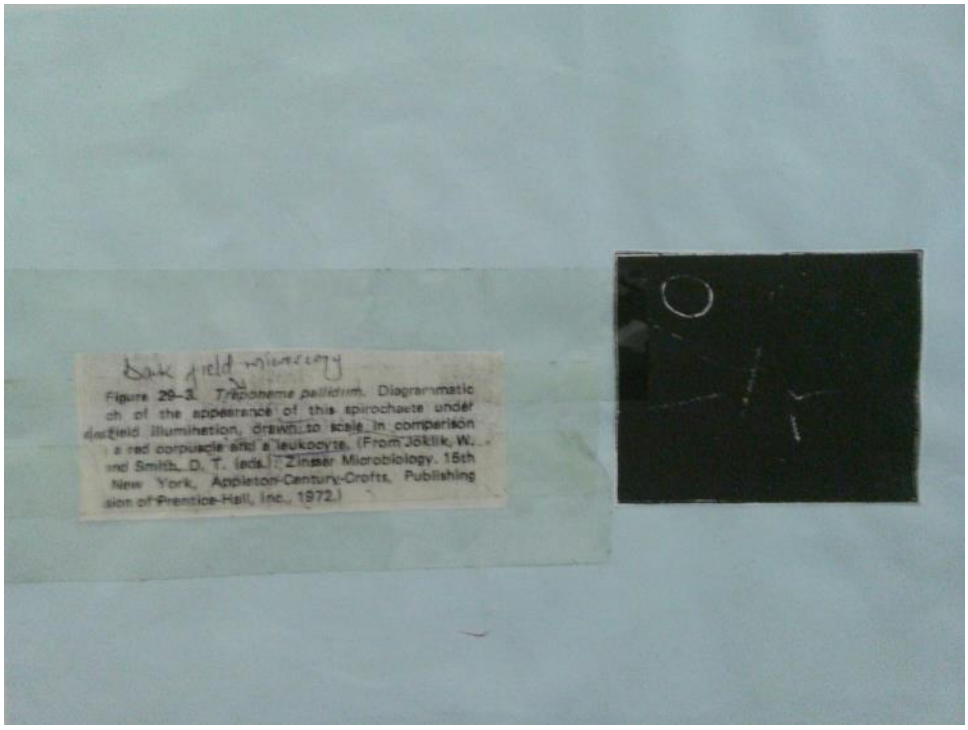
- antigens attached to sheep/rabbit milk
- Hemaglutination if positive
- Tight malt at the bottom of the well if negative

NB: the two bacteria that cause chancre

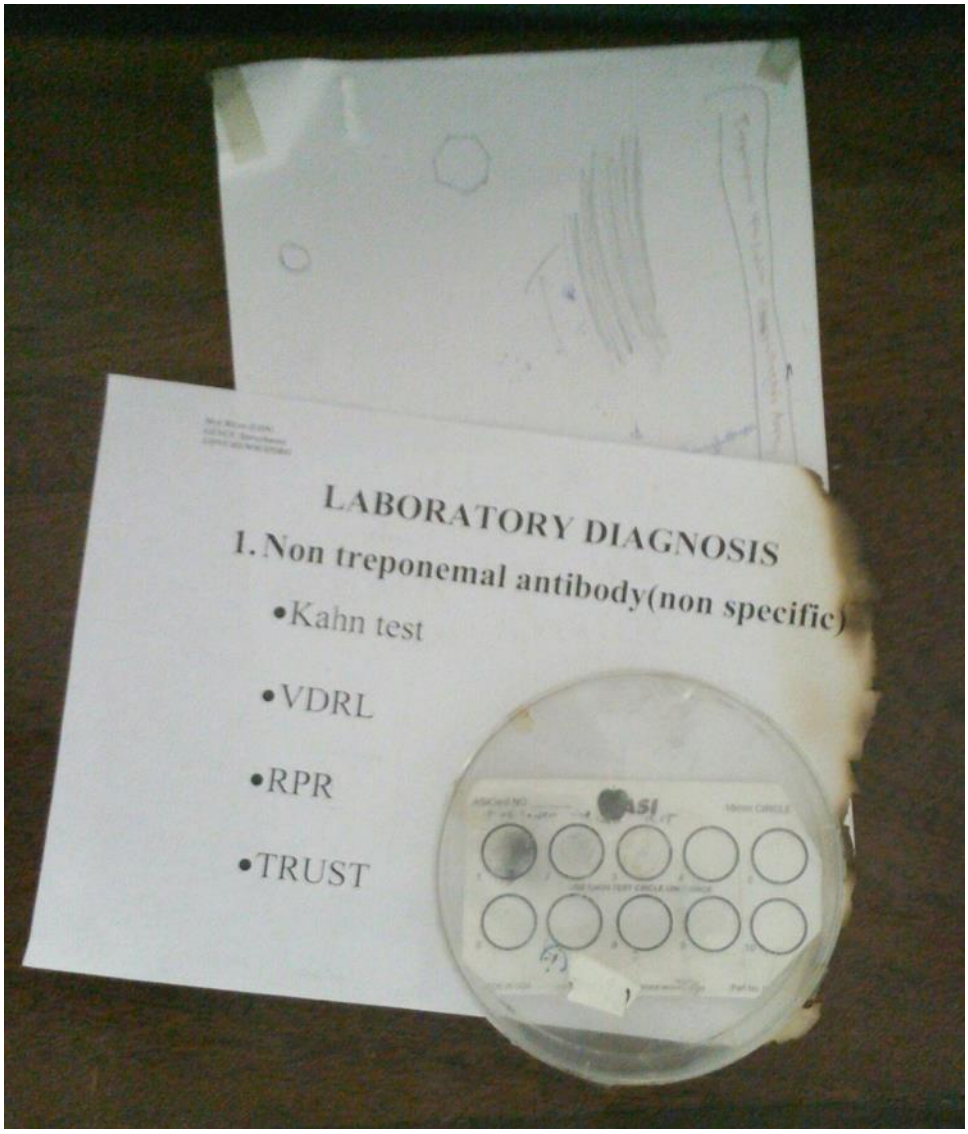
1. H.ducreyi
2. T.palidum

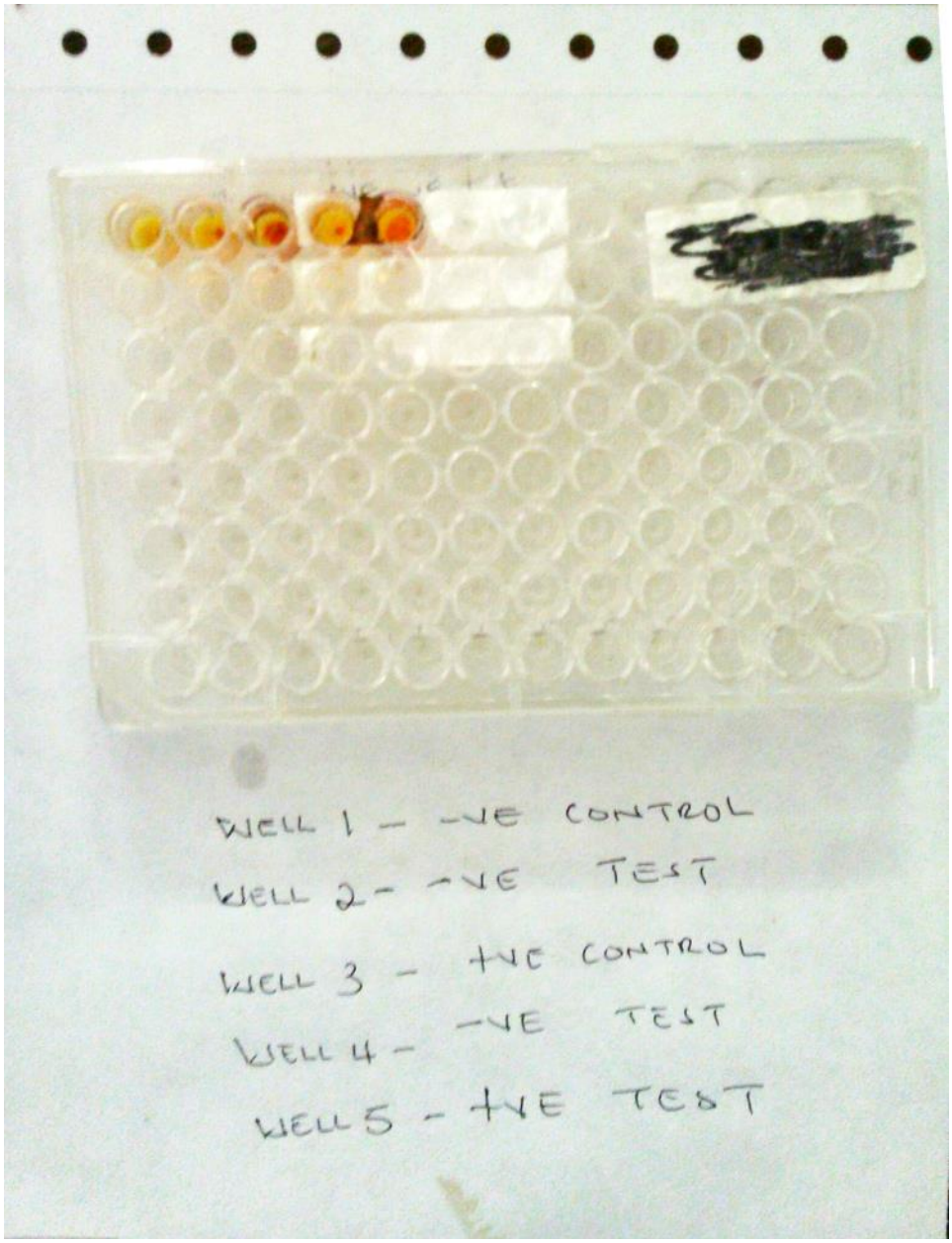


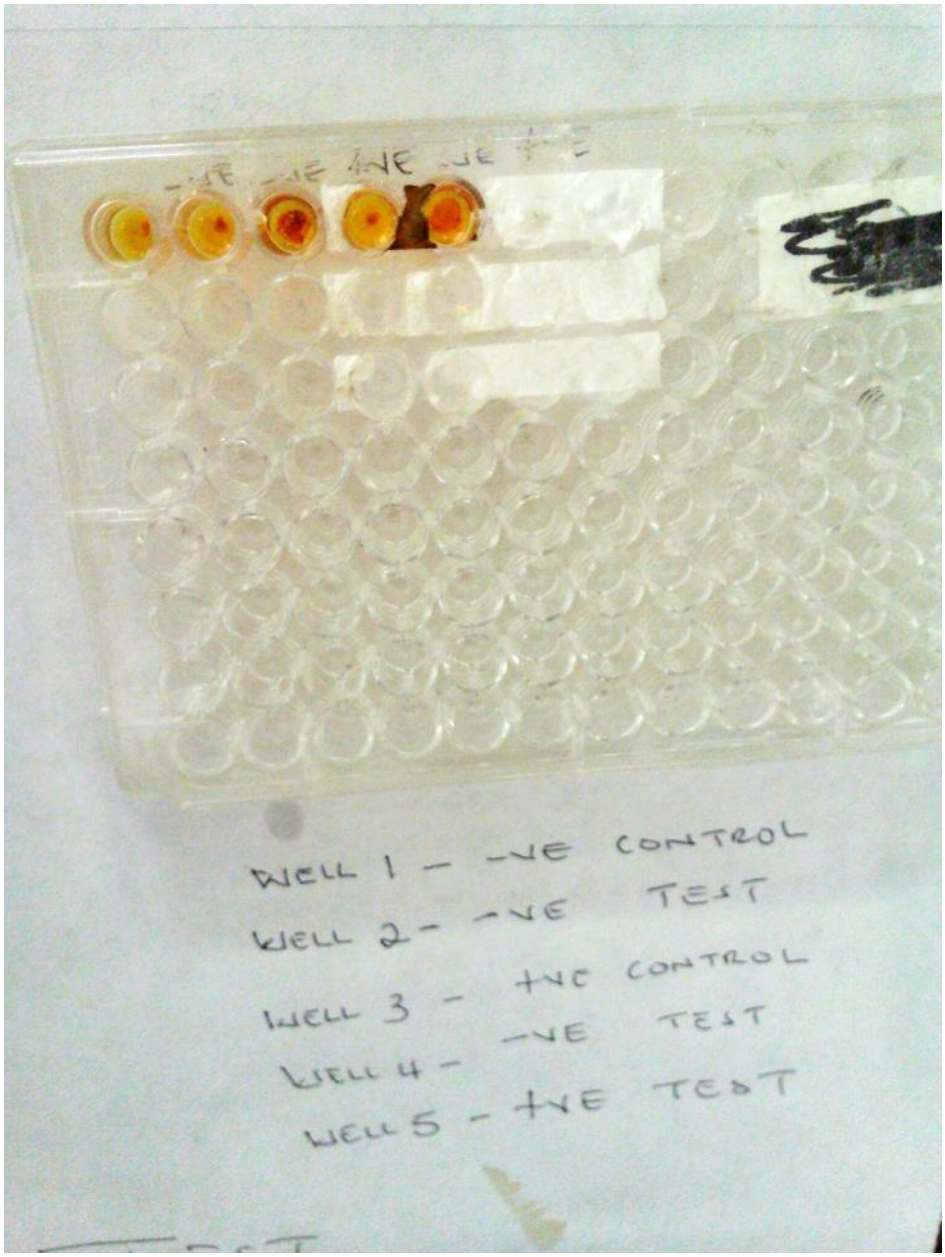


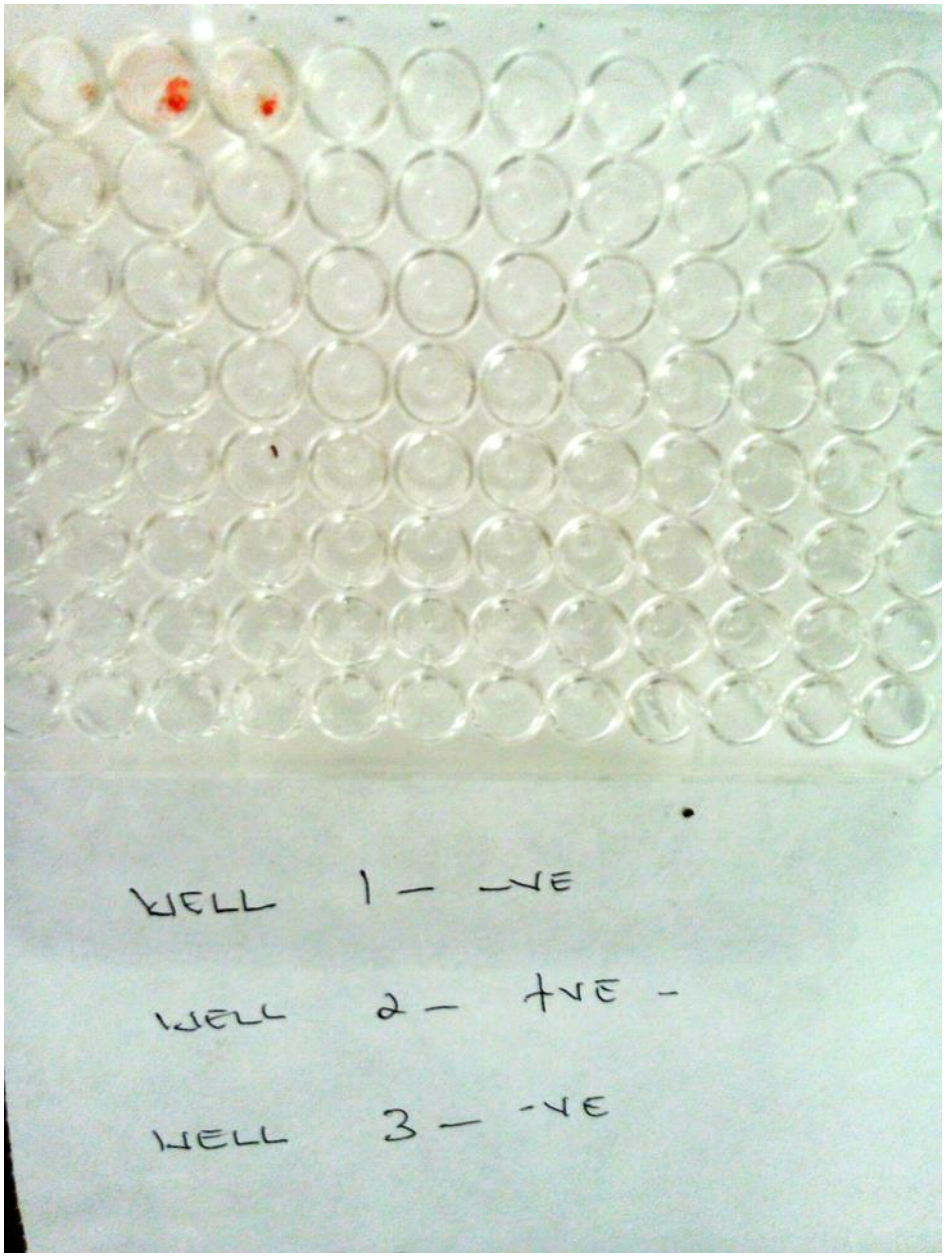

Dark field microscopy
Figure 29–3. Treponema pallidum. Diagrammatic
ch of the appearance of this spirochaete under
dark-field illumination, drawn to scale in comparison
a red corpuscle and a leukocyte. (From Joklik, W.
and Smith, D. T. (eds.): Zinsser Microbiology. 15th
New York, Appleton-Century-Crofts, Publishing
sion of Prentice-Hall, Inc., 1972.)


RPR TEST
DO NOT SHAKE
PLEASE
Lab tests
Spirochetes
RPR
TPHA
Tests
ETC


LABORATORY DIAGNOSIS
1. Non treponemal antibody(non specific)
•Kahn test
•VDRL
•RPR
•TRUST


WELL 1 - -VE CONTROL
WELL 2 - -VE TEST
WELL 3 - +VE CONTROL
WELL 4 - -VE TEST
WELL 5 - +VE TEST


WELL 1 - -VE CONTROL
WELL 2 - -VE TEST
WELL 3 - +VE CONTROL
WELL 4 - -VE TEST
WELL 5 - +VE TEST


WELL 1 – -VE
WELL 2 – +VE -
WELL 3 – -VE