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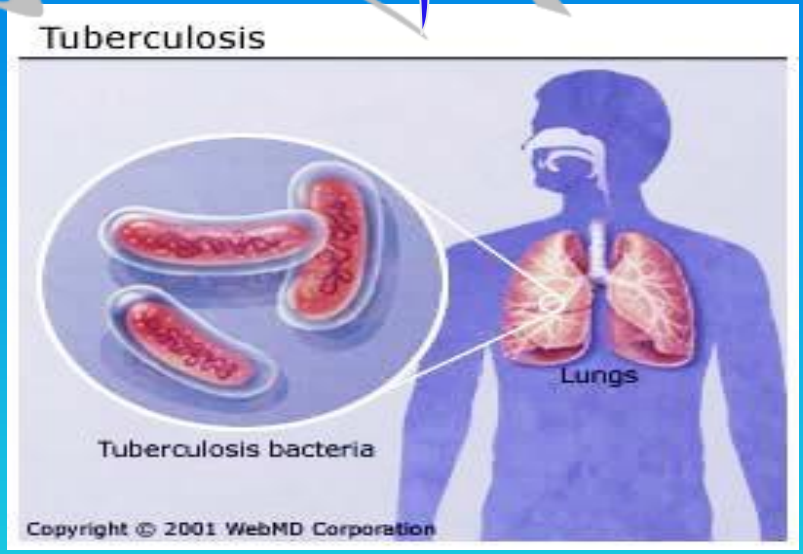


Tuberculosis

World Tuberculosis Day, held every year on 24 March

Prof DR. Waqar Al – Kubaisy

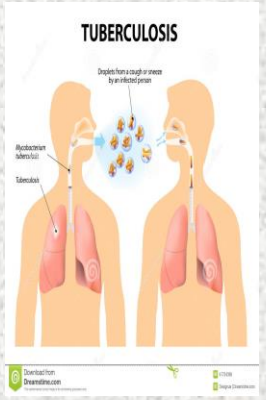
ا. د وقار عبد القهار الكبيسي

7- 10-2024

Introduction

- **Tuberculosis(TB) is a chronic infectious disease that cause by various strain of mycobacteria; usually *Mycobacterium tuberculosis.***

- It is an **airborne infection** spread by **droplets** from **people with active TB disease**
- **bacteria expelled by cough or sneezes**



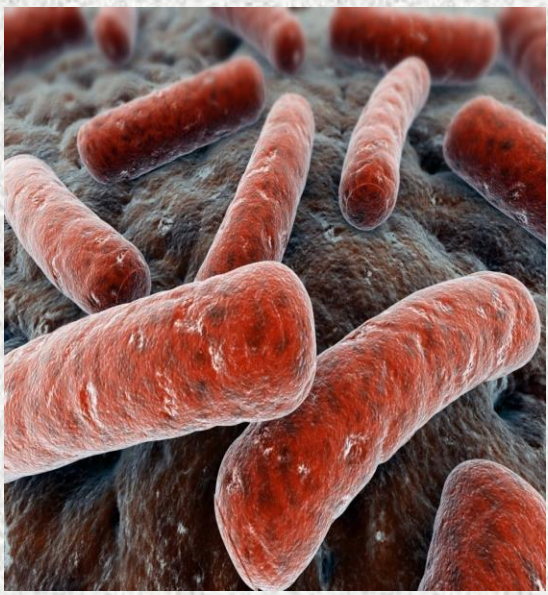
This infection mostly affects lungs (pulmonary TB) other parts of the body can be affected (extrapulmonary TB

Pulmonary TB is common and is most important and is most important epidemiologically

Mycobacterium tuberculosis

Characteristic :

- ❖ **Slow growing bacteria that can only live in people**
- ❖ **always found in the upper lobes of lung**
- ❖ **Cell wall contain mycolic acid – resistance to**
- ❖ **many antibiotics**
- ❖ **Resist dryness for a long period.**
- ❑ **Sensitive to**
  - **heat,**
  - **ultraviolet rays ,**
  - **sunlight, and**
  - **chemical agents** as phenol.



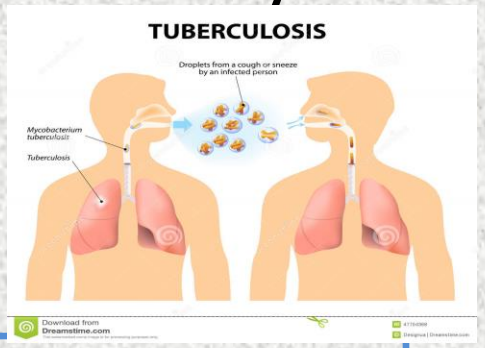
Centre For Disease Control And Prevention (Tuberculosis)

TRANSMISSION

Mycobacterium tuberculosis

Transmission of infection is mainly air borne by

- **droplets,**
- **droplet nuclei and**
- **dust**



thus it is enhanced by overcrowding in poorly ventilated accommodation

The incubation period

The period between the infections till the appearance of **the primary lesion is** about **4-12 weeks**.

the period between the infection till the development of progressive **Pulmonary** or **extra pulmonary TB** is about **6-12 months or may be longer.**

Pathophysiology

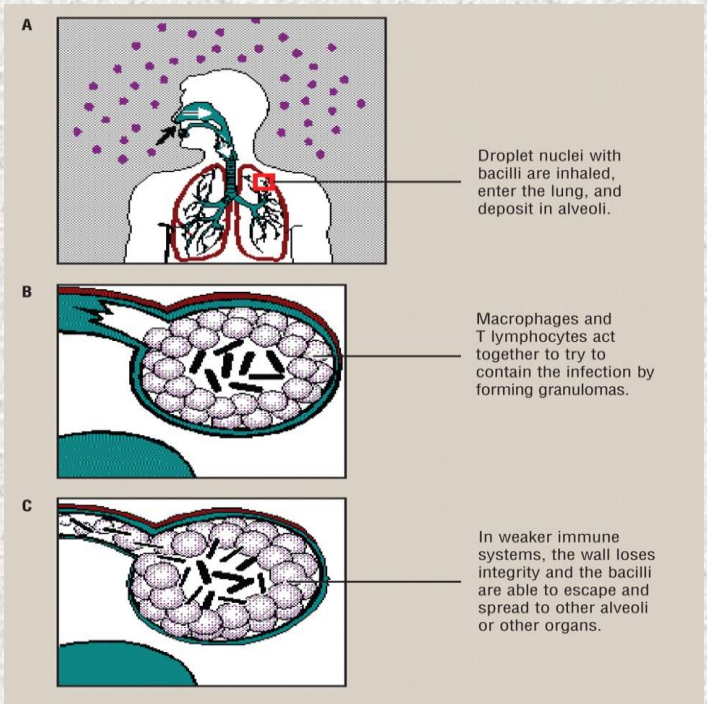
Kumar & Clarks, Clinical Medicine;8th edition

Inhalation of bacilli →

- Innate immune response clear bacilli before reaching lymph node : No infection or memory response

OR

- Formation of Ghon's focus or Ghon's complex : Granulomatous inflammation.
- This will produce :
  - Primary active TB; or
  - Latent TB infection



Pathophysiology For pulmonary TB

Primary Infection

On first infection,

- The initial infection usually goes unnoticed.
- It is asymptomatic primary lung lesions **(Ghon's complex)**

- Commonly heal (**in 95%)** with no residual change except for occasional **pulmonary and tracheo-bronchial lymph node calcifications**
- The patients develop immunity **(cell-mediated type)**.
- However there is a possibility of **reactivation** of the existing lesion

or

re-infection

Cont. Pathophysiology For pulmonary TB

- **re-infection** that may occur resulting in **destruction of lung parenchyma** with **fibrosis** & **cavitation** and hence the **characteristic symptoms appear.**

- **In approximately 5 %** of persons, initial infection may **progress directly to active pulmonary** disease or disseminated leading to:
  - **Miliary tuberculosis**
  - **TB meningitis or**
  - **extra-pulmonary lesions.**

Latent TB infection can be produce reactivate if immune system fails to kill bacteria → Reactivation TB

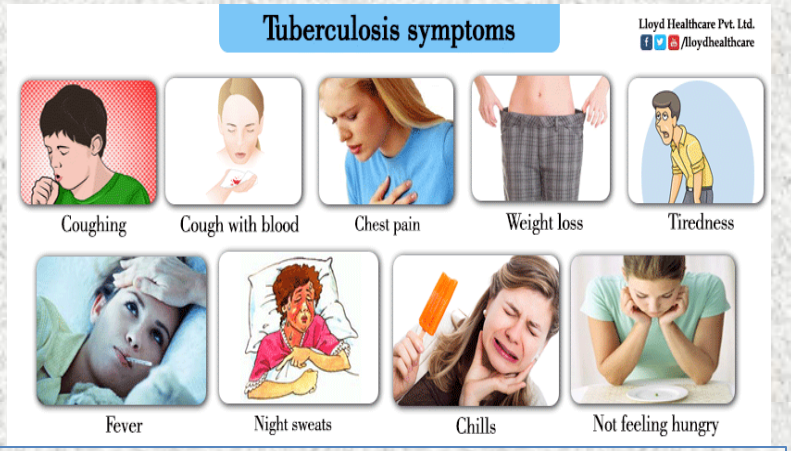
Factors implicated (Involved) in the reactivation of latent TB :

- **HIV co-infection**
- **Immunosuppressant therapy**
- **Diabetes mellitus**
- **End-stage chronic kidney disease**
- **Malnutrition**
- **Ageing**

Clinical Features

TB presents a wide variety

Epidemiologically ,pulmonary TB is most common & important



❑ pulmonary TB : Adult

❖ History of chest symptoms

- Productive cough (unexplained cough lasting more than
- 2 weeks with or without constitutional symptoms
- haemoptysis
- chest pain

❖ Nonspecific constitutional symptoms

- loss of appetite
- unexplained weight loss
- fever
- night sweats
- fatigue

Pulmonary TB : Children

Suggestive of TB

*prolonged fever

* failure to thrive

*unresolving pneumonia

*loss of weight

*persistent lymphadenopathy

Standard cases definition:

Suspected case:

Any patient with cough and expectoration more than three weeks associated with fever, loss of weight and night sweating.

Confirmed case:

- Pulmonary tuberculosis, smear positive cases are those who meet the following:

Confirmed case

Standard cases definition:

+Ve sputum for AFB by direct microscopic examination of two initial specimens.

Confirmed case

OR

+Ve sputum for AFB by direct microscopic

***examination of a single smear specimen and,**

****culture +Ve for AFB.**

OR

+Ve sputum for AFB by direct

***microscopic examination of a**

***single smear specimen and,**

****radiologic abnormalities consistent with active pulmonary TB**

Epidemiology Of TB

One definition of epidemiology is the study of the **distribution** and **determinants** of disease and other conditions in human populations.

Epidemiology is used to identify the distribution of TB geographically and in populations.

Through knowing the distribution of disease and its determinants in **person, place, and time,**

- **strategic planning is facilitated and**
- **the evaluation of interventions and preventive measures is more effective.**

Epidemiology

TB is a **chronic infectious** disease which remains the leading cause of human suffering **all over the world**.

- Since the beginning of the **20th century,** a **marked decline morbidity and mortality** from TB showed in the **industrialized countries**.

❖ **This decline is mainly brought by the ;**

***improvement of living conditions and to lesser extent by**

***the advance in antimicrobial chemotherapy**

- **The disease remained as a public health problem in most developing** parts of the world.
- **In the last two decades** Nowadays,

❖ TB is **re-emerging as a major public health** problem **world wide**.

In 1993, it was **declared** by the **WHO**

.In 1993, it was **declared** by the **W**orld **H**ealth **O**rganization (WHO) as a **global emergency**.

- **The declining trend in TB observed in industrialized countries is leveled or even reversed**

- **In developing countries**, the problem of TB is becoming of **considerable magnitude and serious impact**

- **Despite TB being a preventable and curable disease,**
- **There were cases in all countries and age groups**
- **TB is present all over the world.**

- .About one-quarter of the world's population is estimated to be infected by TB bacteria.
- About one-quarter of the world's population has latent TB, which *means people have been infected by TB bacteria but are not (yet) ill with the disease and cannot transmit the disease*

- Only 5-15% of these people will fall ill with active TB disease

The rest have TB infection but are not ill and cannot transmit the disease.

- Active TB person can infect 5–15 other people through close contact over the course of a year

Cont. ..Epidemiology Of TB

- **TB. Persons with compromised immune systems, such as people living with HIV, malnutrition or diabetes, or people who use tobacco, have a higher risk of falling ill.**
- **Both TB infection and disease are curable using antibiotics**
- Every year, 10 million people globally fall ill with TB

- **1.5 million** people die from TB each year – making it the world's top infectious killer.
- **TB is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS).**
- Over **95%** of TB deaths occur in **low and middle** income countries

1.5 million

Cont. …Epidemiology Of TB

- TB is the **leading killer of HIV-positive** people
- in 2015 with **1 in 3 HIV deaths** was due to TB

- TB is the **leading cause** of death of people with HIV and
- **Without proper treatment,**
  - **Where, 45% of HIV-negative people with TB on average will die**
  - **nearly all HIV-positive people with TB will die.**

- Most of the people who fall ill with TB live in
- low- and middle-income also a major contributor to antimicrobial resistance
- **Multidrug-resistant TB (MDR-TB) remains a public health crisis and a health security threat.**
  - **WHO estimates that there were 484 000 new cases with resistance to rifampicin – the most effective first-line drug,**

❑ **Worldwide In 2020,**

- **an estimated 10 million people fell ill with TB .**
- **5.6 million men,**
- **3.3 million women and**
- **1.1 million children.**
- **TB is present in all countries and age groups.**
- **But TB is curable and preventable.**

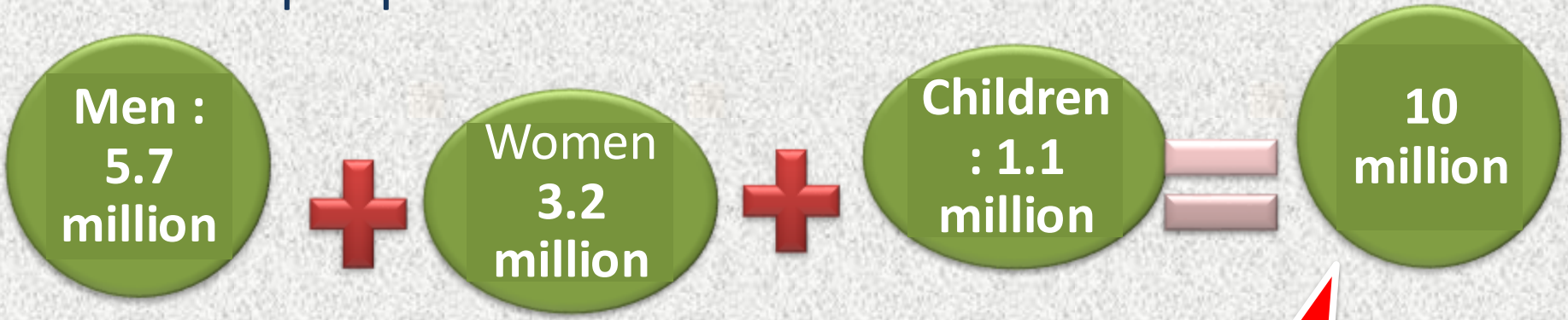
- **Worldwide, in 2020**
- **A total of 1.5 million people died from TB (including 214 000 people with HIV).**
- **TB is the 13th leading cause of death and**
- **the second leading infectious killer**
- **after COVID-19 (above HIV/AIDS).**

Epidemiology

(including 251 000 people with HIV

In 2018 :

10 million people are estimated to have fallen ill with TB.



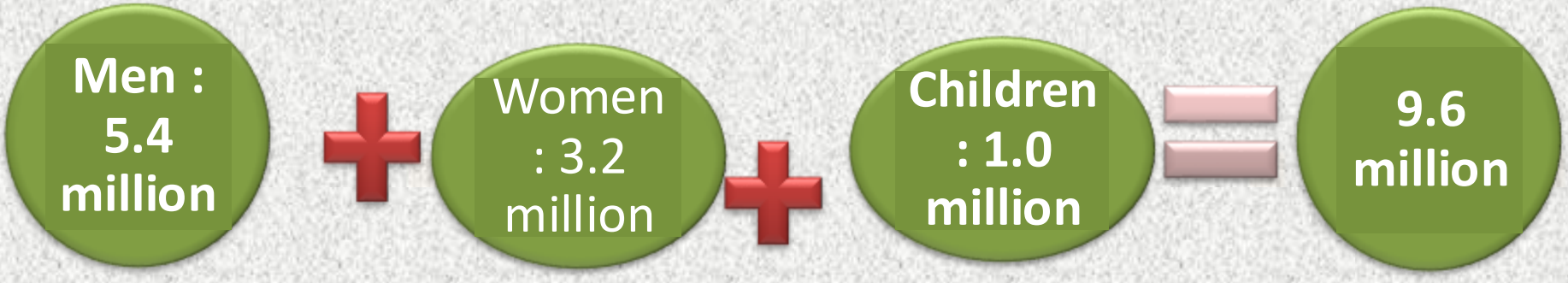
TB is one of the top 10 causes of death and the leading cause from a single infectious agent (above HIV/AIDS).

1.5 million die from TB each year

Epidemiology

In 2014 :

- **9.6 million** people are estimated to have fallen ill with TB.



In 2014 :

TB killed some 1.5 million people in the world

1.1 million HIV negative

0.4 million HIV positive

In Jordan according to the World Bank

Though Jordan incidence of TB is fluctuated substantially in recent years, it tended to decrease through 2001 - 2020

- **ending at 4.7 cases per 100,000 people in 2020.**
- **it tended to decrease through2019 -2020 period ending at 5.5 cases per 100,000 people in 2019.**

In 2020

- **Incidence of TB was 4.7 cases per 100,000 people.**
- **TB death rate = 0.1 per 100,000 people in 2022**

Incidence of TB was 3.8 /100,000 people

TB death rate 0.09%

Jordan

All forms of TB are included, including cases in people living with HIV.

in 2017

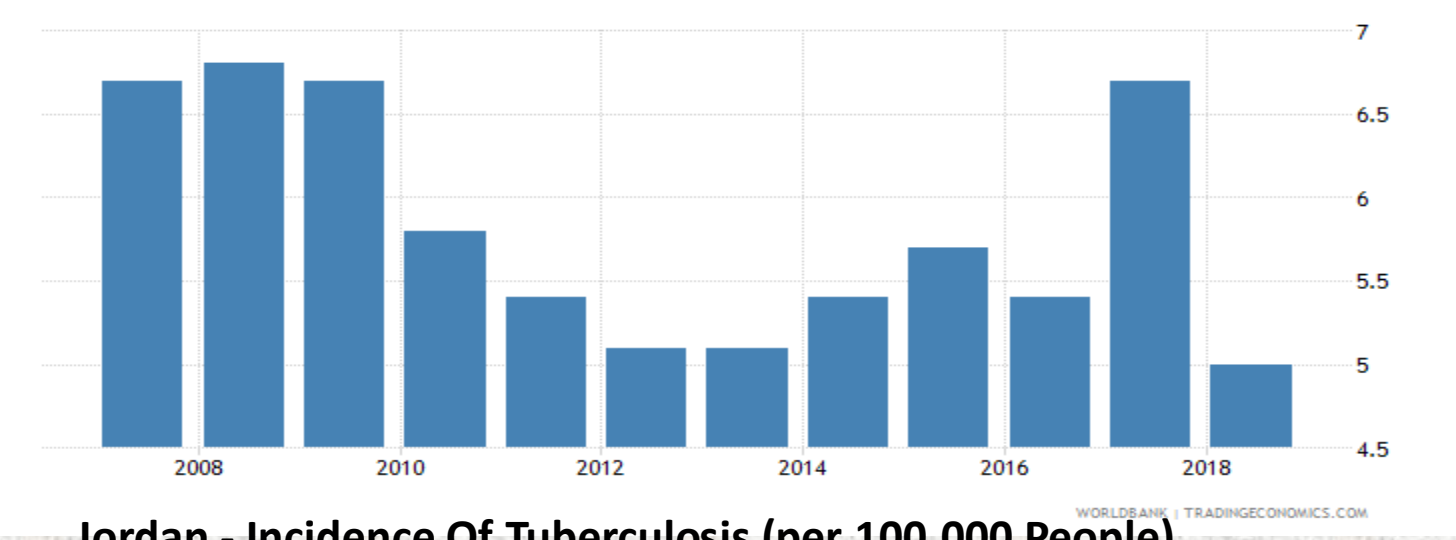
Incidence of TB was 6.8 /100,000 people)

in 2018

Incidence of TB was 5/100,000 people

in 2016

was 5.6 /100,000 people



Jordan - Incidence Of Tuberculosis (per 100,000 People)

Jordan

Epidemiology

Estimated TB incidence by age and sex (thousands)*, 2017			
	0-14 years	> 14 years	Total
Females	0.035 (0.033-0.037)	0. 26 (0.22-0.29)	0.29 (0.24-0.34)
Males	**0.039 (0.036-0.04)**	0. 33 (0.27-0.39)	**0.37 (0.3-0.44)**
Total	0.074 (0.068-0.08)	0.58(0.45-0.72)	0.66(0.5-0.83)

Oct 9, 2023

Age group (years)	
0–4	47 (2.9)
5–14	57 (3.5)
15–24	257 (15.8)
25–34	490 (30.2)
35–44	316 (19.5)
45–54	179 (11.0)
55–64	145 (8.9)
65	132 (8.1)

North Region	500 (30.8)
Central Region	**1,029 (63.4)**
South Region	94 (5.8)

Top four governorates	
Amman	640 (39.4)
Zarqa	293 (18.1)
Irbid	231 (14.2)
Mafraq	218 (13.4

Sex	
Male	**703 (43.3)**
Female	**920 (56.7**

The Jordanian Ministry of Health,
reported that the national TB program **seeks** to
eliminate TB by the end of 2025
Reducing the **incidence** of the disease
to less than **one/100,000** population, and

- Reducing deaths **to less than two cases**,
  so that it no longer poses a threat to public health

- **Among the Ministry's strategies is t**he
- **Rapid diagnosis of TB**, **by offering the new and advanced**
  - **"Gene-Xpert"** test **to those who show initial symptoms of TB**
  - **immediately providing them with a short-term** treatment
  - The Ministry also carries out **regular awareness campaigns**
    in areas where TB is prevalent,
- to encourage citizens to have their lungs x-rayed and
- undergo laboratory tests,

- **Nowadays, TB is re-emerging as a major public health problem for the following reasons:**

1) Inadequate TB control program:

- **The neglect of the disease by governments** has allowed tuberculosis control systems to deteriorate or even disappear in many parts of the world.
- **Poorly managed TB control programs** have contributed to an increase in the burden of disease as well as the **emergence of multi-drug resistant tuberculosis.**
- **The difficulty and the high expenses of treating multi-drug resistant cases of TB** that often fails even in industrialized countries

2) The rapid population growth and its consequences (malnutrition, housing problems, overcrowding, bad ventilation and lack of health services) has contributed to the increase in number of tuberculosis cases.

3) Increase in life expectancy of the population which led to increasing opportunity for the **conversion of a latent TB infection into clinically evident case**

4)The growing problem of HIV/AIDS and its link with tuberculosis led to an explosion of tuberculosis cases in HIV/AIDS endemic areas. HIV infection activates tuberculosis in individuals who are infected with tuberculosis, accelerating the breakdown from infection to diseases.

5)The emergence of multidrug resistant tuberculosis (MDRTB)

❑ Who is most at risk?

- ❖ **Closed TB contacts** ,However, all **age groups are at risk**.
- ❖ TB mostly **affects adults** in their most productive years.
- ❖ Prisoners, **Homelessness**

❑ **Over 95% of cases and deaths are in developing countries**.

❑ **The risk of active TB is also greater in**

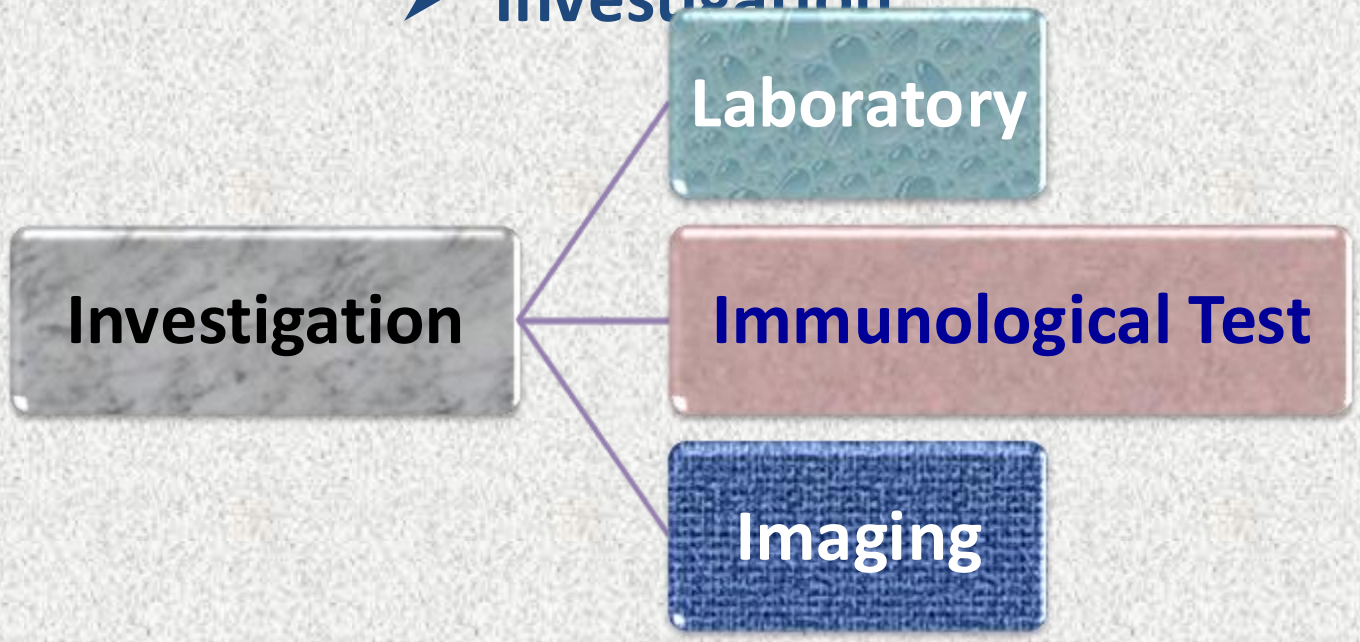
- ❖ **People with HIV are 19 times more likely to develop active TB**
- ❖ **and other conditions that impair the immune system.**
  - ➢ **DM, COPD, End-stage renal failure, Malignancy,**
  - ➢ **Immunosuppressant drugs**
- ❖ **People with under nutrition are 3 times more at risk.**
- ❖ **Alcoholic People are at increase the risk of TB 3.3 times**
- ❖ **tobacco smoking increase the risk of TB disease by 1.6 times**

Diagnosing of TB

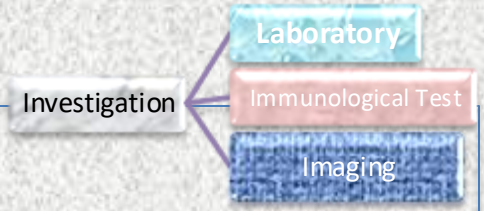
Patients with **active pulmonary** TB **infect 5-15 other persons per year**, **making the diagnosis of active TB essential to both**

- **curing the patient and**
- **preventing new infections.**

- **Clinical Features**
- **Investigation**



Immunological Test



Mantoux Test (Tuberculin skin test)

A delayed hypersensitivity reaction that **assesses the prevalence of TB infection in** the community.

- The Tuberculin skin test (TST) is performed by

- injecting **0.1** ml **of tuberculin purified protein derivative** (PPD) **intradermally** into the inner surface of the forearm.
- Skin reaction should **be read** within **48-72** hours
- The reaction should be **measured in millimetres** of the **induration;** not the erythema

The standard cut-off point for positive tuberculin test is 10 mm area of indurations.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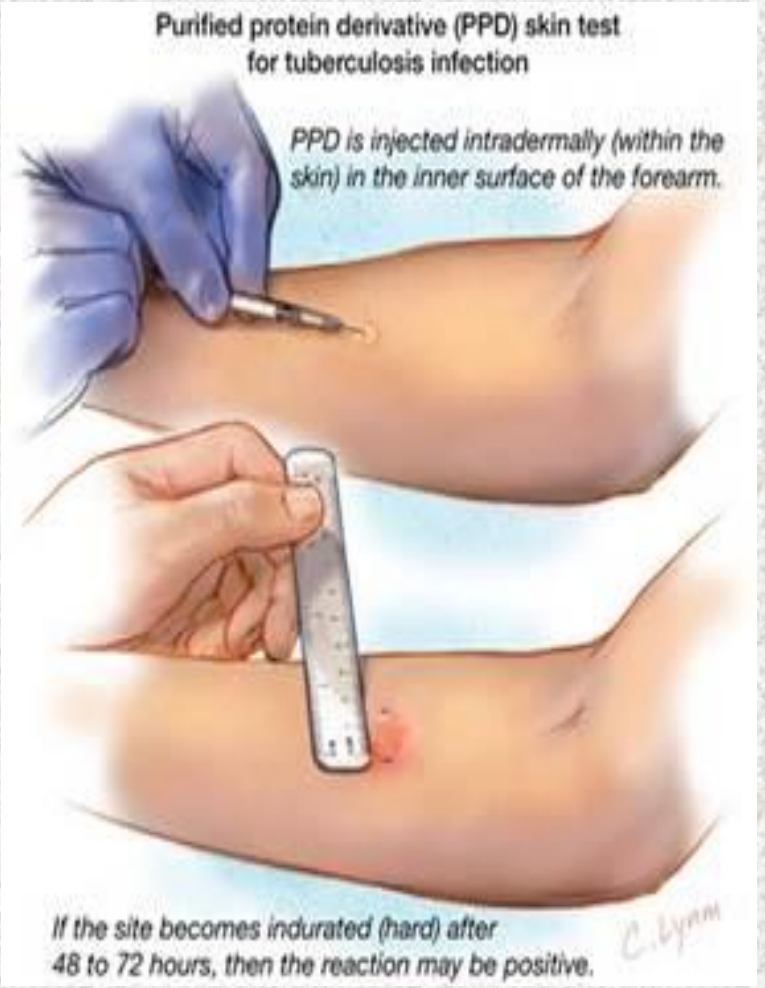

Purified protein derivative (PPD) skin test
for tuberculosis infection
PPD is injected intradermally (within the skin) in the inner surface of the forearm.
If the site becomes indurated (hard) after 48 to 72 hours, then the reaction may be positive.

Interpretation of tuberculin testing:

Positive TST indicates: Sensitivity to tubercle bacilli resulting from:

- previous BCG vaccination,
- old healed primary lesion **or**
- active disease.

The standard cut-off point for positive tuberculin test is **10 mm indurations**

a cut-off level of 5 mm is considered positive test

In the following situations :

- HIV infection
- **Contacts** of **smear positive** pulmonary TB cases.
- Chest **radiographs** consistent with **active** or old **healed lesion**
- **Clinical** evidence of TB.
- patient who are **immunosuppressed**

❑ The importance of TST

- **Identify TB negative** who are eligible for vaccination.
- However BCG could be given to subjects whatever the tuberculin status.
- **Evaluation of BCG vaccination** as it converts tuberculin **negative** into **positive** persons.

❑ TST is of little value as a diagnostic tool for case finding of TB because:

- It **can not** be used to differentiate **between natural** infection and **previous BCG** vaccination.
- **False negative** and **false positive** results

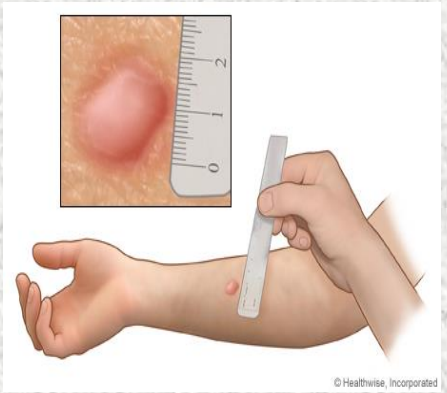
❑ Causes of false -Ve TST

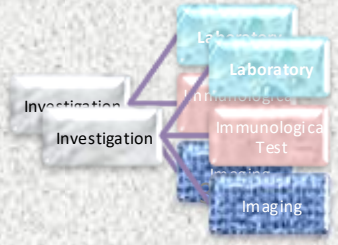
Pre-allergic state (incubation period of infection)

1. High fever and exanthemaus diseases (measles)
2. Advanced pulmonary TB, TB meningitis & milliary TB.
3. Immuno-suppression.
4. In late stage of pregnancy.

❑ Causes of false TST +Ve :

- Infection with atypical mycobacterium.
- Tuberculoid leprosy
- Cutaneous leshmaniasis.





Laboratory diagnosis

Diagnosis of TB based → detection of AFB on smears & cultures from clinical specimens. The TB bacillus is **Gram-positive**, but because of its waxy coat it does not stain with the standard procedure.

- identification of the **organism** on **examination** of
  - **sputum** and other pathological specimens (CSF, urine, pleural fluid or gastric washings). by the **Ziehl-Neelsen method,**
- **At least 2 sputum specimens** for microscopic examin.in all patients suspected of having pulmonary TB
- **at least one sputum from early morning**

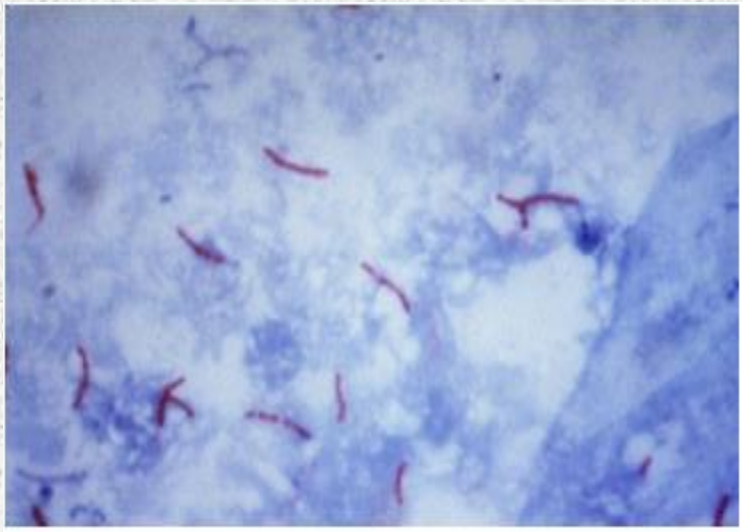
- **At least 10,000 bacilli/Ml requires to detect the ca**

absence of a positive smear result does not exclude active TB infection

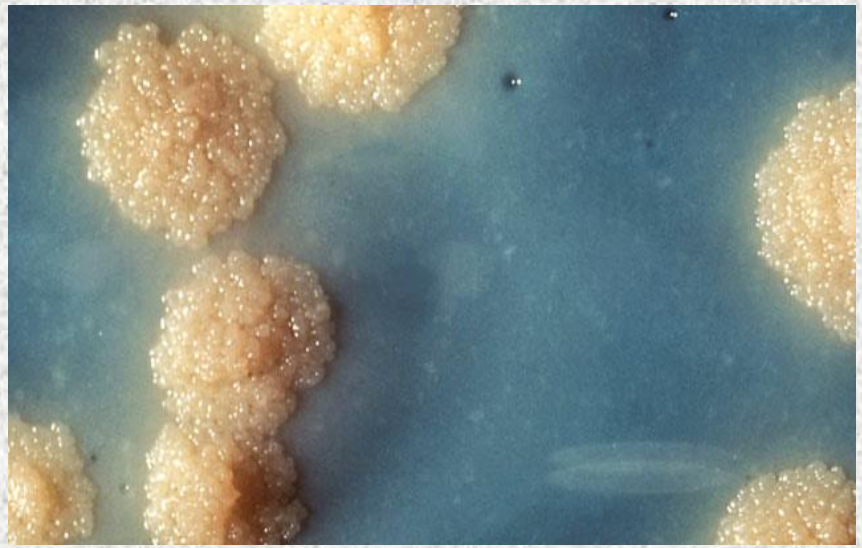
- **The organism can be isolated**
  - **on culture using special media, or by inoculation into guinea pigs.**
  - **DNA amplification by PCR are available in special centres.**

- The organism can be isolated
  - on culture using special media, or by inoculation into guinea pigs.
  - DNA amplification by PCR are available in special centres

SMEAR



CULTURE



Laboratory diagnosis

- Tuberculosis (TB) causes 10 million cases and
- 1.5 million deaths annually and it is estimated that
- 3 million cases go undiagnosed each year

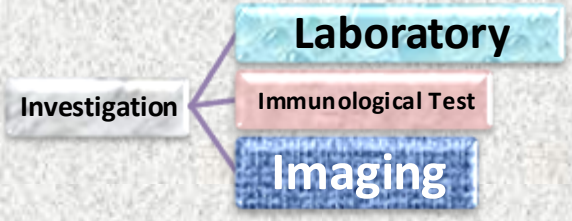
- **In 2011, WHO endorsed the use of**
- **Xpert MTB/RIF** for diagnosis of TB and detection of RR, ***rapid TB diagnostics and drug susceptibility testing (DST)***

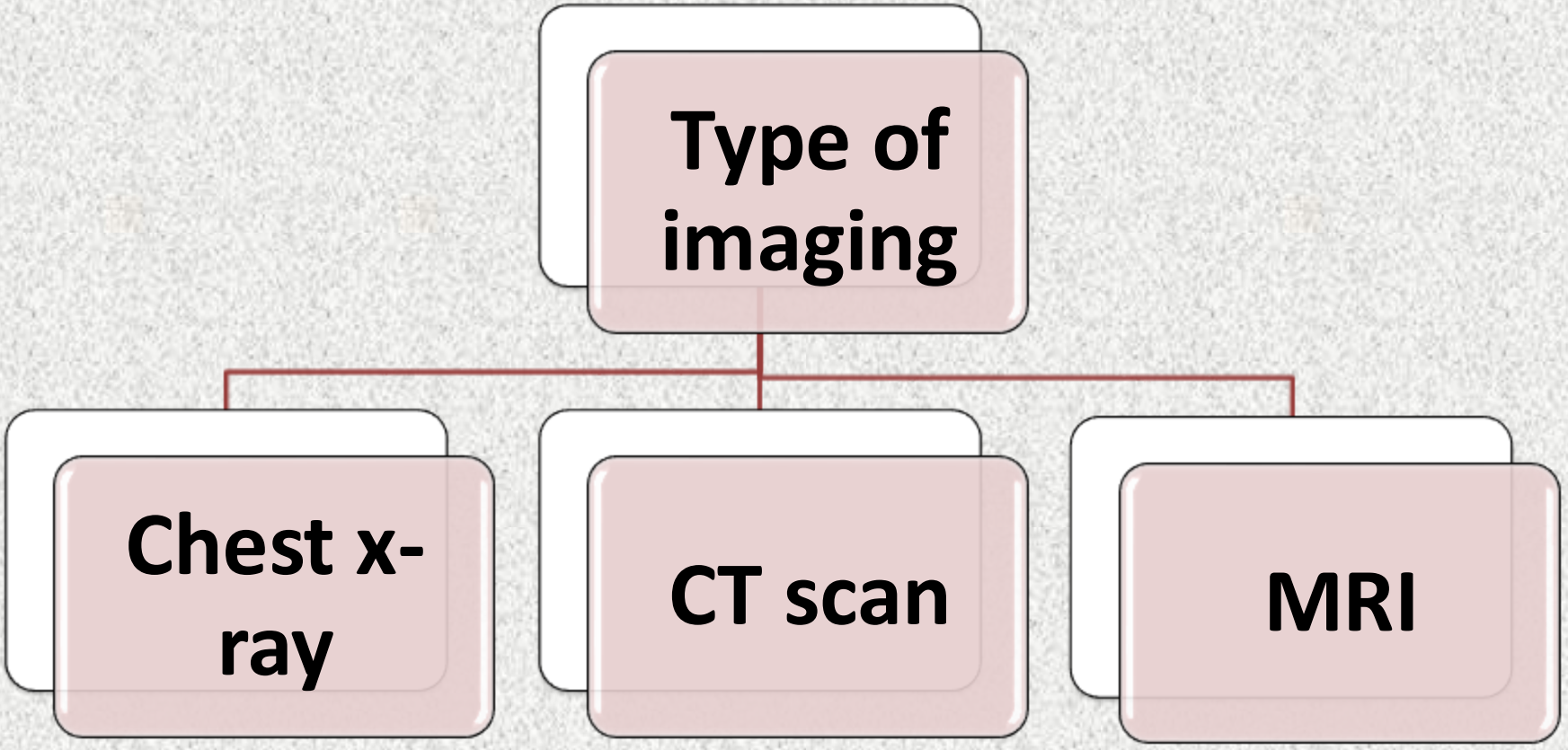
  The test simultaneously detects *Mycobacterium tuberculosis* MTB) and resistance to rifampicin (RIF) in less than 2 hrs.

- **a major step** forward **for improving the diagnosis of TB** and rifampicin resistance (RR) detection globally.
- **should be available** to all persons with signs & symptoms of TB
- **to meet** the targets of **the End TB Strategy..**
- **The Xpert® MTB/RIF Ultra assay** (Ultra) has been developed next-generation assay to overcome these limitations,.

Imaging

CPG Management Of Tuberculosis 3rd Edition

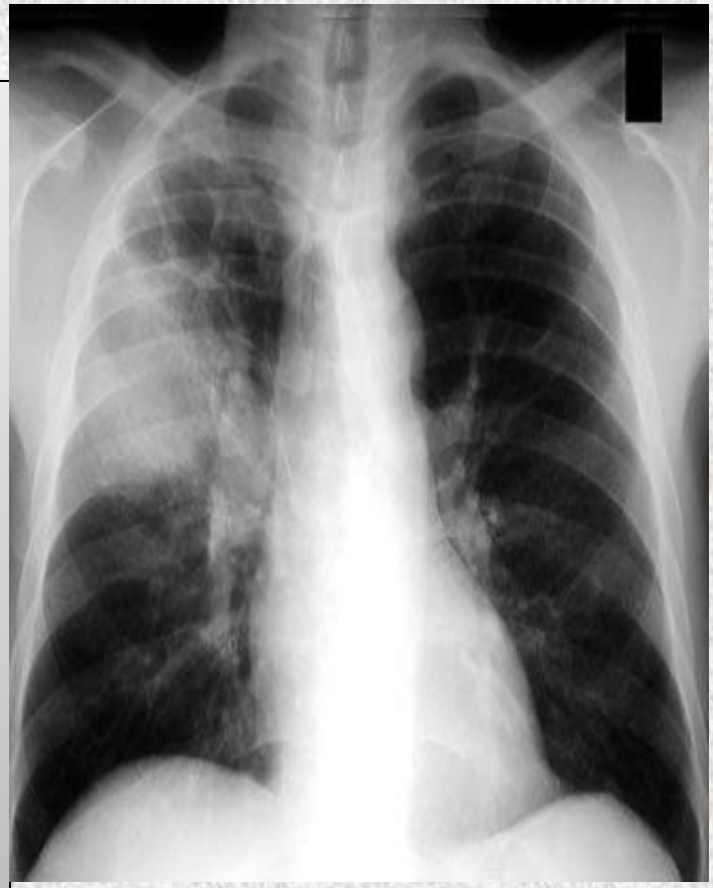




Imaging

1. Chest x-ray

- Remains the primary imaging modality for pulmonary TB
- **Consolidation** with **cavitation** is hallmark of adult-type of pulmonary TB
- **Normal chest** x-ray seen up to **15%** patient of primary TB



Imaging

CPG Management Of Tuberculosis 3rd Edition

2. CT scan

- More sensitive in demonstrating **endobronchial spread**, **lymphadenopathy** and **pleural complication** than chest radiography
- **Useful high** clinical **suspicion of TB with normal chest x-ray**

3. MRI

- **Consider in special circumstances** (children & pregnant women) → **no ionizing radiation**
- Has better soft tissue characterization → useful in **assess pleural and lymph node complications**

MANAGEMENT

- **Cure the disease**
- **Reduce risk of transmission**

Prevention & Control

Prevention

- Improving the socio-economic conditions.
- Apply basic preventive measures of respiratory diseases.
- BCG vaccination

However control of TB should receive higher priority than its prevention

Control program of TB

I Chemotherapy:

Direct observation therapy (DOTS) with short course chemotherapy is the recommended strategy for TB control.

- **Criteria for potent DOTS:**

- Short course therapy: the duration is six months.
- Under observation of a health care worker either at home or in a health facility.

- **Four drugs:** (INH, rifampicin, Pyrazinamide, ethambutol)
  - in the **first initial two months (Intensive phase)**
    - aims to **kill the actively growing bacilli rapidly**
- followed by **two drugs** (INH and rifampicin) within
  - **four months** as a continuation phase. **Maintenance phase**
    - aims to **sterilize by destroying all the bacilli,** especially the intracellular ones.

- In the case of **TB infection** (the patient is infected with TB bacteria but not ill),
- **TB preventive treatment** can be given to stop the onset of disease.
- Recent treatment options have shortened the duration to treatment **to only 1 or 3 months**, as compared to 6 months in the past.

DOTS

the priority clinical TB case eligible for treatment with DOTS is smear positive pulmonary case

- ❑ The treatment should be monitored with the sputum smear examination at the end of initial phase and at the end of the course

❑ Advantages of DOTS:

- Rapid cure: i.e. elimination of both rapid and slow complication from the patient's body
- Reduction of emerging drug resistant strains.
- Low failure rate.
- Improved patient's compliance.

The only disadvantage is the high cost

❑ Control program of TB

Best control measure is **case finding & chemoprophylaxis.**

I.Case finding:

A. Sputum examination:

B. Sputum culture: .

C. Xpert MTB/RIF for diagnosis of TB and detection of RR, ***rapid TB diagnostics and drug susceptibility testing (DST)***

D. Tuberculin skin test

II vaccination (BCG):

❑ II vaccination (BCG):

- Live attenuated vaccine prepared from bovine TB bacilli.
- given in a dose **(0.1) ml intra-dermal** in the left deltoid regio
- **In newborn** the dose is **(0.05)** ml because the skin is rather thin and intra-dermal injection with dose may penetrate the skin to deeper tissue leading to obsess formation and enlarged axillary's lymph nodes.

❖ given immediately after birth since cell mediated maternal immunity can not be transferred to the fetus.

❖ **>80%of neonates** and infants in countries where it is part of the national childhood immunization programme.

❑ Efficacy of BCG:

- It is more than **80 %** in preventing miliary TB and tubercle's meningitis in children.
- BCG does not prevent infection in adults
- It does not prevent primary infection and, more importantly,
- does not prevent reactivation of latent pulmonary

- It does not prevent primary infection and, more importantly,
- does not prevent reactivation of latent pulmonary infection the principal source of bacillary spread in the community.
- The impact of BCG vaccination on transmission of Mtb is therefore limited

❑ Indications of BCG vaccination:

I. If the prevalence of TB is high:

❖ Administration of BCG at birth is recommended; thus give
❖ the vaccine to the newborns *as part of the national childhood immunization programme*).

➢ In newborn tuberculin test is not required before vaccination which is part of the EPI **Expanded Programme on Immunization**

II. If the prevalence of TB is low:

BCG is restricted to the high risk groups as:

- Health care personnel
- Tuberculin negative contacts of positive sputum pulmonary TB cases.
- Industrial workers exposed to silica.

Contraindications of BCG vaccination:

- Immuno-compromized as HIV, cancer.
- Immuno-suppressive drugs used
- Patients suffering from eczema

❑ III Other measures for cases

A. **Isolation:** isolation of cases at home if suitable is a cost effective strategy otherwise hospitalization is required.
B. **Concurrent and terminal disinfection** of patient sputum is recommended.
C. **Rehabilitation:** the aim is to help the patient to live as an active member in the society within his limited physical abilities.

❑ IV Measures for contacts

- ❖ Health education
- ❖ Investigations
- ❖ Tuberculin testing.

Barriers to TB control programs in developing countries

- **Unfavorable socio-economic** conditions which are linked to dissemination of TB.
- **Difficulties in case finding activities due to limited diagnostic resources both in quality and quantity**.
- **Failure of treatment leads to substantial defaulters, who spread the infection to others.**
- **Emergence of drug resistant strains**.
- **The chronic nature of the disease**

World Tuberculosis Day, held every year on 24 March

Thank You

Qs ???