Microbiology

Doctor 2018 | Medicine | JU

Sheet Slides

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This lecture is divided into 2 parts

Neglect the number of pages :P

This lecture is INTERESTING, its related to clinical situations, enjoy what you you're studying fellows!

Mycobacterium

Classification:

***Order: actinomycetales**

*** Family: *mycobacteriaceae***

Genus: *mycobacterium

There are three major species of this family:

A) Mycobacterium tuberculosis complex(MTC)→ That causes tuberculosis مرض السل

B) Mycobacterium leprae→ causes leprosy مرض الجذام

C) Mycobacterium avium intracellularie/ mycobacterium avium complex(MAI/ MAC).

NTM (non-tuberculos mycobacteria): also known as environmental mycobacteria. They are a group of mycobacteria that don't cause neither tuberculosis nor leprosy.

In other words, they are a nontuberculous, nongranulomatous category of mycobacteria that causes infections in different sites of the body (causing lung disease- other than tuberculosis, lymphadenitis, skin infections and others with **NO** "typical granuloma")

*(NTM) frequently infect patients with AIDS. Also, they are opportunistic pathogens in other immunocompromised individuals, and occasionally cause disease in patients with normal immune systems.

Principal pathogen that causes tuberculosis in human is ***Mycobacterium tuberculosis*** [Mtb]

BUT there are other species that can cause tuberculosis, collectively called ***"mycobacterium tuberculosis complex- MTC"***

This group (MTC) can cause **Tuberculosis** disease in humans and other livings. 11 members are in this group, they are for you to memorize or at least to be familiar with, try to make your own mnemonics for them☺ :

- M. tuberculosis (Mtb), Mycobacterium africanum, Mycobacterium bovis, Mycobacterium oryx

- Mycobacterium microti, Mycobacterium caprae, Mycobacterium canetti

- Mycobacterium suricatte, Mycobacterium mungi, Mycobacterium dassie, and Mycobacterium pinnipedii.

Doctor Nader suggested the following question for those:

ALL OF THE FOLLOWING ARE MEMBERS OF MYCOBACTERIUM TUBERCULOSIS COMPLEX EXCEPT

*(choices will include one wrong answer, giving you for example one of **NTMs** that we mentioned before. The question may be introduced for you in the exam vice versa. i.e. all of the following are NTMs except one).

*Note: mycobacterium **bovis** was the major pathogen causing tuberculosis in the past, but when **pasteurization** method arised it has been abolished nearly completely yet it is still used in VACCINATION –**BCG vaccine**- to be discussed later in this lecture.*

MORPHOLOGY

Obligate intracellular, obligate aerobes, non-motile, non spore forming and acid fast bacilli.

An exception- motile mycobacterium: mycobacterium marinum was observed to be **motile inside macrophages. This bacteria causes 'fish aquarium granuloma disease'.

*In tissue, tubercle bacilli are thin,

straight rods measuring about

0.3 ~ 3 µ m.

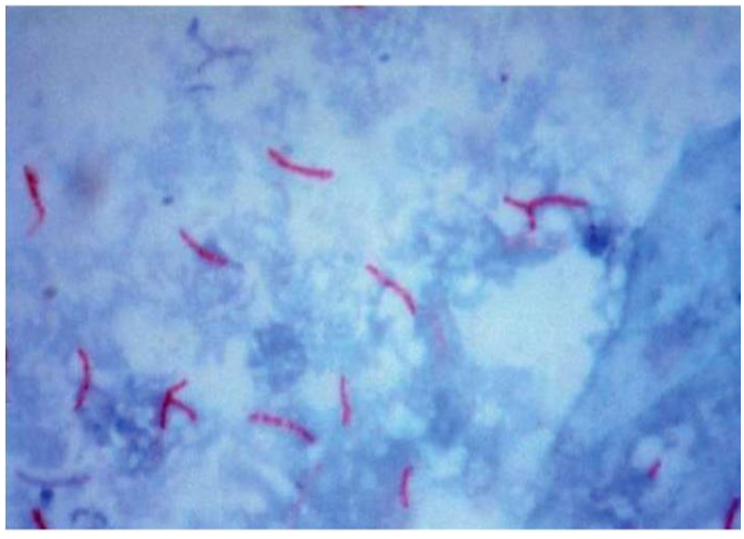
*Mycobacteria are ***obligate aerobes***

and derive energy from the oxidation of many simple carbon compounds.

Brainstorming/ controversial studies upon: active vs passive internalization of mycobacteria inside macrophages

Is it that mycobacteria favor macrophages and follow their steps to occupy them, or is it that alveolar macrophages were the 1st to pick it up?
who nagged the other frist?

*Mycobacteria are **ACID-FAST bacilli** i.e. the stain which we use to identify mycobacterium is acid-fast stain (or zeihl-neelsen stain). Robert Koch utilized (ZN stain) and discovered the causal agent of the disease Tuberculosis (TB); Mtb or Koch bacillus.



Good to know: we refer acid-fast bacilli to two genera; MYCOBACTERIA and NOCARDIA.*

→Some **details** regarding **acid-fast staining** method (just understand the general idea because the doctor explained it in the lecture, Not in the slides):

a red stain called "carbol fuchsin", is used to stain the sample which is usually taken from the **sputum** of the patient.

-heat off the sample – to facilitate penetration of the stain

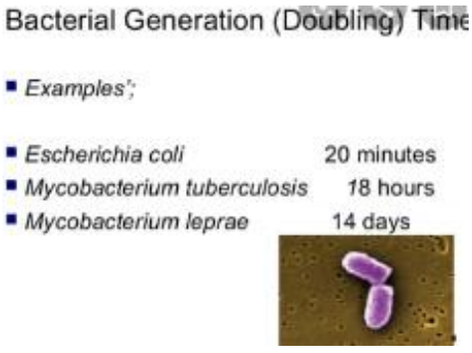
-add hydrochloride acid – to wash off the stain, "decolorization" in other words.

-counterstain the sample with methylene blue

Now, acid fast bacilli will RETAIN the 1st dye(carbol fuchsin) and resist the acid treatment (they fast from the acid), so they appear red under the microscope and don't counterstain with the blue stain→ True tubercle bacilli are characterized by "acid fastness" i.e. resistant to decolorization by **acids**—that is, 95% ethyl alcohol containing 3% hydrochloric acid (acid-alcohol) which quickly decolorizes all bacteria *except the mycobacteria.*

Just keep in mind, MYCOBACTERIA are ACID-FAST BACILLIIIIII

MYCOBACTERIA INSIDE HUMAN BODY ARE OBLIGATE INTRACELLULAR



Its mentioned in the slides that it is facultative, only to illustrate the idea that it is **culturable** and to explain other situations regarding mycobacteria that you are not required to know now

(as in, if it's not facultative OUTSIDE the human body, it won't be cultured)

Inside human body? Mycobacteria are OBLIGATE Intracellular.

Keep in mind that they prefer the niche of alveolar **MACROPHAGES**.

The growth rate of mycobacteria is much slower than that of most bacteria. The doubling time of tubercle bacilli is about 18-24 hours, comparing it to E.coli for example which divides nearly every 20 min clarifies the long doubling time.

This slow doubling time has many consequences on many areas. In diagnosis for instance: **culture results** are lately revealed, preventing fast diagnosis

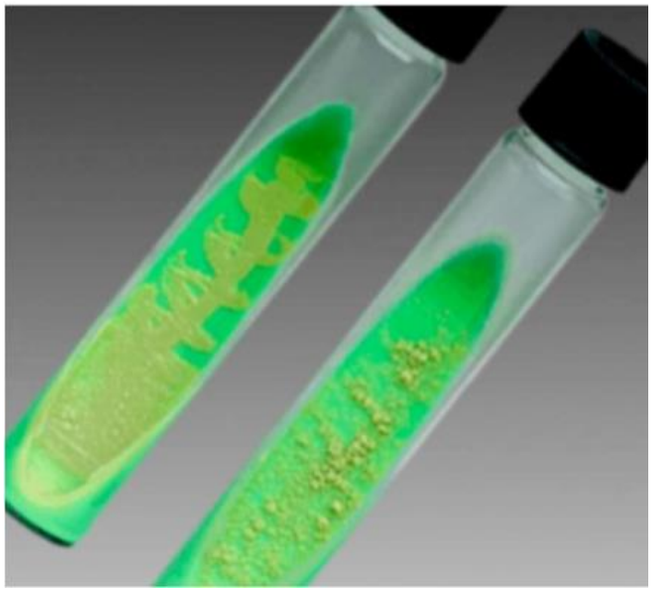
Treatment: **prolonged** period of medication administration (up to 2 years)

Mtb CULTURE

The media for primary culture of mycobacteria should include a nonselective medium and a selective medium, it's of 3 types:

-**Semisynthetic agar media**— eg, Middlebrook 7H10 and 7H11. These media contain defined salts, vitamins, cofactors, oleic acid, albumin, catalase, and glycerol.

-**Inspissated egg media**— eg, Löwenstein- Jensen. these contain defined salts, glycerol, and complex organic substances (e.g. fresh eggs or egg yolks, potato flour, and other ingredients in various combinations



*We add Malachite green along with it, which will inhibit the growth of bacteria other than mycobacteria, notice the green color in the figure aside→

-**Broth media**— (eg, Middlebrook 7H9 and 7H12) support the proliferation of small inoculates – unfortunately it has low specificity and sensitivity.

تأمل الشكل المرافق ثم صِف الشكل النموذجي لمستعمرات البكتيريا المسببة لمرض السل وغيره من الأمراض:

This is a typical mycobacterium colony, its unique in a way.It’s described as **raised, rough and CLUMPED.**

A problem we face in culturing, is that it doesn’t always give us positive even though the bacteria is there!

Mtb Cell wall

Most of the properties of this sophisticated bacteria are referred to the COMPLEXITY OF ITS CELL WALL, mainly the lipid component in it.

The mycobacterial cell wall is a complex structure that is essential for cell growth[1], resistance to antibiotics[2] and virulence[3].

It consists of an ***inner layer*** and an ***outer layer*** that surround the plasma membrane.

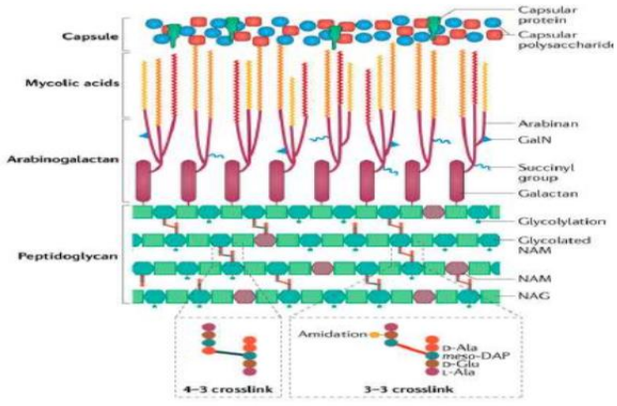
The ***inner*** compartment is composed of three distinct macromolecules —

1)peptidoglycans (PG)

2) Arabinogalactans (AG)

3) Mycolic acids (MA)

— covalently linked together to form a complex known as the MA-AG-PG complex.



*The **peptidoglycan** layer surrounds the plasma membrane and comprises long polymers of the repeating disaccharide N-acetyl glucosamine–N-acetyl muramic acid (NAG–NAM) that are linked via peptide bridges.

*Most of the **arabinan** is ligated with long-carbon-chain mycolic acids, which form the characteristic thick waxy lipid coat of mycobacteria and are major contributors to the impermeability of the cell wall and to virulence.

***Mycolic acids** (long-chain fatty acids C78–C90), waxes, and phosphatides , can be found in Mtb cell wall and make up 50% of the dry weight of the mycobacterial cell envelope.

Outer layer: is a capsule- like that contains polysaccharides, lipids and proteins. It contains a lot of bacterial virulence factors such as **LAM- lipoarabinomannan and LM- lipomannan.**

ركز معي شوي

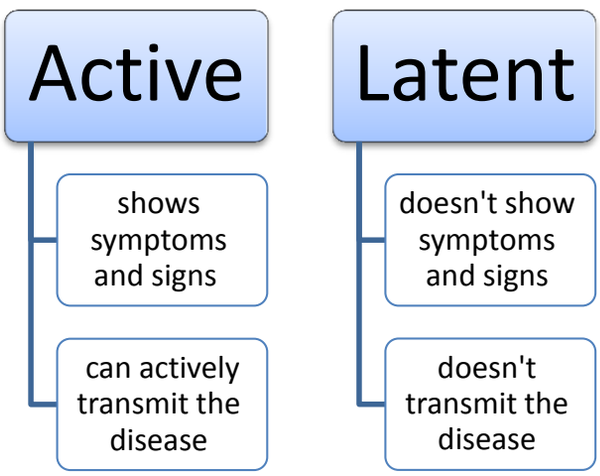
Usually these mycolic acids are esterified to glycerol and trehalose. Trehalose (a disaccharide) can bind one or two molecules of mycolic acid forming trehalosedimycolates ***(TDM/ Cord Factor)*** *and trehalose monomycolates(TMM).*

* Trehalose dimycolates (TDM) (Cord Factor)= are important virulence factors. They are also responsible for the CLUMPING morphology of mycobacterial colonies.

Have a break, have a KitKat 

Epidemiology

Before we proceed here you need to differentiate between 2 clinical entities of TB (tuberculosis):



*Latent TB could **reactivate** and cause the disease, mainly in the first 2 years of latency.

*Keep in mind: IMMUNOCOMPROMISED PATIENTS such as AIDS patients are at high risk of REACTIVATION…WHY?

Remember that TB is an **intracellular** pathogen, so the MAIN mechanism of elimination by immune system is **through CELL-MEDIATED IMMUNITY** (CD4+ cells), so in the case of AIDS patients, cell mediated immunity is not there to get rid of it.

Combination of AIDS + TB = fatal situation!

So, ACTIVE TB can arise in two types,

1)*primary* active disease **2)*secondary***-from reactivation of latent TB

In primary infections, the involvement may be in any part of the lung but is most often at the base, **well oxygenated areas= where the oxygen tension (PO_2) is highest**. i.e. **mainly the lower part of the upper lobe and the upper part of the lower lobe of the lung which makes sense because they are obligate aerobes**. (Remember, they're obligate aerobes)

*risk factors of Mtb:

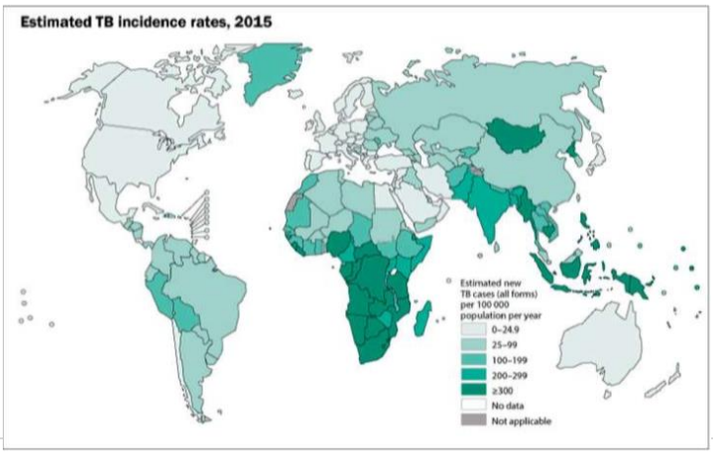
poverty, malnutrition, overcrowdedness (we observe many cases of TB in **jails**), patients who utilize immunosuppressant drugs(are at high risk of REACTIVATION of latent TB) as in the case of **rheumatoid arthritis patients.**

Now lets go over some statistics:

*Incidence rate of TB in Jordan is 25-50 cases per 100,000

*WHO, 2015: about 11 million new cases of active TB are recorded, 1.5 millions of them died. Actually this is not a good indicator as we are in 2019 and yet an INFECTIOUS agent is still causing these huge numbers.

-About one third of the world's population is infected with TB bacteria (latent TB). However, only small proportion of those infected will become sick with active TB.



Have a look on the map, lighter the color -> less incidence rate.

*South Africa and Swaziland are major countries having high incidence rate for TB, in Swaziland for example it reaches 10,000 per 100,000!!!

*One of the reasons for such high number is due to high HIV rates there.

Transmission

TB is considered an **airborne** infectious disease. Although, *M. tuberculosis* complex organisms can be spread through unpasteurized milk, direct inoculation, cough, sneezing and other means.

Patients with TB should be isolated for 2-4 weeks after we start the treatment.

The underlying pathophysiology of TB is the "10/3/1 formula", which states the following:

= if ***10 people*** are exposed to *mycobacterium* TB, **three** of them will develop LATENT TB, and **one** will develop ACTIVE TB

=notice that 6 of them cleared the bacteria somehow by their immune system and didn't develop anything.

Note: less than 10 bacterial particles are enough to establish the disease (virulent)

Mtb can withstand dryness and weak DISINFECTANTS that droplets out of patient may face!!

--

Pulmonary vs extrapulomonary tuberculosis

The primary site of TB is usually the lung "***pulmonary***", from which it can get disseminated into other parts of the body.

The other routes of spread can be **1)contiguous involvement,** in other organs by adjacent tuberculous lymphadenopathy or **2) primary involvement** of extrapulmonary organ. * 90% of infections by TB are **pulmonary** TB.

Extrapulmonary TB are infections that affect other organs than lungs, such as: the pleura, pericardium, kidney.

some of which are given special names, examples:

-TB can affect lymph nodes(**cervical tuberculous lymphadenitis** is called **scrofula**), *other NTM can cause scrofula (called *Mycobacterium scrofulaceum*, to be mentioned at the end of the lecture).

-TB can affect the bones = **Pott disease**, in which TB infects the vertebrae of the vertebral column

-It can affect the abdomen = **abdominal TB**

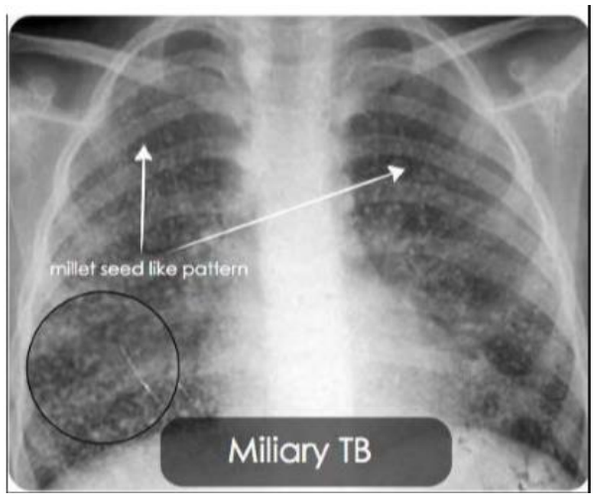
-It can affect the brain, causing **tuberculous meningitis**

-It can spread through the blood circulation, causing **miliary TB**

MILIARY TB AND TUBERCULOUS MENINGITIS ARE VERY SERIOUS CONDITIONS!

**Pulmonary and extrapulmonary can happen together or each on its own.*

Meliary TB



It is a condition where TB enters the blood circulation (i.e. **hematogenous spread**).

→One suggested mechanism by which this occurs is that TB *erodes* from its GRANULOMA to adjacent blood vessels.

Diagnostic feature of meliary TB: MILLETs- which are seed like patterns in the lungs, each of which is *a mycobacterium TB surrounded by a granuloma*.

يلاع الثانية :P

MYCOBACTERIA CONT.

Transmission and Pathogenesis of TB

Mycobacteria are present in respiratory droplets. when infected persons cough, sneeze, or speak. The droplets evaporate, leaving organisms that are small enough, when inhaled, to be deposited in alveoli.

• Inside the alveoli, the host's immune system responds by release of **cytokines and lymphokines** that stimulate monocytes and macrophages.

• These amazing bacteria begin to multiply within ***macrophages*** after it escapes killing mechanisms such as [phagosomes or lysosome, ROS, RNOS and others]. Some of the macrophages develop an enhanced ability to kill the organism, but others may be killed by the bacilli.

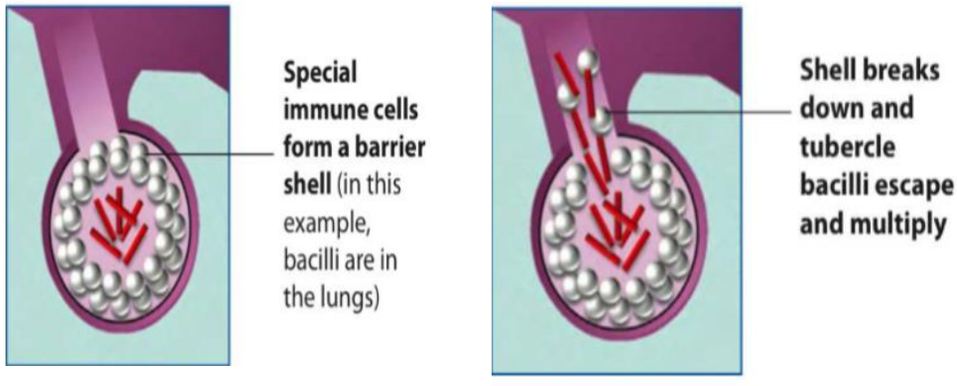
Granuloma formation
'breifly': infected macrophages recruit other macrophages, then adaptive immunity cells come there(T and B lymphocytes) and finally, surrounding the sick cell a fibrous rim is produced.

• The cells form a barrier shell, called a ***granuloma***, that keeps the bacilli contained and under control (LTBI= latent TB infection).

Granuloma is a hall mark for TB infection (intracellular infections generally)

note: less than 10 bacterial particles are enough to establish the disease

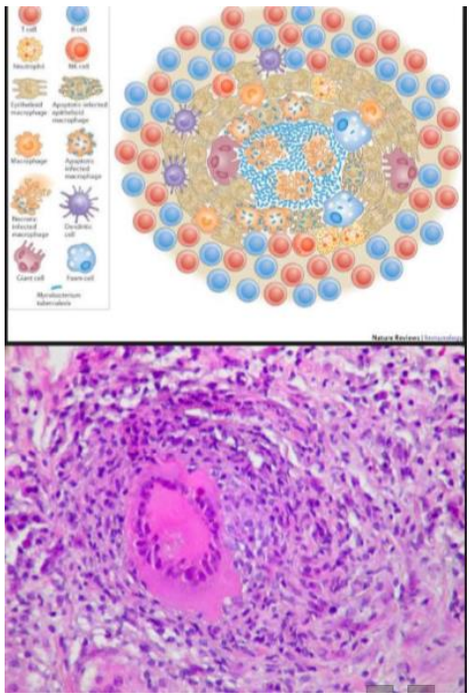
• If the immune system cannot keep the tubercle bacilli under control, the bacilli begin to multiply rapidly (active TB disease).



Pathology

this subject wasn’t explained in class, but it's present in the slides. So, read what's written here..

-the following states the present understanding of inflammation occurrence in TB from a pathological (histological) perspective. There are two types that could occur concurrently:



* **Exudative type** (also called pneumonia type)— This consists of an acute inflammatory reaction with edema fluid; polymorphonuclear leukocytes; and, later, monocytes around the tubercle bacilli. This type is seen particularly in lung tissue, where it resembles bacterial pneumonia. And is seen in serous cavities’ infections with TB.

***Productive type**—(also called granuloma type) When fully developed, this lesion, a chronic granuloma, consists of three zones: (1) a central area of large, multinucleated giant cells containing tubercle bacilli; (2) a mid zone of pale epithelioid cells, often arranged radially; and (3) a peripheral zone of fibroblasts, lymphocytes, and monocytes

Note: granuloma surrounding Mtb (but not in the case of meliary TB) is called ***Ghon focus***; which is a small area of granulomatous inflammation detected by x-ray. If ghon focus involves infection of adjacent lymphatics, it is known as **Ghons complex** (complex means involvement of draining lymph nodes.

Clinical manifestations : Classic clinical features associated with active pulmonary TB are coughing, weight loss/anorexia, **fever**, **night sweats**, **haemoptysis** (coughing blood), dyspnea (chest pain) and malaise/fatigue

*Tuberculosis , named also consumption disease (consumes patients with weight loss), white plaque (extreme pallor seen among patients).

*Tuberculosis is usually a **chronic disease**; it presents slowly with weight loss, low-grade fever, and if it is extrapulmonary; symptoms would be related to the organ system infected. Because of its slow course, it may be confused with cancer. *Whenever you have an infection of any organ system, tuberculosis will be somewhere on your differential diagnosis list. ☺

Laboratory diagnostic methods

Note: Specimen is usually taken from sputum of the patient [children mostly can't give us sputum sample so we use [BAL: Broncho-alveolar lavage] procedure instead.

Smear microscopy

• Three specimens from each patient with suspected TB should be examined microscopically for Acid Fast Bacilli AFB (classically Ziehl-Neelsen) or

 mycobacteria can be demonstrated by yellow fluorescence after staining with auramin.

Culture

• Both liquid and solid mycobacterial cultures should be performed for every specimen, and recovered isolates should be according to standard criteria (Lowenstein-Jensen or Middlebrook 7H10), Radiometric broth culture (BACTEC radiometric system) and mycobacterial growth indicator tube (MGIT).

• **Culture for acid fast bacilli is the most specific** test for TB and allows direct identification and determination of susceptibility of the causative organism, but again remember it takes long time to give the result [about 8 weaks].

A nucleic acid amplification test (NAAT).

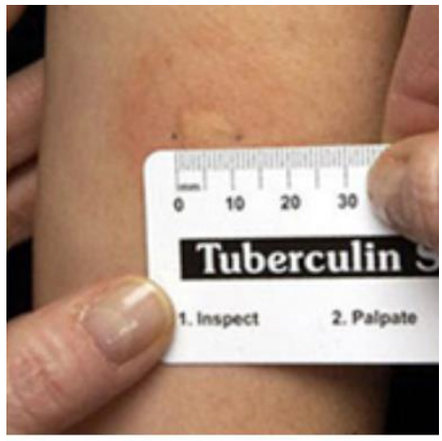
*Tests that are used in diagnosis of **latent** TB:

Tuberculin skin tests (TSTs), Interferon-gamma release assays (IGRAs) are commonly used.

****TST**(also called purified protein derivatives), steps:

-The TB skin test is performed by injecting a small amount of fluid- purified protein derivative (called tuberculin) into the skin(intradermally) on the lower part of the arm

-A person given the tuberculin skin test must return back to clinic within 48 to 72 hours to look for a reaction on the arm and read the results



Reading the result of a TB skin test

-The result depends on the size of the **raised, hard area or swelling { the induration**}, so we measure the size of induration by a ruler-→

Positive skin test: This means the person's body was infected with Mtb. Additional tests are needed to determine if the person has latent TB infection or TB disease. We also interpret numbers measured after we observed +ve results as following:

-If induration size > 15 mm--→ normal healthy individual

-Induration size > 10 mm ---→ intermediate risk group

-Induration size > 5 mm---→ HIV patient [which makes sense as we don't expect patient with HIV to have large induration due to compromised immunity].

Disadvantages of TST:

-You need the patient to come back after 48 hours

-Interpretation may give me FALSE POSITIVE (FP); which may arise in 2 cases that you are required to know guys:

1) patient who is immunized [he took BCG vaccine throughout his life]

2) infection with NTM (nontuberculos mycobacteria) may also give you FP

So, to overcome these problems, another technique is developed:

Interferon-gamma release assays (IGRAs) test

In this test, a blood sample is taken from the patient and distributed on different tubes that contain very specific antigens for Mtb. It works by measuring the body's immune response to TB infection (based on amount of IFN-gamma released or cells that release it).

--->So by that we can exclude FALSE POSITIVE results

Note: both tests (IGRA AND TST) are used for **screening** purposes because they just give you an answer of (had the body faced Mtb before or not?) and don't tell you whether the body faced Mtb now or in the past.

But normally if these tests give us POSITIVE result and the patient DOES NOT show symptoms and signs, we consider him to have **{LATENT TB}**

Prevention

The best way to prevent mycobacterial infections is to **diagnose** and isolate infectious cases (TB)rapidly and to administer appropriate treatment in special labs*(biosafety level 3 lab)* which is not available in Jordan of course☺ until patients are rendered noninfectious (usually 2–4 weeks after the start of proper treatment) and the disease is cured. *Also, many developed countries applies " contact racing" i.e. they look for any place or person with which the patient dealt in the previous month. They make sure that non of them has active TB.*

-Vaccine: **BCG** (Bacillus Calmette–Guérin), an attenuated vaccine derived from Mycobacterium bovis[live attenuated vaccine].

It is the only licensed vaccine against tuberculosis (TB)

*Attenuation= weakening of the microbe by removing many of its virulence factors.

Note: because it is a live attenuated pathogen, we **don't** give this vaccine to those who suffer from problems in cell mediated immunity (like AIDS patients) as its still an alive pathogen!

* here in Jordan we give it for neonates at the age of 1 month.

❖ It's given in the upper left arm and usually leaves a scar- check yours :P

Note: many developed countries **don't give** this vaccination in its **national vaccination program (NIP)** anymore as the disease is much less prevalent now and the vaccine has some problems such as:

-giving "false positive" results in many tests (more details are at the end of this sheet).

-additional problem with BCG vaccine is that it has different degrees of EFFECIENCY among people. Efficiency ranges are from 0-80 (zero means no protection even though the vaccine is given before, and 80 means 80% protection against TB). So not everyone who took it is fully protected.

Then why do developing countries still give this vaccine? Most important reason is that it protects against **2 serious forms of the TB diseases we mentioned before: tuberculous meningitis (most importantly in babies ☹) and meliary TB.**

Treatment

The course of TB treatment depends on whether the individual is in the **latent** or **active** stage, and on his or her probability of risk. This treatment is given for about (6-12) months.

Treatment of TB usually involves a drug cocktail, or a mixture of multiple drugs, with an **intensive** initial 2-month phase followed by a **slower** 4 to 6 months **continuation** phase. The main anti-tuberculosis drugs used in the

chemotherapy of TB are: isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and either ethambutol (EMB) or streptomycin (SM).

*All four are given in intensive phase (initial 2 months)

*In slower continuation phase (remaining 4 months or more), we give the patient mainly 2 drugs of all -**rifampin and isoniazid**.

All these drugs have annoying side effects ☹. For example, **rifampin** changes the color of body fluids such as urine into [orange or red]. **Isoniazid** is autotoxic, nephrotoxic and causes sideroblastic anemia. **Pyrazinamide**, causes hyperuricemia (first step of gout). **Ethambutol** causes optic neuritis.

→Isoniazid preventive therapy **IPT,** is the recommended treatment for **LTBI** but the regimen's (the prescribed treatment's) main drawback is the **long duration of therapy.**

- As you see this is a long period of treatment [as long as this sheet ☺], so many patients quit. They neglect the drug before 6 months as they feel better, and this creates many problems(no compliance with the treatment course leads to development of DRUG RESISTANT strains) such as:

☒ MDR-TB [multi drug resistant TB] that is resistant to **isoniazid and rifampin**

☒ EDR-TB [extensively drug resistant TB], resistant to oral drugs: isoniazid, rifampin, flouroquinolones AND to injectable drugs: kanamycin,capreomycin and amikacin. ☐

to overcome this problem, a new style is used in treatment arised; called **"DOT"**- directly observed treatment in which the patient is forced to come every day and take his medication in front of medical personal.

OTHER MYCOBACTERIA

A) NTM [nontuberculous mycobacteria]. Also called environmental bacteria

They are classified by two criteria as following

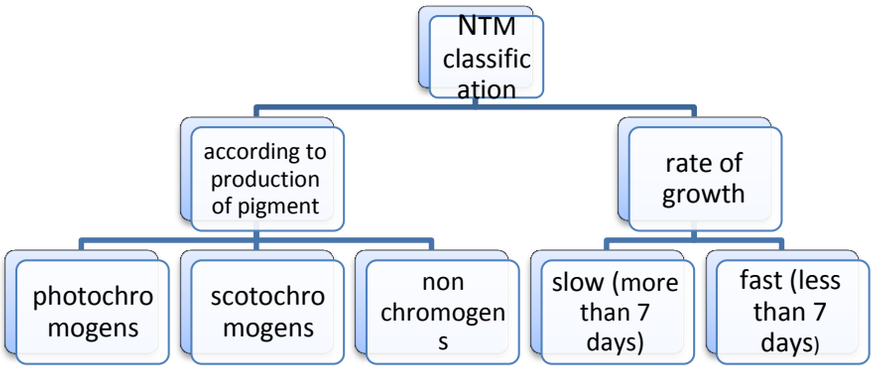
According to production of carotene pigment:

1) **Photochromogens**: produce pigmented colonies in the presence of light (carotene pigment) and non pigmented ones in the dark.
2) **Scotochromogens**: produce pigmented colonies in the presence and **absence** of light.
3) **Nonchromogenic**: don't produce the pigment neither in present nor absent of light.

According to rate of growth

1) Rapidly growing species: they form clearly visible colonies in less than 7 days

2) Slowly growing species: more than 7 days



Apply previous criteria to the following bacteria:

- *Mycobacterium* ***kansasii*** ,*Mycobacterium* ***marinum*** and *Mycobacterium* ***ulcerans*** → Photochromogenes, *slow* **{ group 1}**

- *Mycobacterium* ***scrofulaceum*** [remember it causes **scrofula**, TB of the lymph nodes: tuberculosis lymphadenitis] → scotochromogens, slow **{ group 2}**

- *Mycobacterium* ***avium intracellularae complex***, or (**MAI**) →nonchromogens, slow **{ group 3}**
- *Mycobacterium* ***fortuitum Complex*** ,*Mycobacterium* ***chelonae-abscessus*** → nonchromogens, fast { **group 4}**

B) Mycobacterium leprae: leprosy disease

Pathogenesis: 3 types of leprosy;

- **TUBERCULOID** leprosy (**TL**): cell mediated immune response is apparent and **strong**, and there is a **granuloma**, so number of bacterial particles is **limited**. Accordingly, if we applied lepromin test which is **similar to tuberculin skin test** TST it would give a POSITIVE result due to strong cell mediated immunity.
- **LEPROMATOUS** leprosy (**LL**): cell mediated response is **poor** (not apparent) , number of bacteria is **high** and consequently; lepromin test gives **negative** result.
  - Patients of ***this type*** shed the bacteria from their **nasal secretions**, so its very dangerous and contagious (transmissible).
- **BORDERLINE** lepromatous (BL): intermediate form between the two extremes: **Tuberculoid** and **Lepromatous**

More about lepromin test:

This test is used to dermine **what type** of leprosy a person has.

It depends on the amount and the magnitude of **cell mediated immune reaction** against it. **NOT** the amount and number of organisms present, that's why it's positive in tuberculoid leprosy and negative in lepromatous leprosy.

Clinical manifestation

-The lesions involve the cooler tissue of the body(optimum temp for this bacteria is about 30 C), including the skin (skin histiocyts) **– causing painless skin nodules,** superficial nerves(Schwan cells)- **causing sensory loss**, nose, pharynx, larynx, eyes, and testicles.

The onset of leprosy is insidious.

Notice the LION LIKE FACE!!

Diagnosis

*skin or nasal mucosa or a biopsy of earlobe skin are smeared on a slide

- Smears are stained by the **Ziehl-Neelsen** technique.

*Biopsy of skin or of a thickened nerve gives a typical histologic picture; **granuloma**.

*No serologic tests are of value because it is an **intracellular** infection and the role of **humoral** immunity is **limited**

Don't forget!

****** this bacteria is NOT culturable in the lab, only in vivo******

Treatment

Treatment is given for at least 2 years. Sulfones such as **dapsone** are first-line therapy for both tuberculoid and lepromatous leprosy **RMP(rifampin/ rifampicin)** or **clofazimine** generally is included in the initial treatment Regimens.

العِبرة بكمالِ النّهايات لا بنقصِ البدايات.

–ابن تيميّة.

(برعاية الفاينل)