

# ***Treatment of the MDR-TB***



## ***Monitoring the Response***

**W.H.O.**

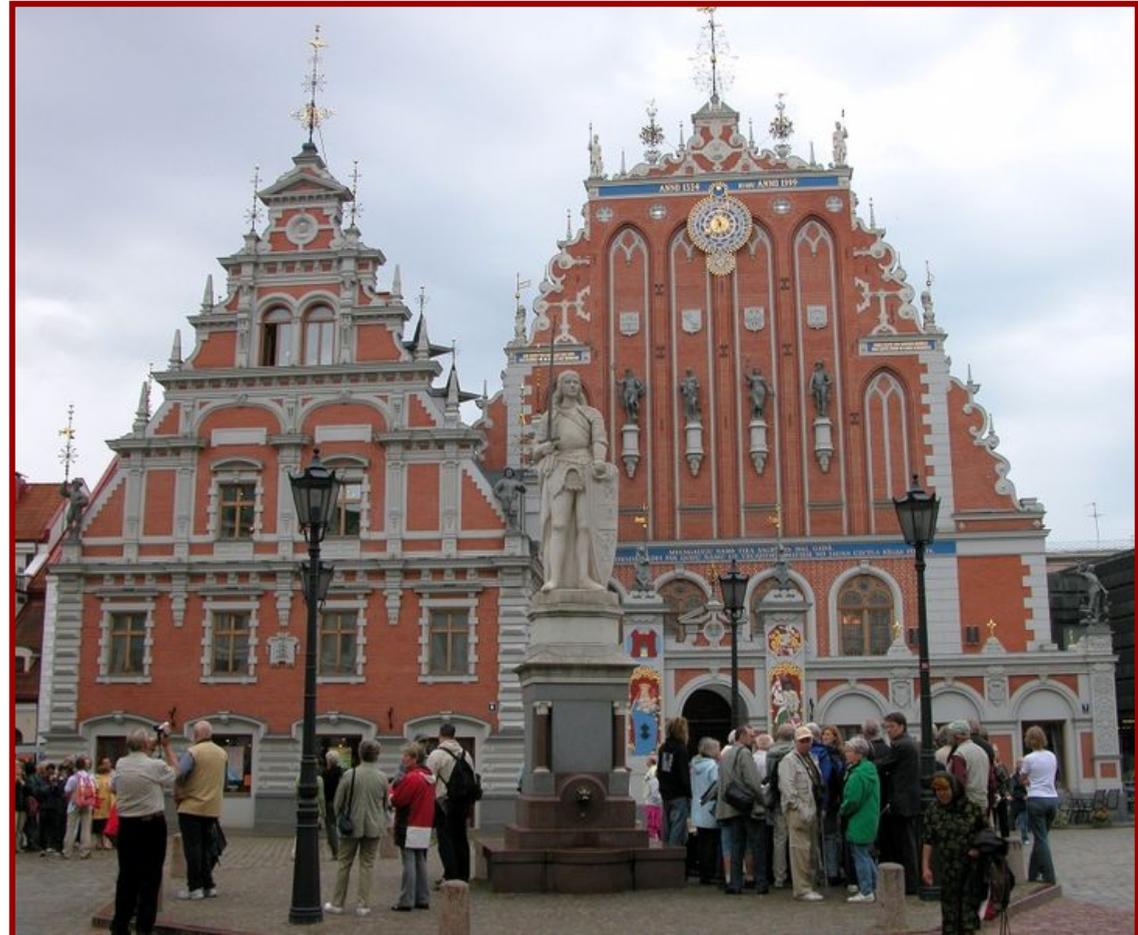
***Second MDR-TB Consultant  
Course***

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# ***Treatment of the MDR-TB***



## ***Monitoring the Response***

### ***- Objectives***

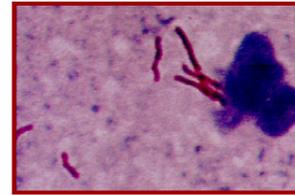
- 1.- To evaluate the Clinical and Bacteriological **response** to the Treatment***
- 2.- To monitor the **Adverse** Reaction to the Anti-Drugs***

# Diagnosis of TB disease

**1. Clinical Evaluation**



**2. Microbiology**



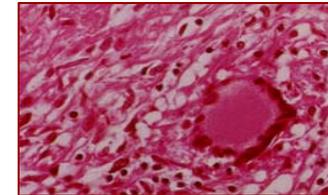
**3. Radiology**



**4. Tuberculin Test**



**5. Anatomical pathology**



**6. Non-Conventional and New Methods**

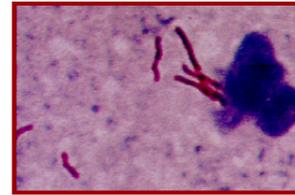


# Diagnosis of TB disease

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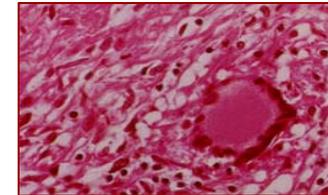
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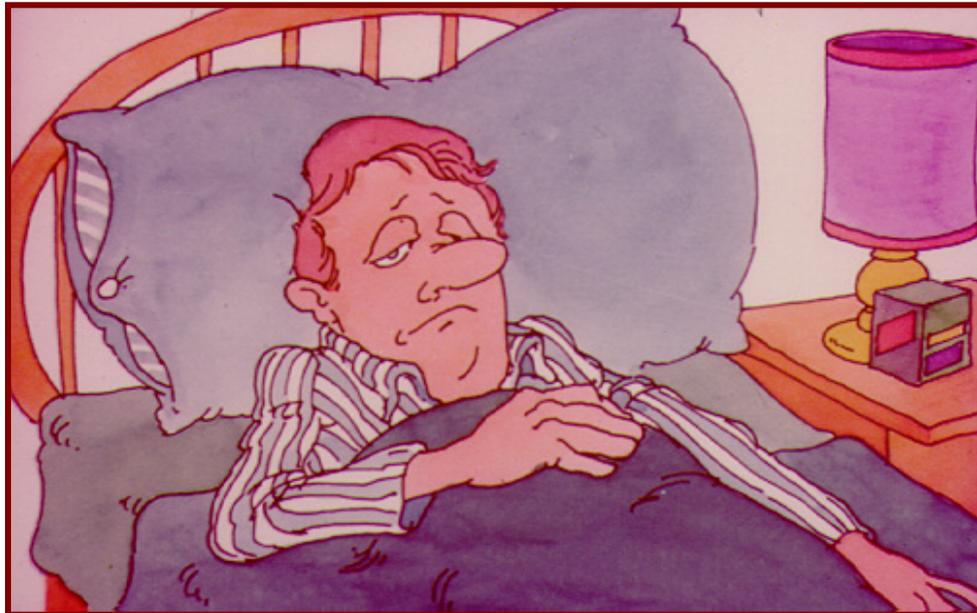
**6. Non-Conventional and New Methods**





# ***Clinical and X-ray film*** ***Manifestations of the TB***

***The Importance in the Follow-up***  
***and in the suspect of Failure***



# ***Limitations of the Clinical and X-ray film in the Dg of MDR-TB and in the suspect of Failure***

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- ***The not Improvement in the clinical and/or x-ray film manifestations during the treatment are very not specific data to diagnose MDR-TB***
- ***Other Disease, frequently associated with TBC (Bronchiectasias, Resp. Infections, etc), can justify this not improvement***
- ***These data must be evaluate only as a data more in the context of the patient***

***Never accept MDR-TB or a Failure only based in Clinical and/or X-ray film criteria***



# ***Radiological Manifestations of TB***

## ■ **In the diagnosis**

- Very easy and of great value in suspected diagnosis
- Unspecific: All X-ray patterns can be found in other diseases

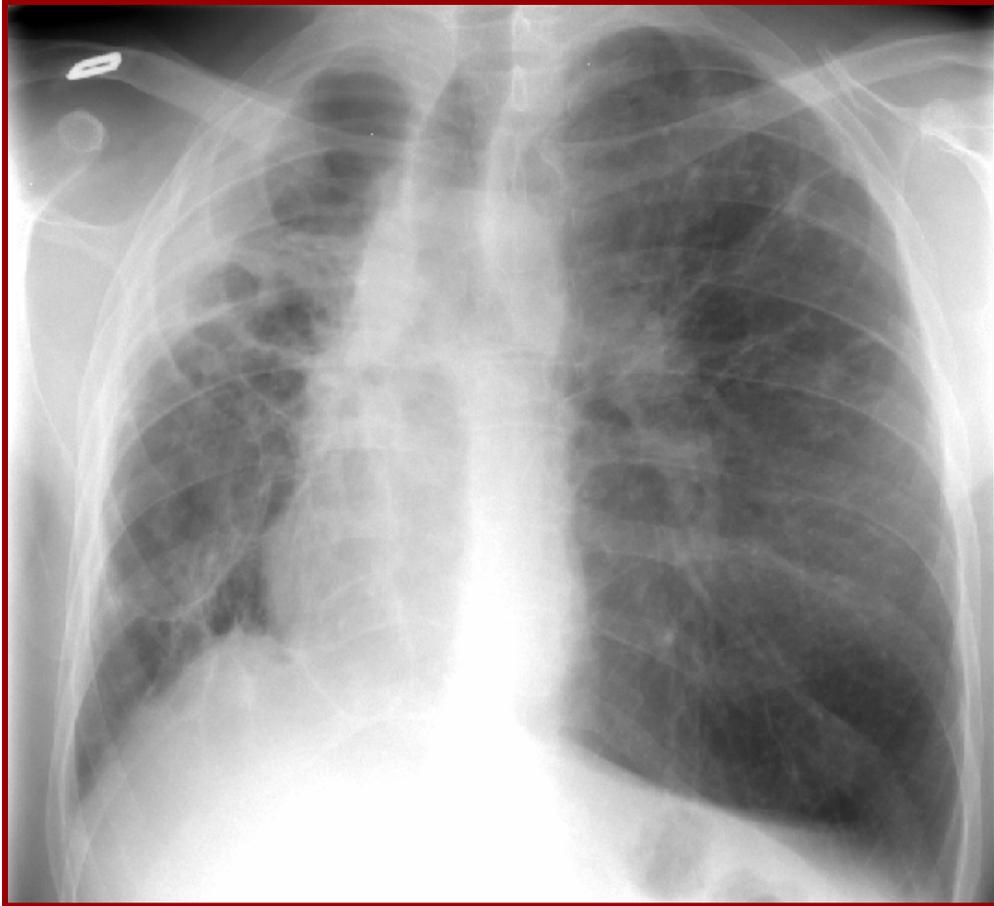
## ■ **In the prognosis** and in treatment response, it is not of decisive value either

- % deterioration in 1-2 months of treatment
- It is only indicated to take two chest X-rays for TB patients, at the start and end of treatment

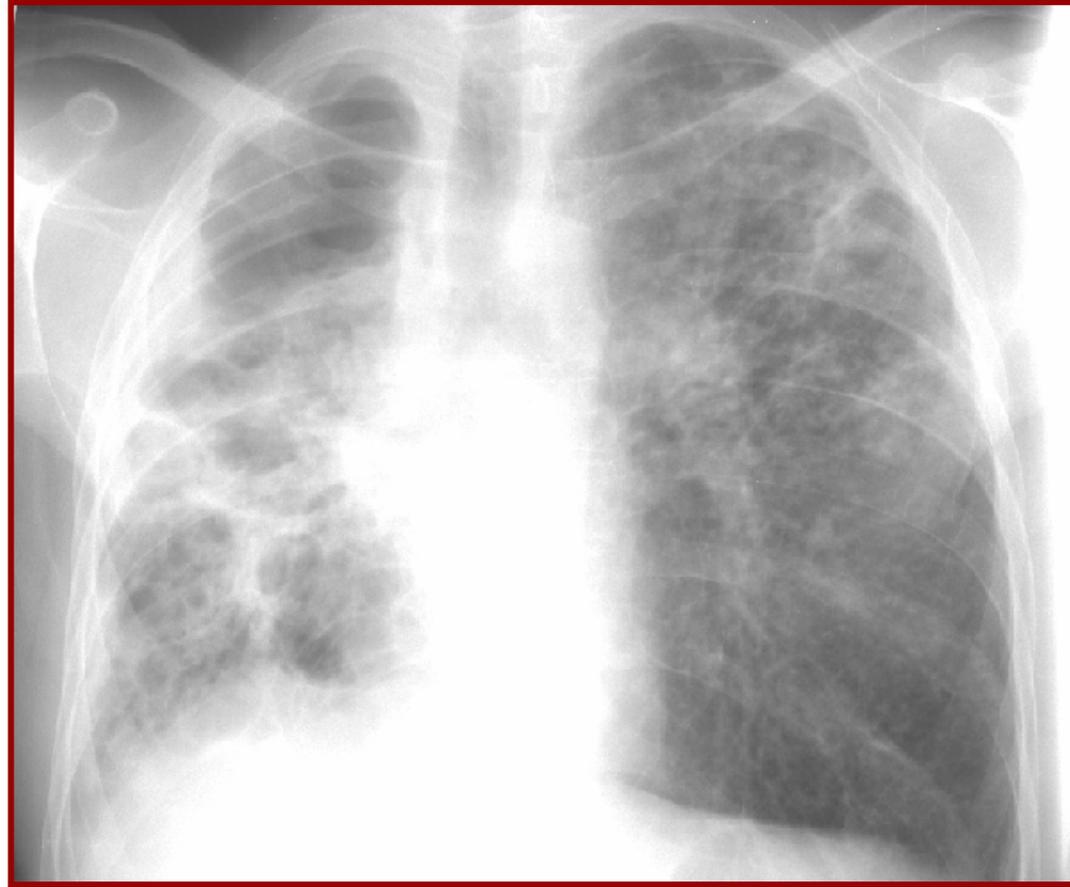


***Not Differences with MDR-TB***

# ***Radiological Manifestations of TB***



***MDR-TB at the beginning the Treatment***



***MDR-TB, 2 m Tr., good bacteriol. evolution***

# ***Conventional Microbiological Techniques in TB Diagnosis***



***1.- Bacilloscopy - Smear***

***2.- Culture***

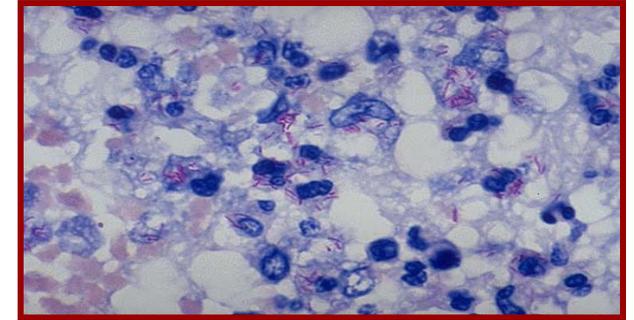
***3.- Identification***

***4.- Antibigram (DST)***



# **Limitations of the Direct Smear in the Dg of MDR-TB and in the suspect of Failure**

- **Relative Importance in the Follow-up (Died Bacillus)**



- **Limitation to Classify the Failure (Bk- 4<sup>o</sup> Mes)**

- **Contamin./Apparition other Mycobacteria**

- **Necessary CULTURE to Ident. and DST**

Anyway, Sm is very **important** in the Follow-up



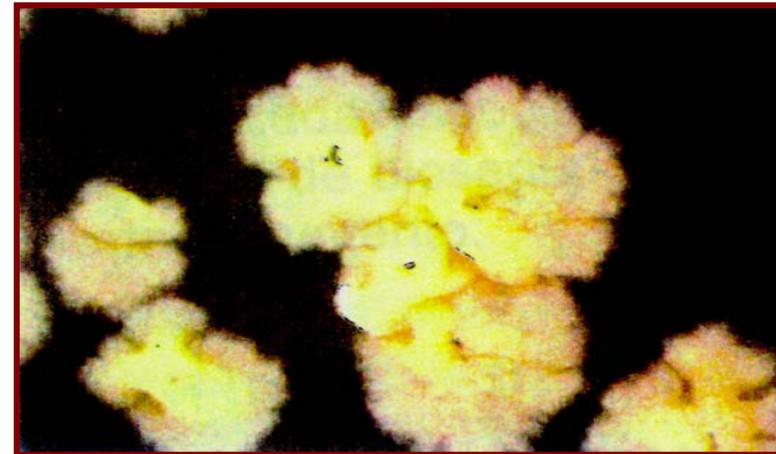
# ***Mycobacteria Culture***

## ***ADVANTAGES***

- *the only Diagnosis confirming TB*
- *more sensitive KB (detects 10 KB / ml)*

## ***DISADVANTAGES***

- *Very Slow Growth (3-8 Weeks)*
- *Less accessible than KB*
- *More expensive than KB*



*Pivotal in the Diagnosis and Follow-up of **MDR-TB***



**2 Concept that can Complicate the Follow-up of the patients with TB sensible and MDR**

***Died Bacillus***

***Bacillary Escapes***



# ***Conventional Microbiological Techniques in TB Diagnosis***

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## **4. Drug Susceptibility Test (DST)** **(Antibiogram)**



**Although all the *MDR-TB* must be *confirmed* by DST, these tests have important *Limitations*. This *Limitations* increase if we perform a DST *during* the *MDR-TB Treatment***

# *What is the true value of the Drug Susceptibility Test?*

## *First Line Drugs*

- Very Good for H and R
- Less for S and E (More reliable the Susc. Result)
- Z needs BACTEC in many countries



# *What is the true value of the Drug Susceptibility Test?*

## *Second Line Drugs*

- *Relatively good for **Aminoglycosides**  
and **Quinolones***
- *Low Reliability in the others, above all:*
  - *Eth/Pth, Cs, PAS*



# ***Monitoring Response Treatment***

1.- To evaluate the **Clinical and Bacteriological response** to the Treatment

## **1. INITIAL Phase (usually Hospitalized). MONTHLY**



- **Clinical evaluation → Above all to control the Side effects**
- **Smear and Culture**
- **X-ray film → Every 6 months**

## **2. CONTINUATION Phase. Ambulatory. Every 2-3 Months**

- **Clinical evaluation → Above all to control the Side effects**
- **Smear and Culture**
- **X-ray film → Every 6 months**

**DST only should be requested when a new Failure was accepted → Interpretation?**

# ***Treatment of the MDR-TB***



## ***Monitoring the Response***

### ***- Objectives***

- 1.- To evaluate the Clinical and Bacteriological response to the Treatment***
- 2.- To monitor the **Adverse** Reaction to the Anti-Drugs***

# *Most Common **Adverse** Anti-TB Drugs Reactions*

*(AATDR)*

*Suspected **Agents** Involved and  
Suggested **Management** Strategies*



# *Adverse ATDR. Hepatitis*

Suspected Agents: Z, H, R, Th, Of, L, Cx, Eth, PAS

## Suggested Management Strategies



- 1) Stop therapy
- 2) Rule out other potential causes of hepatitis
- 3) Re-introduce drugs grouped serially while monitoring liver function, with most likely agent introduced last

\* History of prior hepatitis should be carefully analysed to determine most likely causative agent(s); these should be avoided in future regimens

\*\* Generally reversible upon discontinuation of suspected agent



# *Adverse ATDR. Renal failure*

Suspected Agents: S, Km, Am, Cm



## *Suggested Management Strategies*

- 1) Discontinue suspected agent
- 2) Consider using Cm if an aminoglycoside had been prior parenteral in regimen

\* History of diabetes or renal disease is not a contraindication to the use of the agents listed here, although patients with these co-morbidities may be at increased risk for developing renal failure

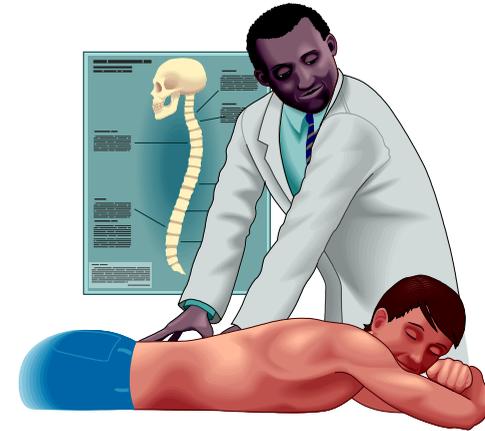
\*\* Renal impairment may be permanent

# *Adverse ATDR. Arthralgias*

Suspected Agents: Z, Of, L, Cx

## *Suggested Management Strategies*

- 1) Therapy with non-steroidal anti-inflammatory drugs
- 2) Initiate exercise regimen
- 3) Lower dose of suspected agent, if this can be done without compromising regimen
- 4) Discontinue suspected agent if this can be done without compromising regimen



\* Symptoms of arthralgia generally diminish over time, even without intervention

\*\* Uric acid levels may be elevated in some patients but are of little therapeutic relevance and anti-gout therapy (e.g. allopurinol, colchicine) is of no proven benefit in these patients



# *Adverse ATDR. Gastritis*

Suspected Agents: PAS, Th, H, Eth, Cfz, Z

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## *Suggested Management Strategies*



- 1) Antacids (e.g. Calcium carbonate, H<sub>2</sub>-blockers, proton-pump isoniazidibitors)
- 2) Hold suspected agent(s) for short periods of time (e.g. one to seven days)
- 3) Lower dose of suspected agent, if this can be done without compromising regimen
- 4) Discontinue suspected agent if this can be done without compromising regimen

# *Adverse ATDR. Nausea and vomiting*

Suspected Agents: PAS, Th, H, Eth, Cfz, Z

## Suggested Management Strategies

- 1) Rehydration
- 2) Initiate anti-emetic therapy
- 3) Lower dose of suspected agent, if this can be done without compromising regimen
- 4) Discontinue suspected agent if this can be done without compromising regimen



# ***Adverse Anti-TB Drugs Reactions. SEIZURES***

Suspected agent(s): **Cs, H, Of, L, Cx**

## **Suggested Management Strategies**

- 1) Initiate anti-convulsant therapy  
(e.g. phenytoin, valproic acid)
- 2) Increase pyridoxine to 300mg daily
- 3) Lower dose of suspected agent, if this can be done without compromising regimen
- 4) Discontinue suspected agent if this can be done without compromising regimen

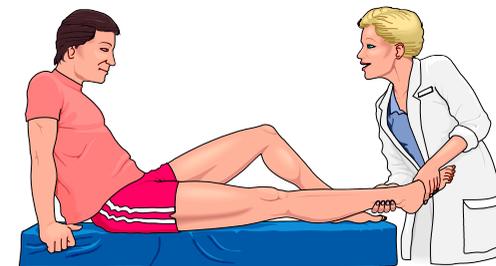




# ***Adverse ATDR. Peripheral Neuropathy***

**Suspected Agents: S, Km, Am, Cm, Th, Cs, Eth, Of, L, Cx**

## **Suggested Management Strategies**



- 1) Increase pyridoxine to 300mg daily
- 2) Change parenteral to Cm if patient has documented susceptibility Cm
- 3) Begin exercise regimen, focusing on affected regions
- 4) Initiate therapy with tricyclic anti-depressant drugs
- 5) Lower dose of suspected agent, if this can be done without compromising regimen
- 6) Discontinue suspected agent if this can be done without compromising regimen
- 7) Initiate therapy with neurontin

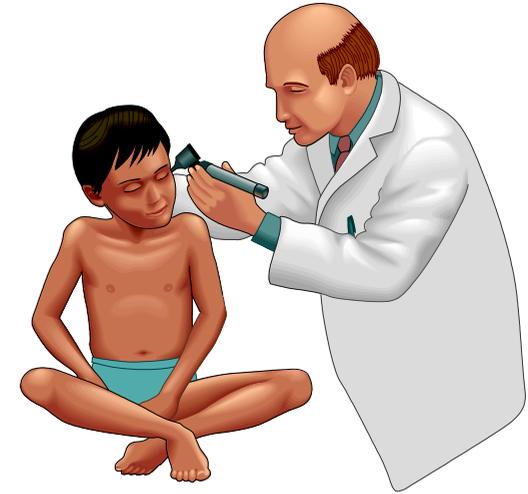


# ***Adverse ATDR. Hearing loss***

**Suspected Agents: S, Km, Am, Cm, Clr**

## **Suggested Management Strategies**

- 1) Change parenteral to Cm if patient has documented susceptibility Cm
- 2) Lower dose of suspected agent, if this can be done without compromising regimen
- 3) Discontinue suspected agent if this can be done without compromising regimen



\* If patients have received prior treatment with aminoglycosides, they may start therapy with hearing loss \*\* Hearing loss is generally not reversible

# ***Adverse ATDR. Psychotic symptoms***



**Suspected Agents: Cs, Of, L, Cx, H, Th**

## **Suggested Management Strategies**

- 1) Initiate anti-psychotic drugs
- 2) Hold suspected agent for short period of time (one to four weeks) while psychotic symptoms brought under control
- 3) Lower dose of suspected agent, if this can be done without compromising regimen
- 4) Discontinue suspected agent if this can be done without compromising regimen



# *Adverse ATDR. Depression*

**Suspected Agents:** Socio-economic circumstances, Cs, Of, L, Cx, H, Th

## *Suggested Management Strategies*

- 1) Improve socio-economic conditions
- 2) Group or individual supportive counselling
- 3) Initiate anti-depressant drugs
- 4) Lower dose of suspected agent, if this can be done without compromising regimen
- 5) Discontinue suspected agent if this can be done without compromising regimen





## *Adverse ATDR. Hypothyroidism*

Suspected Agents: PAS, Th, especially when given in combination

### *Suggested Management Strategies*

- 1) Initiate thyroxine therapy
- 2) Substitute equally efficacious agent for Tha or PAS



### *Comments*

- Completely reversible upon discontinuation of PAS or Tha

# ***Monitoring Response Treatment***

## **2.- To monitor the *Adverse* Reaction to the Anti-Drugs**

### **1. *INITIAL* Phase (usually Hospitalized). *MONTHLY***

- *Clinical evaluation* → Above all to control the Side effects
- *Serum creatinine, potassium, Liver enzymes, Hemogram*
- *Thyroid stimulating hormone* → Every 6 m. if Eth/PAS



### **2. *CONTINUACION* Phase. Ambulatory. Every *2-3 Months***

- *Clinical evaluation* → Above all to control the Side effects
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# Treatment of the MDR-TB

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- Serum creatinine, potassium, Liver enzymes, Hemogram
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- X-ray film → Every 6 months



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**DST** only should be requested when a new **Failure** was accepted → **Interpretation?**