Current Standards of Care for HIV-TB some clinical issues

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- ADDIS ABABA August 2010

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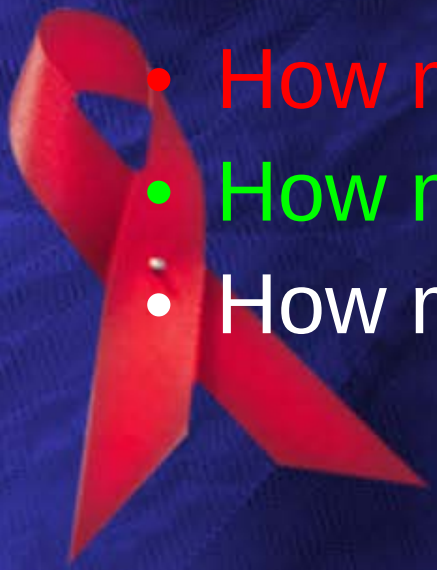
Goal of TB & HIV Collaborative Activities

To decrease
the burden of TB and HIV
in co-infected patients

At your institution ?

- How many doors to knock from a cough to a TB diagnosis including HIV prevention and care ?
- How many faces to meet for HIV care that includes TB screening?
- How many queues?
- How many messages?
- How many infectious germs transmitted?
- How many patients lost in between?



Vincent Tihon

HIV & TB Collaboration and Integration

TB program

HIV program

Collaboration : level of relationship and coordination between the two programs to ensure the provision of a comprehensive service to co-infected patients in a most effective and efficient manner

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Integration is where both TB and HIV prevention and care provided simultaneously to the co-infected patient . It is holistic patient centred care

HIV & TB Collaboration and Integration

TB program

HIV program

Infection control

Highly susceptible patients + TB contagious patients

One patient

Two diseases (or more)

One consulting room

Hospital entry points

- TB entry
  - HIV counselling & Testing (ICF)
  - HIV prevention
  - ARV therapy
  - Cotrimoxazole
  - HIV care and support
- HIV entry
  - TB screening (ICF)
  - INH prophylaxis
  - TB treatment
  - TB care and support

Integration at entry points

- TB entry
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Staff skills& competency in HIV and TB

Information :literacy sessions for both HIV &TB

Infection control

Consulting rooms STI friendly

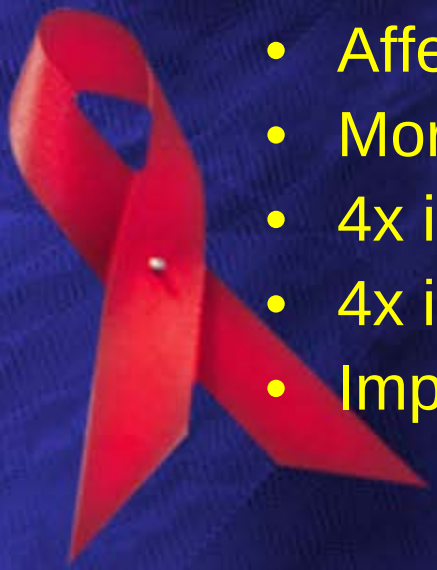
Appropriate place for sputum collection

Standardised recording

Ensure integrated supportive supervision

TB is different in HIV Co-infection

- HIV mimics TB.
- Increased TB incidence .
- Faster progression from infection to disease.
- Alters clinical presentation.
- Alters radiological appearance.
- Affects yield of diagnostic tests.
  - Smear, culture
- Affects treatment: drug toxicity, drug interactions,
- More paradoxical IRIS reactions.
- 4x increase in relapse of TB (~4 increased)
- 4x increase in mortality
- Impacts on response to treatment



Specific issues with HIV/TB

- TB more difficult to diagnose in HIV patients
- Drug adverse events and toxicities
- Paradoxical IRIS reactions
- INH preventive therapy
- When to start ARV in TB patients

Changes in TB clinical presentation with HIV

	HIV Neg.	Early HIV	Advanced HIV (low CD4 Counts)
Site of Infection	PTB:80% EPTB:16% Both:4%	Inter-mediate	PTB:20% EPTB:50% Both:30% (disseminated and more Blood culture +)
CXR	50-70%-upper lobe, fibro-cavitatory	Mixed typical & atypical	Atypical- effusions, lower zone infiltrates, adenopathy, miliary, normal (poor granuloma formation)
Smear +ve	70-80%	50%	25 - 40% (paucibacillary disease)

Screening for TB in all HIV clients before ARVs and IPT.

Screening tool for Intensive case finding

- Fever > 2w
- Drenching Night sweats > 2w
- Weight loss of > 5% over 1 month
- Cough >2w.

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(≥ 2 symptoms: sensitivity near 100% & specificity of 88%)

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TB workup : 2 smears for AFB If AFB –ve

-CXR , 3rd AFB, S-Culture, Antibiotics,

Clinical assessment (BF-C,US, LN Aspirate, LP, X-Ray)

Screen all HIV clients for INH preventive therapy

- BENEFIT
  - Treats latent TB preventing progress to Active TB
- EXCLUDE
  - Active TB
  - patients with liver disease or active alcohol abuse
- INCLUDE
  - Asymptomatic HIV clients not eligible for ARV (CD4 >350)
  - Patients on ARV
    - who are asymptomatic and stable
    - if previous TB, completed TB treatment more than 18m ago
- DOSE
  - INH 5mg/kg /day up to 300mg daily for 6m
  - Also give pyridoxine 25 mg daily

RIF reduces levels of NNRTI and PI

- Rifampicin induces CYP3A4 (P450 enzyme system)
- NRTI
  - EFV (22%) NVP (37%) reduction
  - Trough levels of EFV sufficient
  - Do not need to increase doses
  - Avoid NVP shared toxicity (hepatotoxicity)
- PI
  - Single PI not recommended with RIF
  - Boosted PI (Lip/Rit) ie Kalitra /Aluvia
    - Give Liponovir 400mg and Ritonovir 100+300=400mg BD

ARV with TB treatment

- Change NVP to EFV
- LIP/RIT add 300mg of Ritonovir

- 3TC, AZT,TDF, ABC Ok

Shared Toxicities

	TB medication	ART
Hepatitis (ALT>200 or Bilirubin >44)	Rifampicin INH PZA	NNRTIs (NVP > EFV) Protease inhibitors ("super-boosted")
Drug rash	All TB medication (RIF INH,PZA,ETH)	NNRTIs (NVP>EFV)
Neuropathy	INH	D4T ddI
Nephrotoxicity	Aminoglycosides Rifampicin	Tenofovir
Nausea and vomiting	All TB medication (PZA)	AZT ddI Protease inhibitors (Rit)

Severity of drug reactions

Asymptomatic mild LFT derangement

Life threatening hepatic failure

HEPATITIS

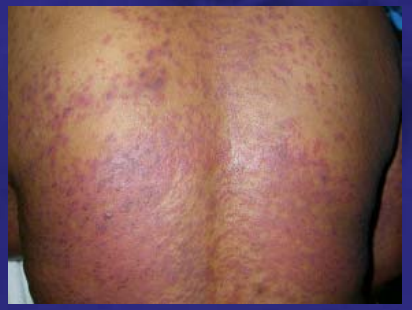
Mild maculopapular rash

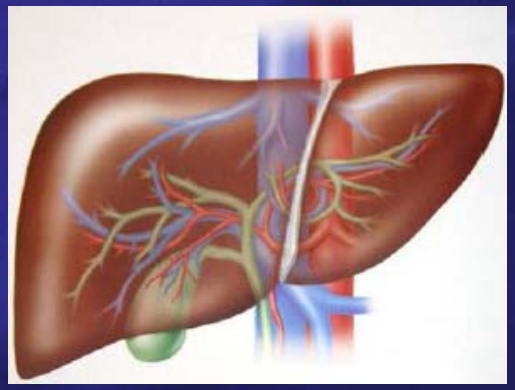
Stevens Johnson TENS

RASH

Severe Hepatitis/Rash

- Hospitalization
- Interrupt drugs
  - Also clotrimoxazole
- Monitor LFT
- Re-challenge regime (various complex regimes/timing)





Paradoxical TB-IRIS

Patient diagnosed with TB and started on TB treatment

⬇

Typically improving on TB treatment then start ART

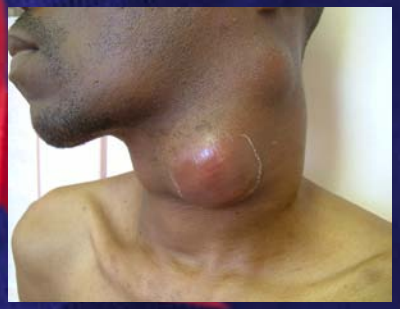
⬇

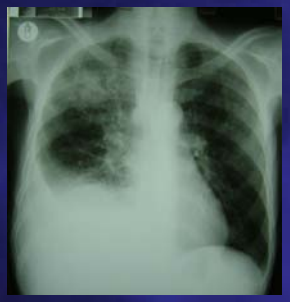
Recurrence of TB symptoms and new or recurrent clinical manifestations of TB

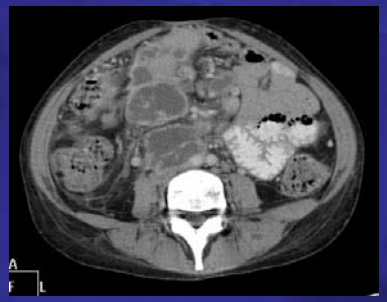
(Usually 1-4 weeks after starting ART)

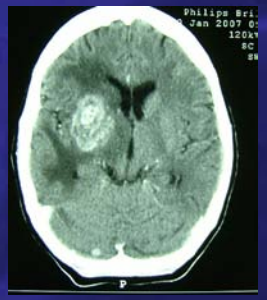
25% of patients starting ART are on TB treatment in Cape Town

8-43% of patients on TB treatment when starting ART develop paradoxical TB-IRIS









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Paradoxical TB-IRIS is a diagnosis of exclusion

ALTERNATIVE DIAGNOSIS

Bacterial infections
Fungal infection
PCP
NTM
Lymphoma
Kaposi's sarcoma

DRUG RESISTANT TUBERCULOSIS

DRUG REACTION

Drug fever vs TB-IRIS fever
Hepatic involvement

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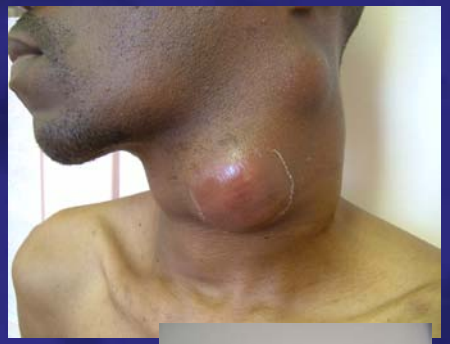
TB IRIS Diagnosis

- No confirmatory diagnostic test

- Diagnosis relies on
  - Clinical deterioration with features of TB
  - Temporal relationship to ART initiation
  - Exclusion of alternative diagnoses
  - (Demonstration of response to ART)

Management

- Corticosteroids mostly used
  - Prednisone
    - 1 mg/kg/d (max 60 mg) for 2 weeks then
    - 0.75 mg/kg/d for 2 weeks
- Reported benefit
  - Decreased hospitalization
  - Improved symptoms and Quality of Life
- Potential risks
  - More milder infections
  - Kaposi's sarcoma
  - Herpes virus reactivations
  - If undiagnosed MDR-TB, may worsen condition
- Other
  - Aspiration of pus collections
  - NSAID



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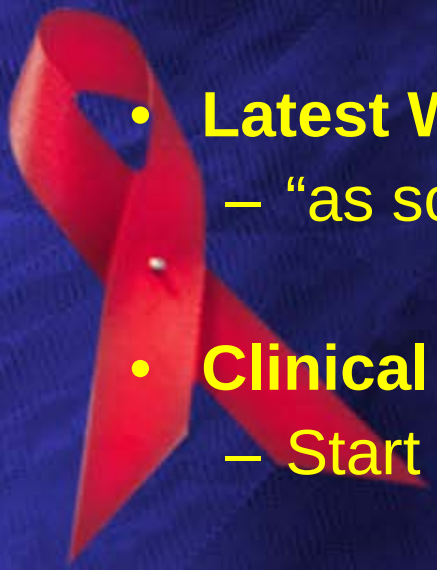
When to start ART in TB patients?

- **New SA DOH guidelines**
  - All HIV-TB patients with CD4 < 350 eligible
- **Major issue**
  - Balancing risk of mortality from TB-IRIS vs mortality from delaying ART
- **Latest WHO guideline**
  - "as soon as possible after starting TB treatment"
- **Clinical trials evidence awaited**
  - Start at 2 weeks vs 2 months?

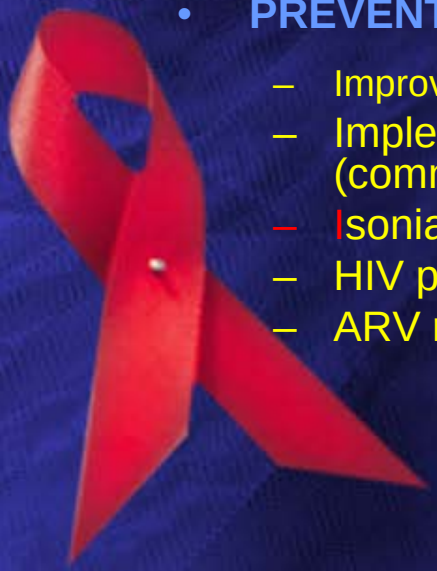


- **COLABORATE & INTEGRATE**

- **FIND**
  - Intensive case finding to identify patients earlier
  - More difficult to Diagnose TB in HIV Patients
  - Explore new diagnostics (Molecular, MODS)
  - Improve availability of culture in high HIV prevalent settings

- **TREAT AND SUPPORT**
  - Appropriate standardized treatment
  - Special issues with HIV/TB treatment (IRIS, Drug adverse events, clinical picture)
  - Information Patient literacy
  - Community support

- **PREVENT**
  - Improved TB program decreases generation of TB & MDRTB
  - Implement Infection control to prevent Air borne transmission of all TB strains (community, clinics , hospitals)
  - Isoniazid Preventive Therapy
  - HIV prevention strategies
  - ARV rollout



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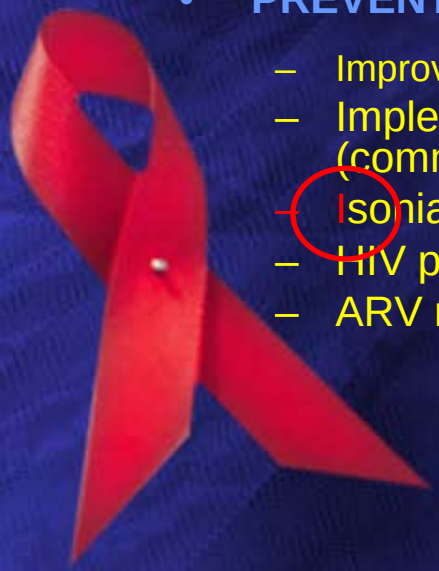

New TB Drugs?

- Ingest Innovative Ingredients

Thank You

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