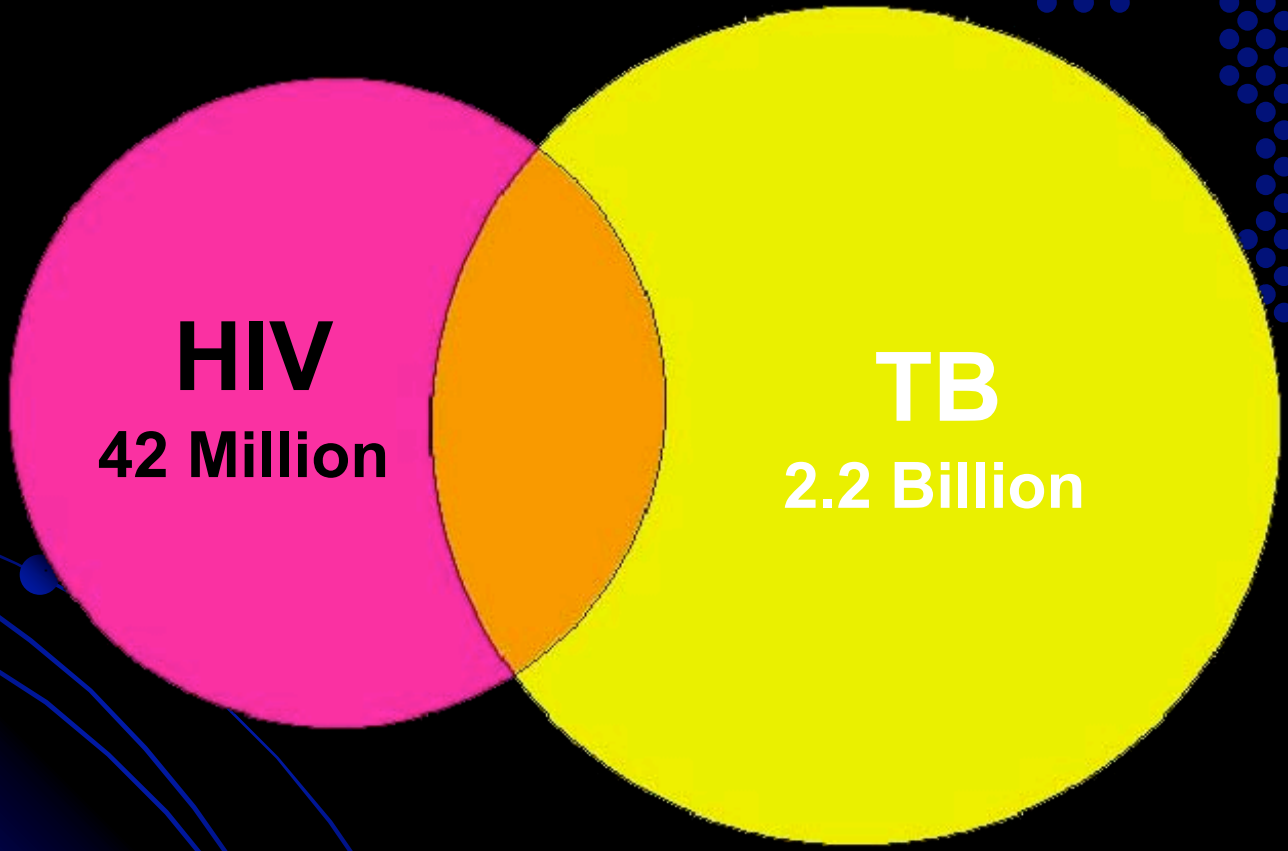
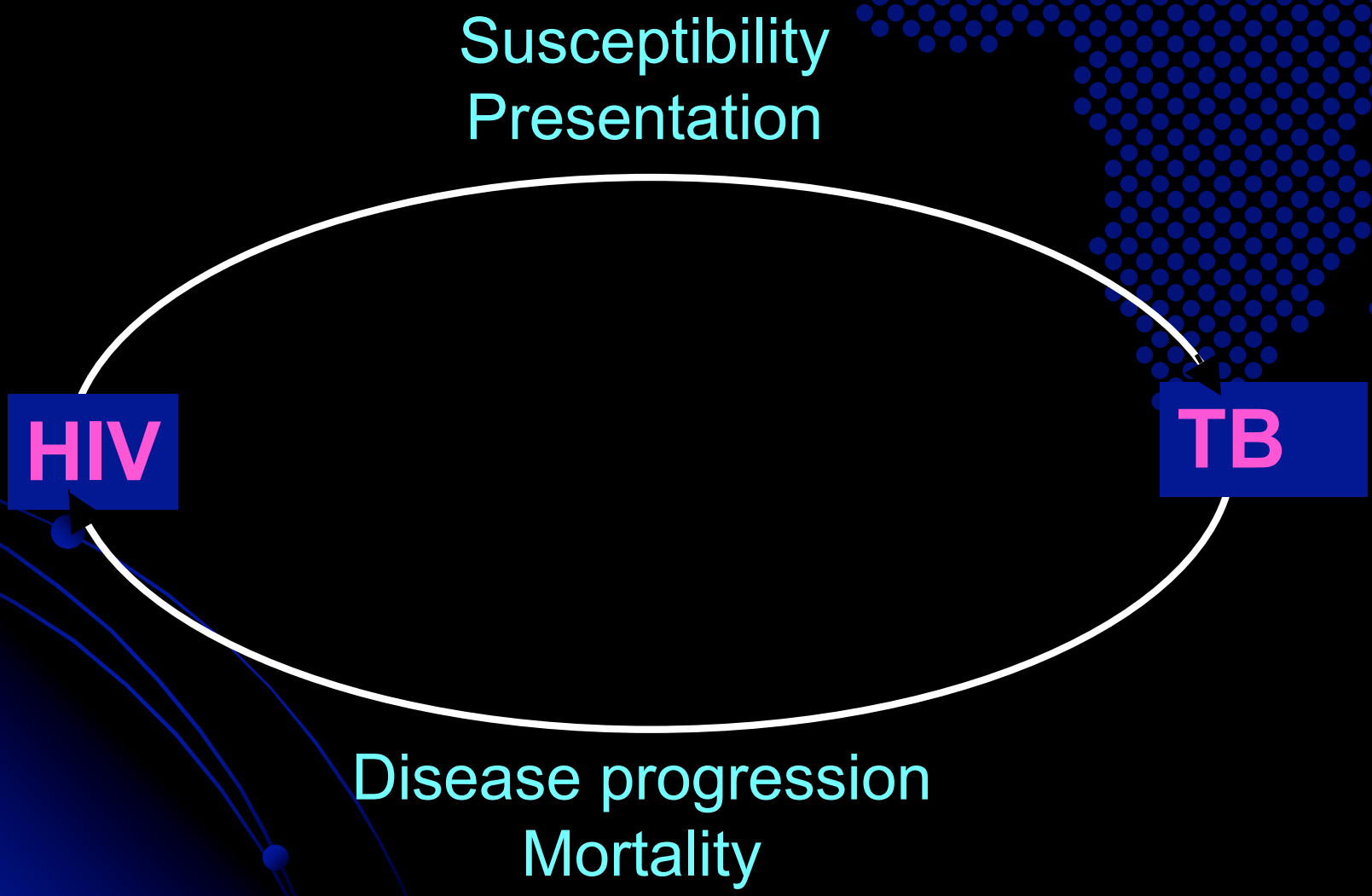
MANAGEMENT OF TB IN PATIENTS CO-INFECTED WITH HIV

F MUGUSI

The Dual Epidemic



Dual Infection: HIV and TB



MTB Disease in AIDS Patients

- 75 % of patients have pulmonary disease
- 20 – 59 % have hilar or mediastinal adenopathy
- 12 – 28 % have pleural effusions
- 7 – 18 % have miliary pattern
- 12 % have normal CXR, positive sputum culture
- Other diseases masquerade as TB

Dual Epidemic: Response

- Early detection of active TB disease
- Prompt treatment of TB
- HIV testing among TB patients
- TB Preventive therapy

Collaboration between HIV and TB efforts

Identification and Testing

- Offer HIV testing for all TB patients
- Evaluate all HIV patients for TB

In 3 U.S.-based studies, < 50 % TB cases offered HIV testing.

NEJM, 1999

Management of TB in HIV involves

- Management of Latent TB infection
- Management of active TB disease
- Cotrimoxazole prophylaxis against OIs in TB/HIV patients

Antiretroviral Therapy and TB experiance

- Improved immune responses to TB with HAART
- Reduction in case rates of TB during HAART era
- HAART could reduce risk of primary infection, relapse, and re-infection

Challenges of TB treatment in HIV positive patients

- Drug drug interactions
- Added drug toxicity
- Pill load → may affect adherence
- Immube reconstitution syndrome

Antiretroviral Therapy and TB Treatment

- Drugs commonly used for TB treatment include: Isoniazid (H), Rifampicin (R) Pyrazinamide (Z) and Ethambutol (E)
- Rifampicin and Isoniazid→ the cornerstone for anti TB theerapy
- Many HIV medications have significant drug interactions with Rifampicin, a cornerstone of TB therapy.

Effects of Rifampicin on HIV Drugs

- Three main groups of ARVs used in Tanzania➔ NRTIs, NNRTIs, PIs
- ART is made up of a combination of:
  - Triple NRTIs
  - 2NRTIs +1 NNRTI
  - 2NRTI + PI (boosted)
- Rifampicin activates liver enzymes (CYP450) that accelerates the elimination of PIs and NNRTIs

Effects of Rifampicin on HIV Drugs

- Protease inhibitors
  - Saquinavir 80 % decrease
  - Ritonavir 35 % decrease
  - Indinavir 92 % decrease
  - Nelfinavir 82 % decrease
  - Amprenavir 81 % decrease
- Nonnucleoside reverse transcriptase inhibitors (NNRTI)
  - Nevirapine 37 % decrease
  - Delavirdine 95 % decrease
  - Efavirenz 26 % decrease

TB Treatment in HIV infected patients

- Treat HIV+ TB patients the same as HIV–
- Early clinical response to therapy appear to be similar for HIV positive and Negative
- Rates of TB relapse may be higher in HIV positive compared to negative patients
- Current TB treatment in TZ: HRZE for 2 months, followed by HR for 4 months

TB Treatment in HIV Co-infected Patients

- Response rates similar between HIV+ and HIV– patients
- Components of successful therapy:
  - Resistance testing
  - DOTS
- Multiple-drug-resistant TB will emerge and spread with inadequate treatment programs

Issues in initiating antiretroviral therapy in HIV patients with TB

TB and HIV: Immediate vs. Delayed Therapy (1)

- TB treatment must be given urgently.
- The urgency of HIV treatment depends on predictors of HIV disease progression (HIV RNA level, CD4 cell count, prior HIV-related diagnoses).

TB and HIV: Immediate vs. Delayed Therapy (2)

Arguments to withhold potent HIV therapy until TB is treated:

1. HIV is a chronic disease.
2. Adherence may be compromised.→pill load, added drug toxicity, complexity of regimen
3. Toxicity management is more complex.
4. Immune restoration may produce “paradoxical reactions.”

TB and HIV: Immediate vs. Delayed Therapy (3)

Arguments to initiate potent HIV therapy at the onset of TB:

1. TB is associated with immune activation, increases HIV replication, and HIV disease progression.
2. Potent antiretroviral therapy can reduce HIV RNA levels, improve immune function and slow HIV disease progression.

- HIV therapy reduces risk of developing opportunistic infections
- Improves quality of life

Antiretroviral Therapy Options

- Triple NRTI with Rifampicin
- NNRTI (EFV)* with Rifampicin
- Ritonavir + saquinavir with rifampicin
- Other rifamycins (eg. Rifabutin) with Protease inhibitor (IDV, NFV, APV)*

*Dose adjusted

Guidelines on the management of TB in HIV infected patients in Tanzania

- In patients who have both TB and HIV priority is to treat TB
- ART and anti-TB treatment may be required in severely immunocompromised patients

Management of TB in HIV infected patients in Tanzania

2 scenarios

- Patient on ART develops TB
- Patient develops TB before starting ART

PT on ART develops TB

- ART should be continued throughout TB treatment, with changes as follows:
- 1st line drugs: Substitute Nevirapine for Efavirenz.
- 2nd line drugs replace LPV/r with SQV/r

TB before starting ART

- If the patient has a CD4+ count >350 cells/mm3, ART is not yet needed. reassess on completion of TB treatment.
- If the patient has h/o WHO Stage 4 illness and/or a CD4+ count of 200 –350 cells/mm3, complete 2 months of TB therapy before commencing ART.
- If the patient has a CD4+ count <200 cells/mm3 or or current WHO stage 4 illness start ART. As soon as patient tolerates anti-TB

Special considerations of ART in TB and HIV co-infected patients

CD4 > 350	Treat TB first, re-asses for ART after completion of TB treatment
CD4 200 – 350	Treat TB first for two month before starting ART
CD4 < 200 or CD4 < 15% or WHO HIV stage 4	Begin ART as early as 2 weeks after TB treatment initiation

Drugs of choice

- 1st line drugs
  - AZT or d4T+3TC+EFV (NVP)
  - (TDF+FTC+EF)
- 2nd line drugs
  - ABC+ddI+SQV/r

  (Replace LPV/r with SQV/r (400mg/400mg))

Cotrimoxazole preventive therapy (CPT) in HIV positive TB patients

- CPT proven to be beneficial to HIV, including HIV+ TB patients
- Prevents several secondary bacterial, fungal and parasitic OIs.
- This reduces morbidity and hospital admission for OI significantly.
- The 6-8 months TB treatment provides a unique opportunity to provide CPT concurrently since adherence to treatment is a major concern for both TB treatment and CPT.

Summary: HIV/TB Treatment Approach

- Treat TB first as a priority
- Determine urgency of treating HIV
- Start antiretroviral therapy if CD4 < 200
- Consider drug interactions in HIV regimen selection
- DOTS and careful monitoring
- Prophylaxis against OIs using cotrimoxazole