TB and Comorbidities

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Comprehensive TB Nurse Case Management
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San Antonio, Texas

Adriana Vasquez, MD, has the following disclosures to make:

- No conflict of interests
- No relevant financial relationships with any commercial companies pertaining to this educational activity

HEARTLAND NATIONAL TB CENTER
A PARTNERSHIP OF UT HEALTH NORTHEAST AND TCID

TB and Comorbidities

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June 2024

Agenda

- TB and HIV
- TB and DM
- TB in patients with chronic kidney disease
- TB and tobacco
- TB in patients with liver disease

TB and HIV

WORLDWIDE TUBERCULOSIS IS THE LEADING CAUSE OF DEATH AMONG PEOPLE LIVING WITH HIV.

Patient with TB /HIV and Bipolar Disorder

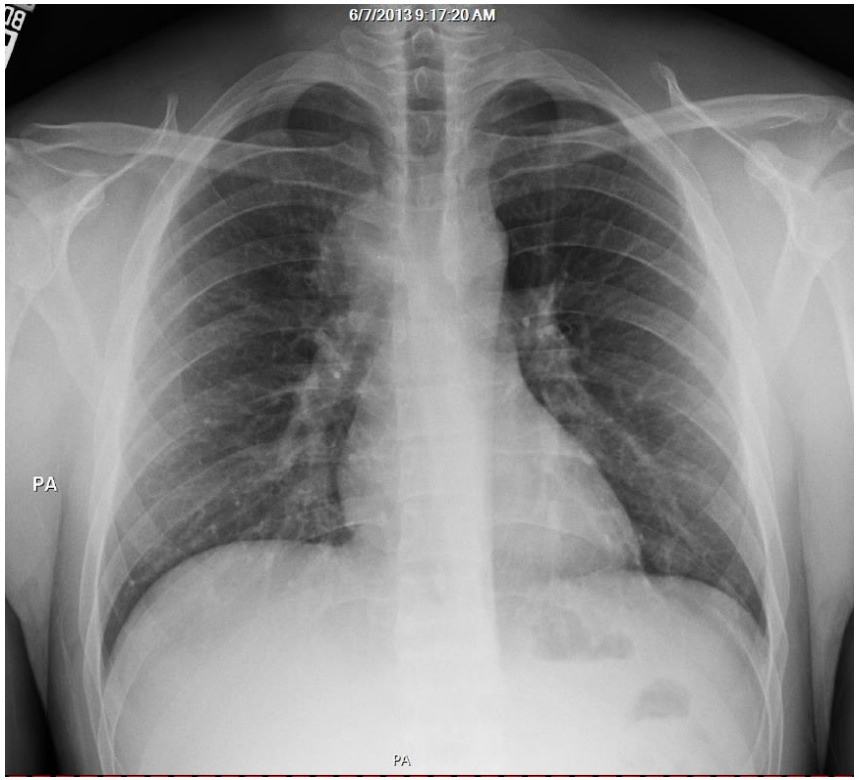
- **30-year-old Hispanic male who was referred to TCID for treatment of pulmonary tuberculosis with history of HIV infection, bipolar disorder, HCV, substance abuse and lack of housing.**
  - **Chest X-ray normal**
  - **Sputum AFB smear negative cultures positive for *MTB, pan-susceptible*.**

Hospital Course

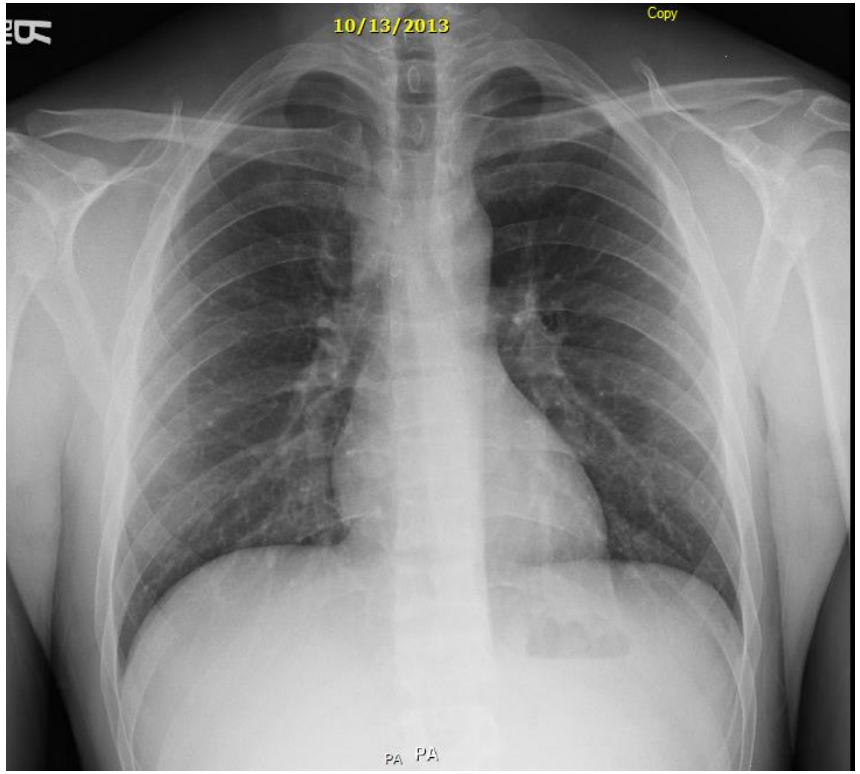
- Admitted to TCID and
  - Started on Rifampin/INH/PZA/EMB
  - Became manic and left against medical advice
- Readmitted under court order one month later

- After 2 weeks was started on antiretrovirals
  - Dolutegravir 50 mg BID and Truvada 1 tab Qday
- Developed IRIS, treated with prednisone

CXR 6 weeks after ART

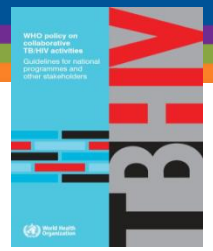


CXR at the end of Therapy



Treatment Outcomes Person with TB HIV Infection and Bipolar Disorder

- **Completed TB treatment at TCID under court**
- **Discharged with undetectable HIV viral load**
- **Discharged with psychiatry and HIV physician follow up**



HIV Associated Tuberculosis

- **Persons co-infected with TB and HIV are 19 times more likely to develop active TB disease than persons without HIV**

- **Risk of progression from TBI to TB disease is 10% per year versus 10% lifelong in HIV negative patients**

- **TB is the leading cause of death among people with HIV**

» https://www.who.int/tb/areas-of-work/tb-hiv/tbhiv_factsheet.pdf?ua=1

COLLABORATIVE TB/HIV ACTIVITIES: RESPONSE & PROGRESS

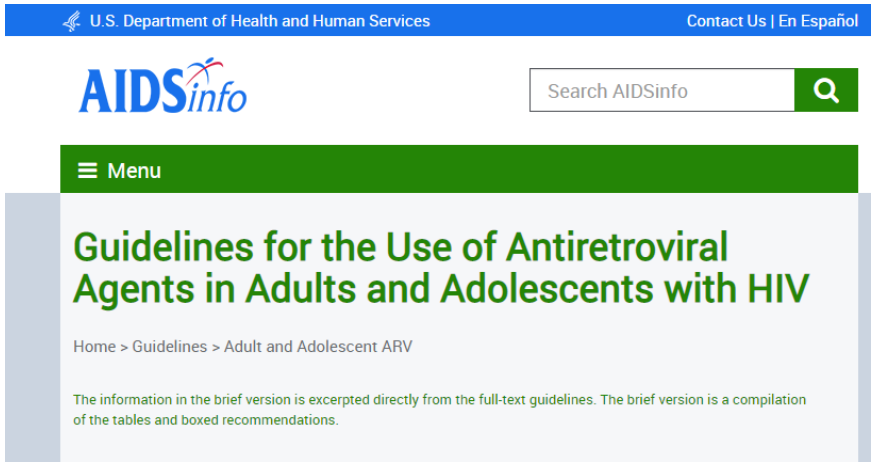
- **HIV testing should be offered to all patients with TB**

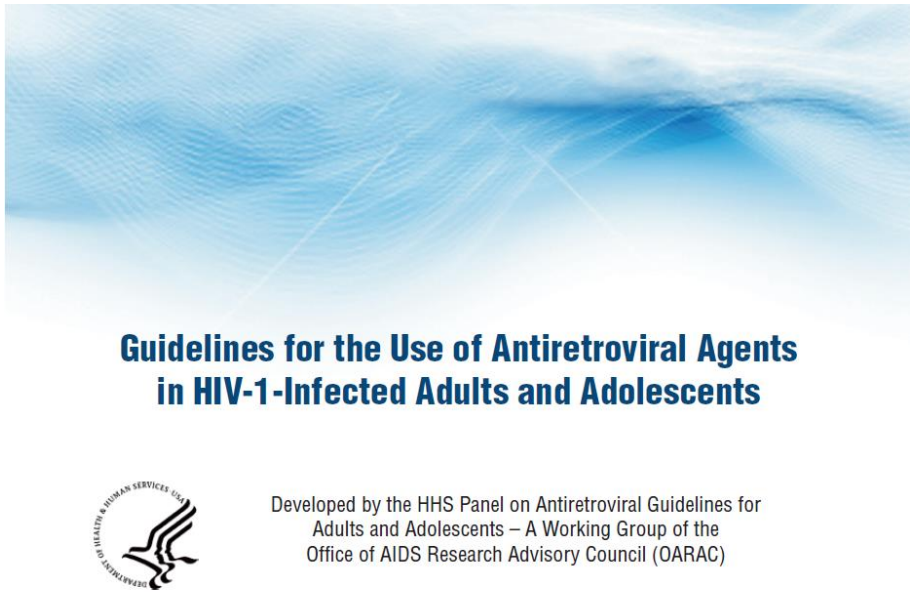
- **Antiretroviral therapy (ART) should be given to all TB patients living with HIV, irrespective of their CD4 counts.**

https://www.who.int/tb/areas-of-work/tb-hiv/tbhiv_factsheet.pdf?ua=1

Clinical Presentation of TB in HIV

	Early Stage HIV CD4>200	Late Stage HIV CD4 <200
Clinical picture	Often resembles post-primary pulmonary TB	Often resembles primary pulmonary TB
Sputum Smear	Often positive	More likely to be negative
Chest x-ray	Upper lobe infiltrates with or without cavitation	Infiltrates any lung zone, no cavitation, miliary; normal





http://aidsinfo.nih.gov/guidelines

Recommended TB Treatment

- **Intensive phase with RIPE for 2 months**
- **Continuation phase with INH and rifampin for 4 months**
- **Extend therapy to 9 months for patient with**
  - **Positive cultures at 2 months or delayed treatment response**
  - **Patients not receiving ART during TB therapy**

https://www.cdc.gov/tb/publications/factsheets/treatment/treatmenthivpositive.htm

ART is Recommended in all HIV-Infected Persons with TB

- **Person already on ART, start TB treatment immediately**
  - **Adjust ART to reduce risk of drug-drug interactions**

- **ART-naïve patients**
  - **CD4 count is <50 cells/mm3, Initiate ART as soon as possible, but within 2 weeks of starting TB therapy (AI)**

  - **CD4 count >50 cells/mm3, initiated ART within 8 weeks of starting TB treatment (AI)**

- **With TB meningitis: When initiating ART early, patients should be closely monitored as high rates of adverse events and deaths have been reported in a randomized trial (AI)**

https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/27/tb-hiv
Last uptdated December18,2019

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IRIS
(Immune Reconstitution Inflammatory Syndrome)

- **Initial response to therapy then clinical and radiographic worsening due to ART –induced immunity restoration**

- **Diagnosis of Exclusion, differential includes**
  - **Treatment failure, drug resistance?**
  - **Other opportunistic infections**
  - **Drug reaction**

- **Treatment**
  - **Mild cases use NSAIDS**
  - **More severe cases use steroids**
  - **Don't stop TB treatment or ART**

Prednisone Dosing for IRIS

- **In patients on a rifampin-based regimen: prednisone 1.5 mg/kg/day for 2 weeks, then 0.75 mg/kg for 2 weeks**
- **In patients on a rifabutin plus boosted PI based regimen: prednisone 1.0 mg/kg/day for 2 weeks, then 0.5 mg/kg/day for 2 weeks**
- **A more gradual tapering schedule over a few months may be necessary in some patients.**
- **Pre-emptive prednisone regimen: 40 mg/day for 2 weeks then 20 mg/day for 2 weeks**

  - https://aidsinfo.nih.gov/guidelines/brief-html/4/adult-and-adolescent-opportunistic-infection/325/mycobacterium-tuberculosis
  - Revised December18, 2019

Effects of HIV on TB

- **HIV and TB → AIDS-defining illness**
- **HIV infection accelerates TB progression**
- **HIV increases the risk of extra pulmonary and disseminated TB**
- **TB is more difficult to diagnose in HIV infected patients**
  - **Sputum often AFB smear negative**
  - **Atypical presentation**

Neil A. Martinson; Proc Am Thorac Soc Vol 8. pp 288–293, 2011

Effect of TB on HIV

- **TB increases the risk of death in HIV + patients**
- **TB worsens HIV infection**
- **TB is harder to diagnose in HIV-positive people.**
- **TB occurs earlier in the course of HIV infection than many other opportunistic infections.**
- **TB increases HIV viral load**

Badri M, Association between tuberculosis and HIV disease progression Int J Tuberc Lung Dis. 2001;5(3):225.

Drug Interactions: Rifamycin and TB Treatment

- **Rifampin interacts with many medications use to treat HIV**
- **Rifabutin can be substituted for rifampin to decrease the drug-drug interaction with ART**
- **As new ART agents and more pharmacokinetic data become available, these recommendations are likely to change**

» https://aidsinfo.nih.gov/guidelines/brief-html/4/adult-and-adolescent-opportunistic-infection/325/mycobacterium-tuberculosis

» Last updated December18,2019

Case Management

- Consult an expert in management HIV and TB
- Close attention to adherence to ART and TB meds
- Drug-drug interactions
- IRIS
- Side effects of medications
- TB treatment failure and relapse

» https://www.cdc.gov/tb/publications/factsheets/treatment/treatmenthivpositive.htm

TB and Diabetes

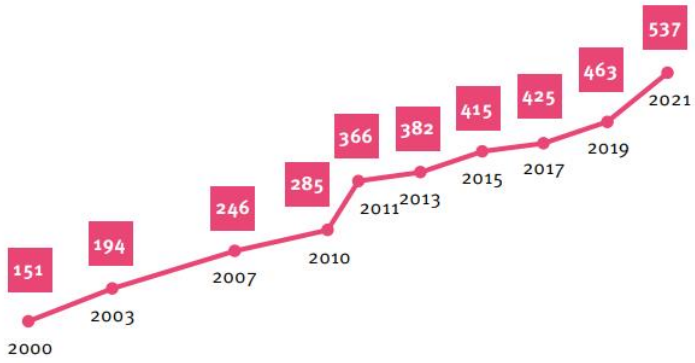
International Diabetes Federation

IDF Diabetes Atlas

10TH edition

2021

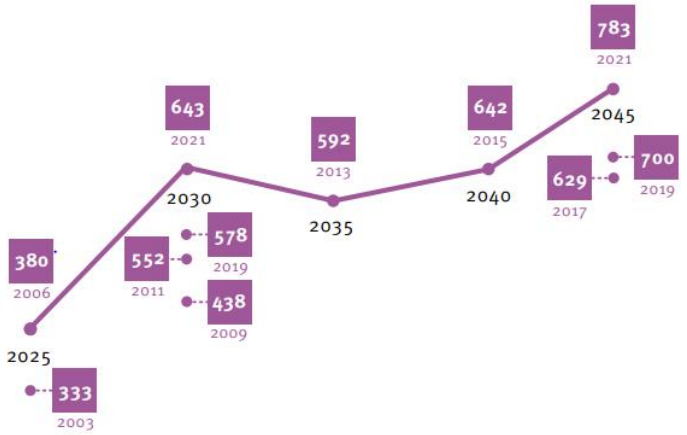
Estimates of the global prevalence of diabetes in the 20–79 year age group (millions)



Key

151 Number of people with diabetes in millions

Projections of the global prevalence of diabetes in the 20–79 year age group (millions)



Key

333 Projection in millions

2003 Year projection made

International Diabetes Federation

IDF Diabetes Atlas

2021

10TH edition

World

2045	783 million
2030	643 million
2021	537 million

46% increase

North America & Caribbean (NAC)

2045	63 million
2030	57 million
2021	51 million

24% increase

Europe (EUR)

2045	69 million
2030	67 million
2021	61 million

13% increase

Western Pacific (WP)

2045	260 million
2030	238 million
2021	206 million

27% increase

South & Central America (SACA)

2045	49 million
2030	40 million
2021	32 million

50% increase

Africa (AFR)

2045	55 million
2030	33 million
2021	24 million

134% increase

Middle East & North Africa (MENA)

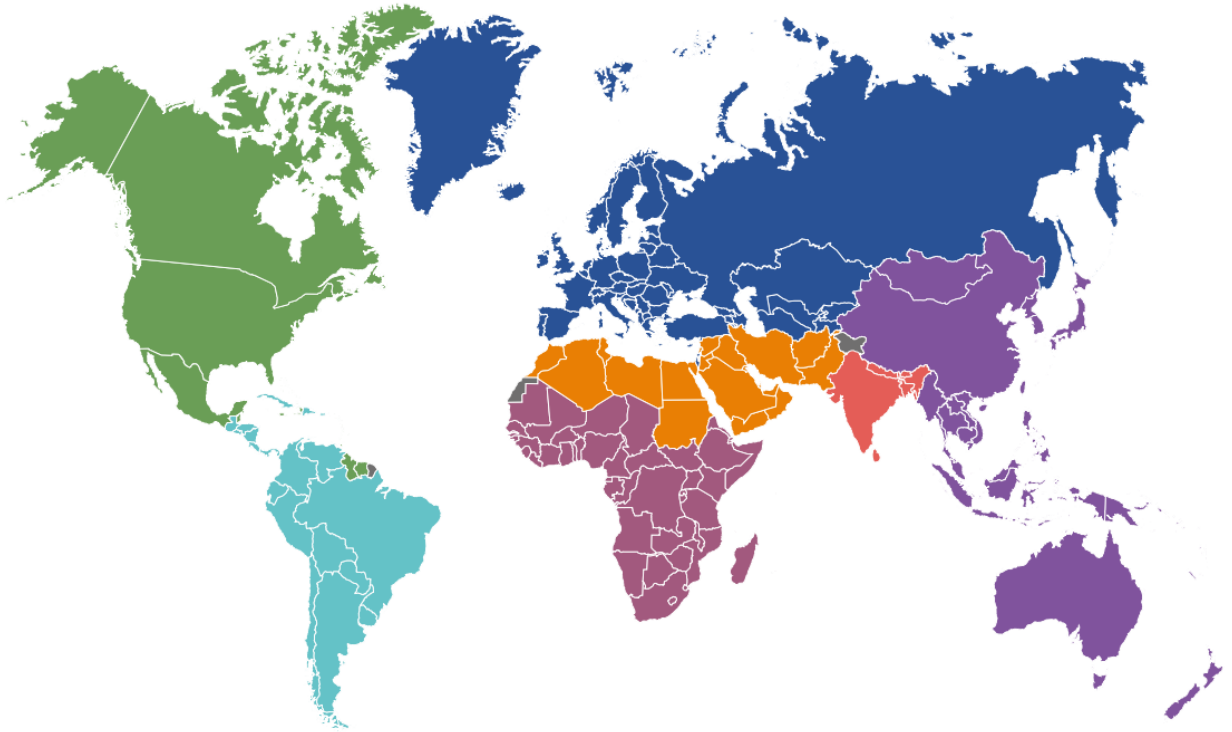
2045	136 million
2030	95 million
2021	73 million

87% increase

South-East Asia (SEA)

2045	152 million
2030	113 million
2021	90 million

68% increase



TB Risk and People with Diabetes

- 1 in 4 people with TB disease also has diabetes
- In 2022, diabetes was the most reported medical risk factor among people with active TB disease
- Patient with diabetes are at increased risk for developing active TB and experience worse treatment outcomes.

Benefits of Physical Activity

- Lowers risk of HTN, stroke
- Improves mental health and cognitive function
- Prevents weight gain, DM, heart disease and cancer
- If you could package physical activity into a pill, it would be the most effective drug on the market

Not getting enough physical Activity Costs Money

- $117 billion in annual health care costs are associated with inadequate physical activity

- Only half of adults get the physical activity they need to help reduce and prevent chronic diseases.

Diabetes and Tuberculosis

- **Patients with diabetes, incidence of Tuberculosis 2-4 x higher**
- **80% of people with DM live in developing countries**
- **10% of TB cases globally are linked to DM**

The Impact of Diabetes on Tuberculosis Treatment Outcomes:

- **A systematic Review of 33 studies:**
  - **Diabetes is associated with an increased risk of TB treatment failure and death during TB treatment.**
  - **Diabetes is associated with an increased risk of death – 4.95 greater- in the studies that adjusted for age and other potential confounding factors.**
  - **Diabetes is associated with an increased risk of TB relapse 3.89 greater**
    - » **Baker et al. Bio Med Central, Medicine, 2011**

Challenges Associated with TB Treatment in Diabetes

- Absorption: Gastroparesis and malabsorption
- Comorbidities: CKD, cardiovascular disease, non-alcoholic Steatohepatitis
- Rifampin: Strong hepatic enzyme inducer leading to decreased drug levels of oral medications for DM
  - Sulfonylureas, Thiazolidinediones,

Rifamycins and Anti-Diabetic Agents: Drug-Drug Interactions

General Tuberculosis (TB) Therapy Information

Developed by Kelly Bujnoch, PharmD Candidate 2011 with the assistance of Regina Tabor, RPh, DPh, Robert Petrossian and Barbara Seaworth, MD

Many diabetic medications are metabolized via the Cytochrome P450 (CYP450) enzymatic system in the liver. Rifampin is a potent inducer of the Cytochrome P450 and accounts for many of the drug interactions that occur during TB therapy.

Rifabutin is a weaker inducer of the Cytochrome P450 system, potentially interacting with some of the same medications as Rifampin.

Enzyme induction effects can last 2-4 weeks after discontinuation of rifampin. Glucose levels should be monitored and diabetic medications should be readiusted at the end of treatment.

BIGUANIDE (METFORMIN) BASED

BRAND	GENERIC	CLINICAL EFFECT	RIFAMPIN (RIF) DRUG-DRUG INTERACTIONS	RECOMMENDATIONS
Glucophage®	**Metformin**	↓Production of glucose by the liver ↓Absorption of glucose by intestines ↑Insulin sensitivity	None noted	No contraindications
Glucovance®	**Glyburide+ Metformin**	Glyburide: ↑Secretion of insulin from the pancreas Metformin: ↓Production of glucose by the liver ↓Absorption of glucose by intestines ↑Insulin sensitivity	↓Glyburide levels 39% Metformin: None noted	•Consider glipizide as first choice sulfonylurea to minimize interactions •Increase monitoring •Consider dose adjustment of antidiabetic agents or alternative glucose control therapy. Metformin: •No contraindications
Metaglip®	**Glipizide+ Metformin**	Glipizide: ↑Secretion of insulin from the pancreas Metformin: ↓Production of glucose by the liver ↓Absorption of glucose by intestines ↑Insulin sensitivity	↓Glipizide levels 22% Metformin: None noted	
Janumet®	**Sitagliptin+ Metformin**	Sitagliptin: ↑Secretion of insulin from the pancreas • delays gastric emptying ↓Appetite ↓Glucagon release after meals Metformin: ↓Production of glucose by the liver ↓Absorption of glucose by intestines ↑Insulin sensitivity	May ↓ sitagliptin levels Metformin: None noted	Sitagliptin: • Increase monitoring; interaction may be minimal and require no adjustments Metformin: •No contraindications
SULFONYLUREA BASED				
Micronase®	**Glyburide**	↑Secretion of insulin from the pancreas	↓Glyburide levels 39%	•Consider glipizide as first choice sulfonylurea to minimize interactions •Increase monitoring •Consider dose adjustment of antidiabetic agents or alternative glucose control therapy.
Amaryl®	**Glimepiride**	↑Secretion of insulin from the pancreas	↓Glimepiride levels 30%	
Glucotrol®	**Glipizide**	↑Secretion of insulin from the pancreas	↓Glipizide levels 22%	
Glucovance®	**Glyburide + Metformin**	Glyburide: ↑Secretion of insulin from the pancreas Metformin: ↓Production of glucose by the liver ↓Absorption of glucose by intestines ↑Insulin sensitivity	↓Glyburide levels 39% Metformin: None noted	•Consider glipizide as first choice sulfonylurea to minimize interactions •Increase monitoring •Consider dose adjustment of antidiabetic agents or alternative glucose control therapy. Metformin: •No contraindications
Metaglip®	**Glipizide+ Metformin**	↑Secretion of insulin from the pancreas Metformin: ↓Production of glucose by the liver ↓Absorption of glucose by intestines ↑Insulin sensitivity	↓Glipizide levels 22% Metformin: None noted	
Avandaryl®	**Pioglitazone + Glimepiride**	Pioglitazone: ↑Insulin sensitivity (body and liver cells) Glimepiride: ↑Secretion of insulin from the pancreas	↓Pioglitazone levels 54% ↓Glimepiride levels 30%	Pioglitazone: •Increase monitoring •Consider dose adjustment of antidiabetic agents or alternative glucose control therapy. •Consider glipizide as first choice sulfonylurea to minimize interaction Metformin: •No contraindications
Duetact®	**Rosiglitazone + Glimepiride**	Rosiglitazone: ↑Insulin sensitivity (body and liver cells) ↓Production of glucose by the liver ↑Cell uptake of glucose Glimepiride: ↑Secretion of insulin from the pancreas	↓Rosiglitazone levels 54-65% ↓Glimiprde levels 30%	Rosiglitazone: •Increase monitoring •Consider dose adjustment of antidiabetic agents or alternative glucose control therapy. •Consider glipizide as first choice sulfonylurea to minimize interaction Metformin: •No contraindications

COMBO DRUGS

APRIL 16, 2012

Rifamycins and Cardiovascular Agents: Drug - Drug Interactions

General Tuberculosis (TB) Therapy Information

Many cardiovascular agents are metabolized via the Cytochrome P450 (CYP450) enzymatic system in the liver . Rifampin is a potent inducer of the Cytochrome P450 and accounts for many of the drug interactions that occur during TB therapy.

Rifabutin is a weaker inducer of the Cytochrome P450 system, potentially interacting with some of the same medications as Rifampin.
Rifapentine is also a potent inducer of CYP450 enzymatic system in the liver with drug-drug interactions of a severity similar to those of rifampin.

Generic	Clinical Effect	Interactions	Recommendations
Angiotensin Converting Enzyme (ACE) Inhibitors			
(Class Effect)	↓blood pressure	RIF: ↓ACEI levels ~30% (poor evidence, no studies)	Increase BP monitoring; Consider ACEI dose adjustment.
Angiotensin Receptor Blockers (ARBs)			
(Class Effect)	↓blood pressure •renoprotective	RIF: ↓ARB levels ~35% (poor evidence, no studies)	Increase BP monitoring; Consider ARB dose adjustment.
Beta Blockers			
metoprolol	↓blood pressure	RIF: ↓metoprolol levels 33%	Increase BP monitoring; Consider dose adjustment.
propranolol	↓blood pressure	RIF: doubled apparent oral clearance	Increase BP monitoring; Consider dose adjustment.
bisoprolol	↓blood pressure	RIF: ↓bisoprolol levels 34%	Increase BP monitoring; Consider dose adjustment.
Calcium Channel Blockers (CCBs)			
nifedipine	↓blood pressure	RIF: ↓nifedipine levels 92-97% (Contraindicated *)	Increase BP monitoring; Consider dose adjustment; Consider switching to other antihypertensive agents with less interaction. *Major interactions occurr between orally administered nifedipine and rifampin. IV administration significantly reduces the potency of the interactions.
amlodipine	↓blood pressure	RIF: theoretically ↓ amlodipine levels	Increase BP monitoring; Consider dose adjustment; Consider switching to other antihypertensive agents with less interaction.
diltiazem	↓blood pressure	RIF: ↓diltiazem levels	Increase BP monitoring; Consider dose adjustment; Consider switching to other antihypertensive agents with less interaction.
verapamil	↓blood pressure	RIF: ↓verapamil levels 93-99%	Increase BP monitoring; Consider dose adjustment; Consider switching to other antihypertensive agents with less interaction.
Thiazide Diuretics			
(Class Effect)	↓blood pressure	none noted	no contraindications
HMG CoA Inhibitors (Statins)			
atorvastatin	↓cholesterol levels ↓stroke •cardioprotective	RIF: ↓atorvastatin levels 80%	Increase BP monitoring; Consider alternate lipid lowering agent to minimize effect; Consider increasing Statin dose; Consider using Rifabutin in place of Rifampin.
rosuvastatin	↓cholesterol levels ↓stroke •cardioprotective	RIF: may ↓rosuvastatin levels	Increase BP monitoring; Consider increasing Statin dose; Consider using Rifabutin in place of Rifampin.
simvastatin	↓cholesterol levels ↓stroke •cardioprotective	RIF: ↓simvastatin levels 82-97%	Increase BP monitoring; Consider alternate lipid lowering agent to minimize effect; Consider increasing Statin dose; Consider using Rifabutin in place of Rifampin.
pravastatin	↓cholesterol levels ↓stroke •cardioprotective	RIF: theoretically ↓statin levels	Increase BP monitoring; Consider alternate lipid lowering agent to minimize effect; Consider increasing Statin dose; Consider using Rifabutin in place of Rifampin.
lovastatin	↓cholesterol levels ↓stroke •cardioprotective	RIF: theoretically ↓statin levels	Increase BP monitoring; Consider alternate lipid lowering agent to minimize effect; Consider increasing Statin dose; Consider using Rifabutin in place of Rifampin.
fluvastatin	↓cholesterol levels ↓stroke •cardioprotective	RIF: ↓statin levels ~50%	Increase BP monitoring; Consider alternate lipid lowering agent to minimize effect; Consider increasing Statin dose; Consider using Rifabutin in place of Rifampin.
Ionotropic/Chronotropic Agents			
digoxin	↑cardiac output •heart rate control with atrial arrhythmias	RIF: ↓levels ~30%	Measure digoxin levels prior to rifampin therapy and then intermittently thereafter. Increase digoxin dose as necessry to maintain therapeutic levels.
Antiplatelet Agents			
clopidogrel	↓platelet adhesion	↑metabolism of clopidogril to active metabolite	Monitor for increased antiplatelet effects such as bruising or bleeding.

Managing TB in Persons with DM

- TB medication absorption is poor in people with DM
  - Consider drug levels
- Extend TB treatment to 9 months if slow culture conversion or clinical response
- If diabetic nephropathy is present adjusted doses of pyrazinamide ad ethambutol
- Administer B6 to prevent INH induced peripheral neuropathy
- Observe closely for TB treatment failure

Managing DM in Persons with TB

- **Check glucose and HbA1C**
- **Reinforce lifestyle changes diet and exercise**
- **Refer patients to diabetes clinic for long-term DM care**
- **Review drug interactions between DM medications and rifampin, adjust doses accordingly**

Sci Transl Med. 2014 Nov 19;6(263):263ra159. doi: 10.1126/scitranslmed.3009885.

Metformin as adjunct antituberculosis therapy.

Singhal A[1], Jie L[2], Kumar P[2], Hong GS[3], Leow MK[4], Paleja B[2], Tsenova L[5], Kurepina N[6], Chen J[2], Zolezzi F[2], Kreiswirth B[6], Poidinger M[7], Chee C[3], Kaplan G[8], Wang YT[3], De Libero G[9].

⊕ Author information

- **Metformin in MTB infected mice:**
  - **Improves the immune response to TB infection**
  - **Reduces intracellular MTB growth**
  - **Facilitates phagosome-lysosome fusion**
  - **Reduces chronic inflammation**
  - **Enhances the efficacy of anti-TB meds**

Clin Infect Dis. 2018 Jan 6;66(2):198-205. doi: 10.1093/cid/cix819.

Metformin Use Reverses the Increased Mortality Associated With Diabetes Mellitus During Tuberculosis Treatment.

Degner NR[1], Wang JY[2], Golub JE[1,3,4], Karakousis PC[1,4].

- This study suggests that despite multiple potential confounding variables
  - There was a significant association between metformin use and decreased mortality during TB treatment, suggesting a potential role for this agent as adjunctive, host-directed therapy
  - DM poses an increased risk of adverse TB treatment outcomes

Yu et al. BMC Infectious Diseases (2019) 19:859
https://doi.org/10.1186/s12879-019-4548-4

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Impact of metformin on the risk and treatment outcomes of tuberculosis in diabetics: a systematic review

Xinyu Yu[1†], Ling Li[2†], Liangtao Xia[1], Xin Feng[1], Fan Chen[3], Shiyi Cao[3*] and Xiang Wei[1,4,5,6*]

- Retrospective review of databases through March 2019
- 12 observational studies, 6980 cases

- Results
  - Metformin prescription was not related to lower risk of TB infection
  - Metformin prescription decreased risk of TB disease among diabetics (TBI to TB disease)
  - Metformin use resulted in higher probability of smear conversion at 2 months
  - Metformin medication during treatment for TB disease reduced mortality
  - Relapse was not reduced by metformin prescription

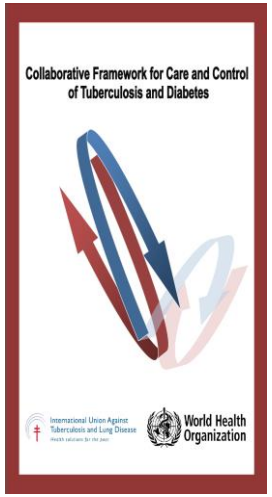
Benefits of Metformin in TB

- **Lower TB mortality rate**
- **Increased TB treatment success rate**
- **Enhanced culture conversion**
- **Reduced risk of developing active TB**

World Health Organization Recommends Bidirectional Screening

- **All people with TB should be screened for DM**
  - **Fasting/random blood sugar or 2 hour glucose tolerance test**
  - **HgbA1c**

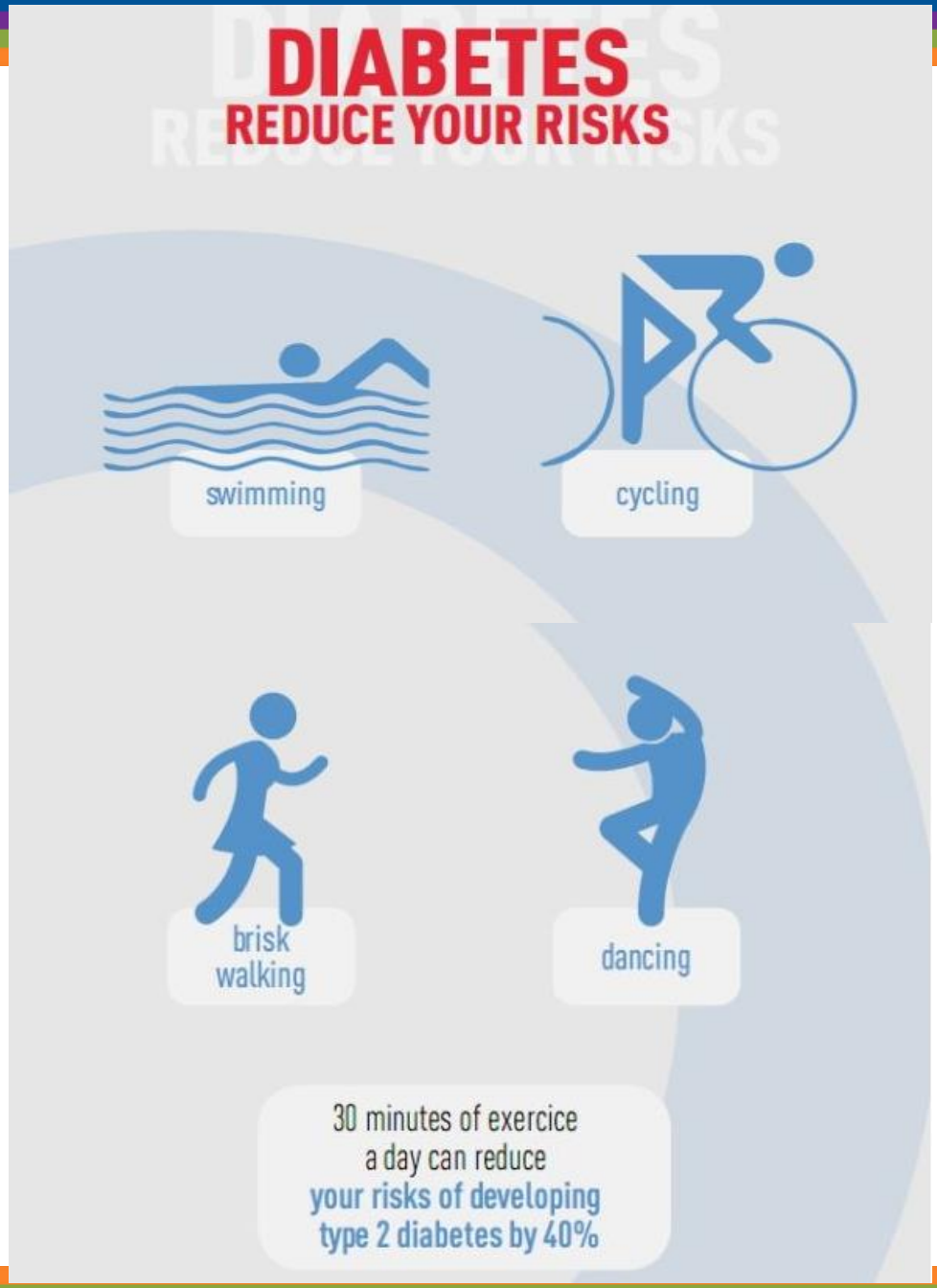
- **All newly diagnosed patients with DM, need screening for TB symptoms, further workup if clinically and epidemiologically indicated**
  - **Radiograph**
  - **Sputum AFB smear, cultures or other tests**



- Healthy weight
- Balance diet
- Smoking
- Stress and depression
- Waist circumference, High risk for DM and heart disease:

  > 40 inches for men

  >35 inches for women
- Sleeping patterns: Both short <6h and > 9h associated with DM

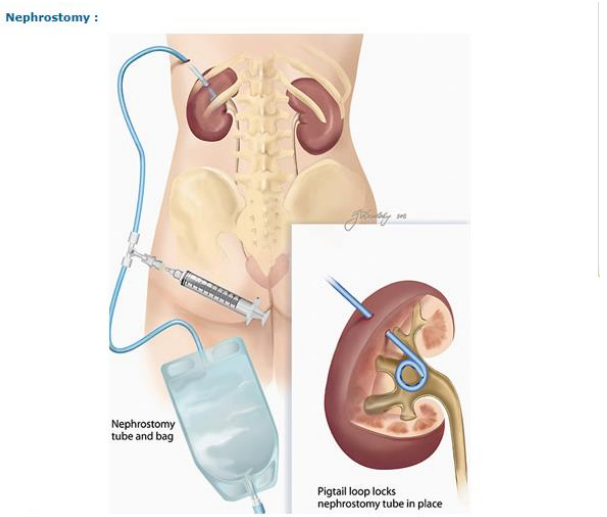


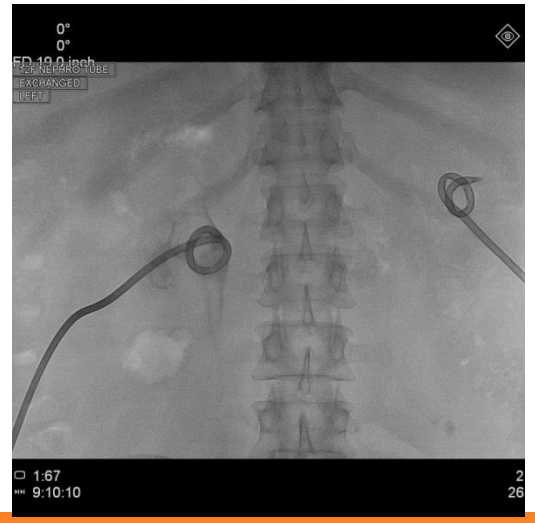
IDF Diabetes Atlas Sixth Edition Update, International Diabetes Federation 2014

TB IN PERSONS WITH CHRONIC KIDNEY DISEASE (CKD)

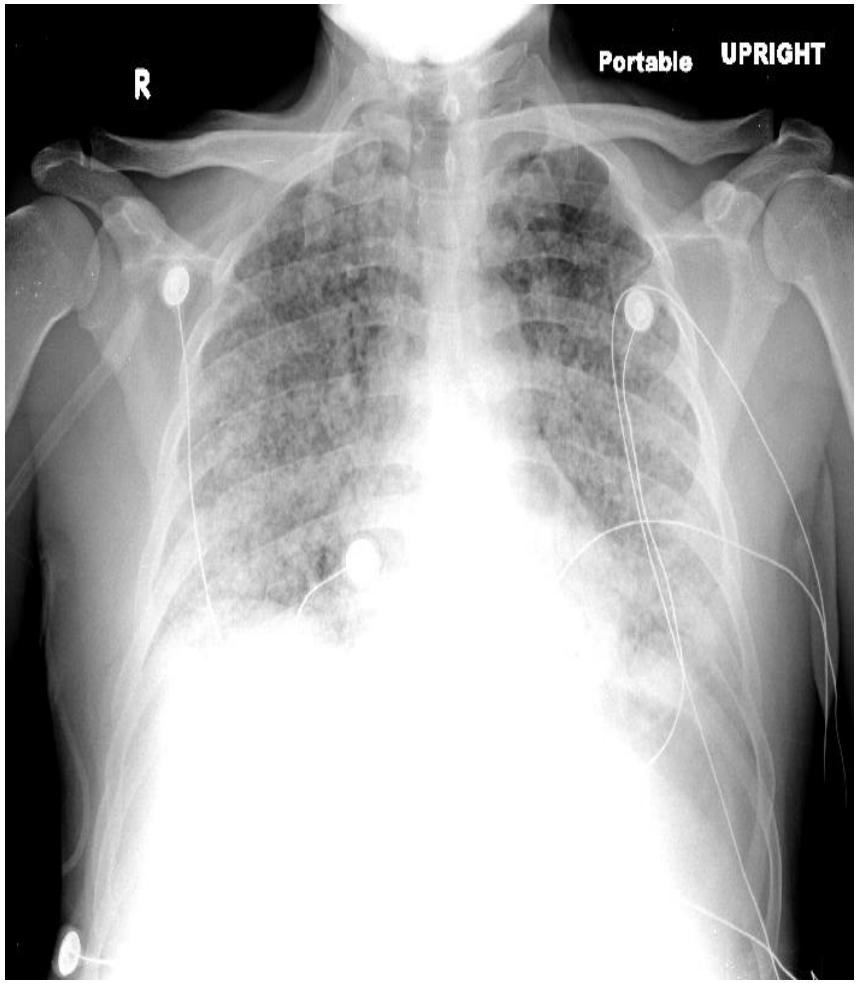
Patient with TB-DM-CKD

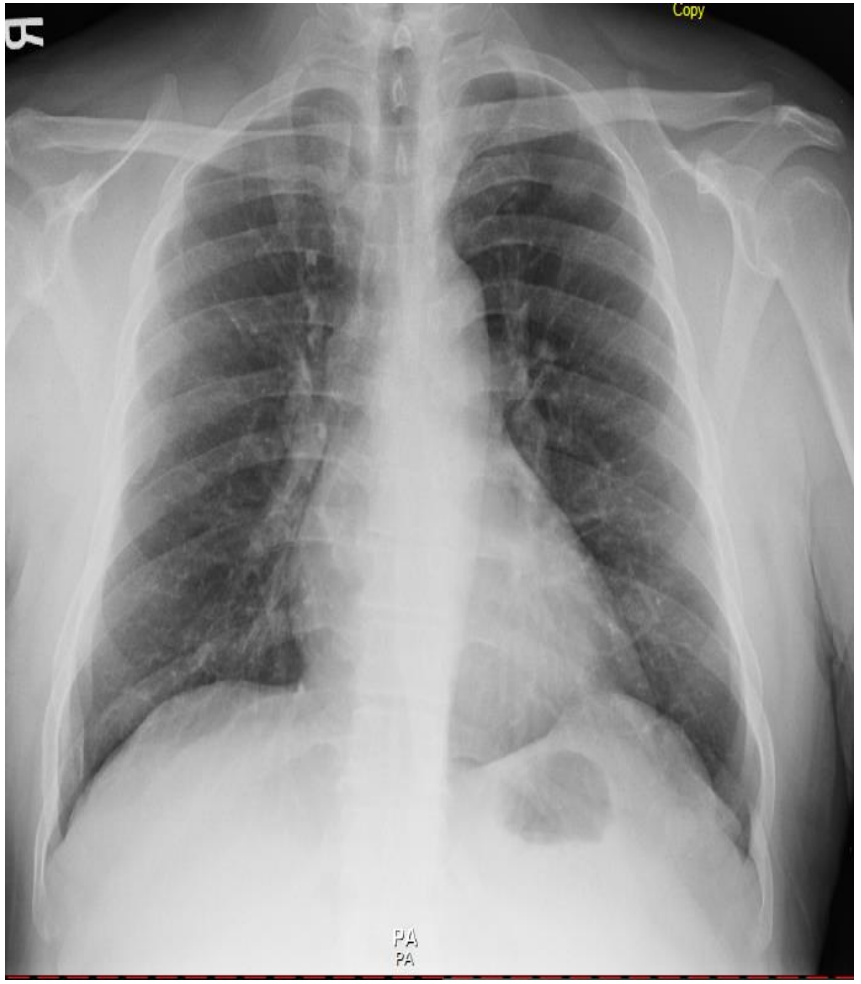
- 46 y/o M with DM disseminated TB involving lungs, both ureters and kidneys
  - Kidney failure, creatinine 8, ureteral strictures
  - Respiratory failure
- Discharged with bilateral nephrostomy tubes
- Multiple UTI's





Initial and End of TB Treatment CXR





Chronic Kidney Disease Increases TB Risk

- **Increased risk of progression from TB infection to active TB disease**
- **Difficulty diagnosing & treating patients on dialysis**
- **Symptoms often mistaken for complications of dialysis**
  - **Cough (congestive heart failure, fluid overload), fever (bacterial infection)**

TB Screening in Persons with CKD

- **TB skin test or IGRA**
  - **At diagnosis of CKD**
  - **Thirty days prior to admission to hemodialysis unit**
  - **Thirty days prior to scheduled renal transplant**
  - **Annual/periodic**
    - **If TST negative Two step should be done**
      - » **California TB Controller Association (CTCA) Recommendations**

Presentation of TB in Persons on Dialysis

- **Atypical presentation of pulmonary TB**
  - **Fever – most common sign!**
  - **Weight Loss**
  - **Anorexia**
  - **Cough (may be present)**

- **Consider TB Disease in ANY patient with:**
  - **Recurrent pneumonia**
  - **Pneumonia not improved within 2 weeks of antibiotics – avoid fluoroquinolones May mask TB!**

Presentation of TB in Persons on Dialysis

- **Extra pulmonary TB**
  - **More common in dialysis patients**
  - **Don’t forget to do SPUTUMS!!**
  - **Abdominal – (Peritoneal, liver, bowel, adenopathy)**
    - **TB peritonitis can be difficult to distinguish from bacterial**
  - **Any site possible - evaluate if abnormal**

CXR Findings in Persons with TB and CKD

- **In late stage CKD cavitation, upper lobe infiltrates are less common**

- **CXR may be normal or atypical**
  - **Infiltrate lower lobes , diffuse, miliary, resembling pulmonary edema, pleural effusions**

TABLE 15. Dosing recommendations for adult patients with reduced renal function and for adult patients receiving hemodialysis

Drug	Change in frequency?	Recommended dose and frequency for patients with creatinine clearance <30 ml/min or for patients receiving hemodialysis
Isoniazid	No change	300 mg once daily, or 900 mg three times per week
Rifampin	No change	600 mg once daily, or 600 mg three times per week
Pyrazinamide	Yes	25–35 mg/kg per dose three times per week (not daily)
Ethambutol	Yes	15–25 mg/kg per dose three times per week (not daily)
Levofloxacin	Yes	750–1,000 mg per dose three times per week (not daily)
Cycloserine	Yes	250 mg once daily, or 500 mg/dose three times per week*
Ethionamide	No change	250-500 mg/dose daily
p-Aminosalicylic acid	No change	4 g/dose, twice daily
Streptomycin	Yes	12–15 mg/kg per dose two or three times per week (not daily)
Capreomycin	Yes	12–15 mg/kg per dose two or three times per week (not daily)
Kanamycin	Yes	12–15 mg/kg per dose two or three times per week (not daily)
Amikacin	Yes	12–15 mg/kg per dose two or three times per week (not daily)

Treatment of Active TB in Persons with CKD on Dialysis

- **Initial Phase (first two months):**
  - **INH 300mg daily or 900 mg thrice weekly**
  - **Rifampin 600mg daily or thrice weekly**
  - **Ethambutol 15-25mg/kg thrice weekly**
  - **PZA 25-35mg/kg thrice weekly**
  - **Vitamin B6 50mg thrice weekly**

- **Continuation**
  - **INH and Rifampin x 4 – 7 months**

- **All doses should be given AFTER DIALYSIS**

TB and Smoking

Smoking and Tobacco Use in the US

- **Smoking leads to disease, disability and harms nearly every organ of the body**
- **Smoking is the leading cause of preventable death in the US**
- **Smoking accounts for 20% of deaths in the US**
- **Smoking is highest among persons with lower education, lower income and serious psychological distress**
- **Smoking has declined from 20.9% in 2005 to 14% in 2017**

– https://www.cdc.gov/tobacco/data_statistics/fact_sheets/index.htm?s_cid=osh-stu-home-spotlight-001

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Tobacco Smoke, Indoor Air Pollution and Tuberculosis: A Systematic Review and Meta-Analysis

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- Review of 33 papers on smoking and TB
- Smokers have an increased risk of
  - Having a positive TST
  - Developing active TB disease
  - Dying from TB

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Smoking and TB recurrence

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Smoking increases risk of recurrence after successful anti-tuberculosis treatment: a population-based study

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- **After controlling for other variables,**
  - **Persons who smoked >10 cigarettes have double the risk of TB recurrence compared to never/former smokers.**

- **To reduce the risk of recurrence, effective measures of smoking cessation should be included in TB control programs, as recommended by the World Health**

Systematic Reviews and Meta-Analyses Evaluating tuberculosis and Cigarette Smoking

- **Approximately 13% of the TB cases in the world each year may be attributable to tobacco exposure.**

- **“Tobacco cessation must become an integral part of all TB control programs.”**

Explore Ways to Quit Smoking

- **Sign up for SmokefreeTXT, at smoke free.gov**
  - **24/7 advice, tips and encouragement to quit**
- **Call 1-800-QUIT-NOW (1-800-784-8669)**

TB in Patients with Liver Disease

TB Treatment in Patients with Advanced Liver Disease

- **Likelihood of drug induced liver injury may be higher**

- **TB may involve the liver, and hepatic abnormalities may improve with TB treatment**

» **Treatment of Tuberculosis : MMWR, June 20, 2003**

TB Regimen Recommended for Persons with Advanced Liver Disease

- **Treat with only one potentially hepatotoxic drug**
  - **Rifamycins should be retained**
  - **Avoid Pyrazinamide**
  - **Additional agents include ethambutol, fluoroquinolone, cycloserine, Linezolid**
- **Treatment duration with such regimens should be extended, depending on the severity, disease response and medications used**
- **Obtain TB expert consultation**

» **Treatment of Tuberculosis : MMWR, June 20, 2003**

TB Treatment without PZA in Persons with Liver Disease

- **PZA can cause severe and prolonged liver injury**
- **Treat with INH, rifampin and ethambutol for 2 months follow by a continuation phase with INH and rifampin for 7 months**

» **Treatment of Tuberculosis : MMWR, June 20, 2003**

Conclusions

- Encourage patients with HIV infection to have HIV viremia goal undetectable and discuss TB meds with HIV doctor
- Encourage patients to adhere to ART / diabetes/ BP medications
- Integrate physical activity every day in every way
- Obtain consultation when treating TB patients with HIV infection, CKD and advance liver disease

Questions?