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Antituberculosis Medications in Liver and Kidney Disease

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Disclosures : None

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Objectives

- Describe the association of chronic liver and kidney disease with tuberculosis
- Discuss medications that are less/least hepatotoxic
- List dosing recommendations of antituberculosis medications for adults with reduced renal function/hemodialysis
- Discuss strategies for using antituberculosis medications in liver and kidney disease

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TB Disease and Medications in Liver Disease

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TB in Patients with Cirrhosis

JOURNAL ARTICLE

Cirrhosis as a Risk Factor for Tuberculosis Infection —A Nationwide Longitudinal Study in Taiwan

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Yi-Ting Lin , Ping-Hsun Wu , Chun-Yu Lin , Ming-Yen Lin , Hung-Yi Chuang , Jee-Fu Huang ✉ , Ming-Lung Yu , Wan-Long Chuang

American Journal of Epidemiology, Volume 180, Issue 1, 1 July 2014, Pages 103–110, https://doi.org/10.1093/aje/kwu095

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▸ Epidemiol Infect. 2000 Apr;124(2):221–225. doi: 10.1017/s0950268899003593

Incidence and prognosis of tuberculosis in patients with cirrhosis of the liver. A Danish nationwide population based study.

A M Thulstrup [1], I Mølle [1], N Svendsen [1], H T Sørensen [1]

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PMCID: PMC2810904 PMID: 10813146

Patients with liver cirrhosis are at increased risk for tuberculosis

Taiwan study – showed particularly those with **alcoholism and hepatitis C**

Denmark study – showed highest incidence was seen in men, > 65 years of age,

Patients with cirrhosis who acquired TB had a poorer prognosis

Patient Case 1

74-year-old US born male, status post treatment for colon cancer in 2020, chronic alcohol use was diagnosed with **drug susceptible cavitary pulmonary TB** in February 2025.

Smear negative on sputum but smear + on BAL,
CT with cavity in RUL (5 x 1.6 x 4.2 cm)
History of alcohol use but no known withdrawal or hospitalizations related to this

Patient Case 1

Feb 2025
RIPE started

April 2025
LFT 5x higher than normal
RIPE Stopped
(No clear evidence that he was consuming alcohol at this time as residing in a Nursing facility)

Mid May 2025
LFT improved to a safe range
Rifampin restarted with plan to start each drug serially

Patient Case 1

June 2025

LFT elevation once INH added

(asymptomatic but “drinking” a “little bit “)

July 2025

Patient reported that he could stop alcohol

Rif and INH reintroduced again

July 2025

Hospitalized for syncope and alcohol withdrawal

Patient Case 1

Rif + INH + alcohol →

Date	AST	ALT	Total Bili
7/12/25	131 (range 13-39)	39 (range 7-52)	0.51 (range 0.2-1)
7/22/25	225	63	1.3

Albumin 3.3-3.8
Platelets range 90-100
Renal function not elevated
WBC/ANC/HBG/Alk Phos in normal range

Total Dose Count since Feb 2025: 44

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Case Report 1: (Audience Poll)

Which option would you like to use for TB treatment in this setting of alcohol use disorder that is not well controlled and elevated Liver function tests?

A) Treat with RIPE , introducing one drug at a time as LFTs permit, for 6-9 months

B) Treat with lesser/least hepatotoxic regimen even if longer duration (9-12 or more months)

C) Try Bpal/BpalM as 6-month regimen (Bedaquinile, Pretomanid, Linezolid +/- Moxifloxacin)

D) Treat with 4-month HPMZ regimen (Isoniazid, Rifapentine, Moxifloxacin, Pyrazinamide) as shortest regimen in the above options

Patient Case 1 Challenges

- Finding the least or lesser hepatotoxic regimen that the strain is susceptible to, which the patient can tolerate
- Deciding duration of treatment based on disease severity, medications used and patient tolerance to medications
- Managing interruptions in therapy and potential resistances that develop due to intermittent therapy

Child Pugh Classification of severity of Cirrhosis

Parameter	Points assigned		
	1	2	3
Ascites	Absent	Slight	Moderate
Bilirubin	<2 mg/dL (<34.2 micromol/L)	2 to 3 mg/dL (34.2 to 51.3 micromol/L)	>3 mg/dL (>51.3 micromol/L)
Albumin	>3.5 g/dL (35 g/L)	2.8 to 3.5 g/dL (28 to 35 g/L)	<2.8 g/dL (<28 g/L)
Prothrombin time (seconds over control) or	<4	4 to 6	>6
INR	<1.7	1.7 to 2.3	>2.3
Encephalopathy	None	Grade 1 to 2	Grade 3 to 4

Modified Child-Pugh classification of the severity of liver disease according to the degree of ascites, the serum concentrations of bilirubin and albumin, the prothrombin time, and the degree of encephalopathy. A total Child-Pugh score of 5 to 6 is considered Child-Pugh class A (well-compensated disease), 7 to 9 is class B (significant functional compromise), and 10 to 15 is class C (decompensated disease). These classes correlate with one- and two-year patient survival: class A: 100 and 85%; class B: 80 and 60%; and class C: 45 and 35%.

INR: international normalized ratio.

Graphic 78401 Version 16.0

Antitubercular Therapy in Cirrhosis

Kumar N *et al*. Antitubercular therapy in cirrhosis

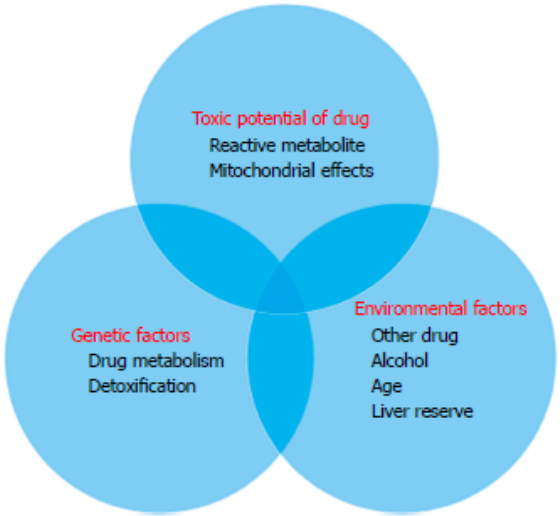

Figure 1 Interaction of factors to produce hepatotoxicity in cirrhosis.

DILI Differential Diagnosis and/ or Contributors

- Alcohol-induced (AST>ALT)
- Acute or chronic viral hepatitis
- Hepatic involvement with TB (cholestatic)
- Acetaminophen (>2g/d)
- Statins, anti-retrovirals, other drugs
- Anatomic/mechanical biliary obstruction

Curry Guide

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Antituberculosis Medications and Liver Effects

- **INH and PZA** most often associated with Hepatotoxicity
- **Rifampin – cholestatic pattern**, lack of rifamycin in regimen usually leads to longer duration of treatment
- **Levofloxacin less hepatotoxic than Moxifloxacin**
- **Combination of medications can be additive for toxicity profile**

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With Clinical Judgement

May Need to Alter this response/thresholds for patients with underlying liver disease

Drug-Induced Liver Injury (DILI)

CLASS	SYMPTOMS	TIMING	LAB	RESPONSE
Adaptation	None	<8 weeks	AST/ALT 1-3x ULN	Continue Monitor
Hepatocellular –Mild	Fatigue, anorexia, N/V (or none)	1-8 weeks	AST/ALT 3-5x ULN Bilirubin ≤2.5 PT INR ~1.0	Stop therapy Follow at weekly intervals
HC--Moderate	As above	1-8 weeks	AST/ALT 5-10x ULN Bilirubin variable PT INR variable	Stop therapy Follow at weekly intervals
HC--Severe	As above plus Icterus Mental status changes	1-8 weeks	AST/ALT ≥10x ULN Bilirubin ≥2.5↑ PT INR >1.0↑	Stop therapy Urgent referral for hospital care
Cholestatic	None or icterus	<4 weeks	AST/ALT <3xULN Bilirubin ≥2.5↑ (mostly direct) AP 2-3x ULN	Monitor Stop rifamycin if bilirubin climbs

Curry Guide

TB in the setting of Liver Disease

If the liver disease is not imminently life-threatening and is Child Pugh classification A or B, the use of one or two hepatotoxic drugs can be considered in a TB regimen. Because of the efficacy of rifamycin, **consider a rifamycin challenge** (before other hepatotoxic drugs) if the isolate is susceptible, e.g., for INH mono-resistance.

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TB in the setting of Liver Disease

- **If the patient has end-stage liver disease and further worsening could be life-threatening** (transplant is challenging in the setting of TB disease), **consider avoiding all hepatotoxic drugs.** Consider LFX, EMB, an amino-glycoside, and CS, if appropriate. LZD, BDQ (precautions noted in **Table 1**), and CFZ are additional alternatives.

Medications Not strongly associated with hepatotoxicity

Ethambutol
Linezolid
Clofazimine
Cycloserine
Aminoglycosides
Quinolones (Levofloxacin even less hepatotoxicity than Moxifloxacin)

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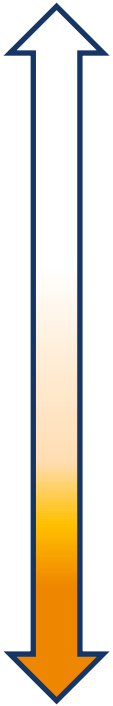
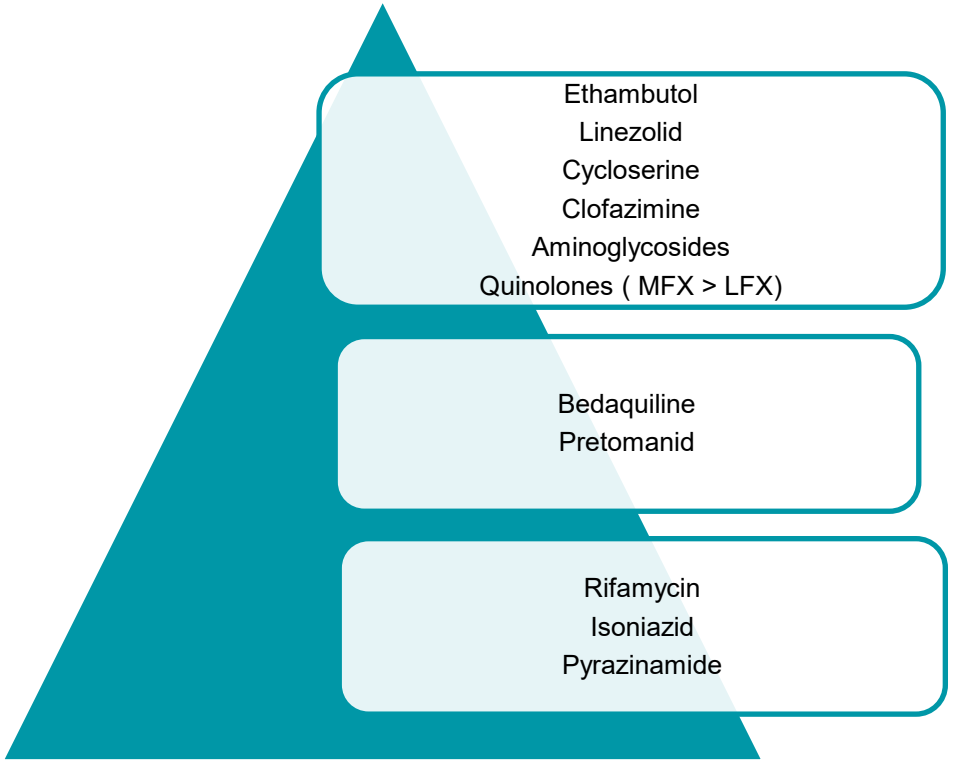
Antituberculosis Medications and Hepatotoxicity

Less Hepatotoxic



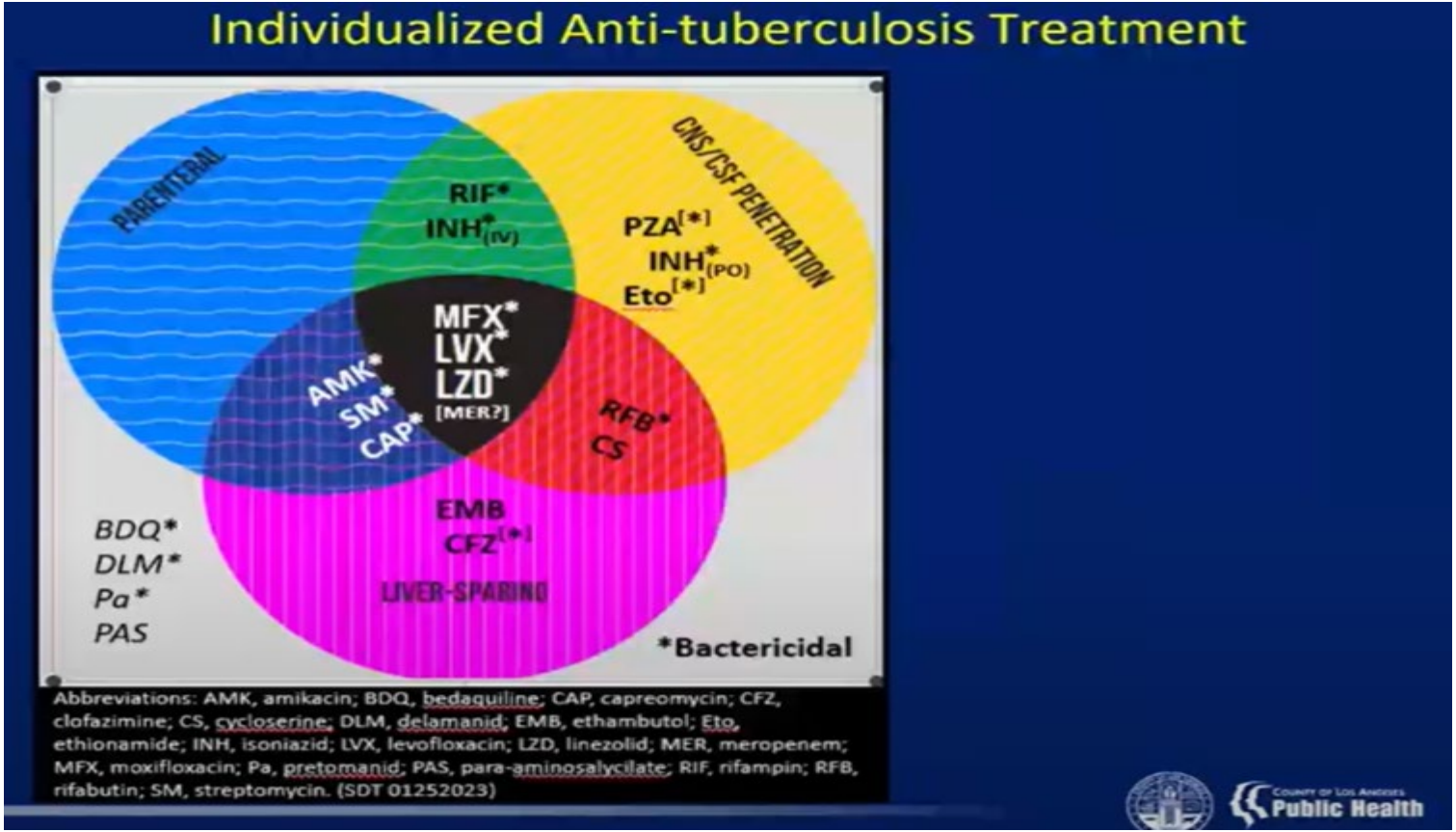
More Hepatotoxic



Medications inside each box are not arranged in any particular order

TABLE 1 **Anti-TB medications and their effects on the liver**

Drug	Effect on liver
Isoniazid (INH)	INH is most likely to cause hepatitis. In patients with normal hepatic function, the hepatotoxic effects are usually reversible if the drug is stopped as soon as symptoms are evident. INH hepatotoxicity appears to be increased when rifampin (RIF) is used.
Rifampin (RIF)	RIF more commonly causes a cholestatic jaundice but can potentiate the hepatocyte damage caused by INH.
Pyrazinamide (PZA)	PZA causes fewer episodes of hepatotoxicity than INH, but the events can be severe and prolonged, and worsen even after stopping therapy. PZA is thought to cause the most severe liver toxicity.
Ethionamide (ETA) **Para-aminosalicylate (PAS)**	ETA and PAS have also been implicated in hepatotoxic drug reactions.
Fluoroquinolones	Moxifloxacin (MFX) has been associated with occasional cases of liver damage. However, levofloxacin (LFX) is thought to have less hepatoxicity and has been used in "liver-sparing" regimens following hepatotoxicity (both LFX and MFX have been successfully used with close monitoring).
Pretomanid (Pa)	There is uncertainty about the effect of Pa on the liver. Early trials of regimens including Pa and other liver-toxic medications like PZA showed some hepatotoxicity. Studies using BDQ and LZD have found rare hepatotoxicity.
Bedaquline (BDQ)	Not associated with hepatotoxicity in most observational studies. The BDQ package insert states that because it has not been studied in patients with severe liver disease, it should be used with caution and only when risks outweigh benefits in these patients.
Aminoglycosides **Clofazimine (CFZ)** **Cycloserine (CS)** **Ethambutol (EMB)** **Linezolid (LZD)**	Not commonly associated with liver dysfunction.


Individualized Anti-tuberculosis Treatment
PARENTERAL
RIF*
INH*(IV)
CNS/CSF PENETRATION
PZA[*]
INH*(PO)
Eto[*]
MFX*
LVX*
LZD*
[MER?]
AMK*
SM*
CAP*
RFB*
CS
EMB
CFZ[*]
LIVER-SPARING
BDQ*
DLM*
Pa*
PAS
*Bactericidal
Abbreviations: AMK, amikacin; BDQ, bedaquiline; CAP, capreomycin; CFZ, clofazimine; CS, cycloserine; DLM, delamanid; EMB, ethambutol; Eto, ethionamide; INH, isoniazid; LVX, levofloxacin; LZD, linezolid; MER, meropenem; MFX, moxifloxacin; Pa, pretomanid; PAS, para-aminosalycilate; RIF, rifampin; RFB, rifabutin; SM, streptomycin. (SDT 01252023)
County of Los Angeles Public Health

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Hepatic Disease TB Treatment Durations

- Durations Vary based on medications used, site of disease, resistances ,etc
- Severe , unstable liver disease leading to regimens with little or no hepatotoxicity are often longer

FIGURE 1. **Building an individualized treatment regimen for MDR-TB**
2019 ATS/CDC/ERS/IDSA DR-TB guideline stepwise guidance for building a regimen using a prioritized ranking of drugs (with comparison to WHO 2020)

During the intensive phase choose **5 drugs**, then drop to **4 drugs** during the continuation phase.

ATS / CDC / ERS / IDSA				WHO
1.	Choose one FQ	Levofloxcin **or** Moxifloxacin	**LFX** **MFX**	**WHO Group A:** Include all three
2.	Use BDQ and LZD	Bedaquiline	**BDQ**	
		Linezolid	**LZD**	
3.	Use CFZ and CS	Clofazimine	**CFZ**	**WHO Group B:** Add one or both
		Cycloserine	**CS**	
4.	Add inj. as needed	Amikacin (**or** Streptomycin[1])	**AK** **(SM)**	**WHO Group C:** Add to complete the regimen WHO rank order: **EMB** **DLM** **PZA** **IMP/MPM** with **CLV** **AK (SM)** **ETA** or **prothionamide** **PAS**
5.	Add as needed	Delamanid[2]	**DLM**	
		Ethambutol	**EMB**	
		Pyrazinamide	**PZA**	
6.	Add as needed	Ethionamide	**ETA**	
		Imipenem-cilastatin **or** Meropenem (**plus** clavulanate)	**IPM** **MPM** **(+CLV)**	
		p-aminosalicylic acid	**PAS**	
		High-dose Isoniazid	**INH**[HD]	

Challenges of managing TB with underlying liver disease

- Likelihood of developing drug induced hepatitis may be higher
- Monitoring of drug induced hepatitis may be confounded in presence of underlying liver disease
- Outcomes of drug induced hepatitis with compromised liver function may be poor
- Durations need modified based on medications, tolerance and site of disease

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TB Disease and Medications in Kidney Disease

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Tuberculosis (TB) and Chronic Kidney Disease (CKD)

Tuberculosis and chronic kidney disease: an emerging global syndemic

Kamila Romanowski[1], Edward G. Clark[2], Adeera Levin[3], Victoria J. Cook[4] and James C. Johnston[4]

[1]Faculty of Medicine, Division of Infectious Diseases, University of British Columbia, Vancouver, British Columbia, Canada; [2]University of Ottawa, Ottawa Hospital Research Institute, Kidney Research Centre, and Division of Nephrology, The Ottawa Hospital, Ottawa, Ontario, Canada; [3]Faculty of Medicine, Division of Nephrology, University of British Columbia and British Columbia Provincial Renal Agency, St. Paul's Hospital, Centre for Health Evaluation and Outcomes Research, Vancouver, British Columbia, Canada; and [4]Faculty of Medicine, Division of Respirology, University of British Columbia and TB Services, British Columbia Centre for Disease Control, Vancouver, British Columbia, Canada

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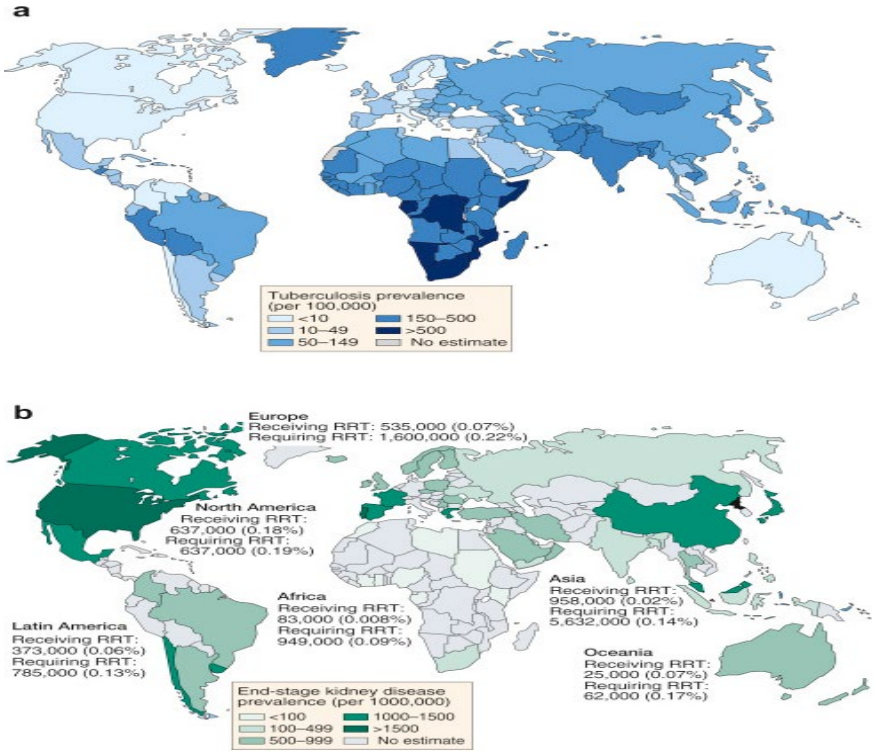
Tuberculosis and chronic kidney disease: an emerging global syndemic



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TB and Chronic Kidney Disease (CKD)

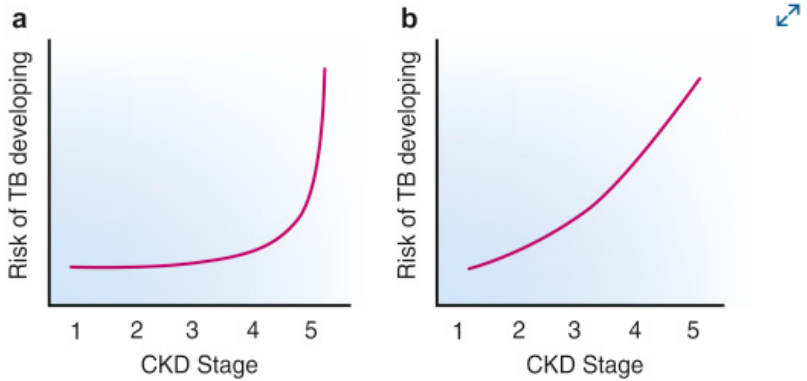

Figure viewer

Figure 2 Hypothesized relationship between CKD stage and risk of the development of TB. (a) Impaired cell-mediated immunity in late-state CKD leaves patient susceptible to infectious complications, such as active TB. (b) Pathophysiology of CKD-related immunodeficiency suggests early stage CKD patients may also be susceptible to TB. CKD, chronic kidney disease; TB, tuberculosis.

K Romanowski et al.: TB and CKD

Table 1 Tuberculosis screening guidance for chronic kidney disease populations

Society	Year	CKD	Dialysis	Transplant
American Thoracic Society[37]	2000	—	TST for immune compromised. No specific recommendations for dialysis	TST for immune compromised. No specific recommendations for transplant candidates
American Transplant Society (donor)[38]	2012	—	—	All living donors should be screened with a TST or IGRA
American Transplant Society (recipient)[39]	2011	—	—	All transplant candidates should be screened with TSS or IGRA
British Thoracic Society[29]	2010	CKD patients should receive a TB risk assessment and if appropriate an IGRA	All dialysis patients should receive a TB risk assessment and, if appropriate, an IGRA	All transplant candidates should be screened with an IGRA
Canadian Thoracic Society[40]	2014	—	TST or IGRA recommended for immune compromised. No specific recommendations for dialysis	TST or IGRA recommended for immune compromised. No specific recommendations for transplant candidates
Canadian Transplant Society[41]	2005	—	—	All transplant candidates should be screened with TST
European Centre for Disease Prevention and Control[42]	2011	—	IGRA with concurrent TST for immune compromised. No specific recommendations for dialysis patients	IGRA with concurrent TST for immune compromised. No specific recommendations for transplant candidates
National Institute for Health and Clinical Excellence[43]	2011	—	IGRA or IGRA and concurrent TST for immune compromised. No specific recommendations for dialysis	IGRA or IGRA and concurrent TST for immune compromised. No specific recommendations given for transplant candidates
World Health Organization[36]	2015	—	Screen all dialysis patients with TST or IGRA	Screen all transplant candidates with TST or IGRA

CKD, chronic kidney disease; IGRA, interferon gamma release assay; TST, tuberculin skin test.

Chronic Renal Failure and TB

Compared to general population , patients with chronic renal failure undergoing hemodialysis are at a **3-25-fold increased risk of** developing TB disease once infected

Data regarding clearance of anti-TB drugs are best documented for patients with CrCl < 30mL/minute or those undergoing dialysis

Data for patients with mild renal failure or undergoing peritoneal dialysis is less available

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Patient Case 2 (Audience Poll)

60 yr old male with ESRD on hemodialysis gets diagnosed with mediastinal lymph node TB. Culture is pan sensitive . Which treatment option would you start with.

A) Rif 600mg daily, INH 300 mg daily, ETH 15-25mg/KG day , PZA 25-40 mg/Kg/day

B) Rif 600 mg , INH 300 mg, ETH 15-25mg/kg and PZA 25mg/kg 3 times a week

C) Rif 600 mg daily, INH 300 mg daily, Eth 15-25mg/kg 3 time a week, PZA 25mg/kg 3 times a week (Give meds after hemodialysis)

TB Medications in renal disease

For TB drugs that are cleared by the kidney, the general strategy is to increase the interval between dosing rather than to decrease the dose.

TABLE 2. **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 patients receiving hemodialysis
Isoniazid (INH)	No change	300 mg once daily
Rifampin (RIF)	No change	600 mg once daily
Pyrazinamide (PZA)	Yes	25–35 mg/kg/dose 3x/week (not daily)
Ethambutol (EMB)	Yes	15–25 mg/kg/dose 3x/week (not daily)
Levofloxacin (LFX)	Yes	750 –1000 mg/dose 3x/week (not daily) for creatinine clearance <50 mL/min
Moxifloxacin (MFX)	No change	400 mg daily
Cycloserine (CS)	Yes	250 mg once daily, or 500 mg/dose 3x/week*
Ethionamide (ETA)	No change	15–20 mg/kg/day (can be in divided doses)
Para-aminosalicylate (PAS)	No change	4,000 mg/dose twice daily
Linezolid (LZD)	No change	600 mg daily
Clofazimine (CFZ)	No change	100–200 mg daily
Amikacin (AK)	Yes	12–15 mg/kg/dose 2–3x/week (not daily)
Capreomycin (CM)	Yes	12–15 mg/kg/dose 2–3x/week (not daily)
Kanamycin (KM)	Yes	12–15 mg/kg/dose 2–3x/week (not daily)
Streptomycin (SM)	Yes	12–15 mg/kg/dose 2–3x/week (not daily)

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Specific TB medications needing renal adjustments

Ethambutol (EMB)

- Up to 80% cleared by the kidney
- Incompletely dialyzed
- Dose should be adjusted as shown in **Table 2**, but there may be an increased risk of accumulation of the drug and eye toxicity in the setting of renal failure
- Drug levels may be helpful in cases where EMB is important for the regimen
- In some circumstances (e.g., peritoneal dialysis, moderate renal failure without dialysis), the use of EMB should be considered carefully (and avoided, if appropriate)
- Little data are available regarding anti-TB drug dosing for patients on continuous ambulatory peritoneal dialysis (CAPD) and no guidelines currently exist; however, a dose of 15 mg/kg/dose every 48 hours has been used successfully
- Peak serum concentrations (2 to 3 hours post-dose) generally should be maintained within the normal range of 2 to 6 mcg/mL
- The initial dose of EMB should be based on ideal body weight rather than total body weight if the patient is above his/her ideal body weight (see link to calculator in ***Estimated creatinine clearance calculations box***, at the bottom of **Table 2**)
- Monitor carefully for red-green color discrimination and visual acuity changes

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Specific TB medications needing renal adjustments

Levofloxacin (LFX)

- Cleared more extensively by the kidney than is moxifloxacin (MFX).
- A dose of 750 to 1000 mg/dose 3x/week (not daily) is recommended for treatment of TB if creatinine clearance <50 mL/min. The manufacturer's literature for dosing LFX for non-tuberculosis infections suggests using smaller doses that may not be adequate. Again, drug concentration monitoring might be beneficial and general toxicity monitoring is imperative.

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Specific TB medications needing renal adjustments

Cycloserine (CS)

- Cleared by the kidney; toxicity appears to be closely related to elevated serum concentration
- Peak serum concentrations (2 hours post-dose) generally should be maintained within the normal range of 20 to 35 mcg/mL

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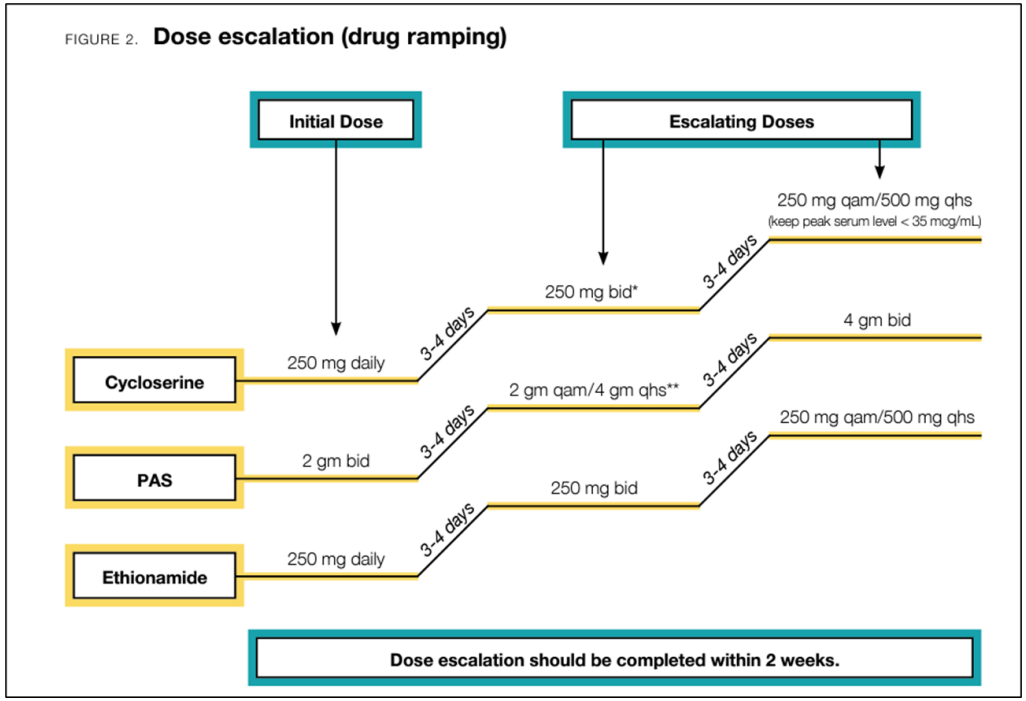
Cycloserine

Cycloserine

Obtain Peak concentrations within the first 1–2 weeks of therapy and monitor serially during therapy

Peak concentration should be kept below 35 mcg/mL

Baseline and monthly monitoring for depression using a tool such as the PHQ9 or Beck Depression Index should be done



Drug-Resistant Tuberculosis: A Survival Guide for Clinicians, 3rd edition / 2022 Updates

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Specific TB medications needing renal adjustments

Aminoglycosides (Streptomycin [SM] and Amikacin [AK])

- Cleared nearly entirely by the kidneys and only about 40% of the dose is removed by dialysis.
- There may be some accumulation of the drug and this might increase the risk of ototoxicity. These patients should be monitored closely for ototoxicity (both hearing loss and vestibular dysfunction). Serum drug concentrations can be used to verify that adequate peak concentrations are achieved (for efficacy). Predialysis trough concentrations may be above the usual target ranges since these patients will be unable to clear the drugs without the help of dialysis.
- The aminoglycosides have sometimes been instilled with peritoneal dialysate with careful serum concentration monitoring.
- The serum level of AK is most readily available in commercial labs. The aminoglycoside doses should be based on ideal body weight rather than total body weight if the patient is above his/her ideal body weight (see calculator at bottom of **Table 2**).
- For patients with creatinine clearance less than 30 mL/min or those receiving hemodialysis, 12-15 mg/kg 2 to 3x/week is recommended. Some experts would recommend considering 3x/week dosing for patients with creatinine clearance 50-70 mL/min, and twice-weekly dosing if less than 50 mL/min.

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TB Disease and Medications in Solid Transplant Patients

TB and Solid organ Transplant (SOT)

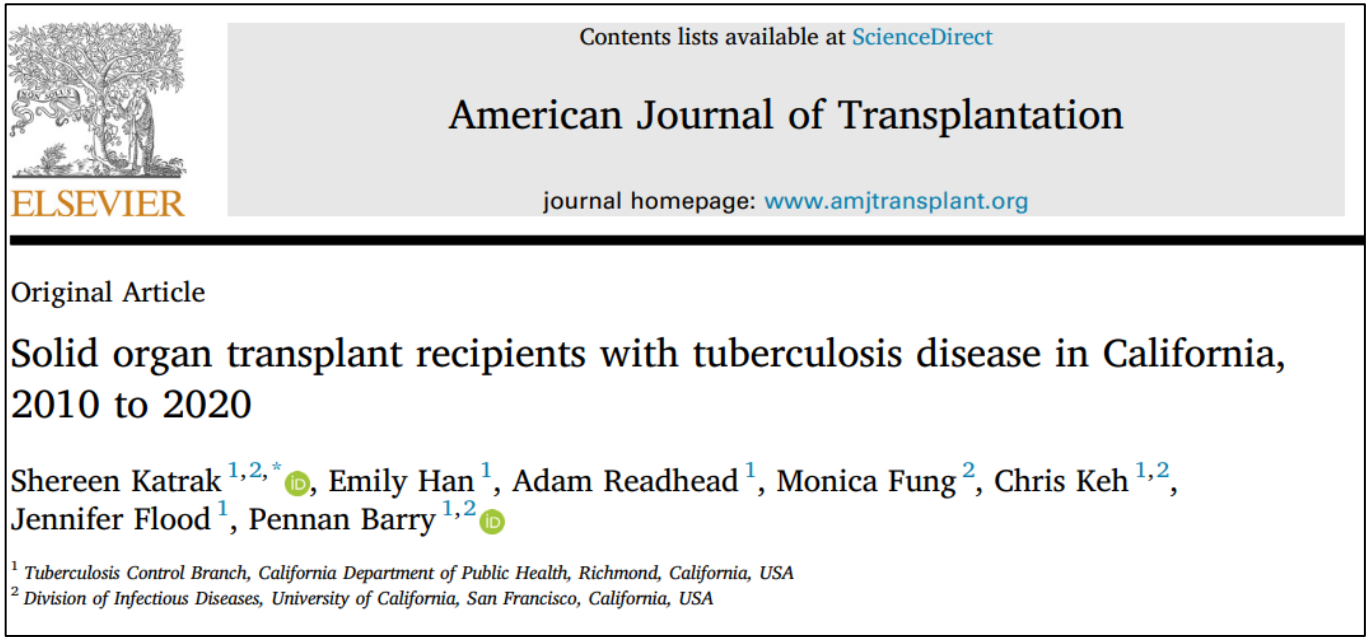
- TB is estimated to be 20-74 times higher in SOT population
- Most TB cases occur during first 6 months post transplant
  - For renal transplant patients, onset can be later
- Diagnosis can be challenging due to atypical symptoms, lack of traditional risk factors, wide range of radiographic manifestations

TB in SOT

TB can occur in a person who has received a SOT for the following reasons:

1. Reactivation of latent TB infection (LTBI)
2. Relapse of previously treated TB
3. TB transmitted by the transplanted organ (donor-derived TB)
4. New transmission of TB after organ transplantation
5. Person with active TB requiring urgent transplantation (e.g., drug-induced hepatotoxicity)

SOT recipients with TB



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Original Article

Solid organ transplant recipients with tuberculosis disease in California, 2010 to 2020

Shereen Katrak [1,2,*], Emily Han [1], Adam Readhead [1], Monica Fung [2], Chris Keh [1,2], Jennifer Flood [1], Pennan Barry [1,2]

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S. Katrak et al, American Journal of Transplantation 23 (2023) 401–407

SOT Recipients with TB (California 2010-2020)

Table 3
Incidence of posttransplant tuberculosis disease in California, 2010-2020, by organ type.

Transplant type	Number of California transplants	Number of TB cases[a,b]	Person-years of transplant follow-up[c]	Incidence rate (cases per 100 000 person-years)
All solid organs	37 064	96	171 455.2	56.0
Heart[d]	3680	6	15 866.6	37.8
Intestine	64	0	356.7	0.0
Kidney	23 148	54	111 702.5	48.3
Liver	9289	26	41 186.7	63.1
Lung	2412	12	8735.2	137.4
Pancreas	866	0	4770.2	0.0

S. Katrak et al, American Journal of Transplantation 23 (2023) 401–407

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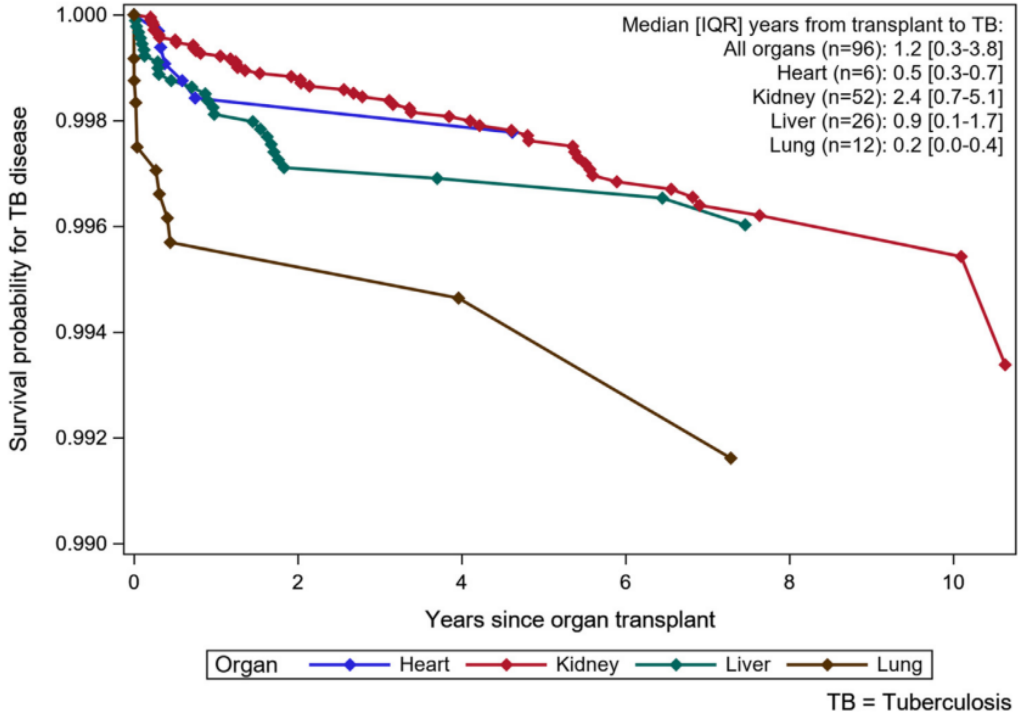
SOT Recipients with TB (California 2010-2020)



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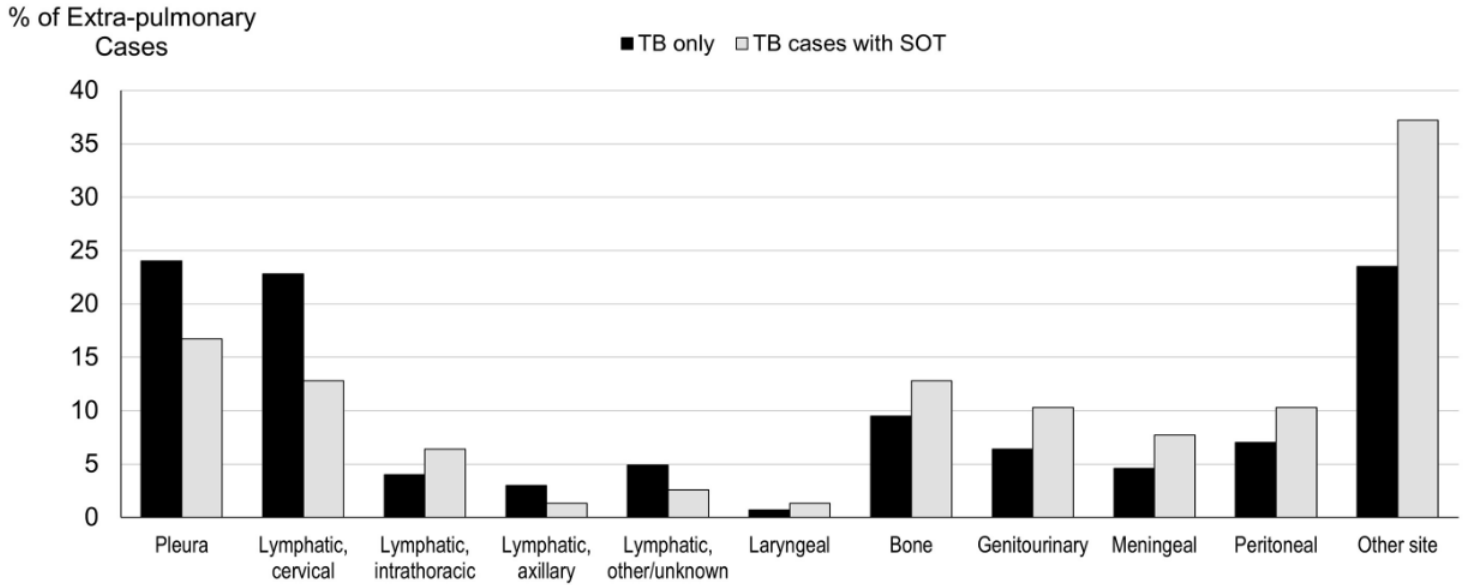
SOT Recipients with TB

Supplemental Figure 1. Extra-pulmonary sites of disease, by SOT status



Other extra-pulmonary sites in TB cases with SOT include: Liver (5), blood (4), pericardium (4), small intestine (4), bone marrow (2), colon (2), spinal cord (2), appendix (1), brain (1), breast (1), cranial, spinal, peripheral nerve (1), pancreas (1), rectum (1), skin (1), not specified (1).

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Patient Case 3 (Audience Poll)

47-year-old male (US born) S/P kidney transplant, and history of LTBI S/P 9 - month INH gets diagnosed with cervical and retroperitoneal TB 4 months after transplant. Patient is on Tacrolimus, Mycophenolate and Prednisone for immunosuppression. Which option would you start TB treatment with (Renal function and LFT currently normal, Susceptibilities pending).

A) Rifabutin, Isoniazid, Pyrazinamide, Ethambutol
B) Rifampin, Isoniazid, Pyrazinamide, Ethambutol (RIPE)

Patient Case 3

- LTBI treatment reduces risk of infection to disease progression , need to have a high index of suspicion in the right scenario even in patients who have completed LTBI treatment
- Understand drug interactions with immunosuppressive medications for adjustments and collaborations with clinical pharmacist /transplant teams etc
- Cautious regarding resistances with previous LTBI treatment
- Collaboration with the transplant team regarding safely reducing immunosuppression if at all possible

TABLE 3. **Interactions between immunosuppressants and commonly used DR-TB medications**

Immunosuppressant	Rifampin (RIF)*	Isoniazid (INH)	Bedaquiline (BDQ)	Pretomanid (Pa)	Cycloserine (CS)	Clofazamine (CFZ)	Moxifloxacin (MFX) or Levofloxacin (LFX)	Linezolid (LZD)
Corticosteroids	Decreased serum concentration of corticosteroids with potential increased risk for organ rejection	May decrease the serum concentration of INH	None	None	Overlapping toxicity: caution and close monitoring recommended for neurologic (mood, psychiatric) changes	None	Increased risk of tendonitis	None
Cyclosporine A	Decreased cyclosporine serum levels with potential increased risk for organ rejection	May increase serum concentration of cyclosporine	None	None	None	May increase serum concentration of cyclosporine	May increase cyclosporine levels (usually LFX only)	None
Tacrolimus	Decreased serum concentration of tacrolimus with potential increased risk for organ rejection	May increase serum concentration of tacrolimus.	Increased risk and enhancement of QTc prolongation	None	None	Increased risk and enhancement of QTc prolongation; may increase serum concentration of tacrolimus.	None	None
Rapamycin/ sirolimus	Decreased serum concentration of sirolimus with potential increased risk for organ rejection	May increase serum concentration of sirolimus.	None	None	None	May increase serum concentration of sirolimus	None	None
Mycophenolate mofetil (CellCept®)	Decreased serum concentration of active metabolite, mycophenolic acid with potential increased risk for organ rejection	None	None	May increase the serum concentration of mycophenolate	None	None	May decrease mycophenolate level	None
Azathioprine	None	None	None	None	None	None	None	May increase risk of bone marrow suppression

* Given the predicted significant decrease in levels of multiple immunosuppressants with RIF, leading to increased risk for organ rejection, most experts would not use RIF in combination with these agents. Some experts may consider using rifabutin (RFB), in very close coordination with ID pharmacy and transplant providers

Resources

- Clinical consultations
  - Rutgers, UVA
- Curry Guide (online)
- Rifampin Drug interactions
- Collaborations multidisciplinary teams
  - Clinical pharmacist /other specialties(GI/Hepatology/Nephrology/ Transplant teams)

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2) Yi-Ting Lin, Ping-Hsun Wu, Chun-Yu Lin, Ming-Yen Lin, Hung-Yi Chuang, Jee-Fu Huang, Ming-Lung Yu, Wan-Long Chuang, Cirrhosis as a Risk Factor for Tuberculosis Infection—A Nationwide Longitudinal Study in Taiwan, *American Journal of Epidemiology*, Volume 180, Issue 1, 1 July 2014, Pages 103–110, https://doi.org/10.1093/aje/kwu095

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