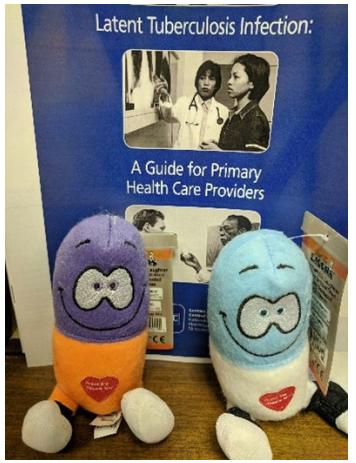
Southern Regional Specialty Chest Clinic

STOP TB

Camden County DHHS
Cooper University Hospital
NJ Tuberculosis Program

Cooper Medical School of Rowan University



Monitoring and Managing Adverse Events of Tuberculosis Treatment
8/19/21

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Case 1

- A 63 year old Vietnamese-born woman is diagnosed with smear-positive pulmonary tuberculosis, GeneXpert® MTB/Rif: MTB positive, RIF^R not detected
- She is started on 4 drug anti-tuberculous therapy with RIPE + Vit. B6 and is receiving her treatment by DOT
- About two weeks into treatment she complains to her clinic nurse that the medications are “making me sick” and she wants to stop them
- What do you do now?

Objectives for this Session

- Understand how we define and monitor for adverse events (adverse drug reactions) from TB medications
- Recognize the most common types of adverse drug reactions: minor → major
- Understand which medications most commonly cause which types of problems
- Provide practical approaches to managing the most common ADRs including GI toxicity, hepatotoxicity, skin rashes, and others

➢ Focus on 1st-line meds (RIPE, RFB, RPT) and FQ

What is an ADR?

- Several different definitions used
- WHO definition: “a response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease”
  - Type A (augmented) vs. Type B (idiosyncratic)
- **Side effects** vs. **ADR (Reactions)** vs. **ADE (Events)**
  - “Side effect” is a less precise term (and hated by pharmacists), often refers to milder, predicable effects from taking a medication. Example: orange urine from RIF
  - ADE vs. ADR: ADE used in clinical trials, but may not be “causal”
- Other adverse events: Drug interactions

What is a “significant” ADR?*

- Requires discontinuing the drug
- Requires changing the drug therapy
- Requires modifying the dose
- **Necessitates admission to a hospital**
- **Prolongs stay in a health care facility**
- **Necessitates supportive treatment**
- **Negatively affects prognosis**
- **Results in temporary or permanent harm, disability, or death**

*Am. Soc. Of Health-System Pharmacists (ASHP)

Monitoring for ADRs

- A process starting before initiating treatment and continuing through the entire treatment course
- Assessment for factors increasing risk of an ADR **or** factors that delay recognition if an ADR occurs
  - e.g., increased age, underlying medical conditions: liver disease, peripheral neuropathy
  - Concomitant medications as well as supplements
  - Behavioral risk factors: e.g., alcohol
  - Barriers to effective monitoring: language/cultural, psychiatric issues, “illness anxiety disorder” (related to side effects)
- Baseline laboratory monitoring

Prescribing Anti-tuberculous Therapy: A Risk Benefit Analysis

Source: h.fraimow

- Treatment for TB Disease
  - Benefits always outweigh the risks
  - Those at higher risk need more careful monitoring
- Treatment for LTBI
  - Weigh risks (toxicity) vs. benefits of treatment
  - Those at highest risk of TB disease should always be treated (e.g., HIV+, infant contacts) despite risks of treatment
  - Risks may outweigh benefit for a few, but **most** can (and should) be treated with shorter, safer regimens

➢ *Baseline evaluation incorporates risk assessment*

Source: h.fraimow

We know what the benefits of treatment are, can we modify the risks?

By choice of regimen: e.g., less hepatoxic if high risk

Behavioral interventions: e.g., alcohol

By having a strong monitoring plan

By reacting quickly if problems do arise

Common Types of Drug Toxicity (ADRs)

- **Gastrointestinal toxicity**
- **Hepatotoxicity**
- **Hypersensitivity (allergic) reactions**
- **Other dermatologic reactions**
- Joint symptoms
- Neuropathy
- Visual symptoms
- Drug fever
- Other: nephrotoxicity, hearing loss, cardiac

Prospective Monitoring for ADRs

- Collaboration between client, prescribers, and TB program
- Client education
  - Educate about potential serious ADRs from their regimen? *But <u>how</u> to educate without creating unnecessary anxiety*
  - Educate about need to report symptoms (but don't presume they will)
- Staff education
  - Awareness of potential serious ADRs from different TB meds
  - Assess for ADR symptoms at each and every interaction
  - Document and communicate!
- Interactions: monthly med pick ups, DOT visits, phone calls, any other

Consequences of ADRs

- Minor: May respond to interventions, without change in treatment
- Severe: Worst cases: severe morbidity and even death
- Need for more intensive clinical/ laboratory monitoring
- Need for alterative, more protracted and potentially less effective treatment regimen
  - *Treating TB with multiple ADRs as challenging as treating MDR disease, often requiring alternate medications*
  - *Multiple ADRs may be more common than MDR*
- Negative impact on compliance and outcomes

What drug can do what?
ADRs to First Line Agents and FQ*

Reaction	INH	RIF	EMB	PZA	FQ
Gastrointestinal	X	X	X	X	X
Hepatotoxicity	X	X		X	X
Cutaneous	X	X	X	X	X
Periph. Neuropathy	X		X (rare)		X (rare)
Optic Neuritis	X (rare)		X		
Arthralgia	X	X (rare)		X	X
Gout			X (rare)	X	
Tendonitis					X
Flu-Like Syndromes		X			
Drug Fever	X (rare)	X (rare)	X (rare)	X (rare)	X (rare)
Hematologic	X	X	X (rare)	X (rare)	X (rare)
QT Prolongation					X
CNS	X				X

*Levofloxacin or Moxifloxacin

How common are ADRs to TB meds?

- LTBI Treatment Regimens
  - Generally healthy, limited number of drugs (1 or 2)
  - Many years of data on INH toxicity, increasing data for risks with other regimens for LTBI
  - Comparative data: recent large clinical trials; meta-analyses
    - 9 mos of INH vs. 12 weeks of INH plus Rifapentine
    - INH vs. Rifampin
- TB Disease Treatment Regimens
  - Multi-drug regimens, overlapping toxicity
  - May be more difficult to assign “blame” for an ADR

Risk for INH Toxicity by Age Group

Table 1. Hepatoxicity rate, adjusted for compliance with therapy, by age groups.

Age range	Adjusted incidence hepatoxicity per 1000
0 – 19	0.8
20 – 34	2.8
35 – 54	9.1 (or 17.2*)
> 54	31.0

Adjusted incidence by age group (criteria from Table 2 applied to age subgroups). References [28-36] were used.
*Reference [29] included in 35 – 54 group (based on mean age of participants = 50). If this study is excluded, rate for 35 – 54 is 17.2.

Forget and Menzies. Exp. Opinion in Drug Safety 2006

	9INH[2] N (%)	4RIF[2] N (%)	Risk Difference[3] (4RIF- 9INH in %, 95%CI)	P value
Total randomized (MITT)	3,416	3,443		
Total taking at least one dose of therapy	3,205	3,280	---	
Total Grade 3-5 Adverse events judged possibly or probably due to study drugs	75 (2.3)	31 (0.9)	-1.4 (-2.0, -0.8)	<0.001
Rash or other allergy	2 (0.1)	6 (0.2)	0.1 (-0.1, 0.3)	0.163
Drug Interaction	0 (0.0)	2 (0.1)	0.1 (-0.1, 0.2)	0.5
Hepato-toxicity	65 (2.0)	11 (0.3)	-1.7 (-2.2, -1.2)	<0.001
GI intolerance	1 (0.0)	3 (0.1)	0.1 (-0.1, 0.2)	0.326

9INH vs 4RIF
Menzies et al
NEJM 2018

Medication error	37 (1.0)	27 (0.7)	0.12
All other adverse events	584 (15.5)	531 (13.1)	0.003
Attribution — no. (%)¶			
Related to drug	206 (5.5)	332 (8.2)	<0.001
Hepatotoxicity‖	103 (2.7)	18 (0.4)	<0.001
Rash	21 (0.6)	31 (0.8)	0.26
Possible hypersensitivity**	17 (0.5)	152 (3.8)	<0.001
Other drug reaction	65 (1.7)	131 (3.2)	<0.001
Not related to drug	410 (10.9)	226 (5.6)	<0.001
Severity of adverse event — no. (%)††			
Grade 1 or 2	341 (9.1)	310 (7.7)	0.03
Grade 3	202 (5.4)	193 (4.8)	0.24
Grade 4	42 (1.1)	36 (0.9)	0.32
Nongraded events	31 (0.8)	19 (0.5)	0.05

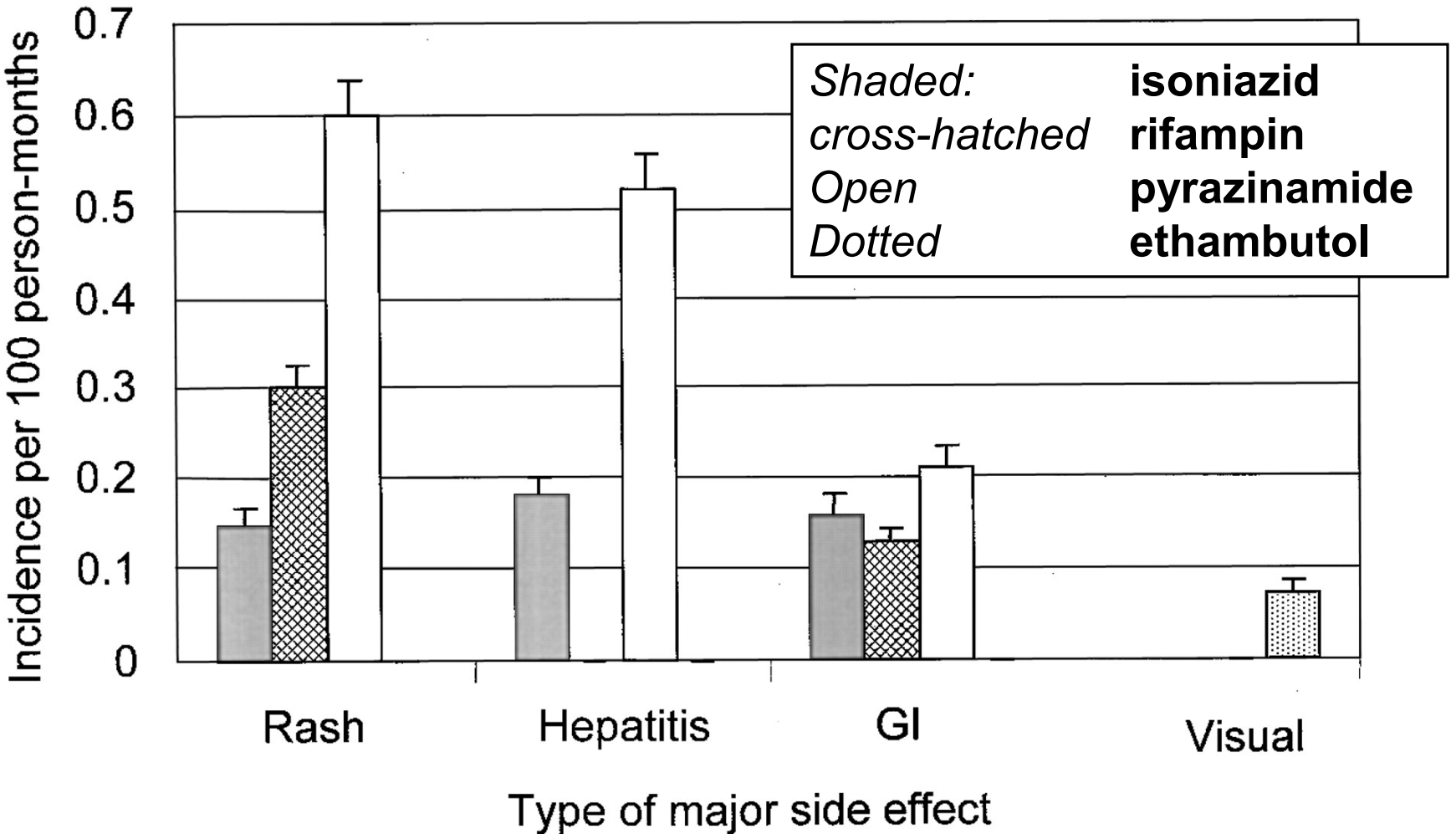
Prevent TB Trial
Sterling et al
NEJM 2011

Incidence of Adverse Events during TB Disease treatment – Montreal Chest Institute

- Retrospective review: 403 adult patients
  - **9.2%** (37/403) major ADRs leading to D/C'ing a drug
  - 9 had 2nd adverse reaction (total 46 events)
- Rash/fever 4%, Hepatitis 2.9%, other GI 2%
- Risks:
  - Female > Male
  - Age > 60

Yee, et al AJRCCM 2003;167(11): 1472-1477

Incidence of Serious Side Effects by Type and Drug



AJRCCM 2003;167(11): 1472-1477

ADRs in Some Other Studies

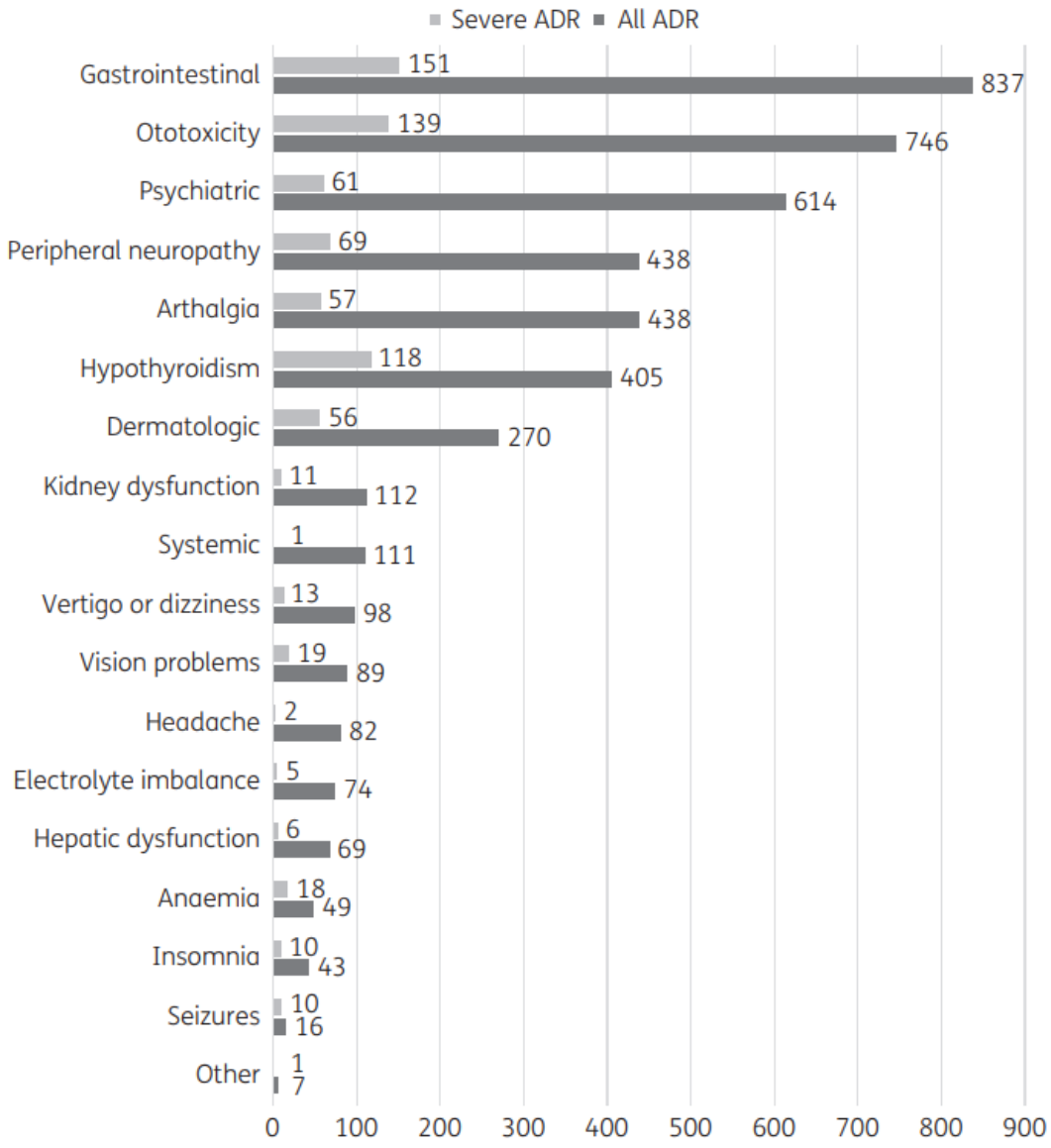
- Tuber. and Lung Disease, 1996 (UK)
  - 5.1% ADRs requiring treatment modification
  - Increase with increasing age:
  - 2.3% 0-19, 8.3% over 60; female > male
- PLOS 1, 2011 (Lima, Peru)
  - Risks for ADRs (in multivariate analysis)
    - Age, obesity, anemia, smoking, MDR
- Int. J. of Env. Res. Pub. Health 2016 (China)
  - 462 patients, **22.1% ADRs**, 3.1/100 patient mo.
  - 37% of these liver toxicity, 24% GI toxicity

Why are there such variations in ADR rates?

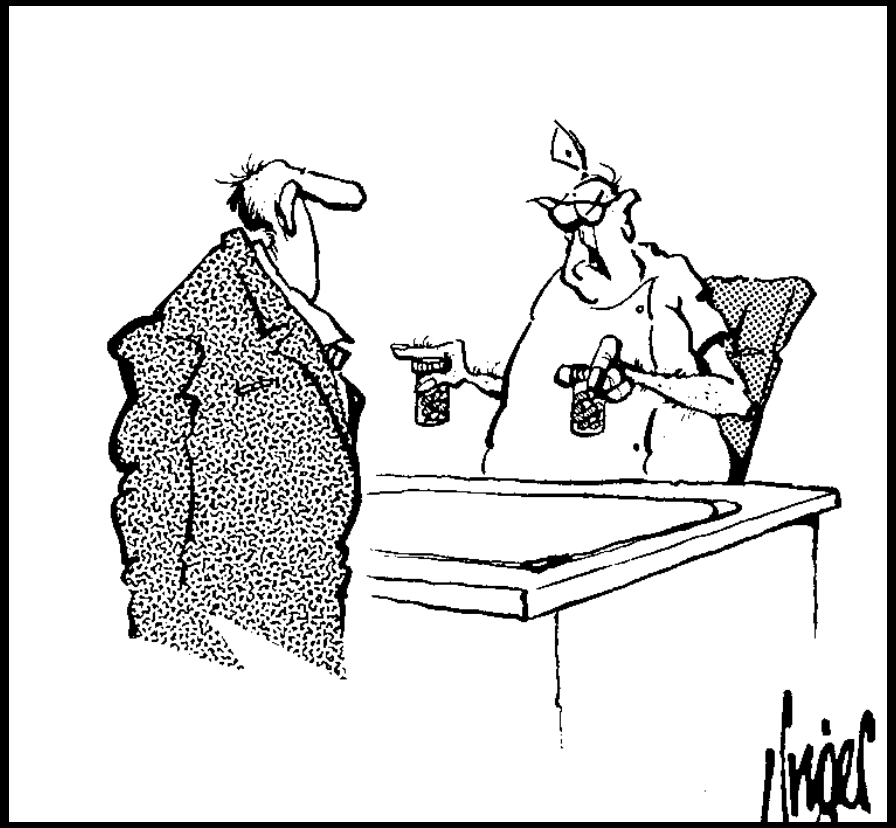
- Rates of ADR requiring stopping Rx vary from 5-20%
- Why such variability?
  - Where were the studies done? What was the make up of the treated population?
- Pharmacogenetics:
  - Altered metabolism may result in higher drug exposure Example: slow vs. rapid acetylators of INH (NAT2)
  - Other genes where SNPs (mutations) have been implicated in potential toxicity: CYP2E1 and GSTM1

ADRs in Drug-Resistant TB Treatment

- Schnippel K, et al. *ADRs during **drug-resistant TB treatment** in high HIV prevalent settings: a systematic review and meta-analysis*. JAC 2017; 72:1871-9.
  - **83%** of patients had ≥1 ADR
  - **24%** of patients had ≥1 severe ADR
  - No significant association between HIV infection and drug-resistant TB treatment ADR

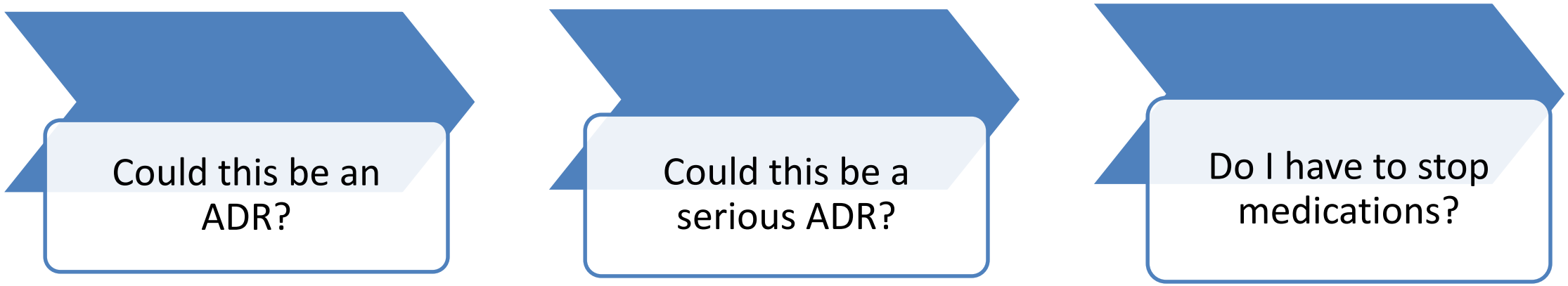


Management of Some Common ADRs to Anti-tuberculous Therapy: State of the Art



"Don't take any of these red pills, and if that doesn't work, don't take any of the blue ones"

Dr. F's Thought Process in Thinking Through Potential ADR Symptoms



Do I need to see them?
Do I need lab work?
What do I tell them?

Do I stop one/some/all meds?
Do I need to start new meds?

General Principles and Approach

- Pre-emptive monitoring for ADRs (baseline exam/labs)
- Evaluate likelihood that signs/symptoms due to a TB medication
  - Any risk factors for toxicity?
- Rule out other common, or less common (but potentially more alarming) causes of the current presentation
  - Medication-induced nausea/vomiting vs. hepatotoxicity
- Evaluate severity of ADR → informs action plan
  - Self-limiting, supportive care, or need for alternative treatment
- Follow-up monitoring including treatment adherence

Case 1

- When further interviewed (using interpreter phone) our client says that when she takes her TB pills, she feels “sick to her stomach” like she might throw up and can’t eat. She has not vomited, does not have abdominal pain or dark urine. She has lost 2 lbs.
  - She has blood work done
  - ALT 51 (ULN 32, baseline was 23 before treatment); AST 38 (at ULN), Bilirubin 0.9
- What do we do now?
- What interventions can we try?

Q1. The most likely explanation for her symptoms is:

1. Gastrointestinal toxicity from INH
2. Hepatotoxicity from INH
3. Gastrointestinal toxicity from PZA
4. Gastrointestinal toxicity from any of her anti-tuberculous medications

Gastrointestinal (GI) Toxicity

- Nausea
- Vomiting
- Diarrhea
- Bloating
- Anorexia
- Abdominal pain

➢ Overlap of GI toxicity and hepatotoxicity symptoms: Can’t tell without difference without checking LFTs

Which drugs are most likely to cause GI toxicity (and when?)

- Almost any drug can potentially cause GI toxicity
- Often occurs early (first few weeks) of Rx
- Hierarchy: PZA > INH > RIF > EMB
- Fluoroquinolones can also cause GI toxicity but less commonly than PZA or INH
- Many of other 2nd-line drugs can cause GI toxicity (rarely injectables)

Q2. How would you try and manage her symptoms?

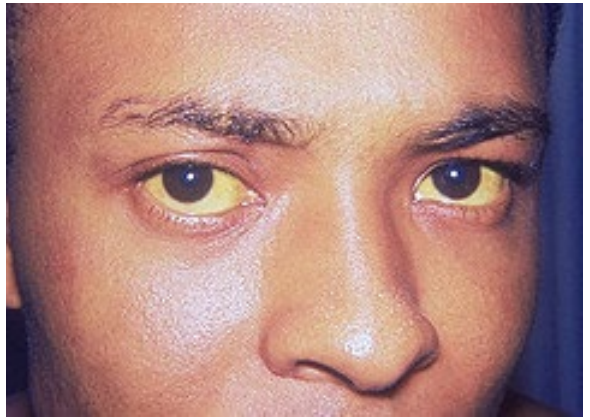
1. Stop all anti-tuberculous medication and re-introduce them one at a time
2. Try giving medications with food or at a different time
3. Try giving medication with an anti-emetic
4. Stop the PZA and see if symptoms resolve

Management of GI Symptoms (after excluding hepatotoxicity)

- Change the timing of the dose
- Give meds with food (how much food?)
- Daily dosing with fewer pills rather than intermittent therapy with more pills
- Antacids 2hr before or after
- Anxiolytic if nausea occurs prior to swallowing pills
- Anti-emetics:
  - Ondansetron (Zofran®), prochlorperazine (Compazine®), promethazine (Phenergan®), hydroxyzine, metoclopramide

Back to our Case

- What if her LFTs are elevated?
- What if her LFTs are:
  - ALT 732 (ULN 55)
  - AST 444 (ULN 50)
  - Bilirubin 3.4
- How should her symptoms be managed?



Q3. How should her symptoms be managed?

1. Stop all anti-tuberculous medications until LFTs return to 2X ULN
2. Stop INH and follow LFTs
3. Stop INH and PZA and follow LFTs
4. Stop INH, RIF, and PZA, continue EMB and add 2 new, low-hepatotoxic risk anti-tuberculous agents

Hepatotoxicity: Drug Induced Liver Injury (DILI)

- Elevation in liver enzymes: ALT (AST, Bili)
- Confounders: Other drugs/supplements, alcohol, viral hepatitis, other liver/biliary tract disease, rarely TB involvement of liver
- Spectrum of hepatotoxicity
  - Can be symptomatic or asymptomatic
    - Asymptomatic, mild AST increases in up to 20% on INH, can monitor
  - ATS **symptom-related** threshold to **stop therapy** ALT 3x ULN
  - ATS **asymptomatic** threshold to **stop therapy** ALT 5x ULN
  - Fulminant hepatitis (rare)
  - Fatal hepatitis: Estimates 4-7/100,000 INH courses

Some Risk Factors for Hepatotoxicity from Anti-tuberculous Therapy

- Increasing age > 35
- Malnutrition or hypoalbuminemia
- PZA in regimen
- Other hepatotoxic agents
- Alcohol
- Pregnancy or post-partum (3 mos)
- Elevated baseline ALT
- HIV infection
- Multiple medical problems
- Pre-existing chronic liver disease
- Chronic viral Hepatitis: Hepatitis B and/or C
- Slow acetylators
- Other genetic risks

Treatment Limiting Thresholds

- **Stop if ALT > 3 X ULN with N,V, abd. pain OR ALT > 5 X ULN in all**
- If moderate or severe TB, then continue at least 3 drugs
  - Rifampin, EMB, fluoroquinolone
  - Full hepatic sparing regimen (no Rifampin): EMB, FQ, injectable or linezolid
- Assess for confounders
  - Concomitant meds, OTC, supplements, herbals, EtOH
  - Acute viral hepatitis testing:
    - IgM anti–Hep A Ab; hepatitis B S Ag and IgM anti–Hep B core Ab; anti-HCV Ab and/or HCV RNA
    - Note: If unstably housed or injection drug user, think Hepatitis A!!
- In some instances, increased LFTs can be due to TB disease especially if disseminated disease

From: Am J Respir Crit Care Med. 174; 935–52, 2006

So now we've stopped treatment, what then? Practical aspects of re-challenge

- Can restart once ALT falls to < 2 X ULN
- Many can even return to original regimen and tolerate it
- Weigh risks based on severity of hepatotoxicity
- Different strategies:
  - Sequential re-challenge: most useful to sort out hepatotoxicity cause; re-introduce a drug every ~7 days with LFT monitoring
    - Start RIF +/- EMB, then INH, +/- PZA
    - If symptoms or LFTs ↑→ stop last drug added
    - If RIF and INH are tolerated, and **hepatitis was severe,** might not add back PZA

Severe INH Liver Injuries among Persons being Treated for LTBI in US 2004-2008: MMWR 2010

- 17 cases reported to CDC (unable to determine a rate)
  - Rates in older studies up to 0.43 per 1000
- 5 died, 5 required liver transplantation
- Can occur anytime in treatment: 9 of 17 beyond the 3rd month
- Can occur in children: 2/17
- Hepatitis diagnosis by other than prescribing physician: 10/17
- Did **NOT STOP** medication when symptoms developed: 8/17

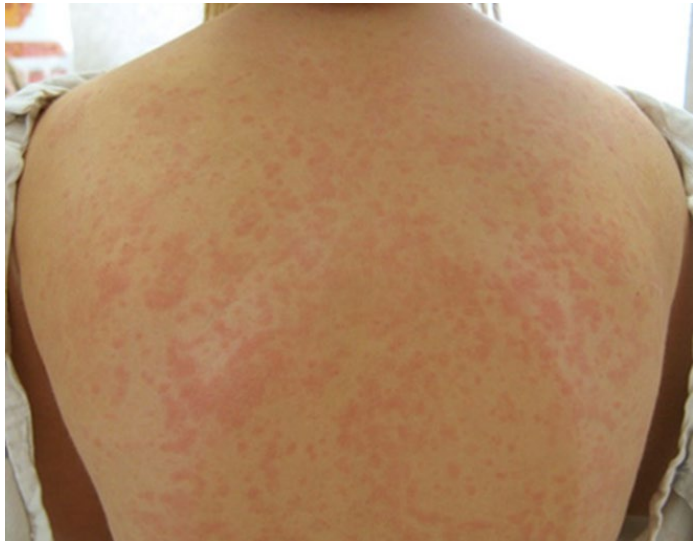
An idiosyncratic reaction that can occur later in treatment
Keep monitoring until the end of therapy!!

What about Rifampin Hepatotoxicity?

- Transaminitis (increased AST, ALT) is much less common than hepatotoxicity from INH or PZA
- Most common liver injury pattern is **cholestatic hepatitis**
  - Elevated bilirubin and alkaline phosphatase
  - Often with fever
  - Often other manifestations of hypersensitivity reaction
  - Almost always need to stop the drug
- Some with RIF liver injury have tolerated Rifabutin

Back to our Patient

- You made some adjustments in timing of her medications
- She takes a small snack prior to taking her pills, and has ondansetron as needed
- She remains on RIPE and is doing much better
- At her one month clinic visit, weight is stable and cough is better. But she now says she feels “itchy” and you note a **diffuse erythematous macular rash** on her back



Q4. How should this reaction be managed?

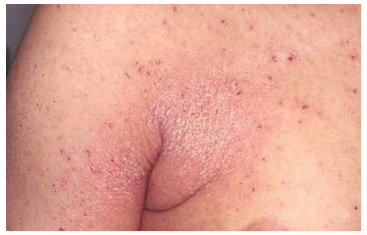
1. Stop all anti-tuberculous medications until the rash subsides
2. Obtain more history about the rash
3. Treat with antihistamines
4. Check for fever, mucous membrane involvement or generalized erythema and stop medications if any of these are present

Cutaneous Adverse Drug Reactions (CADRs) to Anti-tuberculous Drugs

- Can be confined to the skin or part of a more systemic hypersensitivity syndrome
- Epidemiology and rates of CADRs less well defined than for other toxicities
  - Montreal Chest Institute study: PZA > Rif > INH, but in other studies (and our clinic) EMB skin reactions also very common
- Severe CADRs more common in HIV+ and in those with multiple drug allergies

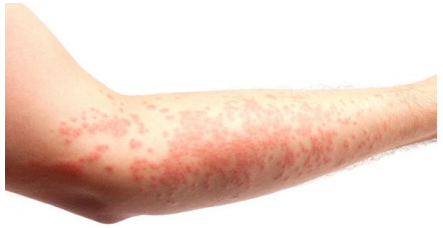
Drug Rashes for the Non-Dermatologist (Us)

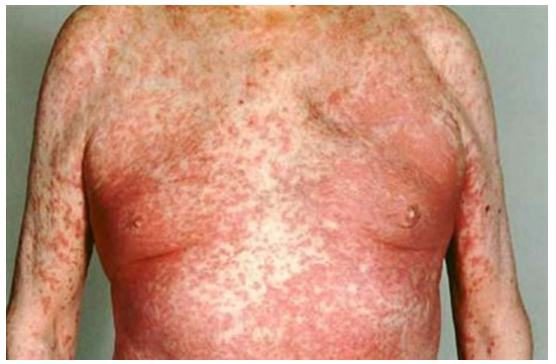
- **Where…**
  - did it start?
  - has it spread?
- **What…**
  - does it look like?
  - makes it better or worse?
- **When** did it start?
- **Who** (else) has it?



DDx of skin rashes besides TB Rx

- Insect bites, scabies, bed bugs
- Other drugs
- Contact dermatitis
- Acne/folliculitis
- Immunologic/hypersensitivity reactions
- Sunburn
- Pellagra
- Eczema
- Dry skin
- Skin infections

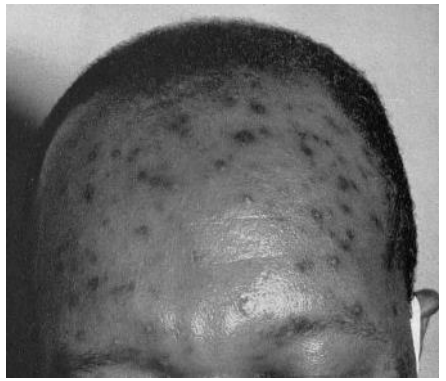


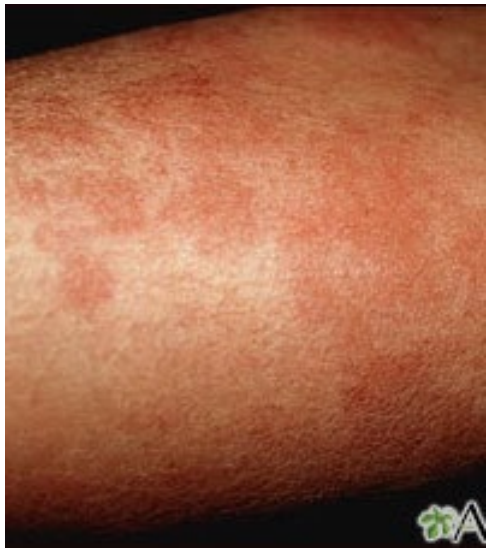


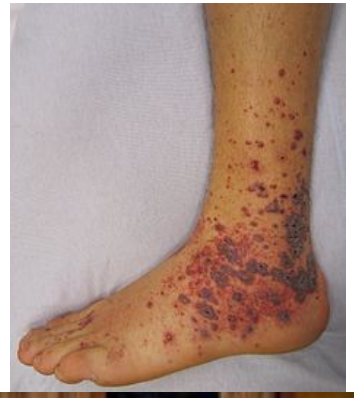
Note: Your clients will always blame the medications, regardless of the cause

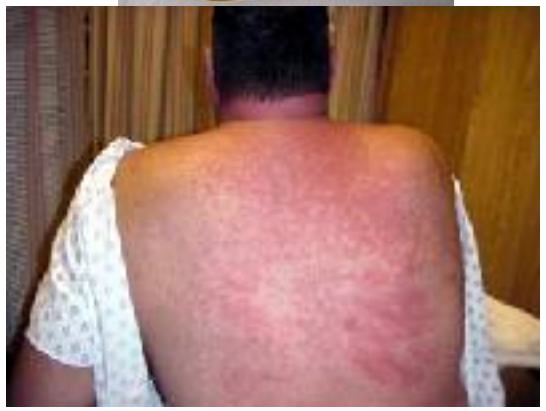
Skin Reactions with Specific Anti-TB Drug Association

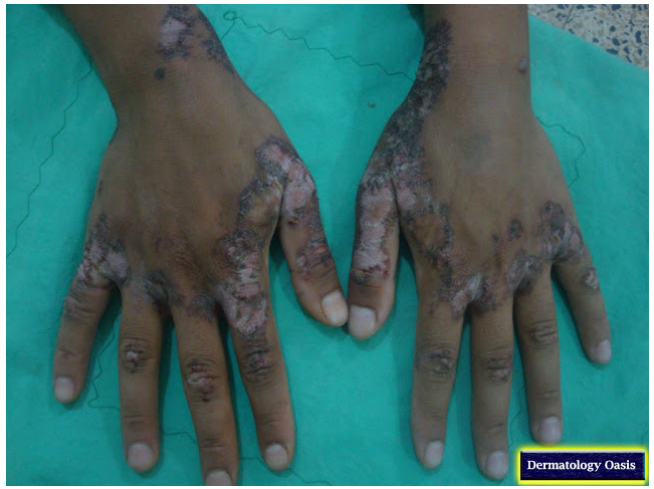
- Acne (INH, RIF)
- Photosensitivity (PZA, FQ)
- Purpura (RIF,INH)
- SLE-like syndrome (INH)
- Pellagra (INH)
- Urticaria **(Any)**
- Exfoliative dermatitis **(Any)**
- Toxic epidermal necrolysis **(Any)**
- Stevens-Johnson syndrome **(Any)**











“Minor” Itchy Rashes

- May be localized, may be more pruritic than actual visible rash, not progressing over time
- Can be maculopapular – ensure NO involvement of mucous membranes or systemic signs (fever)
- **Continue** all TB medications (with careful monitoring)
  - May resolve after first several weeks without stopping
  - Monitor for progression
- **Symptomatic treatment** (antihistamines)
  - **Diphenhydramine** 25-50 mg PO before TB meds and q6 hours PRN
  - **Hydroxyzine** 25 mg PO every 6 hours
  - **Loratadine** 10 mg PO once daily before TB medications
  - Topical corticosteroid – **hydrocortisone cream**
  - Low-dose **prednisone** 10-20 mg/day for refractory cases

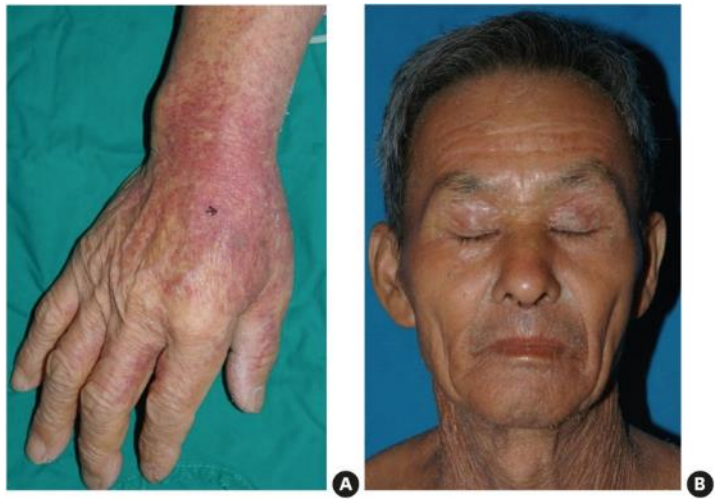
Other Dermatologic Reactions

- **Flushing reactions**
  - Flushing and/or itching or redness involving the face and scalp
  - Occurs 2-3 hours after taking medications, usually due to **RIF or PZA**
  - Mild and resolves without therapy, can use **antihistamines**
- **Photosensitivity**
  - Concern especially with **PZA or FQs**
  - Limit sun exposure and use sunscreen
- **Petechial rashes**
  - Check platelet count; if low: presume rifampin is culprit and stop it
- **Hives and Urticaria**
  - Can be caused by **ANY** TB medication
  - **STOP** all potentially responsible medications
  - Ensure initial reaction was **NOT** severe – no signs of anaphylaxis, angioedema, or airway compromise
  - **Graded rechallenge** after reaction resolves, start with most important drug

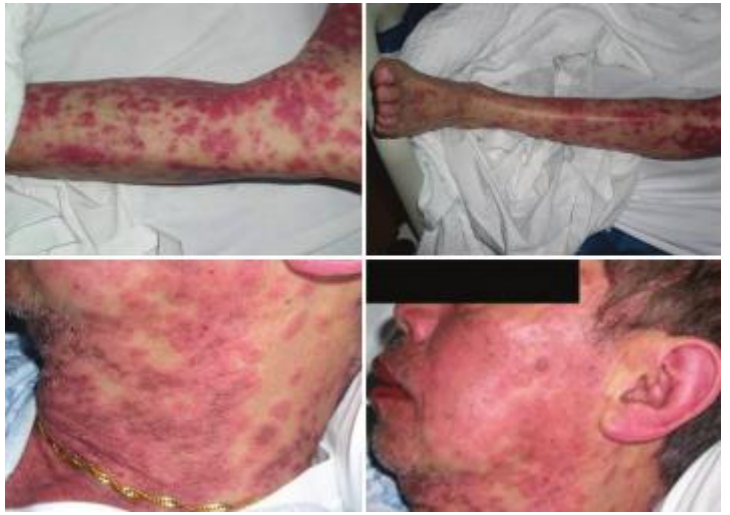
Generalized Erythematous Rashes

- Any drug can cause this
- Stop all drugs immediately
  - Especially if fever and/or mucous membrane involvement
  - Concern for toxic epidermal necrolysis (TEN)/ Steven Johnson / DRESS
  - If severe TB disease, use 3 **new** drugs
  - ? Systemic steroids
- Once rash significantly improved
  - Re-challenge serially
  - Reintroduce new drug every 2 – 5 days
    - R, H, E, (Z)
- Adjuvant testing: CBC (eosinophil count)

➢ Dermatology evaluation and skin biopsy



Jung et al. Allergy Asthma Immunol Res. 2019



Kaswala J Family Med Prim Care. 2013

My Patient had an ADR to Rifampin- What can I do?

- Rifamycins remain our most important drug→ need much longer treatment regimens without it
- Can I give them **rifabutin** instead?
  - More than 50% of patients who have problems with rifampin can take rifabutin but depends on the reaction
  - GI and hepatotoxicity usually can
  - Some skin rashes yes, but severe hypersensitivity less likely
  - Thrombocytopenia generally would not use

Common Types of Drug Toxicity (ADRS)

- **Gastrointestinal toxicity**
- **Hepatotoxicity**
- **Hypersensitivity (allergic) reactions**
- **Other dermatologic reactions**
- Joint Sx: PZA arthralgias and Gout, INH, FQ tendon rupture
- Neuropathy: INH
- Visual symptoms: Ethambutol
- Drug fever (any) and “Flu” like symptoms (RIF)
- Other: Hematologic, QT prolongation, nephrotoxicity, CNS

Case 2

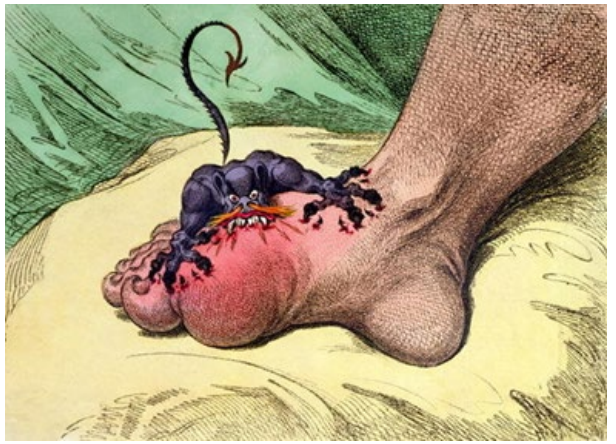
- 74 year-old man with pulmonary TB, AFB smear positive, GeneXpert® RIF-susceptible MTB
- Hx of diabetes mellitus, chronic kidney disease and coronary artery disease. Ht 68 inches, wt. 134 lbs, Creatinine is 1.7 (Calc Cr.Cl ~35)
- Started on INH 300 mg, RIF 600 mg, PZA 1500 mg, EMB 1200 mg and B6 daily
- Seen two weeks later. His cough is better, he gained 2 lbs, but complains of aches in knees and ankles. On exam left knee is mildly swollen and tender

Q5. How should his joint symptoms be managed?

1. Check uric acid and stop PZA if uric acid is elevated
2. Start allopurinol
3. Hold all medications until symptoms stop and rechallenge
4. Continue all medications and treat symptomatically with an NSAID

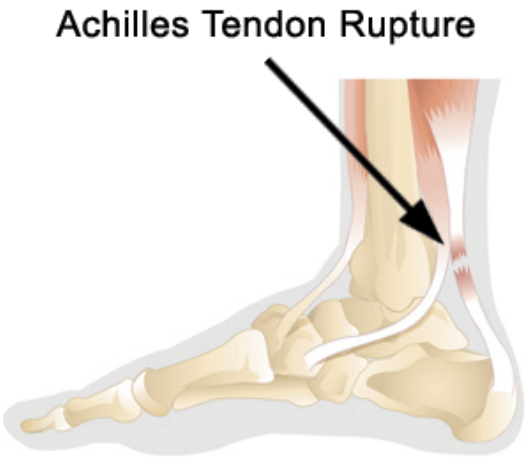
Joint Complaints: PZA and other

- Arthralgias common with PZA:
  - 8% with joint symptoms, 2% will stop drug
  - Elevated uric acid common
  - Treatment is NSAIDS, allopurinol generally not helpful
- PZA rarely can cause acute gout flares; history of gout a relative contraindication, but elevated uric acid alone is not
- Other drugs and arthralgias
  - INH and RIF (much less common than PZA)
  - Fluoroquinolones
- Gout from other drugs: EMB (rare)



Other Musculoskeletal ADRs of Anti-tuberculous Therapy

- Tendonitis and tendon rupture
  - Fluoroquinolone use
  - Risk with increased age, steroids
  - **Now a black box warning**



WARNING:
Fluoroquinolones, including LEVAQUIN®, are associated with an increased risk of tendinitis and tendon rupture in all ages. This risk is further increased in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart or lung transplants [See *Warnings and Precautions (5.1)*].

ADRs to First Line Agents (and FQ)

Reaction	INH	RIF	EMB	PZA	FQ
Gastrointestinal	X	X	X	X	X
Hepatotoxicity	X	X		X	X
Cutaneous	X	X	X	X	X
Periph. Neuropathy	X		X (rare)		X
Optic Neuritis	X (rare)		X		
Arthralgia	X	X (rare)		X	X
Gout			X (rare)	X	
Tendonitis					X
Flu-Like Syndromes		X			
Drug Fever	X (rare)	X (rare)	X (rare)	X (rare)	X (rare)
Hematologic	X	X	X (rare)	X (rare)	X (rare)
QT Prolongation					X
CNS	X				X

Nephrotoxocity and Ototoxicity: Injectables

A Few Key Points

- ADRs common on Rx for LTBI and TB disease and range in severity from minor to major
- Severe, idiosyncratic ADRs rare but have significant implications
- Particular drugs may be more frequently implicated in some ADRS; other reactions can be caused by any first-line TB medication
- Monitoring for ADRs requires risk assessment, client/staff education and awareness, open communication, and careful documentation
- All suspected ADRs need to be addressed, but do not always require stopping/modifying Rx; some drugs can be successfully reintroduced
- We are NOT: Dermatologists or Hepatologists or Ophthalmologists (or other…) so get help with severe/complex ADRs if you need it!

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