MANAGING ADVERSE DRUG REACTIONS

Shu-Hua Wang, MD, MPH &TM
Assistant Professor of Medicine
The Ohio State University

OBJECTIVES

For anti-tuberculosis medications:

- Describe clinical monitoring for adverse drug reactions
- Case Reviews
  - Nursing interventions and medical management
- Review specific drug side effects
- Review adverse drug reactions

CLINICAL MONITORING

- Ongoing Process→→→
- Initial assessment – nurse/physician
  - Identify high risk individuals
  - Check baseline labs
- Staff and Patient education
  - Aware of adverse drug reactions
  - Instruct patient to report signs or symptoms
    - Rash
    - Decrease appetite, nausea, vomiting, abdominal pain
    - Fatigue or weakness
    - Dark urine
    - Persistent numbness in hands or feet

CLINICAL MONITORING

- Document, document, document!
- Encounters
  - Monthly refill visits
    - Rationale for treatment
    - Adherence with therapy
    - **Symptoms of adverse drug reaction**
    - Commitment to continue therapy
    - Limited # doses of medication dispensed
  - DOT visits
- Case management
  - Assessment/PLAN in place
  - Good communication with team: MD, RN, MA, DIS

MINOR SIDE EFFECTS

- Mild reactions
- No lasting effect
- Usually do not require change in TB meds
- Discoloration of body fluid
- Gas, bloating, mild nausea
- Itching, mild rash
- Photosensitivity
- Sleep disturbances
- Headache

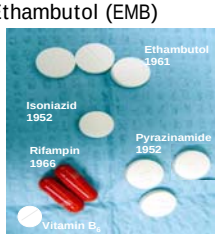
SERIOUS DRUG COMPLICATIONS

- Serious
- May be life threatening
- Require change in medication
- May require hospitalization
- Significant nausea, vomiting, diarrhea
- Hepatotoxiciy
- Toxic skin / systemic reactions
- Hearing loss
- Kidney failure
- Vision loss
- Hematologic reactions
- Electrolyte abnormalities
- Neurologic damage
- Death

ANTIMYOBACTERIAL DRUGS

First-Line Drugs

- Isoniazid (INH)
- Rifampin (RIF)
- Pyrazinamide (PZA)
- Ethambutol (EMB)



Second-Line Drugs

- Streptomycin
- Cycloserine
- p-Aminosalicylic acid
- Ethionamide
- Amikacin or kanamycin*
- Capreomycin
- Levofloxacin*
- Moxifloxacin*
- Linezolid*

* Not approved FDA for TB Treatment

COMMON ADVERSE REACTIONS TO DRUG TREATMENT

Drug	Adverse Reaction	Signs and Symptoms
Any drug	Allergy	Skin rash
Ethambutol	Eye damage	Blurred or changed vision Changed color vision
Isoniazid, Pyrazinamide, or Rifampin	Hepatitis	Abdominal pain Abnormal liver function test results Fatigue Lack of appetite Nausea Vomiting Yellowish skin or eyes Dark urine

COMMON ADVERSE REACTIONS TO DRUG TREATMENT

Drug	Adverse Reaction	Signs and Symptoms
Isoniazid	Peripheral neuropathy	Tingling sensation in hands and feet
Pyrazinamide	Gastrointestinal intolerance	Upset stomach, vomiting, lack of appetite
	Arthralgia	Joint aches
	Arthritis	Gout (rare)
Streptomycin	Ear damage	Balance problems
		Hearing loss
		Ringing in the ears
	Kidney damage	Abnormal kidney function test results

COMMON ADVERSE REACTIONS TO DRUG TREATMENT

Drug	Adverse Reaction	Signs and Symptoms
Rifamycins	Thrombocytopenia	Easy bruising
Rifabutin		Slow blood clotting
Rifapentine	Gastrointestinal intolerance	Upset stomach
Rifampin		
	Drug interactions	Interferes with certain medications, such as birth control pills, birth control implants, and methadone treatment

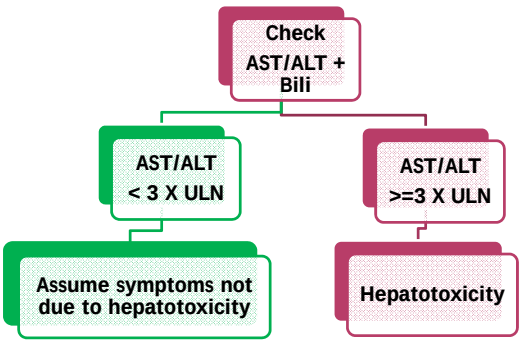
CASE (1)

- 44 year-old male
- Diagnosed with active pulmonary TB disease
  - TST Positive
  - Abnormal CXR
  - Smear positive
  - NAA test positive for *M.tb*
  - Culture pending
- Started on 4 drug anti-TB medications
  - RIF, INH, PZA, and EMB
- Seen in clinic 2 weeks after starting meds with nausea

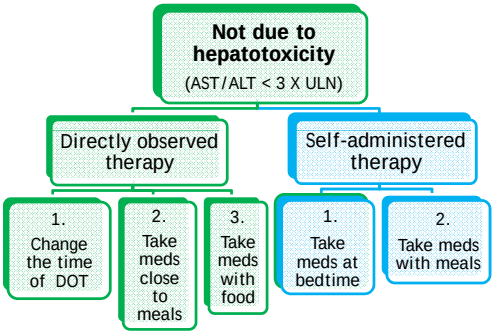
GASTROINTESTINAL UPSET:
NAUSEA, VOMITING, POOR APPETITE, ABDOMINAL PAIN

- GI reactions are common
- Especially in the first few weeks of therapy
- Many anti-TB meds cause GI upset
- Check AST and bilirubin

GASTROINTESTINAL UPSET:
NAUSEA, VOMITING, POOR APPETITE, ABDOMINAL PAIN



GASTROINTESTINAL UPSET:
NAUSEA, VOMITING, POOR APPETITE, ABDOMINAL PAIN



CASE (2)

- 34 year-old female
- TB suspect
  - TST positive
  - Joint pain in elbow X 3months with swelling
  - Surgical I&D (incision and drainage)
  - AFB smear negative
  - NAA test - pending
  - Culture pending
- Started on 4 drug anti-TB medications
  - RIF, INH, PZA, and EMB
- Seen in clinic one week after starting meds with complaints of rash

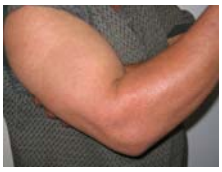
4 W'S OF DRUG RASH
WHERE, WHAT, WHEN, WHO?

- Where is it? Where did it start? Where has it spread to?
- What does it look like? What makes it better or worse?
- When did it start?
- Who has it?

- Insect bites, scabies
- Contact dermatitis
  - New soap, detergent, lotions, perfumes
- Sunburn
- Dry skin
- Other drugs –new
- Other infections

RASH

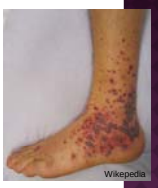
- All drugs used in treating TB can cause rash
- Rash is **minor** –
  - Affecting limited area
  - Predominantly itching
- Antihistamine
  - Symptomatic relief
- Continue anti-TB medications



Localized itching without erythematous rash is common early side effect

RASH-PETECHIAL

- MAY SUGGEST THROMBOCYTOPENIA



If patient is taking RIF

Check platelet count

If platelet count is low, presume RIF hypersensitivity

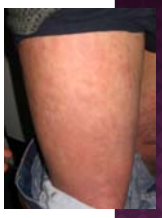
RIF should be stopped and the platelet count monitored until it returns to baseline

RIF should not be restarted

RASH

- GENERALIZED ERYTHEMATOUS RASH (1)

- Stop all drugs immediately
  - Especially if associated with fever and/or mucous membrane involvement
- If patient has severe TB, three new drugs should be started
  - aminoglyocoside and two oral agents
- Rash is substantially improved
- →Restart medication one by one,
- → Add new drug every 2 – 3 days



http://www.japi.org/june_2010/article_15.html

RASH

- GENERALIZED ERYTHEMATOUS RASH (2)

- RIF should be restarted first
  - Least likely to cause rash
  - Most important agent
- Followed by INH
- Followed by EMB or PZA
- If the rash recurs→ stop last drug added
- If no rash appears after the first three drugs have been restarted→ continue first 3 drugs
- Can add fourth drug if…
  - If the rash was relatively mild and
  - If the fourth drug is considered essential therapy.

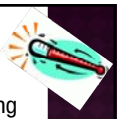
CASE (3)

- 29 year-old male
- Diagnosed with active pulmonary TB disease
  - Sputum AFB smear and culture positive
- Started on anti-TB medications
- Cough and fever resolved, sputum converted AFB smear negative, returned to work
- Seen in clinic 6 weeks after TB meds start →
- Complaints of fever: Comes and goes
- Physical Examination
  - Temp >40^{0}C, BP 120/60, HR 100, RR 18
  - No acute distress, normal examination

DRUG FEVER

- Recurrence of fever in a patient who has been receiving therapy for several weeks
  - Especially if the patient is showing microbiological and radiographic improvement
- Fever from TB may persist for as long as 2 months after therapy has been initiated
- Fever can be a paradoxical reaction
  - Especially in patient with HIV infection
- Patient looks and feels well despite Temp >39^{0}C
- No specific pattern to the fever
- Eosinophilia may or may not be present

MANAGEMENT OF DRUG FEVER

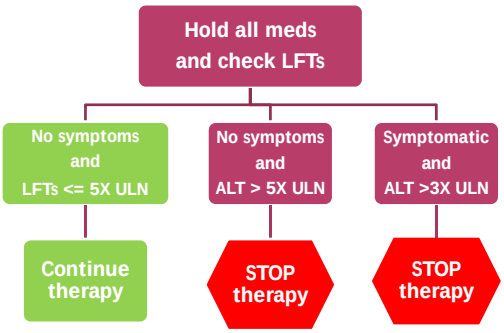


- Ensure there is no superinfection or worsening of TB. Check labs, etc…
- Once potential causes are excluded → Stop all drugs
- Drug-related fever usually resolve within 24 hours
- Patients with **severe TB** should be given at least 3 new drugs (i.e., aminoglyocoside and two oral agents)
- Once the fever has resolved, medication can be restarted one by one, at intervals of 2 – 3 days
- If fever recurs, the last drug added should be stopped

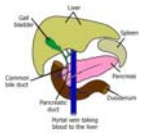
CASE (4)

- 42 year-old female diagnosed with active TB disease
- Smear positive, PCR positive for *M.tb*
- Started on 4 drug therapy (RIF, INH, EMB, PZA)
- Baseline labs:
  - AST-22, ALT-30, T. bili-0.2, Alk phos-45
- Seen in clinic after one month
- AFB smear negative, culture pending
- No complaints, feeling better
  - Repeat ALT 220, AST 98

MANAGEMENT OF HEPATOTOXICITY



INH HEPATOTOXICITY



- Asymptomatic ALT increase in
  - ~20% of patient
- Clinical hepatitis 0.1-0.6%
- Timing: weeks to months of starting drug
- Risk factors:
  - Age
  - Chronic alcohol consumption
  - Active hepatitis B (+HBeAg)
  - Elevated baseline transaminases (AST, ALT)
  - Concomitant use of other hepatotoxic drugs
  - 3rd trimester pregnancy to 3 months post-partum
  - Pre-existing liver disease

AJRCCM, 2006; 174:935-952

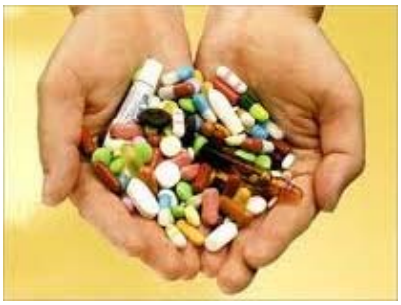
MANAGEMENT OF HEPATOTOXICITY

- Serologic testing Hepatitis A, B, C
- Ask patient symptoms of biliary tract disease
- Exposure to other hepatotoxins
  - Alcohol
  - Other drugs (RX and OTC)
- Hepatitis
  - No symptoms but LFT > 5X ULN or
  - Symptoms and LFT > 3 X ULN
- Start at least 3 nonhepatotoxic drugs
  - Slower schedule for restarting anti-TB medication compared to rash or drug fever
  - **EMB, FQ, strep/amikacin**, (capreomycin, cycloserine)
- Monitor Labs

MANAGEMENT OF HEPATOTOXICITY

- When to restart therapy (RIF, INH, PZA)
- LFTs < 2 X ULN or baseline (abnormal prior to TB meds)
  - Re-challenge medications → One drug at a time
  - Start with RIF
    - Recheck AST after one week→ No increase
  - Add INH
    - Recheck AST after one week→ No increase
  - Add PZA*
- If symptoms recur or AST increases→ stop last drug added
- *If RIF and INH are tolerated, and **hepatitis was severe**
  - Do not add back PZA - assumed PZA was responsible
- Once added back RIF, INH, ± PZA
  - Continue EMB and stop other "liver friendly" drugs added

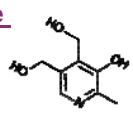
MEDICATION SIDE EFFECTS



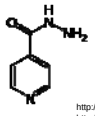
INH NEUROTOXICITY

- Dose related, uncommon
- Risk factors
  - Other conditions with neuropathy:
    - Malnutrition, diabetes, HIV, renal failure, alcohol, pregnant female
- Mild peripheral neuritis - Stocking glove syndrome ~2%
- Retrobulbar (optic) neuritis
- CNS toxicity: Slurred speech, ataxia, seizure, memory

Pyridoxine



INH



http://en.wikipedia.org/wiki/Isoniazid
http://en.wikipedia.org/wiki/Pyridoxine

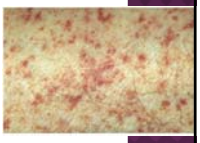
RIFAMPIN TOXICITY

- Orange discoloration of body fluid
- Cutaneous reactions:
  - Mild
  - Generally self-limited
  - Treat symptomatically - antihistamine
- Gastrointestinal symptoms:
  - Nausea, anorexia, abdominal pain
- Hepatocellular injury less common
  - Insidious cholestasis
    - Anorexia, nausea, vomiting, fever, jaundice
  - RIF is much less likely to cause hepatoxicity than INH or PZA

http://connect.in.com/thrombocytopenia/photo-gallery-more.html

RIFAMPIN: HYPERSENSITIVITY REACTIONS

- Flu-like syndrome with fever, chills, headache, & bone pain
  - Can begin 1-2 hrs after medication dose and resolve spontaneously after 6-8 hrs
  - More common in intermittent dosing, higher dose
  - Can try daily therapy if mild
- Severe immunologic reactions – rare, each < 0.1% patients
  - Low platelet count / petechiae
  - Kidney dysfunction
  - Hemolytic anemia
  - Thrombotic thrombocytopenic purpura



RIFAMPIN DRUG INTERACTIONS

- Rifampin induces cytochrome P450 class of enzymes
  - Involved in drug metabolism
- Rifampin interacts with
  - Narcotics (methadone) - ⬇
  - Corticosteroids – ⬇
  - Warfarin (coumadin) – ⬇
  - Phenytoin (dilantin) – ⬇
  - Contraceptives (estrogens) - ⬇
  - HIV protease inhibitors & non-nucleoside reverse transcriptase inhibitors – complex interactions

PYRAZINAMIDE

- Hepatotoxicity: Both dose-dependent & idiosyncratic
- Causes hepatotoxicity less often than INH ***but***
  - *Can be more prolonged*
  - *Can continue after drug discontinued*
  - *Can be most severe*
- Can cause granulomatous hepatitis
  - Fever, rash, lymphadenopathy, elevated ALT

PYRAZINAMIDE TOXICITY

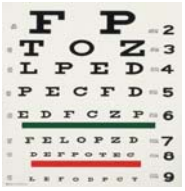
- Gastrointestinal symptoms: nausea, vomiting
- Arthralgias common – Rx symptomatically
- Elevated uric acid
  - PZA is a pro-drug →active compound Pyrazinoic acid →Blocks renal tubular excretion of uric acid →Increase uric acid
  - Allopurinol does not reverse this
  - Routine measurement of uric acid is not recommended
  - Gout is rare
  - Hyperuricemia without gout is not a reason for discontinuing drug

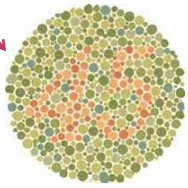
ETHAMBUTOL TOXICITY

- Retrobulbar neuritis: decrease visual acuity or red-green color discrimination
- Increase risk with renal insufficiency
- Peripheral neuritis
- Cutaneous reactions: <1%
- Joint pain

ETHAMBUTOL TOXICITY

- Baseline and monthly
  - Visual acuity test (Snellen chart)
  - Color discrimination test (Ishihara tests)
- Patient education
- Monthly symptom check
  - blurred vision etc
- Opthalmology evaluaion
- Hold medication – for any symptoms





QUINOLONES

- **Arthralgias, tendonitis**, tendon rupture – very rare
  - All ages
  - Greater risk age >60
  - Patients taking corticosteroids
  - Transplant patients
- EKG abnormalities: QT prolongation
- Nausea & diarrhea: 0.5-2%
- Rash/Pruritis/Photosensitivity: 0.2-0.4%
- Avoid in pregnancy

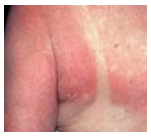
STREP/AMIKACIN/CAPREOMYCIN

- **Ototoxicity**
- **Vestibular toxicity**
- Nephrotoxicity
- Electrolyte disturbances
  - Potassium, calcium, and magnesium depletion
  - Cardiac dysrhythmias
- Local pain at IM injection site
- Avoid in pregnancy

WHAT IS YOUR DIFFERENTIAL DX? ADVERSE DRUG REACTIONS

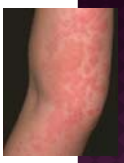
DERMATOLOGIC REACTIONS

- Itching with or without erythematous rash is common early side effect
  - May resolve after 1st several weeks of therapy without stopping medications
  - For mild or localized reaction, continue treatment & treat the rash and pruritis symptomatically – antihistamines, topical steroids
- Photosensitivity
  - PZA, fluoroquinolones

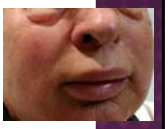


http://emedicine.medscape.com/article/1049648-overview

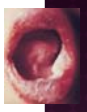
DERMATOLOGIC REACTIONS

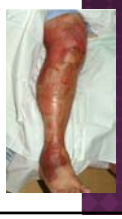


- Hives, urticaria, erythematous rash
  - Any drug
  - Stop all drugs immediately, rechallenge 1 at a time
    - Wait for rash to resolve
    - Start RIF 1st (least likely to be cause)
    - If no recurrence after 2-3 days start INH
    - Continue with EMB or PZA
    - Discontinue any drug which causes recurrence
- Angioedema, anaphylaxis, or airway compromise
  - Stop drug – consider desensitization in ICU



OTHER SERIOUS DERMATOLOGIC REACTIONS





- Spectrum of diseases – generalized, involve mucus membranes, cause fever – epidermis separates from dermis
  - Stevens-Johnson Syndrome
  - Toxic Epidermal Necrolysis (severe form SJS)
- Mortality high
- Quinolones
- Emergency, hospitalization
- Stop offending drug, do not use again

GI UPSET

- Improves if drugs are administered with food or closer to bedtime
- Ethionamide
  - Causes profound GI symptoms
  - Metallic taste, nausea, vomiting that can be severe, loss of appetite, abdominal pain
  - Dose-related
  - May give as split dose
- P-Aminosalicylic Acid (PAS)
  - Significant GI intolerance, less with granular formulation
  - Dose-related
- INH
  - Commercial liquid preparations contain sorbitol which can cause diarrhea

NEUROTOXICITY: PERIPHERAL NEUROPATHY

- Numbness, tingling hands & feet in stocking-glove pattern
- Risk factors: diabetes, alcoholism, HIV, hypothyroidism, pregnancy, poor nutrition, inadequate dietary intake of pyridoxine
- Pyridoxine supplements
  - 10-50 mg daily (should this be routine?) for INH
  - 100-200 for cycloserine &/or ethionamide

PERIPHERAL NEUROPATHY

- INH
  - Dose-related
  - Interferes with biologic function of vitamin B6
- Ethionamide
  - Increased incidence with prolonged use
- Linezolid
  - Increased incidence with prolonged use
  - 600 mg daily instead of twice daily is used to prevent this
- Ethambutol, cycloserine
  - Rare

CNS EFFECTS

- INH
  - Inability to concentrate, irritability, dysarthria, seizures, dysphoria
- Cycloserine (Dr K's mnemonic – cyclo, psycho)
  - Headache, restlessness, psychosis, seizures (dose-related)
  - Pyridoxine 100-200 mg daily to prevent / treat
- Ethionamide
  - Anxiety, depression, psychosis
  - Increased incidence with prolonged treatment
- Fluoroquinolones
  - Dizziness, insomnia, tremulousness, headache

VISION - E - E EYE

- Ethambutol
  - Retrobulbar neuritis
  - Dose related – very rare (if at all) with currently recommended doses
  - Decreased red-green color discrimination (1 or both eyes), decreased visual acuity
  - ↑ With renal disease
- Ethionamide
  - Optic neuritis
  - Dose related

OTOTOXICITY: 8TH CRANIAL NERVE DAMAGE

- Streptomycin
  - Vestibular (balance) and hearing disturbance
  - Related to single dose size and cumulative dose (>100-200 g)
  - Increased with incidence if diuretics are used
  - Monitor with audiogram, Romberg
  - Hearing loss can be permanent – consider stopping
- Amikacin & Kanamycin
  - Less vestibular toxicity than SM
- Capreomycin

These drugs also cause nephrotoxicity & require monitoring

OTOTOXICITY: AMINOGLYCOSIDES

- Injectable agents – 15mg/kg daily or 25 mg/kg TIW
  - Ototoxicity often permanent
    - *Hearing loss ≥ 20 db occurred in 32/87 (37%) patients, 88% had persistent loss at end of follow-up
    - Associated with older age, duration of treatment, & total dose, not to vestibular or renal toxicity
    - Amikacin>Kanamycin >Streptomycin
    - TIW = daily Rx

*Peloquin, et al. Aminoglycoside toxicity…Clin Inf Dis 2004;38:1538-44

STUFF HAPPENS; BE PREPARED

Acknowledgement:
Special thanks to Dr. Dana Kissner , Wayne State University

CASE (5)

- 44 year old female diagnosed with latent TB infection
- 8/3 seen by physician and nurse
  - Started INH
  - Baseline labs:
    - AST-19, ALT-19, T. bili-0.3, Alk phos-68
- 9/1 - Nurse Refill Visit #2
  - Repeat AST on 09/01 was 27
- 10/6 - Nurse Refill Visit #3
- 11/10 – Nurse Refill Visit #4
- 11/30 admitted for "jaundice"

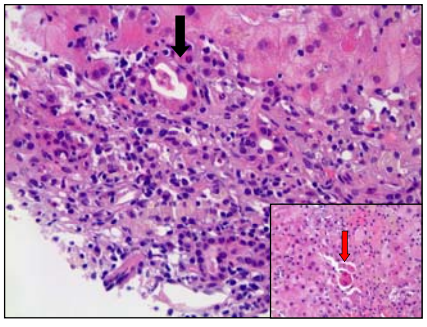
CASE (5)

- No signs or symptoms of any hepatic problems reported at any health dept visits
- 2 weeks prior to admission – ER visit – cough
  - CXR negative
  - Tessalon® perles and hydrocodone cough syrup
- Increasing fatigue, weakness, diarrhea, yellowing of eyes
- Return to hospital
  - **AST-3627→1410**
  - **ALT 2159→1621**
  - **Alk phos 190→179**
  - **Total Bili 25→27.5 (Direct 13→16.6)**

CASE (5)

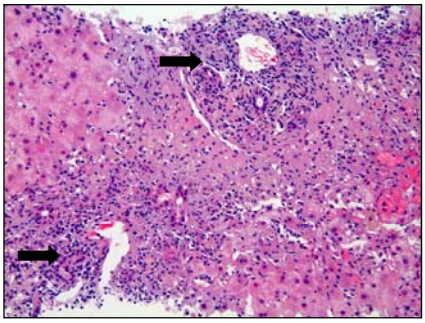
- RUQ ultrasound: no intrahepatic ductal dilation, + cholelithiasis, no cholecystitis, no liver abnormalities
- Abdominal MRI: no biliary ductal dilation, no gallstones, no liver lesions
- Liver biopsy: patchy hepatocellular necrosis with acute and chronic inflammation. mild portal fibrosis, no granuloma/viral inclusions
- Diagnosis: Acute Hepatitis- secondary to INH toxicity

PORTAL AREA WITH A MIXED INFLAMMATORY INFILTRATE OF LYMPHOCYTES, NEUTROPHILS, PLASMA CELLS AND RARE EOSINOPHILS WITH DAMAGED BILE DUCT (BLACK ARROW). THE MIXED INFLAMMATORY INFILTRATE EXTENDS TO THE LOBULE (INSET) WHERE MANY DEAD HEPATOCYTES (RED ARROW) ARE SEEN.



Slide courtesy of Dr Jonathon Rock and OSUMC Clinical Pathology

BRIDGING NECROSIS RUNNING BETWEEN TWO PORTAL AREAS (BLACK ARROWS) EACH WITH A MIXED INFLAMMATORY INFILTRATE OF LYMPHOCYTES, NEUTROPHILS, PLASMA CELLS AND RARE EOSINOPHILS.



Slide courtesy of Dr Jonathon Rock and OSUMC Clinical Pathology

TABLE 1. Reported severe adverse events (N = 17) associated with isoniazid (INH*) treatment for latent tuberculosis infection (LBTI), by patient characteristics — United States, 2004–2008

Characteristic	No.
Age group (yrs)	
≤15	2
16–35	5
>35	10
Sex	
Male	6
Female	11
Race/Ethnicity	
Hispanic	8
Black, non-Hispanic	1
White, non-Hispanic	8
Country of birth	
United States	10
Foreign-born	7
Duration of INH treatment (days)	
Median	104
Range	28–499†
Period from initiation of INH treatment to severe adverse event symptoms (days)	
Median	109
Range	56–502†
Results of testing for viral hepatitis§	
Negative	16
Abnormal	1
Outcome	
Recovered	8
Had liver transplant	5
Died	5¶

Adult median age 39

Dx 2nd and 9th month

HIV, Hep C

MMWR 3/5/10 59(08); 224-229

TABLE 2. Results of onsite case investigations (n = 10) of severe adverse events (SAEs) associated with isoniazid (INH*) treatment for latent tuberculosis infection (LTBI), by case characteristics — United States, 2004–2008

Characteristics	No.
Treated outside of a public health clinic	2
Had clinical monitoring monthly	10
Had laboratory monitoring of serum aminotransferase levels monthly	2
Results of baseline testing of serum aminotransferase†	
Within normal limits	5
Abnormal	0
Never tested	5
Period from SAE symptom onset to discontinuation of INH (days)	
≤2	1
3–6	1
7–10	4
11–14	0
15–20	2
>20	2
SAE diagnosis by different clinician than the one who prescribed INH	7
Serum aspartate aminotransferase (AST) measurement at SAE diagnosis (international units/liter [IU/L])§	
Median	2,200
Range	387–3,000
Serum alanine aminotransferase (ALT) measurement at SAE diagnosis (IU/L)§	
Median	2,192
Range	272–3,000
Putative risk factors for INH-induced liver injury¶	
None	3
Preexisting liver disease	1
Human immunodeficiency virus (HIV) infection	1
Concurrent injection-drug use	0
Concurrent alcohol consumption	3**
Pregnancy or ≤3 months after delivery	1
Older age	5
Concurrent use of non-acetaminophen-containing medications with hepatotoxic potential††	4

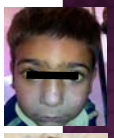
AST

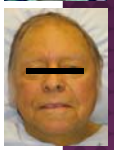
ALT

MMWR 3/5/10 59(08); 224-229

SEVERE INH LIVER INJURIES AMONG PERSONS BEING TREATED FOR LTBI IN US 2004-2008

- Idiosyncratic reaction, independent of dosing
- Can occur anytime in treatment
  - 9/17 beyond the 3rd month
- Can occur in children
  - 2/17 in children
- Diagnosed not by prescribing physician
  - 10/17
- Did NOT STOP the medication when symptoms developed
  - 8/17 continue to take the medication





MMWR 3/5/10 59(08); 224-229
http://en.wikipedia.org/wiki/Jaundice

WWW.TSTIN3D.COM

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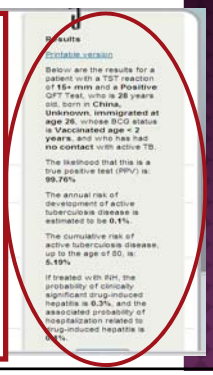
- **PPV 99.76%**
- **Annual risk of developing TB=0.1%**
- **Cumulative risk of active TB disease up to age 80 is 5.19%**
- **If treated with INH probability of significant drug induced hepatitis is 0.3%**
- **Association with probability of hospitalized drug induced hepatitis is 0.1%**


Results

Printable version

Below are the results for a patient with a TST reaction of **15+ mm** and a **Positive** QFT Test, who is **28 years** old, born in **China, Unknown**, **immigrated at age 26**, whose BCG status is **Vaccinated age < 2 years**, and who has had **no contact** with active TB.

The likelihood that this is a true positive test (PPV) is: **99.76%**.

The annual risk of development of active tuberculosis disease is estimated to be **0.1%**.

The cumulative risk of active tuberculosis disease, up to the age of 80, is: **5.19%**.

If treated with INH, the probability of clinically significant drug-induced hepatitis is **0.3%**, and the associated probability of hospitalization related to drug-induced hepatitis is **0.1%**.

CASE (6)

- 25 year old female
- diagnosed with lymph node TB
- started on four drug: RIF, INH, EMB, PZA
- On day 8: developed generalized papulosquamous rashes involving both thighs, legs, trunk, face and oral cavity
- She was admitted outside and was put on antibiotics along with steroids
- Patient improved slightly, was discharged after 5 days. TB meds were continued

http://www.japi.org/june_2011/article_15.html

CASE (6)

- 4-5 days later patient again developed increase generalized body rashes
- Febrile, vitals –stable
- Treated with steroids and TB medication discontinued


Fig. 1 : Clinical photograph showing erthematous patches over both malar prominences with haemorrhagic crusts present over the lips and anterior nares.

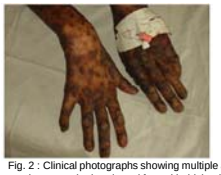


Fig. 2 : Clinical photographs showing multiple areas of erosions over the hands and feet with thick adherent yellow crusts, some showing whitish scales, hyperpigmentation along with thick dystrophic nails

http://www.japi.org/june_2011/article_15.html

ADVERSE DRUG REACTIONS

Place a check mark for the common side effects

	RIF	INH	PZA	EMB
Rash				
GI Intolerance				
Liver toxicity				
Peripheral Neuropathy				
Optic Neuritis				
Gout				
Discoloration of body fluid				

ADVERSE DRUG REACTIONS

	RIF	INH	PZA	EMB
Rash	X	X	X	X
GI Intolerance	X	X	X	X
Liver toxicity	X	X	X	
Peripheral Neuropathy		X		
Optic Neuritis		X (rare)		X
Gout			X	X (rare)
Discoloration of body fluid	X			

ETHIONAMIDE

- **Gastrointestinal Effects – severe**
  - May improve with food or at bedtime
- Hepatotoxicity: 2%
- Neurotoxicity: peripheral neuropathy, optic neuritis, depression, psychosis
- Endocrine disturbances
  - Gynecomastia, hair loss, hypothroidism, impotence
  - Diabetes may be more difficult to manage
  - Acne
  - Irregular menstrual cycles

LINEZOLID

- **Nausea & diarrhea**
- Myelosuppression
  - Dose dependent
  - Reversable
- Peripheral neuropathy
  - Not dose dependent
  - May not be reversible
- Optic neuritis
- Serotonin syndrome
- Rash

PARA-AMINOSALICYLATE (PAS)

- **Gatrointestinal distress:** 11%, ↓dose/stop med
- Hypothyroidism is common
  - Reversible, ↑with ethionamide
  - Goiter can develop
- Hepatitis: 0.3%
- Malabsorption - fat malabsorption
  - Doubling of prothrombin time
    - Vitamin K is a fat soluble vitamin
  - Levels of fat soluble vitamins (A, D, E) can be measured & monitored
- Rash, lymphadenopathy, leukocytosis, arthralgia

CYCLOSERINE

- Central nervous system effects: headaches, restlessness, suicidal ideation, psychosis, seizures (3% 500mg/day)
- Caution in patients with underlying seizure disorders or mental illness
- Pyridoxine 100-200mg/day may decrease neurotoxic side effect
- Peripheral neuropathy
- Rash – skin changes (lichenoid eruptions, Stevens-Johnson Syndrome)