Disclosures

I have nothing to disclose, and I will not be discussing off-label or investigational treatments with specific medications or products in this presentation.
Learning Objectives

• Describe historical parallels between tuberculosis and mental illness

• Identify drug-drug interactions of concern when prescribing medications to treat tuberculosis to patients with mental illness

• Identify and manage challenges arising from comorbid mental illness/substance use disorders that patients may face when confronting tuberculosis treatment
# Brief History of Tuberculosis and Mental Illness

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Sanatorium or Asylum?

The rules are:

• Absolute and utter rest of mind and body—no bath, no movement except to toilet once a day, no sitting up except propped by pillows and semi-reclining. Lead the life of a log, in fact.

• Eat nourishing food and have plenty of fresh air.

Then my own rules to myself:

• Never give way to self pity
• Interest myself as much as possible in outside things
• Try and improve my mind by reading and thinking
Sanatorium or Asylum?
Sanatorium or Asylum?

I awoke the next morning in a horrific sweat, only to find that my experiences were not a dream, but reality. I was actually in the uncomfortable bed in an off-white room. The room was very dull in appearance with only the bed and a small table next to it. A window to my left had a view of a vast field, empty with the morning dew still covering the grass. An attendant came through the door assuring me that everything would be all right and that it was time for breakfast. Breakfast was a very foul tasting slop accompanied by cold coffee and stale bread. After breakfast I learned that it was my day to go out into the yard. The yard was a 10-acre field with gardens, flowerbeds, and a grove of oak trees. The attendant informed me that I was not to go beyond the limits of the hospital.
Sanatorium or Asylum?
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Case Report

- 30 year-old woman from Sudan emigrated to US 9 years prior to presentation

- History of schizophrenia

- History of depression

- History of reactive Mantoux test 2 years prior
  - No history of medications for latent or active TB
Case Report

- Discontinued medications for schizophrenia 6 months prior
- Last psychiatric visit 10 months prior
- Patient and husband say no psychiatric symptoms
- No current psychiatric provider
Case Report

- **Current medications**
  - Etonogestrel implant (hormone-based implantable contraceptive)
    - Prescribed for dysmenorrhea/menorrhagia

- **Social history**
  - Lives with husband
  - Does not use alcohol, drugs, or tobacco

- **Laboratory and imaging studies**
  - Normal LFTs, lytes, CBC, creatinine from 1-2 years prior
  - Chest x-ray from 2 years prior clear without infiltrates (pos PPD)
What do you do next?

A. Start oral isoniazid therapy for nine months
B. Start oral rifampin therapy for four months
C. Check QuantiFERON assay, chest x-ray, and LFTs
D. Tell patient you will see her back when she re-establishes psychiatric care
Case Report

- QuantiFERON 14.53 IU/mL = positive
- LFTs
  - ALT 179 U/L (ref: 7-45)
  - AST 82 U/L (ref: 8-43)
  - Alk Phos 65 U/L (ref: 37-98)
- Ultrasound of liver with slightly coarse echotexture → CT normal
- LFTs normalized within 7 days
What do you do next?

A. Start oral isoniazid therapy for nine months

B. Start oral rifampin therapy for four months

C. Tell patient you will see her back for LTBI therapy when she has re-established psychiatric care
Case Report

- LTBI therapy started with oral isoniazid 300 mg once daily for nine months

- Several days later, patient presents to the ED
  - Auditory hallucinations: voices telling her to kill her husband
  - Visual hallucinations: images of a knife stabbing her husband
  - Disorganized thoughts (like a puzzle she cannot figure out)
  - Referential thinking: home television giving her messages about her husband
  - Decreased sleep
What do you do next?

A. Discontinue isoniazid and admit patient to psychiatric hospital

B. Discontinue isoniazid and discharge patient home with husband

C. Continue isoniazid and admit to psychiatric hospital

D. Start rifampin and admit to psychiatric hospital

E. Start rifampin and discharge home with husband
Case Report

- Isoniazid discontinued
- Psychiatrically hospitalized and stabilized on risperidone long-acting injectable
- LTBI therapy not yet restarted
Case Points

- TB not uncommon in psychiatrically hospitalized patients
- Mental illness not uncommon in hospitalized (or community) patients with tuberculosis
- Mental illness has implications for treatment of TB
- TB has implications for treatment of mental illness
- Why are mental illness and TB interrelated?
Risk Factors for TB and Mental Illness

• Homelessness
• HIV positive serology
• Alcohol and other substance use disorders
• Migrant status (case)
Associations Between TB and Mental Illness

- Patients with psychiatric illness have risk factors associated with progression of LTBI $\rightarrow$ active TB
  - Smoking (Nicotine use disorder)
  - Poor nutrition
  - Diabetes
  - HIV
  - Treatment noncompliance
Associations Between TB and Mental Illness

- 20-40% of psychiatric patients in a variety of settings have positive PPD
  - Rates possibly associated with housing stability

- Depression and anxiety present in up to 70% of patients with TB
  - Higher rates with comorbid illness such as HIV
  - However, rates not as high as in chronic respiratory illness (n = 1 study)

- No known association between TB and suicide
Risk Factors for Mental Illness in Patients with TB

- Depression and anxiety risk factors
  - Medical comorbidities
  - Substance use disorders (especially alcohol)
  - Low educational attainment

- Psychosis risk factors
  - Intracranial tuberculoma
  - Miliary tuberculosis
  - Treatment with anti-TB medications (low but present)
    - But anti-TB meds have been a boon to psychiatry
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Adverse Effects of TB Treatment

• Isoniazid (case)
  • Psychosis rate 1.9/100 patients (1972 data)
  • Rate of psychosis second only to steroids
  • Possible prodrome
    • Weeks long
    • Anxiety, emotional lability, facial twitching

• Mechanism
  • Depletion of pyridoxine (B6), however replacement ineffective
  • MAOI activity → manic psychosis?
Adverse Effects of TB Treatment

• Isoniazid
  • Suicidality
    • Many case studies among various ethnic groups
    • Both suicidal thoughts and behaviors
    • More suicides in TB than other cardio-respiratory illnesses
  • Relationship to depression unclear
Adverse Effects of TB Treatment

- Ethambutol
  - Psychosis in case reports – probably toxicity

- Cycloserine
  - Mania
  - Insomnia
  - Anxiety
  - Psychosis
  - ? Suicidality
  - Contraindicated in patients with agitation
  - Also has been tried as anti-depressant with little success
Drug-Drug Interactions

• Isoniazid
  • MAOI → Can it be prescribed with SSRIs?
    • No reports of serotonin syndrome
    • Case-control study → increased discontinuation in Isoniazid/SSRI group vs SSRI or Isoniazid alone
    • Insufficient evidence to avoid prescribing

• P450 interactions
  • Key drug interaction: carbamazepine
    • Carbamazepine toxicity can result
Drug-Drug Interactions

• Rifampin
  • Potent inducer of many P450 enzymes
  • Key drug interactions
    • Oral contraceptives – decreased efficacy (case)

• Nortriptyline – level decreased, beware of toxicity on discontinuation of rifampin

• Valproate – level decreased, beware of mood destabilization
Drug-Drug Interactions

- Rifampin
  - Potent inducer of many P450 enzymes
  - Key drugs interactions
    - Risperidone – level decreased, beware of psychosis (case)
  - Methadone – level decreased, can precipitate withdrawal
    - Rifampin may be false + on UDAS for opiates
Drug-Drug Interactions

• Check interactions with:
  • Linezolid – serotonin syndrome concerns
  • Fluoroquinolones – QTc
Treatment of TB in Patients with Mental Illness

• Noncompliance major problem
  • Residential treatment if appropriate

• Isolation has been attempted
  • Increases stress levels in patients
  • Not recommended if possible to avoid
Treatment of TB in Patients with Mental Illness

• Managing noncompliance, continued

• Directly-observed therapy
  • Highly effective (up to 90% completion)

• Can be combined with other therapies
  • Methadone programs
  • Monitored disulfiram
  • ACT teams
Treatment of TB in Patients with Mental Illness

- Other challenges
  - Perceived adverse events

- Legal issues
  - Involuntary treatment for TB possible in some areas
  - Involuntary treatment for MI may not be possible in same areas

- Substance use disorders (nicotine, alcohol, IVDA)
  - Concurrent treatment

- Stigma → compounded with MI, TB, HIV, etc.
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So the Wheel Turns…

• MAOIs now rarely used for depression
  • Increased drug resistance for TB, but still first-line

• Phenothiazines occasionally used for psychosis
  • Now being studied for MDR-TB
  • Potentiate efficacy of other antimicrobials

• What new medications or treatment strategies will TB and mental illness share in common?
Learning Objectives

• Describe historical parallels between tuberculosis and mental illness

• Identify drug-drug interactions of concern when prescribing medications to treat tuberculosis to patients with mental illness

• Identify and manage challenges arising from comorbid mental illness/substance use disorders that patients may face when confronting tuberculosis treatment
Questions & Discussion