DIRECTLY OBSERVED 3-MONTH THERAPY TO TREAT LATENT TUBERCULOSIS INFECTION (LTBI)

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Student Health Services
Storrs, CT
No Financial Disclosures
THE UNIVERSITY

- Main Campus in Storrs
- Founded in 1881
- Largest Public University in CT

<table>
<thead>
<tr>
<th></th>
<th>Undergraduate</th>
<th>Graduate</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td># Students</td>
<td>18,826</td>
<td>6,827</td>
<td>25,653</td>
</tr>
<tr>
<td>International</td>
<td>5%</td>
<td>24%</td>
<td></td>
</tr>
</tbody>
</table>
Student Health Services

- Founded in 1926
- Medical Providers:
  - 6 Primary Care MDs
  - 10 NPs
  - 14 RNs
- 8-bed Infirmary
- X-Ray Service
- Laboratory
- Pharmacy
- Full-time RD
- Counseling & Mental Health Service
  - 2 Part-time Psychiatrists
  - 9 Psychologists, 5 Clinical Social Workers, 2 Psychiatric NPs
- Health Education office

Open Mon. 8am-Sat. 3:30pm, Sun. 8am-3:30pm
TUBERCULOSIS

- #1 Infectious disease killer in the world
- Has latent infection phase \( \rightarrow \text{LTBI} \)
- WHO: 1/3 of the world has LTBI
- CDC: 11 million in USA have LTBI
- At UConn:

<table>
<thead>
<tr>
<th>Country</th>
<th>% of Int. Student Pop.</th>
<th>Incidence of Active TB/100,000 pop.</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>55%</td>
<td>68</td>
</tr>
<tr>
<td>India</td>
<td>22%</td>
<td>167</td>
</tr>
</tbody>
</table>
LTBI: -Treat? -Screen?

- Can we treat LTBI? Yes.
  - Isoniazid Daily x9 mos > 90% efficacy, 6 mos > 70% efficacy

- Can we screen for it? Yes.
  - Tuberculin Skin Test (TST)
    - Cheap & easy
    - Requires 2 visits for patient
    - Interpretation subjectivity
    - BCG vaccine interference
  - Interferon-Gamma Release Assay (IGRA) Tests
    - T-Spot & Quantiferon In-Tube Gold
    - Require only one visit for patient
    - Objective result
    - Fewer interferences
    - More expensive & require a lab to do test
LTBI Treatment

- Isoniazid (INH)
  - **Daily**
    - Standard for many years
    - Self-administered by patient
    - Taken x9 mos: >90% protective lifetime efficacy against active TB
    - Taken x6 mos: >70% protective lifetime efficacy against active TB
  - **Directly-observed Therapy (DOT)**
    - Given twice a week
    - Useful in controlled situations like shelters, correctional facilities, long term care

- Rifampin
  - **Daily**
    - Standard second line treatment if cannot tolerate INH or prefer shorter course of treatment
    - Self-administered by patient
    - Taken x4 mos: 70% protective lifetime efficacy against active TB

Recommend: McGill Univ. TB Risk Calculator
The following tool estimates the risk of active tuberculosis for an individual with a tuberculin skin test reaction of ≥5mm, based on his/her clinical profile. It is intended for adults tested with standard tuberculin (5 TU PPDS, or 2 TU RT-23) and/or a commercial Interferon Gamma release assay (IGRA).

For more details about the algorithm used, go to the About page. The current version of the algorithm contains modifications of the original version, which was detailed in a paper by Menzies, et al. (2008). For further information see references, or contact dick.menzies@mcgill.ca

Please select the best response for each field:

TST Size:
Select...  
IGRA Result:
IGRA Not Done

Age at immigration (if person immigrated to a low TB incidence country):
Age:
Select... N/A

Country of birth:
Select...

BCG status: Select...
For more info, visit: BCG World Atlas

Recent contact with active TB: No Contact

Please select all the conditions that currently apply to the patient:
(If none of these conditions apply, please leave boxes unchecked)

- AIDS
- Abnormal chest x-ray: fibronodular disease
- Chronic renal failure requiring hemodialysis
- Diabetes Mellitus (all types)
- Recent TB infection (TST conversion ≤ 2 years ago)
- Silicosis
- Tumor Necrosis Factor (TNF)-alpha inhibitors (e.g. Infliximab/Etanercept)
- Young age when infected (0-4 years)
- Abnormal chest x-ray: granuloma
- Carcinoma of head and neck
- Cigarette smoker (>1 pack/day)
- HIV infection
- Transplantation (requiring immune-suppressant therapy)
- Treatment with glucocorticoids
- Underweight (< 90 per cent ideal body weight or a body mass index (BMI) ≤ 20)
Why Bother with New Regimen?

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>2006-07</th>
<th>2007-08</th>
</tr>
</thead>
<tbody>
<tr>
<td># PPD Done</td>
<td>507</td>
<td>631</td>
</tr>
<tr>
<td># Pos. PPD (%)</td>
<td>55 (11)</td>
<td>100 (16)</td>
</tr>
<tr>
<td># Started Rx (%)</td>
<td>40 (73)</td>
<td>31 (31)</td>
</tr>
<tr>
<td># Finished Rx (%)</td>
<td>17 (43)</td>
<td>17 (55)</td>
</tr>
</tbody>
</table>

Please take your INH!
Yes every day.
Yes for 9 months.
How many times did you forget it??
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td># PPD Tests Done</td>
<td>507</td>
<td>631</td>
<td>1138</td>
</tr>
<tr>
<td># Pos. PPD Tests (%)</td>
<td>55</td>
<td>100</td>
<td>155</td>
</tr>
<tr>
<td>% Started Rx</td>
<td>73%</td>
<td>31%</td>
<td>46%</td>
</tr>
<tr>
<td></td>
<td>(40/55)</td>
<td>(31/100)</td>
<td>(71/155)</td>
</tr>
<tr>
<td>%Finished Rx of Started Rx</td>
<td>43%</td>
<td>55%</td>
<td>48%</td>
</tr>
<tr>
<td></td>
<td>(17/40)</td>
<td>(17/31)</td>
<td>(34/71)</td>
</tr>
<tr>
<td>%Finished Rx of Pos. Tests</td>
<td>31%</td>
<td>17%</td>
<td>22%</td>
</tr>
<tr>
<td></td>
<td>(17/55)</td>
<td>(17/100)</td>
<td>(34/155)</td>
</tr>
</tbody>
</table>
Newest LTBI Treatment: INH + Rifapentine (RPT)

  - TB Trials Consortium PREVENT TB Study Team,
  - Timothy R. Sterling, M.D- Vanderbilt University
  - Randomized 7731 pts 2001-2008: INH+RPT via DOT or Standard Rx w INH only

<table>
<thead>
<tr>
<th>Data Measured</th>
<th>INH + RPT DOT Group</th>
<th>INH Standard Rx Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completion Rate</td>
<td>82%</td>
<td>69%</td>
</tr>
<tr>
<td>#Active TB cases</td>
<td>7</td>
<td>15</td>
</tr>
</tbody>
</table>

- Nov. 2014, CT State Dept. of Public Health- TB Seminar
  - 308 pts 2012-2014 INH+RPT via DOT

<table>
<thead>
<tr>
<th>Data Measured</th>
<th>% of Total Pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completed Rx</td>
<td>86%</td>
</tr>
<tr>
<td>D/C Due to Adverse Event</td>
<td>8%</td>
</tr>
</tbody>
</table>
Patient Selection:
• IGRA test positive, not just TST+
• Screen for s/s active TB
• Current CXR w no signs of active TB.
• No active liver or hematologic disease.

Regimen:
● INH 900mg  ● RPT 900mg  ● Pyridoxine (Vitamin B6) 50mg

Dose Schedule:
• Ideally 12 straight wks but 12 doses w/in a 16 wks.
• Avoid >2wk gap in doses.
• Make doses at least 5 days apart.

Evaluation & Follow-up:
• Baseline LFTs, CBC, & HIV
• CXR (current)
• LFTs & CBC may be repeated every 4-6 weeks.
• Seen wkly by RN.
• Seen by clinician q4-6wks or prn.
• Medication symptom checklist filled out RN/clinician at each DOT visit.

Administration:
• RN will interview patient to determine best weekly dosing time schedule.
• Time schedule for entire 12 wk period reviewed at start.
12-Dose Isoniazid-Rifapentine Latent TB Infection Treatment Dose and Symptom Monitoring: Directly Observed Therapy Log

Patient ___________________________      DOB ________________  Weight _____________ kg  Dose ______mg INH  ______mg RPT

Medical Risk Factors (all that apply):
□ Immunocompromised or immunosuppressed (reason, e.g. medication, medical condition _________________________________________)
□ Chronic renal disease (□ on dialysis)         □ Hepatitis (□ B  □ C )         □ Diabetes (type ________ )        □ Other_________________

Please complete a symptom review at every visit. Visit 1 should reflect baseline symptoms.

<table>
<thead>
<tr>
<th>Date:</th>
<th>1/</th>
<th>2/</th>
<th>3/</th>
<th>4/</th>
<th>5/</th>
<th>6/</th>
<th>7/</th>
<th>8/</th>
<th>9/</th>
<th>10/</th>
<th>11/</th>
<th>12/</th>
</tr>
</thead>
</table>

- No adverse reaction
- Loss of appetite
- Nausea or vomiting
- Yellow eyes or skin
- Diarrhea
- Rash or hives
- Fever
- Sore muscles or joints
- Numbness or tingling
- Fatigue
- Dizziness
- Easy bruising
- Abdominal pain
- Abnormal labs (please attach)
- Other ___________________
- Rx stopped or held* □ □ □ □ □ □ □ □ □ □ □ □

* Contact TB Control Program (860-509-7722) and complete Adverse Event Episode

Adverse Event Episode

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Onset of symptoms</th>
<th>Symptom Duration</th>
<th>Hospitalized</th>
<th>Rechallenge</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><em><strong>/</strong></em></td>
<td>□ &lt; 2 hrs</td>
<td>□ &lt; 1 day ___hrs</td>
<td>□ yes</td>
<td>□ yes → □ INH □ RPT</td>
<td>□ continue INH/RPT</td>
<td></td>
</tr>
<tr>
<td><em><strong>/</strong></em></td>
<td>□ 2-48hrs</td>
<td>□ &gt; 1 day ___days</td>
<td>□ no</td>
<td>□ no</td>
<td>□ Switch to another regimen</td>
<td></td>
</tr>
<tr>
<td><em><strong>/</strong></em></td>
<td>□ &gt;48hrs</td>
<td>□ yes</td>
<td>□ yes → □ INH □ RPT</td>
<td>□ no</td>
<td>□ No further treatment</td>
<td></td>
</tr>
</tbody>
</table>

Final Disposition: □ Completed treatment  □ Stopped treatment -- If stopped, why: □ adverse event  □ lost to follow-up  □ moved  □ other

Final 26 October 2012
LTBI Treatment

- Some UConn SHS LTBI Data:

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>2006-07</th>
<th>2007-08</th>
<th>2015-16 Std Rx Pts</th>
<th>2015-16 DOT Pts</th>
</tr>
</thead>
<tbody>
<tr>
<td># Started Rx</td>
<td>40</td>
<td>31</td>
<td>7</td>
<td>9</td>
</tr>
<tr>
<td># Finished Rx (%)</td>
<td>17 (43)</td>
<td>17 (54)</td>
<td>2 (14)</td>
<td>6 (67)</td>
</tr>
</tbody>
</table>

**DOT PATIENTS**

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>2014-15</th>
<th>2015-16</th>
</tr>
</thead>
<tbody>
<tr>
<td># STARTED</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td># FINISHED (%)</td>
<td>3 (100)</td>
<td>6 (67)</td>
</tr>
<tr>
<td># ON GOING</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td># D/C</td>
<td>-</td>
<td>2 (22)</td>
</tr>
</tbody>
</table>
Rifapentine

- Rifamycin antibiotic – like Rifampin
- Red-orange body fluids
- GI upset – take w food
- CP450 Inducer - Interferes w ALL contraceptive hormones, anticonvulsants, anticoagulants
- Liver toxicity (< INH)
  - LFTs
- Blood cell toxicity
  - Leukopenia, Neutropenia
  - Thrombocytopenia
  - Anemia
- Flu-like, Renal (IN, ATN)
INH

- Liver toxicity
  - Monitor LFTs (?)
  - If AST or ALT rise >3-5x baseline, consider stopping

- GI upset
  - Nausea – take w food
  - At bedtime

- Fatigue

- Peripheral neuropathy
  - Interferes w pyridoxine (vitamin B6) metabolism in nerve function
PLUS/MINUS OF INH + RPT DOT REGIMEN

**PLUS**
- Shorter Rx course
- More sure of dose being taken
- Better completion rate
- Better acceptance of rx in first place

**MINUS**
- Pt must come in for dose
- Costs more
- More potential drug side effects
- More lab monitoring
- More staff work
- Pill burden
DOT BUDDIES!
TB Resources

- ACHA Guidelines - April 2011
  - “TB Screening & Targeted Testing of College & University Students”
- State of CT Dept. of Public Health
- CDC “Core Curriculum on Tuberculosis: What the Clinician Should Know” 6th Ed. 2013
- Regional Training and Medical Consultation Centers (RTMCCs)
  - Global Tuberculosis Institute at Rutgers Univ., Newark, NJ
  - Curry International Tuberculosis Center, Oakland, CA
  - Mayo Clinic Center for Tuberculosis, Rochester, MN
  - Heartland National Tuberculosis Center, San Antonio, TX
  - Southeastern National Tuberculosis Center, Gainesville, FL

WHAT DO I DO, DOC?
THE CONTRACTIONS ARE COMING ONE AFTER ANOTHER!