

INH/Rifapentine Fast Track Treatment for TB Infection

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Rifapentine

- ▶ Longer half life than rifampin
- ▶ Usual rifamycin effects
 - Orange discoloration of secretions, urine, tears
 - Can stain contact lenses
 - Interactions with many medications
 - Examples – Birth control, methadone, coumadin, levothyroxin
- ▶ Rare adverse effects:
 - elevated liver function tests
 - headache and dizziness

TB Trials Consortium Study 26 (PREVENT-TB)

- ▶ Multi-center, sites in US, Canada, Brazil, Spain
- ▶ 8,053 “high-risk” patients
 - 72% contacts of TB cases, 24% TST converters
 - Very few HIV+ or children 2 years and older

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Study 26 – results

- ▶ Both arms similar efficacy
 - 15 cases (0.43%) in 9H arm
 - 7 cases (0.19%) in 3HP arm
- ▶ Completion much higher with 3HP (80%)
- ▶ Toxicity slightly higher with 3HP (5% vs. 3% in 9H)
 - Hepatotoxicity the same
 - “Excess” toxicity was hypersensitivity
 - *(There is some evidence that it may have been over-reported.)*

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Study 26 – Some caveats

- ▶ DOT was used in the study, so there is no data on completion rates for self-administered therapy
 - Ten pills once per week – adherence could be very different
- ▶ Limited data on HIV+ patients
- ▶ No data yet on children <2 years

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TB Prevention Strategy Identify & Treat Those with Latent Infection

- ▶ Until now – few choices
 - Drugs
 - Nothing
 - 90% never develop active



12-Weeks of once weekly INH/Rifapentine AKA – “3HP”

Pros:

- Shorter duration of treatment
- Individuals more likely to complete therapy
- Similar amount of adverse drug events

Cons:

- More Expensive
- Experience with the regimen
- Not clear how to use this regimen in special populations:
 - HIV positive
 - Children under 5

Morbidity and Mortality Weekly Report

Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection

- ▶ INH-RPT – 12 weekly DOT doses
 - recommended as an equal alternative to 9 months of daily self-supervised INH
 - healthy patients aged ≥ 12 years at risk for TB disease:
 - recent exposure to contagious TB
 - conversion of TST or IGRA
 - radiographic findings of healed pulmonary TB

INH-RPT NOT Recommended

- ▶ Children <2 years old
- ▶ HIV-infected patients receiving HAART
- ▶ Pregnant women and women expecting to become pregnant during treatment
- ▶ Where LTBI is presumed to have INH or RIF resistance

Choosing between INH and INH-RPT

- ▶ Feasibility of required DOT
- ▶ Resources available for obtaining drugs
- ▶ Ability of the district to monitor patient
- ▶ Expectations concerning compliance
- ▶ Client and clinician preferences

Virginia Specific Guidelines

- ▶ VDH specific guidelines on TB control web
 - DOT mandatory for this regimen
 - Completion defined as 11 or 12 doses within 16 weeks
 - “Weekly” doses must be separated by > 72 hours to be countable

Monitoring

- ▶ Weekly monitoring for side effects at each DOT visit
- ▶ Monthly clinical assessment including brief physical examination for jaundice, tenderness of liver, or rashes
- ▶ Baseline LFTs for the following clients:
 - HIV-infected clients
 - Clients with liver disorders
 - Clients in the immediate postpartum i.e. < 3 months after delivery
 - Clients with regular alcohol usage
 - Testing clients on other hepatotoxic medications should be considered on a case by case basis.
- ▶ Monthly monitoring of LFTs is not necessary unless baseline testing is abnormal or the client is at risk for liver disease.

Virginia's Experience with INH + Rifampentine therapy for TB Infection

- ▶ 19 of 35 health districts in Virginia have used the 12 week INH/Rifampentine (3HP) regimen through 10/31/14.
- ▶ Data is only received at central office after completion or if discontinued for a serious side effect.
- ▶ 255 know to have started treatment with 3HP
 - 222 (87%) completed therapy
 - 2 still on treatment
 - 28 (10%) stopped treatment
 - 17 (7%) stopped due to side effects
 - 0 stopped due to death
 - 6 (2%) stopped lost to follow-up
 - 5 (2%) stopped other

Virginia's Experience with INH + Rifampentine therapy for TB Infection

- ▶ 10 districts had 1 or more clients with an adverse event form filed.
- ▶ Outcomes from adverse event forms
 - Continued 3HP - 6
 - Switched to INH for 9 months - 5
 - Switched to rifampin for 4 months - 0
 - Stopped any LTBI treatment - 14
 - Unknown - 1

Virginia's Experience with INH + Rifampentine therapy for TB Infection

- ▶ Most frequently reported symptoms associated with treatment being stopped or held
 - Rash/hives - 6
 - Nausea or vomiting - 5
 - Fatigue - 2
 - Appetite loss - 2
 - Sore muscles - 2
 - Diarrhea - 1
 - Numbness - 1
 - Dizzy/faint - 1
 - Abdominal pain - 1
 - Other - 6

Mississippi 3HP Experience (SETBC 10/20/2014)

- ▶ Since deployment in 2011, 1478 patients have started 3HP
- ▶ 1,345 patients have realized completion or have stopped receiving treatment
 - 1,095 patients (81.3%) have successfully completed 3HP
 - 72 (5.3%) starting 3HP completed alternate regimen
- ▶ Overall completion rate for persons starting 3HP and completing any regimen - 86.6%
 - 156 (11.6%) stopped therapy due to adverse reaction
 - 72 (5.3%) stopped by choice or other reason
 - 27 (2%) lost to follow-up

Duval County, FL 3HP Experience (1) (SETBC 10/20/2014)

- ▶ Duval Co. jail screens approximately 45,000 inmates annually
 - House 2500 at any given time
 - Average length of stay is 42 days
- ▶ TB therapy provided
 - 3HP DOT weekly x12weeks
 - 9INH SA x 9 months or 4R SA x4 mo.
- ▶ Contact Investigation in Jail, 40 inmates identified, 35 offered treatment
 - 29 have completed treatment (82%)
 - 2 are still currently being treated
 - 2 have been transferred to state facilities
 - 2 have been 'lost' once released from jail

The Way forward.....

- ▶ Statewide performance for contacts completing treatment for TB infection is **abysmal!**

Virginia NTIP Performance for Contacts Treatment for LTBI Initiated

YEAR	ACHIEVEMENT	# CONTACTS/INFECTED CONTACTS
2009	68.8%	201/292
2010	52.6%	142/270
2011	61.1%	201/329
2012	54.7%	141/258
2013	43.9%*	119/271*

* Incomplete data

Virginia NTIP Performance for Contacts Treatment for LTBI Initiated

YEAR	ACHIEVEMENT	# CONTACTS/INFECTED CONTACTS
2009	60.7%	122/201
2010	74.6%	106/142
2011	66.2%	133/201
2012	62.2%	88/141
2013	57.1%*	68/119*

* Incomplete data

Virginia Reality Performance for Contacts Completed Treatment for Infected Contacts

YEAR	ACHIEVEMENT	# CONTACTS/INFECTED CONTACTS
2009	41.8%	122/201/292
2010	39.3%	106/142/270
2011	40.4%	133/201/329
2012	34.1%	88/141/258
2013	25.1%*	68/119/271*

* Incomplete data

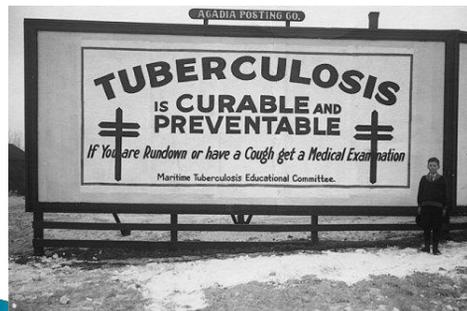
The Way forward.....

- ▶ 3HP **strongly** encouraged for contacts unless contraindicated!
 - INH or rifampin resistant source case
 - Age, medical condition, or drug profile of contact
- ▶ High priority for treatment of LTBI

Still tracking

- ▶ All 3HP outcomes
 - When treatment stops for any reason
 - Fax your 3HP log to 804-371-0248
 - Complete and fax adverse event form when needed

Questions?



Additional Resources

- Recommendations for Use of an Isoniazid-Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w

