



2013 Expert Panel

New Practice Recommendations

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Prevention and Health Promotion Administration**



- **Maryland TB Expert Panel November 25, 2013**
- Discussion based on CTBCP review of published research, published guidelines and recommendations, and review of other state practices by CTBCP staff regarding topics put forward by CTBCP, LHD and Corrections staff.
- Members included MD partners and TB experts from State, LHDs, Corrections, TBESC and JHU.



● Agenda Topics

- Diabetes Screening
- Therapeutic Drug Monitoring
- Using video/mobile devices for DOT
- Use of IGRAs
- Bedaquiline
- LTBI Screening in Corrections
- Counting Doses during Intensive Tx. Phase



Diabetes (DM) Screening



General Facts Re: Diabetes and TB

- **Diabetes Mellitus, especially Type 2 DM, is increasing worldwide**

- WHO estimated in 2010 that 285 million individuals worldwide were affected with DM and projected \uparrow to \sim 438 million by 2030
- DM disproportionately affects those also at greater risk for acquiring tuberculosis
 - lower socioeconomic status
 - ethnic minorities/foreign-born (12%-32%)
 - \geq 45 year age group with 22% among those \geq 65 years

General Facts RE: Diabetes and TB

- The risk for developing active TB if infected for person with DM is 2-3 times more than non-DM
- DM in Maryland:
 - Affects 14% of TB cases vs. 9-11% of general population
 - 8% of TB-DM cases also have renal failure
 - DM in Maryland has doubled since 2003 (4-5%) vs. 2009 (9-11%)

General Facts RE: Diabetes and TB

- TB can worsen glycemic control complicating management of diabetes
- TB-DM patients who smoke ≥ 1 pack/day have 5.8 times increased risk of death vs. non-DM, non-smoker
- DM (especially uncontrolled) is associated with poor TB treatment outcomes
 - Treatment failure, relapse, and death
 - Slower times to culture conversion (5-12 days)
 - Reduced Rifampin concentration

Recommendations for DM Screening

- Applies to all TB patients/suspects on treatment
- Screen for DM, using **blood glucose** or glycemic control (**HgA1c**) at the time of treatment initiation
 - For known diabetic (medical record/self-report):
Review existing HgA1c level
 - For all others: Suspect DM if FBG ≥ 126 mg/dl;
“casual” BG ≥ 200 mg/dl; or HgA1c $\geq 6.5\%$

Recommendations for DM Screening (2)

- If no HgA1c, ***consider*** obtaining HgA1c on known/suspected DM patient

- If HgA1c >7.0%:
 - perform therapeutic drug monitoring within 2-3 weeks of treatment initiation
 - refer known or suspected diabetics for DM evaluation and linkage to appropriate medical care /case management



Therapeutic Drug Monitoring (TDM)



Therapeutic Drug Monitoring: Yes???

- Some TB patients are at higher risk for malabsorption of medications, including those with:
 - co-morbidities such as HIV and DM
 - MDR-TB
- Delayed time to culture conversion (> 2 months) may be an initial sign of a malabsorption problem
- Knowing drug levels allows for early changes in regimen and ↓ chances of resistance or relapse



Therapeutic Drug Monitoring: No???

- Cost: ~ \$80 per drug
- Unlikely to benefit most TB patients as tx. failure and relapse are not common
- Multiple Test Options (2 hour vs.6 hour testing)
 - 2 hour testing is the standard
 - 6 hour testing can differentiate *slow* absorption from *mal*absorption



Recommendations for TDM

- Consider performing TDM for TB patients when ***at least one*** of the following conditions is met:
 - Known diabetic with HgA1c >7.0%
 - Severe TB disease
 - Suspected Treatment Failure or Relapse: defined for this purpose as delayed clinical or microbiological response to treatment (e.g., > 2 months sputum culture conversion)

Recommendations for TDM (2)

- If HgbA1c >7.0%:
 - perform TDM within 2-3 weeks of treatment initiation
- Perform 2 hour test unless otherwise requested by TB consultant
- Dosage changes based on TDM should be made in consultation with a TB expert
- Refer known or suspected diabetics for DM evaluation and linkage to appropriate medical care/case management

Recommendations for TDM (3)

- Submit blood to an approved TDM lab
- High TB burden jurisdictions should have staff certified to perform and submit blood for TDM directly to approved lab to reduce risk of a poor, inadequate, or late sample
- Low burden jurisdictions should submit blood for drug levels to the DHMH TB Lab for shipment per policy
- Dosage changes based on TDM results should be made in consultation with TB Expert and CTBCP

Recommendations for TDM (4)

- Policy becomes effective immediately and will be incorporated into revised MD guidelines
- DHMH 2014 TDM Workgroup Members:

Deb Hardy, HCHD, Ann Inman, PGCHD, Rich Oatis, DHMH Lab., Andrea Palmer, CTBCP, Sherry Roberts, BCHD, Jafar Razeq. DHMH Lab., Kimberly Townsend, MCHD, Kay Tremeloni, PGCHD



Video Directly Observed Therapy (vDOT)



Video DOT (vDOT) : Why ?????

- Directly Observed Therapy (DOT) is the standard of care for providing medications to TB patients
- Endorsed by WHO, recommended by CDC and codified via regulation in MD (*MD COMAR 10.06.01*)
 - Resource intensive
 - Reduced funding in public health necessitates evaluating new cost-effective options to DOT
- vDOT offers a flexible, cost effective option to provide DOT using available (and future) technologies



Recommendations for vDOT

- vDOT is an approved method of DOT in Maryland based on the following criteria
 - Patients receiving care under LHD supervision
 - Excluded for MDR or XDR TB unless approved by CTBCP (requires formal consultation)
 - Patient/guardian must be capable of and demonstrate understanding of tx. plan and handling of video/electronic equipment
 - Demonstrate compliance with treatment plan



Recommendations for vDOT (2)

- Demonstration of Compliance
 - 100% cooperation with **in-person** DOT for the intensive phase of treatment before moving to vDOT
 - Daily dosing 7 days per week X 2 weeks
 - Daily dosing 5 days per week X 3 weeks
 - A minimum of 80% DOT compliance for remainder of treatment (evaluated weekly) OR
 - Approval from CTBCP



Recommendations for vDOT (3)

- Live visual contact time preferable if possible, but if not, review videos/recordings no less than once a week with patient
- Local TB policy must conform with Expert Panel recommendations and must be reviewed and approved by LHD administration; review annually
- Local TB program will monitor and remove any patient from participation for noncompliance
- Document on RVCT as DOT, unless outside standards for vDOT compliance



Recommendations for vDOT (4)

- **Age limits:** Determined on case-by-case basis
 - LHD should obtain signed parental/guardian permission for children ≤ 18 years of age who will self vDOT
 - Signed agreement should be considered for parents who use vDOT to administer meds to own children
- **Use of packets:** Determined on case by case basis with CTBCP review if for ≥ 2 weeks



Recommendations for vDOT (5)

- vDOT workgroup is in process of developing MD policy which will be incorporated into new guidelines
- Until policy is final, please consult with CTBCP prior to using vDOT
- Current vDOT workgroup members include: Maureen Donovan, CTBCP, Bonnie Lewis, Caroline Co., Barb Johnson/Maunank Shah, Baltimore City, Kimberly Townsend, Mont Co. and Jayne McGunigale, Howard Co.



IGRA's :
“Confirmatory “ Tests ???
and
OK for Children ≤ 5 years ???



General Facts Re: Using IGRAs as Confirmatory Tests

- A positive TST followed by negative IGRA does ***NOT*** necessarily rule out TB infection
- Treatment must be considered in those groups at high risk for TB infection
- Treatment of TB infection is critical to decreasing the pool of future active cases



Revised Recommendations RE: Using IGRAs as Confirmatory Tests

- Select one or the other FDA approved test (IGRA or TST) based on population risk and test that is available at LHD
- Routine use of an IGRA as a ‘confirmatory’ test for a positive TST should ***not*** be done in individuals at high risk for progression to disease; ***close contacts***. immigrants and refugees with TB Class B waivers, ***other individuals at high risk for infection***



Use of IGRAs in Children \leq 5 years of age

- IGRAs are more problematic in children <5 yrs old
 - Failed T-SPOT TB more common (<4.7 years)
 - Indeterminate QFT results more common (11% or 14 of 127) in children 0-5 years)
- Very little published data and numbers are small
- More discordant results may be related to:
 - Effects of BCG vaccine
 - Functional status of immune system
 - Nature of pediatric TB infection



Recommendations RE: Use of IGRAs in Children ≤ 5 years of age

- Do not *routinely* use an IGRA for children younger than 5 years old
- Consult with CTBCP or TB Expert prior to use in young children



Screening for TB infection in Correctional Facilities



Screening for TB infection in Correctional Facilities

- TB remains a significant problem in correctional facilities due to close quarters and close proximity of inmates

Maryland Data:

- In 2012, over 21,000 individuals were incarcerated in MD state and federal facilities
- 5 MD counties (predominantly rural) house ICE detainees (numbers vary from year to year)



Screening for TB infection in Correctional Facilities

- Between 2009-2012, there were 9 active TB cases among inmates in MD facilities
 - 8 in local detention centers
 - 1 in a federal facility
- 2009 Expert Panel approved concept of minimal and non-minimal risk definitions as applied to screening and testing for TB in correctional facilities



2013 Recommendations RE: Screening for TB infection in Correctional Facilities

- **Minimal risk facilities** (defined as facilities in jurisdictions with no cases for \geq one year):
 - Use full TB risk screening tool for everyone
 - Test for TB anyone who answers "YES" to any question indicating \uparrow risk for TB
- **Non-minimal risk facilities:**
 - follow CDC guidelines; ***Prevention and Control of Tuberculosis in Correctional and Detention Facilities: Recommendations from CDC; MMWR 2006;55(No. RR-9)*** <http://www.cdc.gov/mmwr/PDF/rr/rr5509.pdf>



Screening for TB infection in Correctional Facilities: 2013 Recommendations (2)

- **Non-Minimal Risk Facilities: Repeat offenders**
 - Use symptom/risk assessment tool for repeat offenders *within same year (12 months)* who have documented history of positive TST or IGRA and negative CXR
 - Test those who answer "YES" to any high risk TB question during risk screening; CXR and medical evaluation required for those whose assessment has changed or who present with TB symptoms
 - Yearly CXR is not needed if symptom screen negative



Bedaquiline for TB Treatment

Bedaquiline (BDQ) for TB Treatment

- The first new class of drugs to obtain FDA approval for a TB indication in 40 years (December 2012)
- Indicated as part of combination therapy in adults \geq 18 years of age with pulmonary MDR-TB
- Drug has a half-life of approximately 5.5 months
- Single regimen costs ~\$23,000

Bedaquiline (BDQ) for TB Treatment

- The recommended dose of Bedaquiline for the treatment of pulmonary MDR in adults:
 - 400 mg given orally once daily for 2 weeks
 - followed by 200 mg orally three times weekly with a total treatment duration of 24 weeks

- Concerns
 - Prolonged QT interval on EKG
 - Death risk after discontinuation due to long half-life

Recommendations RE: Bedaquiline for TB Treatment

- Add to Maryland TB Guidelines
- Use must be approved through CTBCP before drug can be ordered according to both manufacturer and CDC protocols
- Approval for use is based on CDC provisional guidelines, on a case-by-case basis, when an effective treatment regimen is not otherwise available
- Outcomes of all patients on BDQ will be systematically monitored



Counting Doses/Weeks for Completion of Initiation Phase of TB Treatment

Counting Doses /Weeks for Completion of Initiation Phase of TB Treatment

- Confusion with current MD Guidelines over how to count doses/weeks when determining completion of initiation phase of TB tx.
- 2 options for starting TB treatment:
 - Daily dosing X 7 days per week X 2 weeks
 - Daily dosing X 5 days per week X 3 weeks
- Initiation phase then continues for 6 weeks
- When is initiation phase of treatment technically over ?

Recommendations RE: Counting Doses /Weeks to Determine Completion of Initiation Phase

- Initiation phase of treatment is defined as ***a total of 8 weeks*** regardless of regimen chosen for first 14 or 15 days of intensive treatment
- Daily dosing during the first 14 or 15 doses of treatment (depending on regimen selected) does NOT include counting of weekend packets
- Initiation phase of treatment is followed by 4 month continuation phase

NEXT STEPS

- Recommendations as presented can be put in place by local programs effective immediately; except for vDOT which requires consultation with CTBCP until procedure is finalized
- Recommendations are in the process of being incorporated into MD guidelines for publication; members from this audience may soon be asked to assist in final review and editing....stay tuned!

Maryland TB Expert Panel 2013



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