

# Diagnosis and Management of Tuberculosis in Adolescents

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# Disclosures

- I have no disclosures or conflicts of interest to report

# Objectives

- Describe the differences between adolescents and younger children and between adolescents and adults
- Summarize evidence for best practices in diagnosing and treating LTBI and disease in adolescents
- Identify potential strategies to apply these practices in your setting

# Case

- 17yo HIV-uninfected F with 1m of weight loss (18kg), 2 weeks of fever, diffuse abdominal pain
- Born in Mexico, to US 5 yrs ago; prior treatment for LTBI 3-4 yrs ago in S. Texas
- Medication: oral contraceptives
- WBC 5.5k, Hgb 10, plt 230k
- AST/ALT 65/59; pregnancy test: negative



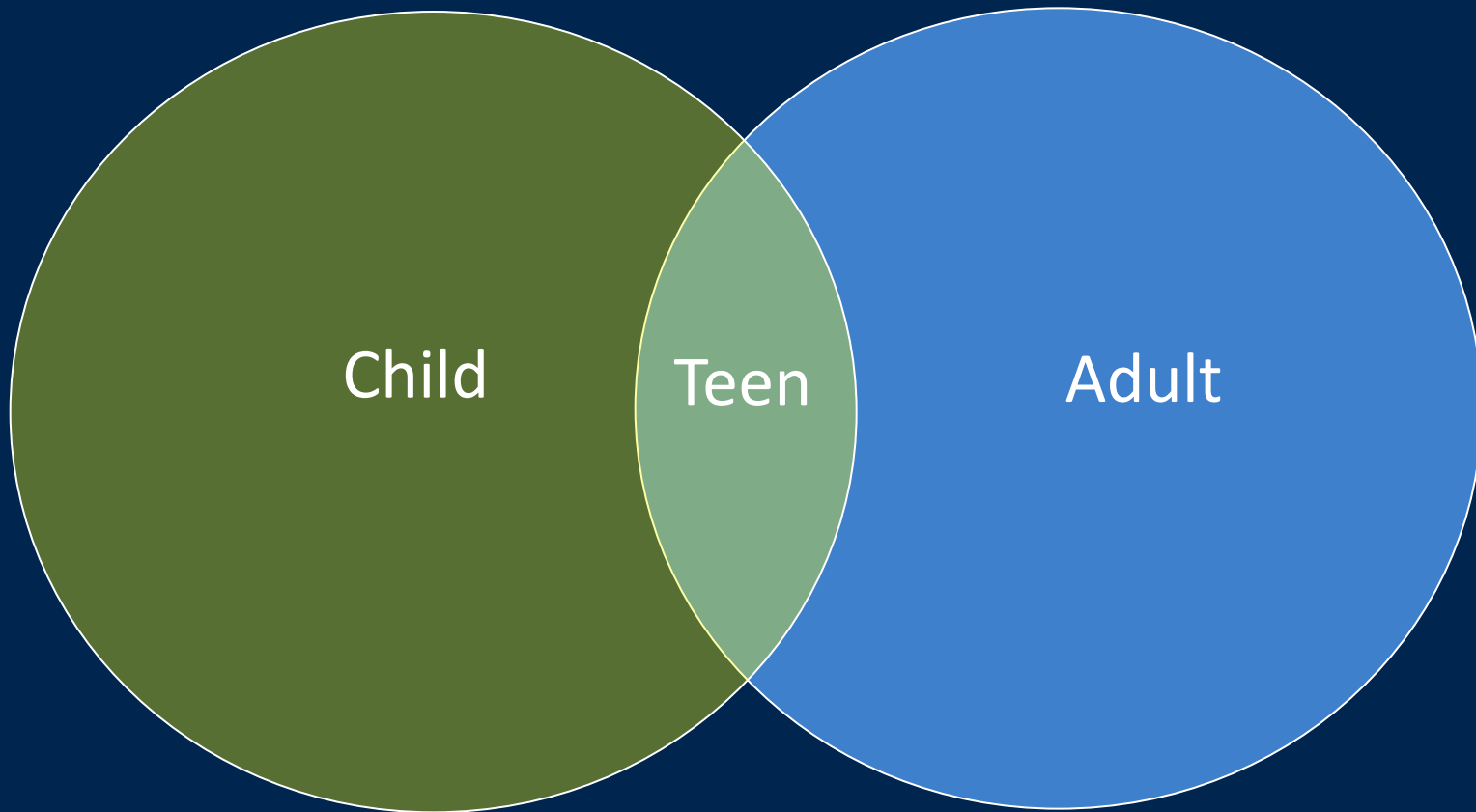
# Case: Initial Diagnostic Results

Source	AFB Smear	AFB Culture
Sputum	Negative	Negative
Induced sputum	Negative	Negative
BAL	Negative	Negative
Lung biopsy	Negative	Positive

# The Adolescent Conundrum

Trait	Pediatric	Adult
Symptoms		X
Radiographic findings	X	
Difficulty in obtaining adequate specimens	X	
Difficulty in securing microbiologic diagnosis	X	
Concern for medication tolerance		X
Consideration for alternative methods of birth control		X
Infection control considerations / public health ramifications		X

# Adolescents





# Epidemiology

- 2660 US cases in persons < 18 yrs old 2008-2010
- 29% were 13-17 yrs old (2% of total cases)

	Total U.S. population	10-14y	15-19y
% of population	N/A	6.9%	7.1%
Foreign born	13%	5%	7%
Below poverty line	15%	19%	20%
Uninsured	16%	10%	15%

# Risk of Progression to Disease, Stratified by Patient Age

Age at Primary Infection (yr)	No Disease (%)	Pulmonary Disease (%)	Miliary or Central Nervous System TB (%)
<1	50	30 to 40	10 to 20
1 to 2	75 to 80	10 to 20	2.5
2 to 5	95	5	0.5
5 to 10	98	2	<0.5
>10	80 to 90	10 to 20	<0.5

Adapted from Marais, et al. Childhood pulmonary tuberculosis: old wisdom and new challenges. *Am J Resp Crit Care Med.* 2006;173:1078–1090.

# Signs and Symptoms of Pulmonary TB by Age

Clinical Feature or Disease Type	Infants	Children	Adolescents
<b>Symptom</b>			
Fever	Common	Uncommon	Common
Night sweats	Rare	Rare	Uncommon
Cough	Common	Common	Common
Productive cough	Rare	Rare	Common
Hemoptysis	Never	Rare	Rare
Dyspnea	Common	Rare	Rare
<b>Sign</b>			
Rales	Common	Uncommon	Rare
Wheezing	Common	Uncommon	Uncommon
Decreased breath sounds	Common	Rare	Uncommon
<b>Location of Disease</b>			
Pulmonary	Common	Common	Common
Pulmonary + Extrapulmonary	Common	Uncommon	Uncommon

# Diagnostic Approaches: LTBI

Performance	TST	IGRA
Sensitivity	90%	92%
Specificity	95%	91%
PPV (overall)	1.5%	2.7%
PPV (high-risk)	2.4%	6.8%
NPVs	99.4%	99.7%

**Adolescents:** Recent IGRA conversion was indicative of an 8-fold higher risk of progression to disease within 2 years of IGRA conversion compared to non-converters (Cape Town)\*

# Diagnostic Approaches: Disease

- Sites of disease
- TSTs/IGRAs
- Radiographic findings
- Smear microscopy yield
- Culture yield

# Childhood TB Disease Sites, US: 1993-2001

Site*	% of cases	Median Age (years)
Pulmonary	76.9	6
Lymphatic	15.5	5
Meningeal	2.1	2
Bone/joint	1.4	8
Pleural	1.1	16
Miliary	1.1	1
Other	1.9	Variable

\*: United States (almost all are normal hosts)

# Tuberculosis in Adolescents

## *A French Retrospective Study of 52 Cases*

- 52 patients

- 12-18 yrs

- 7 HIV+

- Sites:

- 52% pulmonary

- 31% pulmonary +  
extrapulmonary

- 17% extrapulmonary

**TABLE 1. Presenting Symptoms of 52 Adolescents With Tuberculosis (Some Patients had More Than one Manifestation)**

Manifestations	No. (%)
Fever	40 (76.9)
Weight loss	38 (73)
Asthenia	37 (71.2)
Cough	28 (53.8)
Abnormal auscultation	16 (30.8)
Dyspnea	13 (25)
Abdominal pain	6 (11.5)
Neurologic manifestations	6 (11.5)
Abdominal distension	4 (7.7)

# TSTs vs IGRAs: Disease

Assay	Younger children	Teens	Adults
TST sensitivity	55-89%	83-89%	52%
IGRA sensitivity	52-94%	?	60-76% (HIV+), 84-85% (HIV-)



# Brazilian Adolescents

- 904 adolescents treated for pulmonary TB
- 1996-2005

Finding	%
Infiltrate	53.3%
Cavitation	32.4%
Condensation	27%
Pleural effusions	9.3%
Hilar adenopathy	3.2%
Miliary	1%
Normal CXR	6.2%

# Tuberculosis in Adolescents

## *A French Retrospective Study of 52 Cases*

Test		# +	%
CXR	Any anomaly c/w TB	43/52	83%
	Adenopathy	30/43	70%
	Infiltrates*	23/43	54%
TST	> 15 mm	43/52	83%
AFB	Smear	15/52	28%
	Culture	27/52	52%

\*Included: cavitation (14), pleural effusion (11), infiltrates (10), pulmonary nodules (6);  
cavities increased with age: 5% at 12 yrs, 36% at 18 years

**Culture positivity: 23% at 12 years, 71% at 18 years**

# Radiographic Findings

**Table 3:** Comparison of Adolescents with Cavitory and Non-cavitory Pulmonary Tuberculosis

Variable		Total (n=118) †	Cavitory (n= 31)	Non- cavitory (n= 87)	p =
Age	Mean age (years)	15.3	15.8	15.1	0.047
TST	TST ≥ 5 mm	105 (89%)	26 (84%)	79 (90%)	0.32
Microbiology	Cultures attempted	97 (82%)	31 (100%)	66 (76%)	0.001
	AFB smear	24/97 (25%)	13/31 (42%)	11/66 (17%)	0.01
	AFB culture	52/97 (54%)	20/31 (65%)	32/66 (48%)	0.19
Duration of therapy	Mean duration of therapy (months)	7.6	8.5	7.3	0.20
End-of-therapy radiographic findings	Radiograph abnormal	63 (53%)	16* (52%)	47 (54%)	0.83
	Hilar adenopathy	14	1 (3%)	13 (15%)	0.11
	Scarring	37	17 (55%)	30 (34%)	0.06
	Calcifications	2	0	2 (2%)	1
	Effusions	1	0	1 (1%)	1

# Microbiologic/PCR Yield, Pulmonary TB

Assay	Younger children	Teens	Adults
Smear-positivity*	2-3%	10-29%	43-72%
Culture-positivity*	4-7%	21-52%	66-75%
Xpert sensitivity	50-90%	?	76-95%
Xpert specificity	99%	?	95-99%

\* North American, French data; one South African study in 324 adolescents demonstrated positive cultures in 78% (Ann Trop Paediatr 2000;28:5)

# Predictors of Smear-Positivity

- 78 adolescents, Taiwan
- Univariate analysis indicated risk factors for smear-positivity:
  - Cough > 4 weeks (aOR 13.8, 2.3-83)
  - Hemoptysis
  - Multilobar or lower lobe involvement (aOR: 12.6, 1.2-135)
  - Cavitations (aOR 7.7, 1-58)
  - Pleural effusions

# Treatment: LTBI

Regimen	Pros	Cons
INH x9m	~20% benefit over INH x 6m	Adherence (<50% completion)
INH x 6m	Adherence better than 9m	Slightly reduced benefit compared with 9m (assuming both taken as indicated)
RIF x 4m	Adherence, availability	Cost if uninsured; drug interactions
INH/RFP x 12 doses	Adherence	Availability; requirement for DOPT
INH/RIF x 3-4m	Adherence	Slightly increased risk of side effects compared to monotherapy
RIF/PZA x 2m	Adherence	Hepatotoxicity; recommended for patients initially suspected of having disease

# Treatment: Disease

- Follow adult guidelines; routine use of RIPE unless source case is known to have an isolate susceptible to all 1<sup>st</sup> line medications
- For larger adolescents, use ATS/CDC dosing schedule as opposed to Red Book schedule
- Routine use of B6 in adolescents
- Check UPT in all post-menarchal females prior to starting therapy

# Challenges

- Medical:

- Infection control
- Medication tolerance
- Lack of medical home

- Social:

- Substance use and abuse
- Stigma
- Missing school, work



# Infection Control

- Contact investigations: hospital, school, home, ...
  - Same principles apply in all settings
- Lack of negative-pressure rooms in many pediatric facilities
- Complacency on part of pediatric providers, or inadvertent exposure because TB not suspected

# Medication Tolerance

- Metabolize INH, EMB more slowly than younger children, but faster than adults
- Few adolescent-specific data; in our series of 145, 6 (4%) had side effects, 2/6 with transaminitis
- Discuss birth control options with all post-menarchal girls
- Baseline transaminases

- 110 HIV-uninfected children, Toronto 2002-2009
- Deteriorations occurred in 14%, associated with:
  - Weight for age  $\leq$  25<sup>th</sup> percentile
  - Multiple sites at diagnosis
  - Most common site: airway compression from enlarging intrathoracic lymphadenopathy
- Median time: 80 days (range: 10-181 days)

# Lack of Medical Home

- Changes preventive opportunities
- Changes venues where present to care
- TB clinician often serves as their 'real' pediatrician, at least for the next 6-9 months:
  - Opportunity for health maintenance
  - Catch-up vaccinations
  - Screen for other diseases
  - Contraception

Untitled - Message (HTML)

Message Developer Nuance PDF

Reply Reply to All Forward Call IM

Delete Move to Folder Create Rule Other Actions

Block Sender Safe Lists Not Junk

Categorize Follow Up Mark as Unread

Find Related Select Find

You forwarded this message on 2/6/2012 3:50 PM.

From: [REDACTED] Sent: Mon 2/6/2012 9:15 AM  
To: Cruz, Andrea T.  
Cc:  
Subject:

Excuse me will you help I have T.B am takeing med's I know I cant drink but can I smoke weed

Feb 11, 2013, 9:32 AM

What happens if you we're taking the pills for the T-B and you do drugs like lean &dro just once

**Lean:** promethazine + codeine + Sprite +/- Jolly Ranchers

**Dro:** hydroponically-grown marijuana

# Teens, Substance Use & Abuse: 2011

Drug	Prevalence of use
Ethanol	28-41% of high school seniors 6 million teens binge drink
Marijuana	40% use, 23% used in last month
Cocaine	6.8%
Heroin	2.9%
Inhalants	11.4%
Methamphetamines	3.8%
Prescription Stimulants	1.7-3%
Prescription Sedatives	0.4-2.7%
Prescription Opioids	4-12%

**6% of middle- and high-school Canadian adolescents report using prescriptions drugs to get high**

# Stigma

- Guilt over potentially infecting family members, friends, classmates
- Fear about ramifications of contact investigations
- Address social media, messaging
- Judicious sharing of information

*Link between stigma, adherence, and concomitant use of other substances (& other risk-taking behavior)*



# Missing School

- Coordinate with local health departments re: repeat sputum sampling in the field
- Arrange for work to be sent home versus home schooling until they can return to school
- If possible, try to fit appointments during spring break, holidays, etc to minimize time lost

# Conclusions

- Adolescents straddle the line between pediatric and adult TB in terms of presentation, diagnostics, and treatment
- There are few adolescent-specific data available to guide management, and the age group per se poses challenges to providers
- In contrast to the younger child, the adolescent needs to be an active participant in his/her care