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Tuberculosis Exposure, Infection, and Disease Among Children with Medical Comorbidities

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Background

- TB is poorly characterized among HIV-uninfected immunocompromised children in many settings
- This results in lack of uniformity (or lack of mention) in many national subspecialty organization guidelines regarding screening for latent TB infection
- Recent U.S. study found that 25% of children with disease had no identifiable TB risk factors

Toussi *et al.* Clin Infect Dis 2013;57:1318
Winston & Menzies. Pediatrics 2012;130:e1425

Methods

- Design: Retrospective cohort study
- Setting: Houston, TX (4.5/100,000)
- Time period: 1983-2013
- Classified as exposure, infection, or disease as per standard definitions

- Inclusion:
  - 0-18 years of age
  - Immunocompromised
  - Receiving immunosuppressants
  - Pulmonary, hepatic, renal, or hemodynamically significant cardiac disease
- Exclusion:
  - Mild systemic disease

ATS, CDC, IDSA. Am J Respir Crit Care Med 2000;161:S221
Graham *et al*. J Infect Dis 2012;205:S199

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Demographics

Variable	Subgroup	Total (n=69)	Disease (n=22)
Age	Mean (range)	9.5y (2m-18y)	10y (1.2-18y)
Gender	Female	41%	32%
Race/Ethnicity	Hispanic	48%	45%
	Black	29%	27%
	Asian	17%	23%
Country of Origin	US	55%	55%
	Latin America	29%	19%
	Asia	9%	18%
	Africa	7%	9%
BCG status	Received	41%	41%

Comorbidity		Total (n=69)	Disease (n=22)*
Cardiac	**Cyanotic heart disease**	13%	**18%**
Hemoglobinopathy	**Sickle cell disease**	10%	**18%**
Oncologic	**Solid organ**	10%	**9%**
	Hematologic	6%	**14%**
GI	**Crohn's**	3%	**9%**
	Hepatitis	10%	0%
Renal	Dialysis	3%	0%
	Nephrotic	6%	0%
Immunologic	HIV	4%	0%
	Primary I.D.	3%	1%
	Chronic steroids	4%	0%

*Diabetes, Krabbe's, juvenile idiopathic arthritis, spina bifida, developmental delay

Exposure

- 7 children
  - 5 were < 5 yrs old
  - 2 were >5 yrs old but immunosuppressed:
    - HIV
    - Renal transplant recipient
- Completion: 100% completed 8-10 wks of INH
- None have progressed to disease

Infection

- 40 children
  - 25 identified via targeted skin testing
    - 18 foreign birth, 7 foreign travel
  - 9 via contact investigations
  - 6 had no identifiable risk factors
- Completion:

Regimen	Completion Rate	Complications
INH	92% (34/37)	2 children with other hepatic risk factors (antiepileptic use, hepatitis B) developed transaminitis; one mother overdosed her child inadvertently
RIF	100% (2/2)	-
Levoflox/ PZA	0% (0/1)	Hepatitis with coagulopathy; later found to have Wilson's disease

- None have progressed to disease

Disease

- 22 children (13 confirmed, 9 probable)
  - 20 pulmonary, 1 scrofula, 1 cutaneous TB
- **Only 60% had identifiable risk factors**
  - 10 foreign birth, 3 source cases
- 80% had TST ≥5mm
- 4 (18%) died:

Age	Comorbidity	Details
18y	Sickle cell, s/p BMT	Developed disseminated TB after BMT engrafted, died of ARDS; post-mortem blood and lung cultures grew *M.tb*
14m	Congenital heart disease	Developed miliary TB with multiple pulmonary blebs, one of which ruptured, resulting in tension pneumothorax
16y	Sickle cell	Died of cardiac arrest 3 months into treatment
3y	Krabbe's	Died of underlying syndrome 2 months into treatment

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Conclusions

- Many children had comorbidities that would not have deemed them at high risk for LTBI
- Targeted testing would have missed over 40% of children with disease
- Given high mortality in this small cohort, consideration should be given to integrating LTBI testing into initial and ongoing evaluation of certain pediatric populations

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Risk Factor Questionnaire

TABLE 4. ORs and 95% CIs for Logistic Model Predictors of Positive TST Result (≥10 mm) in 29 699 Children

Predictor	OR	95% CI
Child received BCG vaccine	2.31	(1.70,3.13)
Child born outside United States	8.63	(6.16,12.09)
Household member with history of TB	1.53	(1.14,2.04)
Child lived outside United States	2.06	(1.49,2.85)

Number of Factors Affirmed	*n*	Sensitivity (%)	Specificity (%)	PPV (%)
1	16 823	83.5	47.5	1.59
2	5297	66.7	83.9	4.04
3	1514	48.9	95.7	10.4
4	471	25.9	98.8	17.6

Pediatrics 2001;107:e54

What *is* a Positive PPD?

≥ 5 mm	≥ 10 mm	≥ 15 mm
HIV+	Immigrants from high-prevalence areas	Anyone (even if no risk factors)
Other immunocompromise[1]	<4 yrs of age	
Contact with TB case	Exposed to adults in high-risk categories	
Suspected TB disease in the child	Other chronic medical conditions[2]	

1: includes chronic corticosteroids, TNF-alpha antagonists
2: includes chronic renal failure, diabetes mellitus, malnutrition, lymphoma

2012 Red Book, Table 3.75