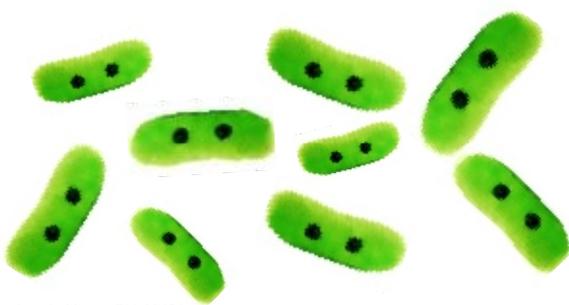


TB Overview & the Basics



Jane L. Moore, RN, MHSA
Director, TB Control and Newcomer Health



TB Case Management Series

Series of videoconferences designed to provide tools needed to be successful in the management of TB cases.

- Package - not independent - requires commitment

Today

- Overview and the Basics

Future sessions

- Friday, March 8th - TB Nurse Case Management
- Thursday, April 11 - Ongoing Monitoring in TB Case Management
- Friday, April 26 - Contact Investigations
- Friday, May 31 - Complex Cases



- TB cases continue to be reported in every state
- Drug-resistant cases reported in almost every state
- Estimated 10-15 million persons in U.S. infected with *M. tuberculosis*
 - Without intervention, about 10% will develop TB disease at some point in life



TB Epidemiology

World

- 1 in 3 people in world infected
- - 8 million new cases of active TB/year
- 2+ million deaths/year

US

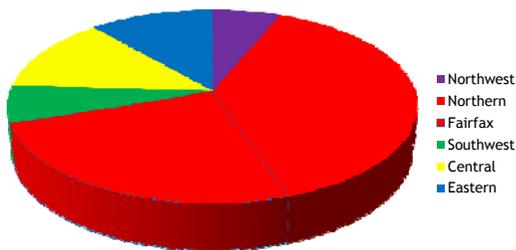
- 10,528 new cases of active TB in 2011 (3.4/100,000)

Virginia

- 221 new cases of active TB in 2011 (2.7/100,000)
- Know your local epidemiology !
- 2012 numbers will be released on March 21



Distribution of TB in Virginia



History of TB

TB has affected humans for millennia

Historically known by a variety of names, including:

- Consumption
- Wasting disease
- White plague

TB was a death sentence for many



Vintage image circa 1919
Image credit: National Library of Medicine



Virginia's Long History with TB

Three sailing ships, the *Godspeed*, *Discovery*, and *Susan Constant*, came ashore at Jamestown, VA in April, 1607. These ships carried 108 settlers.

Many of the early settlers often arrived in Virginia with diseases such as yellow fever and the plague. Just as often, they became sick with other diseases - 'seasoning,' malaria, and consumption (tuberculosis). In an effort to prevent 'seasoning,' the settlers changed their arrival schedule from summer to fall or winter.





Tuberculosis was suspected as a possible cause of Pocahontas's death. She became ill while in England, and died just before setting sail to Virginia with her husband (John Rolfe) and son.



History of TB Scientific Discoveries in 1800s

Until mid-1800s, many believed TB was hereditary

1865 Jean Antoine-Villemin proved TB was contagious

1882 Robert Koch discovered *M. tuberculosis*, the bacterium that causes TB



Mycobacterium tuberculosis
Image credit: Janice Haney Carr

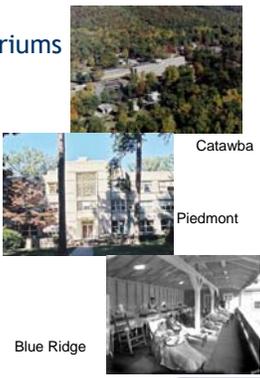


History of TB Sanatoriums

Sanatoria movement began in the 1880s

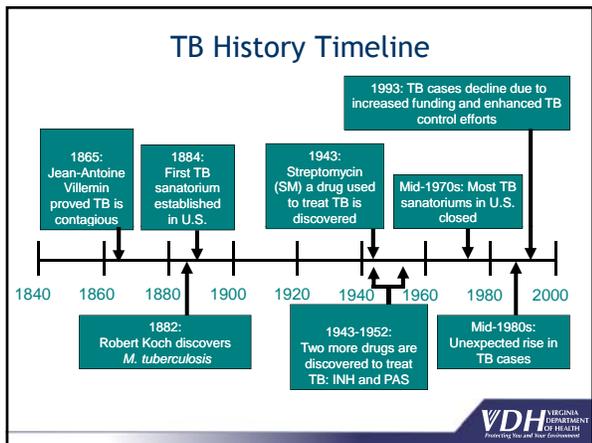
Treatment was a regimen of bed rest, open air, and sunshine

Those who could not afford sanatoriums often died at home



Catawba
Piedmont
Blue Ridge





Virginia Time Line

1600s

- Laws passes in the Colony of Virginia that allows for the collection of data on its residents

1872

- Virginia General Assembly creates the State Board of Health

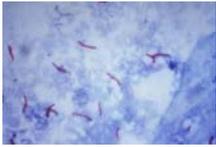
1908

- VA General Assembly reorganizes the State Board of Health
 - Board of Health now includes a commissioner, a bacteriologist and a clerk
 - Appropriates \$40,000 and divides it equally among TB Control and other programs



Tuberculosis

- Airborne disease caused by the bacterium *Mycobacterium tuberculosis* (*M. tb*)
- *M. tb* complex (*M. tb*, *M. bovis*, *M. africanum*, *M. microti*, *M. canetti*, *M. caprae*, *M. pinnipedii*, and *M. mungi*) can cause TB disease
- Majority of TB cases caused by *M. tb*
- *M. tb* organisms also called tubercle bacilli



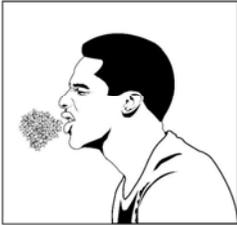
TB Transmission

TB is spread person to person through the air via droplet nuclei

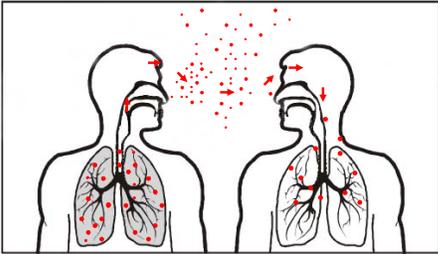
M. tuberculosis may be expelled when an infectious person:

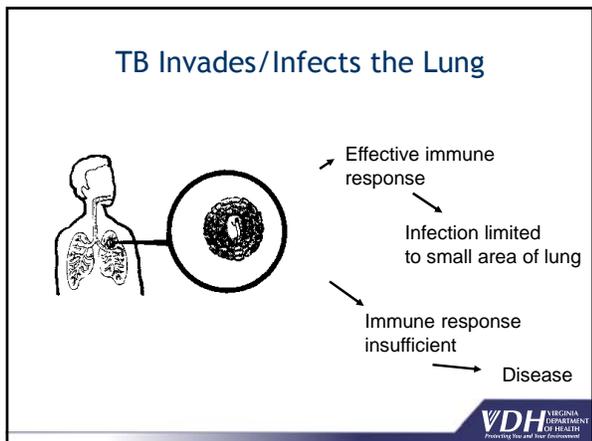
- Coughs
- Sneezes
- Speaks
- Sings

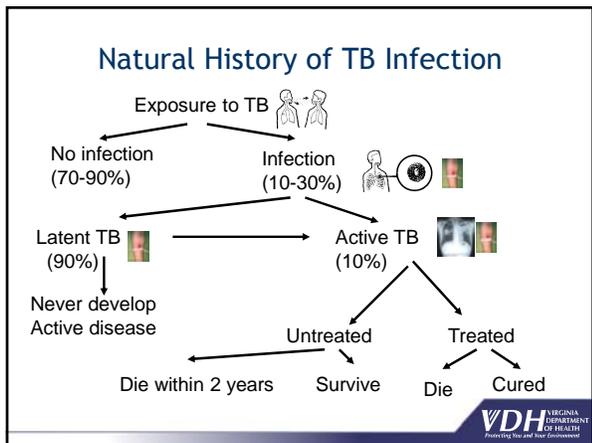
Transmission occurs when another person inhales droplet nuclei



TB Transmission







TB Transmission

Probability that TB will be transmitted depends on:

- Infectiousness of person with TB disease
- Environment in which exposure occurred
- Length of exposure
- Virulence (strength) of the tubercle bacilli

The best way to stop transmission is to:

- Isolate infectious persons
- Provide effective treatment

VDH VIRGINIA DEPARTMENT OF HEALTH
Protecting You and Your Environment

Persons at Higher Risk for Acquiring TB Infection

- Close contacts of persons know or suspected to have active, infectious TB disease
- Foreign-born person from areas where TB is prevalent
 - Beware the 5 years in US statement!
- Residents and employees of selected congregate living settings
- HCWs who serve high-risk populations



Persons at Higher Risk for TB Infection - cont.

- Injection drug users
- Some medically underserved populations
- Certain racial or ethnic minority populations
- Children exposed to high-risk adults



Testing for TB Infection

- Two methods for testing for TB infection
 - Tuberculin skin test - TST
 - -100 years old
 - Imperfect
 - False positive & false negative results
 - Subject to user error & interpretation
 - Interferon Gamma Release Assay - IGRA
 - Blood test
 - Two products available
 - QuantiFeron
 - T-Spot-TB



Testing for TB Infection

- Pros and cons to each test
- Main utility -
 - Part of diagnostic work-up for disease, i.e. is infection present
 - Identifying those who may benefit treatment to prevent future cases of disease



Targeting the Screening Efforts

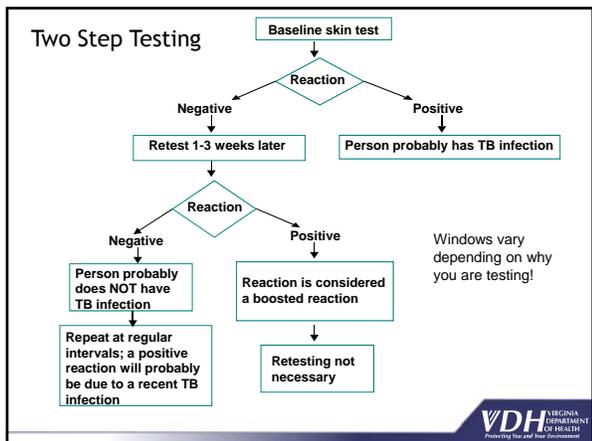
- Focus efforts to those at true risk for TB infection or progression to disease
- Predictive value of the TST
- “A Decision to Test is a Decision to Treat”



TB Control Risk Assessment

- Tool to assist in identifying those at risk for acquiring TB infection or progression to disease if infected
- Current VDH policy is to offer testing for TB infection only to individuals with an identified risk





BCG Vaccination and Tuberculin Skin Testing

- Tuberculin skin testing not contraindicated for BCG-vaccinated persons
- Treatment for LTBI considered for any BCG-vaccinated person whose skin test reaction is ≥ 10 mm

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Protecting You and Your Community

Progression to TB Disease

Some conditions increase probability of LTBI progressing to TB disease

Infection with HIV	Organ transplant
Chest x-ray findings suggestive of previous TB	Silicosis
Substance abuse	Diabetes mellitus
Recent TB infection	Severe kidney disease
Prolonged therapy with corticosteroids and other immunosuppressive therapy, such as prednisone and tumor necrosis factor-alpha [TNF- α] antagonists	Certain types of cancer
	Certain intestinal conditions
	Low body weight

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Progression to TB Disease TB and HIV

TB infection and NO risk factors	TB infection and HIV infection (pre-Highly Active Antiretroviral Treatment [HAART])
	
Risk is 10% over a lifetime with about 5% in the first 2 years and remaining 5% during remainder of life	Risk is about 7% to 10% PER YEAR, a very high risk over a lifetime

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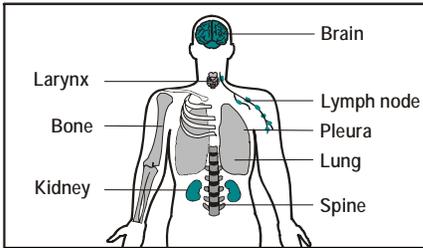
Latent TB Infection vs. Active TB Disease

Latent TB Infection (LTBI)	Active TB Disease
Tubercle bacilli in the body	
Tuberculin skin test reaction usually positive	
Chest x-ray usually normal	Chest x-ray usually abnormal
Sputum smears and cultures negative	Sputum smears and cultures may be positive
No symptoms	Symptoms such as cough, fever, weight loss
Not infectious	Often infectious before treatment
Not a case of TB	A case of TB

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Sites of TB Disease

Bacilli may reach any part of the body, but common sites include:



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TB Disease

M tb actively growing/destroying tissue in one or more locations

- Pulmonary TB
 - Cough > 2 weeks duration
 - Hemoptysis - late symptom
- Systemic
 - Weight loss
 - Fever
 - Night sweats
 - Fatigue
- Extrapulmonary
 - Symptoms vary depending on location



Diagnosis of TB

- Careful history of present illness and examination
- Test for TB infection
 - Tuberculin skin test - TST
 - Interferon Gamma Release Assay - IGRA
 - QuantiFERON
 - T-SPOT-tb
- Chest x-ray - CXR
- Sputum or other samples



Chest X-Ray

- Infiltrates (collections of fluid and cells in lung tissue)
- Cavities (hollow spaces within lung)



Abnormal chest x-ray with cavity



Chest X-Ray

Chest x-rays can:

- Help rule out possibility of pulmonary TB disease in persons who have a positive TST or IGRA result
- Demonstrate improvement in clinical cases, i.e. culture negative pulmonary TB



Chest X-Ray

Chest x-rays cannot confirm TB disease

- Other diseases can cause lung abnormalities
- Chest x-ray may appear unusual or even appear normal for persons living with HIV



Diagnosis of Pulmonary TB

Coughed sputum

- Best specimen when available
- Early AM best, supervise at least one collection
- AFB smear best available tool for assessing infectiousness
- Most likely to yield positive culture
- Multiple specimens recommended to maximize chances for +AFB/culture

Induced sputum

- Watery , mark as induced
- Up to 30 minutes with hypertonic saline

Bronchoscopy



Yield of Smear and Culture from Repeated Sputum Induction for the Diagnosis of Pulmonary TB

Induced sputum (% yield)

specimen	one	two	three	four
AFB smear	64	81	91	98
AFB culture	70	91	99	100

Int J Tuberc Lung Dis. 2001 Sep;5(9):855-60. Al Zahrani K, et al.



Diagnosis of Pulmonary TB

Laboratory tests

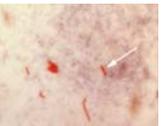
- A continuum of testing
- AFB smear - 24 hours
- NAA - MTD - few days after smear
- Culture -
 - Preliminary result - DNA probe 7-14 days
 - Positive for an Nontuberculous mycobacteria does not rule out TB
 - ID of isolate - confirmation of *M. tb* or not
- Antimicrobial susceptibility testing - 28 days



Laboratory Tests for *M. tb*

AFB smear

- Available in 24-48 hours
- Simple test; requires skilled technologist to read
- Not diagnostic for *M. tb*: All AFB look alike
- Used to assess infectiousness
 - Need for isolation, contact investigation
- Monitor response to treatment
 - Decrease in AFB on smear correlates with effectiveness of treatment





Direct/rapid tests for TB

- Nucleic acid amplification
 - DCLS using MTD
 - Other labs - other technologies - PCR - other names
- Results in 3-5 days
- Automatically done for positive smears by DCLS
- TB Control must request testing on negative smears
- Cannot be on treatment for more than 7 days or within last 12 months
- Beware “the probe”



Laboratory Tests for *M. tb*

Culture and Identification of Isolate



- “Gold standard” for TB diagnosis
- Usually complete in 2-4 weeks
- Not signed out as negative until 8 weeks
- Traditional identification based on growth characteristics, biochemical tests
- Preliminary ID by “probe” now standard
 - Requires isolate (2-4 weeks)
 - Tests DNA - can ID *M. tb complex*, *M. avium*, +/- others
 - More rapid than chemicals, just as accurate
 - Cannot distinguish among *M. tb complex* species (*M. tb* vs. *M. bovis*)



Laboratory Tests for *M. tb*

Antimicrobial susceptibility testing

- Requires TB isolate
- 2-4 weeks after isolate available
- INH, rifampin, ethambutol & PZA testing standard
- Second line drug testing only on request
- 3-10% of VA TB isolates resistant to ≥ 1 first line TB drug
 - Continue all drugs until susceptibility results available



Bacteriologic Examination Types of Drug-Resistant TB

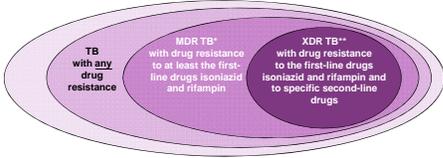
Mono-resistant	Resistant to any one TB treatment drug
Poly-resistant	Resistant to at least any two TB drugs (but not both isoniazid and rifampin)
Multidrug-resistant (MDR TB)	Resistant to at least isoniazid and rifampin, the two best first-line TB treatment drugs
Extensively drug-resistant (XDR TB)	Resistant to isoniazid and rifampin, PLUS resistant to any fluoroquinolone AND at least 1 of the 3 injectable second-line drugs (e.g., amikacin, kanamycin, or capreomycin)



Multidrug-Resistant (MDR) and Extensively Drug-Resistant (XDR) TB

MDR TB caused by bacteria resistant to best TB drugs, isoniazid and rifampin

XDR TB caused by organisms resistant to isoniazid and rifampin, plus fluoroquinolones and ≥ 1 of the 3 injectable second-line drugs




Drug-Resistant TB

Primary Resistance	Caused by person-to-person transmission of drug-resistant organisms
Secondary Resistance	Develops during TB treatment: <ul style="list-style-type: none"> • not given appropriate treatment regimen OR • did not follow treatment regimen



Other Diagnostic Tests

HAIN Test - rapid molecular susceptibility testing for INH and rifampin

- Requires authorization
- Can be done from raw specimen

CDC molecular susceptibilities

- Requires authorization
- Requires growing culture - i.e. preliminary culture report



Examination of AFB Smears

Classification of Smear	Smear Result	Infectiousness of Patient
4+	Strongly positive	Probably very infectious
3+	Strongly positive	Probably very infectious
2+	Moderately positive	Probably infectious
1+	Moderately positive	Probably infectious
Actual number of AFB seen (no plus sign)	Weakly positive	Probably infectious
No AFB seen	Negative	May not be infectious



What do each of these mean??

Result	Interpretation
Positive M.tb Culture	TB confirmed in site tested
Positive DNA probe for M.tb Complex	TB or related bacteria confirmed in site tested
Positive MTD or other NAA for M.tb	M.tb very likely (high sensitivity)
Negative MTD or other NAA for M.tb	M.Tb NOT ruled out, but less likely if smear neg.
Positive AFB smear	Mycobacteria likely present, TB not confirmed
Positive AFB culture	Mycobacteria present, TB not confirmed
Persons with TB symptoms	Potential TB suspect



Treatment of TB Disease

4 regimens approved for drug susceptible disease
Recommendations for HIV-infected same with a few exceptions

- Twice weekly options are not recommended for HIV+ patients with CD4+ cell counts less than 100



Treatment Pearls

Ethambutol can be discontinued once susceptibility to INH and RIF demonstrated

- Must be on PZA
- Requires physician order

PZA must be continued for full recommended 8 week course to qualify for short-course treatment

- Number of doses depends on prescribed regimen
- Dose count required

DOT standard of care for all

Never add a single drug to a failing regimen



Antituberculosis Drugs Currently in Use in the United States

First-line Drugs

- Isoniazid
- Rifampin
- Rifapentine
- Rifabutin*
- Ethambutol
- Pyrazinamide

Second-line Drugs

- Cycloserine
- Ethionamide
- Levofloxacin*
- Moxifloxacin*
- Gatifloxacin*
- P-Aminosalicylic acid
- Streptomycin
- Amikacin/kanamycin*
- Capreomycin



Isoniazid



Preparation

- 50 mg, 100 mg, and 300 mg tablets
- Suspension (can cause diarrhea and cramping)
 - Suspension must be kept at room temperature

Administration tips

- Can be cut or crushed
- Do not take with large fatty meal
- If upsets stomach, take with small amount of food
- Avoid alcohol
- No antacids within 1 hour



Isoniazid



Adverse Reactions and Side effects

- Hepatitis
 - Loss of appetite
 - Tiredness, weakness
 - Stomach pain, nausea, vomiting
 - Yellow skin or dark colored urine
- Can cause flushing with some fish or cheeses
- Peripheral neuritis
 - Numbness or tingling in hands or feet
- Arthralgias
- Optic neuritis



Rifampin



Preparation

- 150 mg and 300 mg capsules

Administration tips

- Store at room temperature - humidity can affect
- Powder from capsules can be mixed with liquid or soft food
- Must be administered immediately after mixing
- Be careful in opening capsules!
- Large number of drug interactions



Rifampin



Adverse Reactions and Side effects

- Affects hormone based birth control!
- Orange staining of body fluids - fast!
 - Will stain soft contact lens
- Rash
- GI upset, flu-like syndrome
- Liver toxicity
 - Unusual tiredness or loss of appetite
 - Severe abdominal pain
 - Fever chills



Ethambutol

Preparation

- 100 mg and 400 mg tablets

Administration tips

- Store at room temperature
- Can be taken with food
- Can be split or crushed and mixed - used immediately



Ethambutol



Adverse Reactions and Side effects

- Visual disturbances - vision changes, blurring, color blindness, trouble seeing, eye pain
- Swelling of face
- Rash, hives, trouble breathing
- Numbness, pain or tingling of hands/feet
- Joint pain
- Fever chills
- Nausea, vomiting, poor appetite, abdominal pain
- Headaches, dizziness



Pyrazinamide

Preparation

- 500 mg tablets

Administration tips

- Store at room temperature
- May be taken with food
- Can be split or crushed
- Use immediately following mixing with food





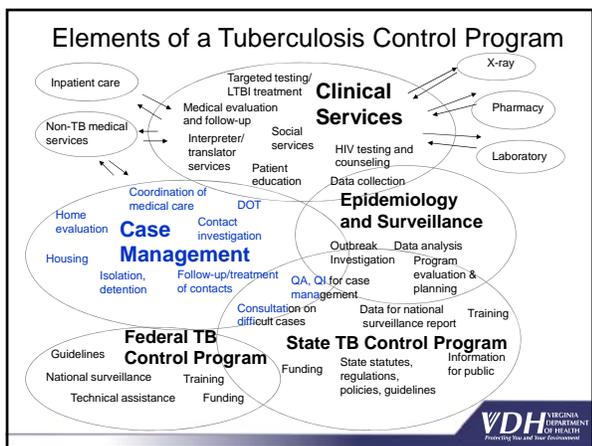
Pyrazinamide

Adverse Reactions and Side effects

- Can cause rash after sun exposure - limit sun exposure
- Gout-like symptoms (pain swelling in joints) and arthralgias
- GI upset
- Liver toxicity -
 - yellow skin/dark urine
 - nausea/vomiting
- Skin rash, severe itching, hives







Definition of Case Management

Primary responsibility for coordination of patient care to ensure that the patient's medical and psychosocial needs are met through appropriate utilization of resources



Responsible and accountable to ensure:

The case

- Completes a course of therapy
- Is educated about TB and its treatment
- Has documented culture conversion
- Has a contact investigation completed, if appropriate



Primary goals of case management

- Render the patient non-infectious by ensuring treatment
- Prevent TB transmission and development of disease
- Identify and remove barriers to adherence
- Identify and address other urgent health needs



VDH TB Prevention and Control Policies and Procedures

Based on USPHS/CDC, ATS, IDSA and Pediatric "Red Book" guidelines
Adapted to address uniquely Virginia issues
<http://www.cdc.gov/tb/publications/reportsarticles/mmwr/default.htm>



Treatment of TB Disease

Overall goals

- Cure the individual patient
- Minimize transmission within the community

Responsibility for successful treatment is assigned to public health department or private provider, not individual patient.

Health department **ultimately responsible** for ensuring adequate, appropriate treatment.



Legal Authority - Reporting

- TB required to be reported - *Code*, § 32.1-50
 - Suspects and cases!
 - Medical providers, facilities (incl. corrections), and labs
- Regulations for Disease Reporting and Control March 2011

www.vdh.virginia.gov/epidemiology/Regulations.htm



Legal Authority - Subsequent Reporting

- TB reporting not a one time event - *Code*, § 32.1-50
 - Secondary report
 - TB infection results
 - Initial and follow-up CXRs
 - Bacteriologic results
 - Treatment regimen
 - HIV status
 - Any contact screening
 - Subsequent reports
 - Change in status
 - Additional reports
 - Adherence issues
 - Treatment ceases



Legal Authority - Treatment Plans

Treatment Plans - *Code*, § 32.1-50.1

- Subject to approval by local health director (designee)
- Approval required for inpatients
- Disagreements between written treatment plan and established standards of care can be addressed and settled by the Commissioner or designee



Legal Authority - Nursing Actions

- Sputum collection -
 - *Code*, § 54.1-2901. A. 28
- TST placement -
 - *Code*, § 54.1-3408. G.



Legal Authority - Consent

- Consent - A minor deemed as an adult for purpose of consent
“Medical or health services needed to determine the presence of or to treat venereal disease or any infectious or contagious disease that the State Board of Health requires to be reported”
 - Code, § 54.1-2969.E.1



Legal Authority - Nursing Guidelines

TB Specific

- Tuberculosis Case Management
- Tuberculosis Contact Investigation
- Directly Observed Therapy (DOT)
- Management of Individuals with Latent TB Infection

Non-TB Specific

- Delegation to Unlicensed Personnel
- Documentation in the Medical Record
- Approved Abbreviations



Legal Authority - Community Control

- Isolation - Health Department with authority
 - Code, § 32.1-48.02 - also see VA TB Control Laws Guidebook on TB website
 - Regulations, pg. 18-22
- Contact Investigation
 - Code, § 32.1-48.02
 - Regulations, pg. 18



TB Case Management Series

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Questions ?

VDH TB Control: 804-864-7906

www.vdh.virginia.gov/tb