Treatment of TB Disease

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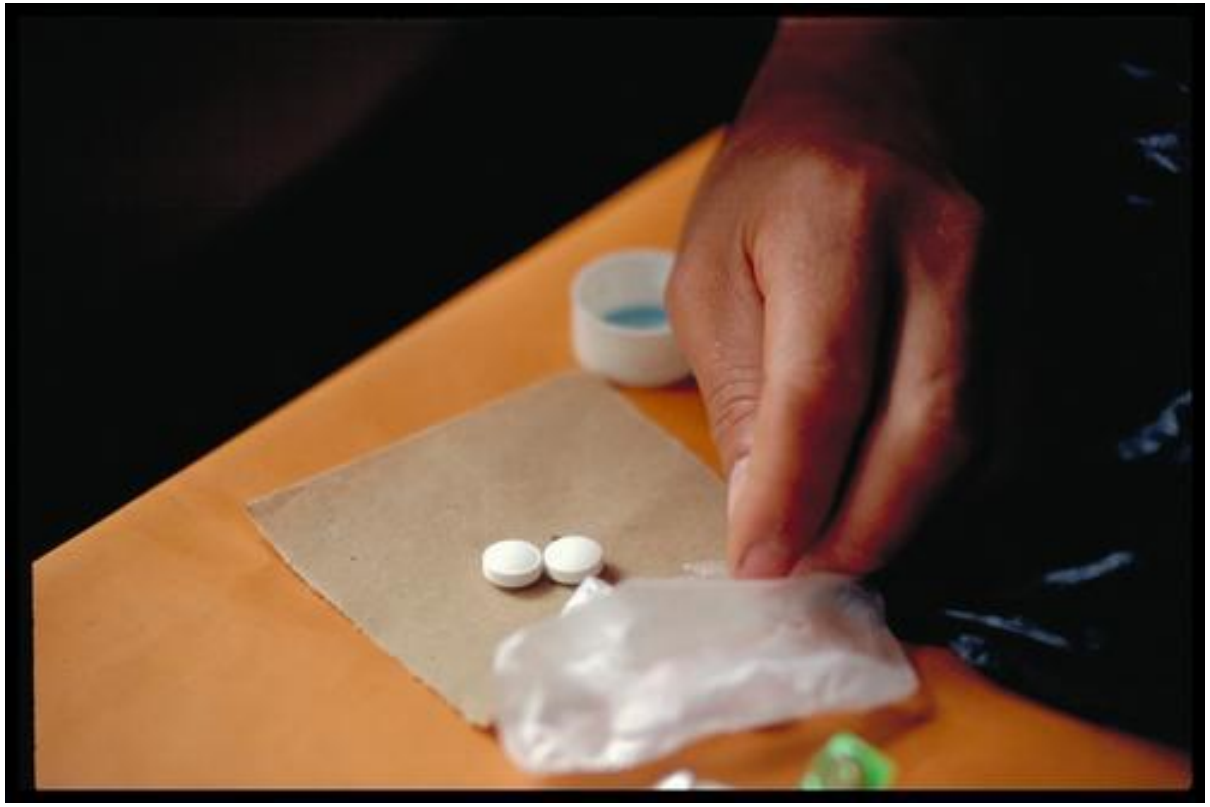
March 22, 2017

Objectives

- Describe the current guidelines for the treatment of TB disease including the newly released CDC guidelines
- Identify the basic principles of drug resistant TB

Treatment of TB Disease
Principles of Therapy



Treatment of Tb Disease

- In order to effect a cure, Tb must be treated with at least *two drugs* to which the organism is *susceptible*
  - Two drugs
    - It is the uncoupling of the drugs leads to drug resistance
  - Susceptibility
    - This is not known when the patient walks into the office
    - It takes time to obtain this information from the laboratory
      - Hours (Xpert testing)
      - Days (MDDR testing)
      - Weeks (Pheontypic testing)

Treatment of Tb Disease

- Current recommendation for initiation of TB treatment:
  - Isoniazid (I or H)
  - Rifampin (R)
  - Pyrazinamide (Z)
  - Ethambutol (E)
- Why do we need four to start if two is curative?

Drug resistance

- Occurs by means of genetic mutations
- The genetic mutations conferring drug resistance will occur spontaneously and randomly in the environment
- These mutations occur at known rates for each of the drugs
- The mutations are independent of each other

Drug Mutations

	Rate of mutation
INH resistance	1/1,000,000
Rifampin resistance	1/100,000,000
Both INH and rifampin resistance	1/100,000,000,000,000

Principle of acquired drug resistance

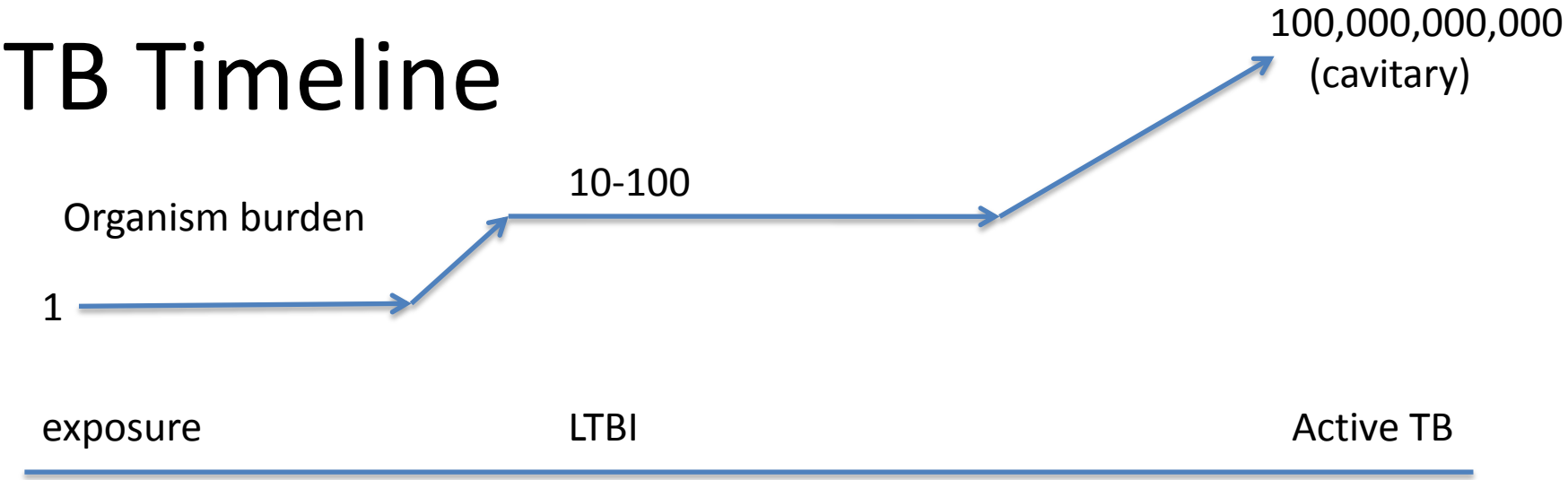
- Drug A kills organisms susceptible to drug A and those resistant to drug B
- Drug B kills organisms susceptible to drug B and those resistant to drug A
- Any organisms that underwent *both* mutations would not be killed by this combination
  - But the probability of one organism undergoing both mutations is small

Organism burden in latent Tb versus cavitary reactivation disease

	Number of organisms present	Number of drugs required
LTBI	Only 10-100	1
Cavitary Tb disease	100,000,000,000	≥2 (start with 4)

We can treat latent Tb infection with only 1 drug (usually isoniazid x 9 months) but we need multiple drugs to treat Tb disease

TB Timeline

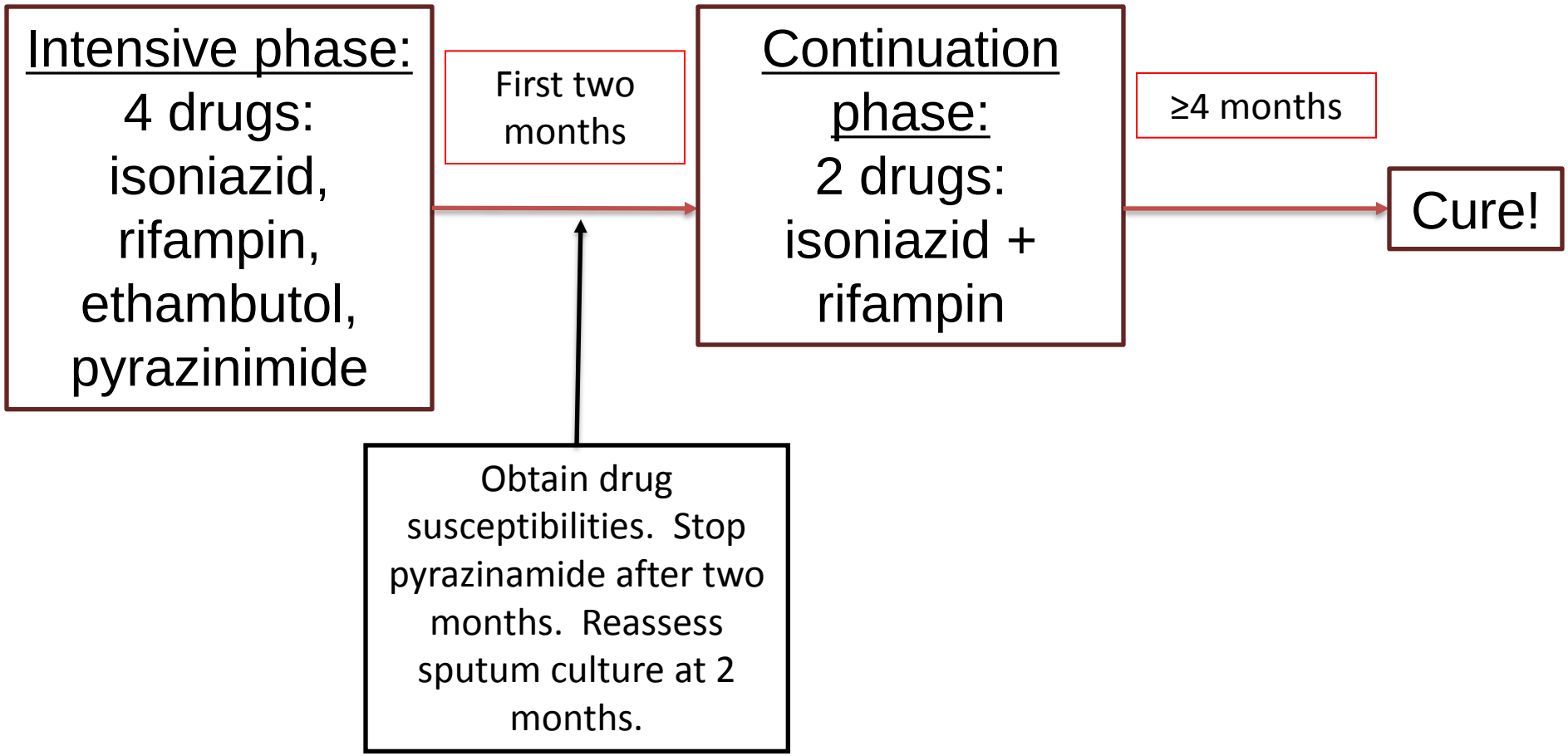


History No testing available	TST IGRA	AFB Smear AFB Culture PCR Based testing Biopsy and Histology
Window Prophylaxis One drug	Primarily one drug regimens (INH or Rifampin) Two drug -12 week- regimen	Initial 4 drug Regimen Tailored if DST available

Exposure to LTBI (test conversion) = 8-10 weeks

LTBI to Active Disease timeline depends on Host Immune System – weeks to years

Treatment


Intensive phase:
4 drugs:
isoniazid,
rifampin,
ethambutol,
pyrazinimide
First two months
Continuation phase:
2 drugs:
isoniazid +
rifampin
≥4 months
Cure!
Obtain drug susceptibilities. Stop pyrazinamide after two months. Reassess sputum culture at 2 months.

The “specialness” of PZA

- PZA does not protect against the emergence of resistance in a companion drug
- It is essential in the first 2 months to allow a short course regiment (BMC trials)

PZA is pH dependent

- Works best in low pH environments – such as in intracellulare lysosomes (where IRE work poorly)
- It does not work well in neutral pH environments such as a cavity or lung parenchyma (where most of the organisms are)
- Compartmentalization of drugs = PZA is not very effective in the lung parenchyma
  - Therefore if the patient was INH Resistant, RX with HRZE is really RX with RZE and the lung is only “seeing” RE (2 effective drugs!)

Definitions

- Primary resistance
  - Resistance appearing on the initial specimen of the patient
- Secondary resistance
  - Resistance that appears during the course of therapy for TB
  - Uncoupling of drugs during the course

Multi Drug Resistant=INH and Rifampin

Primary Drug Resistance

- The latent stage of TB allows the host to carry organisms far from their origin – both in time and in space. A patient may be infected in his youth, but not develop disease for decades
  - Susie is born in Vietnam (where there is significant inh drug resistance)
  - She is infected in childhood
  - Susie moves to USA. At age 50 she becomes ill with TB and infects her friend George
  - George was not found in the contact investigation as he had changed addresses and moved to Rhode Island
  - 2 years later he is ill
  - The history cannot find these links to discover he has INH resistance before his DST returns
  - Thus we start 4 drug regimen until his DST returns
  - This 4 drug regimen prevents emergence of MDR TB in this case
    - If he has INH resistance, his 4 drug regimen means that he is on effective RX with REZ

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Secondary Drug Resistance

- Drug uncoupling has occurred through out the world in multiple ways
  - First treatment regimens were with monotherapy, then sequential addition of monotherapy
  - Patient nonadherence
    - Side effects, misunderstanding, cost
  - Physician nonadherence
    - Lack of recognition of disease
  - Inadvertent nonadherence
    - Malabsoption (DM, HIV, malnutrition)
    - Poor drug formulation

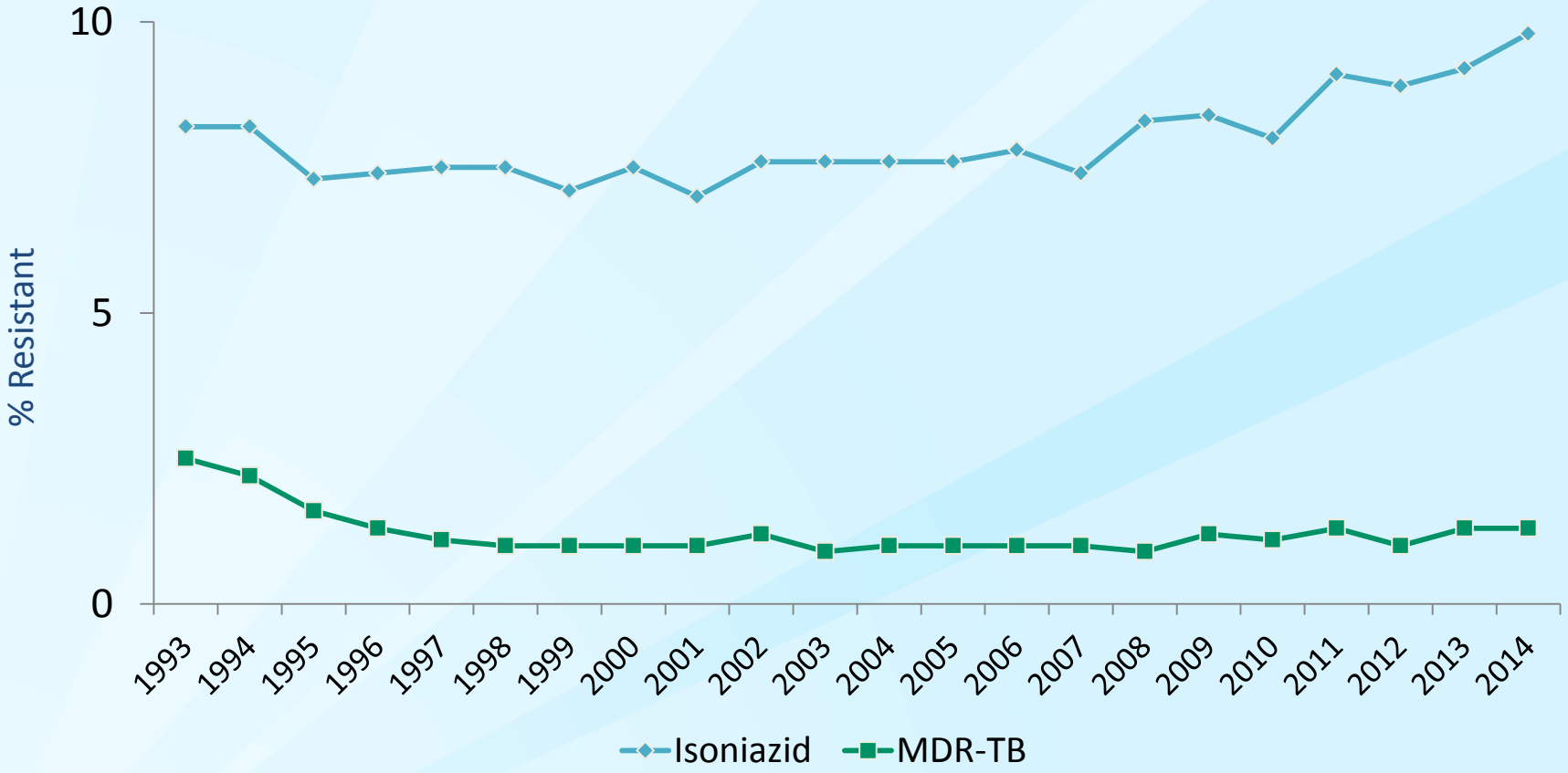
Therapeutic implications

	Length of treatment	# of drugs	Cure rate	
Pansusceptible	6 months	H/R/Z x 2, H/R x 4	99%	
INH resistance	12 months	2 (R/E)	95%	
Rifampin resistance	18 months	2 (H/E)	95%	
INH and Rifampin resistance	18-24 months	4 to include amikacin and a quniolone	70%	Consider surgery
INH, Rifampin plus	24 months after sputum culture conversion	At least 5 to include an injectible	70%	Consider surgery

Treatment: two drugs to which the organism is susceptible

- We do not know this when the patient walks in
- In the past assume susceptible until resistance proven
  - interviewed the patient for risk factors for resistance
- Assume resistance until proven susceptibile
  - Modify the regimen after that is known
  - Begin with 4 drugs in all areas where the rate of INH monoresistance >4%

Primary Anti-TB Drug Resistance, United States, 1993 – 2014*



*Updated as of June 5, 2015.

Note: Based on initial isolates from persons with no prior history of TB. Multidrug resistant TB (MDR TB) is defined as resistance to at least isoniazid and rifampin.

Treatment for Tuberculosis in the 21st Century

- Emphasis on provider/program responsibility
- Focus on individual case management with DOT
- Tailoring treatment regimens to circumstances
- Importance of evaluating response
- Increasingly complicated patients

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Risk Factors for Relapse

Category	Risk Factor	Studies
Microbiological	Colony Count	Hong Kong
	Culture positivity at 2 (or 3) months	East Africa, Hong Kong, Poland, Study 22

Risk Factors for Relapse

Category	**Risk Factor**	**Study**
Demographic	Increasing age	Hong Kong
	White race	Study 22
Clinical	Underweight	Study 22
	Concomitant disease	Poland
Social	Alcohol use	Poland
Radiographic	Extent of disease	Poland, Study22
	Cavitation	East Africa, Poland, Study22

Risk of Relapse (Study22)

Continuation phase, Control, (I/R 2x/wk)

Cavity	**Culture positive at 2 months**	**Culture negative at 2 months**
Yes	21.8%	6.2%
No	5.0%	2.1%

DOTS

- Does not ensure adherence
- Ensures that the physician KNOWS as soon as a patient is not adherent
- DOT- an outreach worker observes each dose to be swallowed
  - Twice or thrice weekly dosing
  - Stop as soon as cure is reached
  - Cure is guaranteed

We know the drugs, but….

- Adherence
- Adherence
- Adherence
- Adherence
- Adherence
- DOT – Directly Observed Therapy

Adherence

- Not determined by socioeconomic status, education status, severity of illness
  - Accuracy in predicting adherence 50%
- Only accurate predictors of non-adherence are untreated mental illness and active drug abuse
- Adherence is a major barrier to Tb care
  - Long treatment regimens (at minimum 6 months)
  - Patients feel better long before cure completed.

DOT-Directly Observed Therapy

- Does *not* ensure adherence
- Ensures that the physician *KNOWS* as soon as a patient is not adherent
- DOT- an outreach worker observes each dose to be swallowed
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Fundamental Responsibility and Approach

- The *provider* (or *program*) is responsible for prescribing an appropriate regimen **AND** ensuring that treatment is completed successfully
- *Direct observation of treatment* (DOT) with individualized *case-management* is the approach of choice

Components of Patient Centered Care

Table 4. Possible Components of a Multifaceted, Patient-Centered Treatment Strategy

Enablers	Incentives
Interventions to assist the patient in completing therapy [130]	Interventions to motivate the patient, tailored to individual patient wishes and needs and, thus, meaningful to the patient [130]
Transportation vouchers [30]	Food stamps or snacks and meals [30]
Convenient clinic hours and locations [30]	Restaurant and grocery store coupons [30]
Clinic personnel who speak the languages of the populations served [428]	Assistance in finding or provision of housing [429]
Reminder systems and follow-up of missed appointments [28]	Clothing or other personal products [30]
Social service assistance (referrals for substance abuse treatment and counseling, housing, and other services) [429]	Books [428]
Outreach workers (bilingual/bicultural as needed; can provide many services related to maintaining patient adherence, including provision of directly observed therapy, follow-up on missed appointments, monthly monitoring, transportation, sputum collection, social service assistance, and educational reinforcement) [428]	Stipends [30]
Integration of care for tuberculosis with care for other conditions [428]	Patient contract [30]

Initiation of Therapy

- Often is based on high index of suspicion
  - Do not delay treatment waiting for smear and culture results, especially in ill patients
  - Absence of AFB on smear or granulomas on biopsy does not rule out tuberculosis, nor does negative TB culture
  - A positive TST is only supportive, may be negative in 25% of cases

Drugs in Current Use

First-line

Isoniazid (INH)
Ethambutol (EMB)
Rifampin (RIF)
Rifabutin* (RBT)
Rifapentine (RPT)
Pyrazinamide (PZA)

Second-line

Cycloserine
Levofloxacin*
Ethionamide
Moxifloxacin*
p-Aminosalicylic acid (PAS)
(Gatifloxacin*)
Amikacin/Kanamycin*
Capreomycin
Streptomycin (SM)

xxx-line

Bedaquiline

***Not approved by FDA for use in tuberculosis*

2016

Roles of "Newer" Agents

- **Rifabutin:** May be used as a primary drug for patients receiving medications having unacceptable interactions with rifampin, especially for patients with HIV infection

- **Rifapentine:** May be used as a primary drug *by DOT* in a twice-weekly initial phase (FDA 2010) and once-weekly continuation phase for highly-selected (HIV-neg) patients; prevention (FDA 2015)

- **Levofloxacin, Moxifloxacin (Gatifloxacin – *not in US*):** Oral agents that can be used when first line drugs are not tolerated or the organism is resistant

Bedaquiline (TMC 207)

- Accelerated FDA approval, November 2012
  - 2 studies involving a total of 440 patients with MDR-TB: time to culture conversion
  - Safety concerns
- Unique mechanism
  - ATP synthase proton pump inhibitor
- Indication
  - as part of combination therapy for the treatment of MDR pulmonary TB in adults
- Phase 3 trial planned for 2013
  - double-blind study: 9 months bedaquiline *versus* placebo, with background regimen

Sirturo® Janssen Therapeutics

Treatment of Culture-positive Pulmonary Tuberculosis

General Conclusions from the Literature

- 6 months (26 wks) is the minimum duration of treatment
- 6 month regimens require a rifamycin throughout and PZA for the first 2 months
- 6 month regimens are effective without INH

Treatment of Culture-positive Pulmonary Tuberculosis

General Conclusions from the Literature

- Without PZA minimum duration is 9 months (39 wks)
  - Without RIF, minimum duration is 12 months (up to 18+ mos)
  - SM and EMB are approximately equivalent in effect

Drug Susceptible TB Drug Regimens

Table 2. Drug Regimens for Microbiologically Confirmed Pulmonary Tuberculosis Caused by Drug-Susceptible Organisms

	Intensive Phase		Continuation Phase				
Regimen	Drug[a]	Interval and Dose[b] (Minimum Duration)	Drugs	Interval and Dose[b,c] (Minimum Duration)	Range of Total Doses	Comments[c,d]	Regimen Effectiveness
1	INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	7 d/wk for 126 doses (18 wk), or 5 d/wk for 90 doses (18 wk)	182–130	This is the preferred regimen for patients with newly diagnosed pulmonary tuberculosis.	Greater
2	INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	110–94	Preferred alternative regimen in situations in which more frequent DOT during continuation phase is difficult to achieve.	
3	INH RIF PZA EMB	3 times weekly for 24 doses (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	78	Use regimen with caution in patients with HIV and/or cavitary disease. Missed doses can lead to treatment failure, relapse, and acquired drug resistance.	
4	INH RIF PZA EMB	7 d/wk for 14 doses then twice weekly for 12 doses[e]	INH RIF	Twice weekly for 36 doses (18 wk)	62	Do not use twice-weekly regimens in HIV-infected patients or patients with smear-positive and/or cavitary disease. If doses are missed, then therapy is equivalent to once weekly, which is inferior.	Lesser

Treatment of Culture-positive Pulmonary Tuberculosis

Regimens Rated A-I *(HIV Uninfected)*

2 mos - I, R, Z, E daily (56 doses, 8 wks) **then**

4 mos - I, R daily (126 doses, 18 wks) **or**

4 mos - I, R 2X / wk (36 doses, 18 wks)

Continuation phase increased to 7 months if initial film shows cavities and sputum is culture-positive at completion of 2 months of treatment.

CDC 2003 ,2016

Tailoring Tuberculosis Treatment Regimens

Rationale for Extending Treatment by 3 Mos

- Continuation of PZA for additional 2 months does not improve outcome
- Prolongation of continuation phase by 2 months decreased relapses in silicotuberculosis from 20% to 3%

Risk Factors for Relapse: Study 22

Continuation Phase, Control (*I/R Twice weekly*)

Cavity	Culture Positive at 2 Mos	
	Yes	No
Yes	**21.8%**	6.2%
No	5.0%	**2.1%**

Tuberculosis Trials Consortium. Lancet. 2002; 360

Sputum Monitoring

Simply Stated

- Obtain sputum every month until culture-negative for at least 2 consecutive months
- For those with *either* delayed culture conversion (beyond 2 months) *or* cavitation on plain CXR, clinicians may extend treatment to 9 months, although 6 mos is acceptable
- For those with *both* cavitation and delayed culture conversion, 9 months is recommended
- Patients with sputum cultures that remain positive at 3 months require further investigation

Preventing Complications: *Drug Selection and Dosing*

- Select individual treatment regimen based on individual risk factors for toxicity, clinical, and life conditions
  - Understand specific toxicities of TB medications
    - *e.g.,* Avoid hepatotoxic medications in patients with active hepatitis
  - Tailor regimen to accommodate lifestyle of patient
    - Case management-DOT → SAT?
- Adjust doses of specific drugs as necessary
  - Use weight-based dosing
  - Reduce doses of specific drugs if metabolism is impaired
    - *e.g.,* Increase dosing interval of EMB in renal failure (3x/wk, with dialysis)
  - Consider drug level testing/monitoring in specific circumstances
    - Malabsorption ?

Table 3. Doses[a] of Antituberculosis Drugs for Adults and Children[b]

Drug	Preparation	Population	Daily	Once-Weekly	Twice-Weekly	Thrice-Weekly
First-line drugs						
Isoniazid	Tablets (50 mg, 100 mg, 300 mg); elixir (50 mg/5 mL); aqueous solution (100 mg/mL) for intravenous or intramuscular injection. Note: Pyridoxine (vitamin B6), 25–50 mg/day, is given with INH to all persons at risk of neuropathy (eg, pregnant women; breastfeeding infants; persons with HIV; patients with diabetes, alcoholism, malnutrition, or chronic renal failure; or patients with advanced age). For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100 mg/d.	Adults	5 mg/kg (typically 300 mg)	15 mg/kg (typically 900 mg)	15 mg/kg (typically 900 mg)	15 mg/kg (typically 900 mg)
		Children	10–15 mg/kg	. . .	20–30 mg/kg	. . .[b]
Rifampin	Capsule (150 mg, 300 mg). Powder may be suspended for oral administration. Aqueous solution for intravenous injection.	Adults[c]	10 mg/kg (typically 600 mg)	. . .	10 mg/kg (typically 600 mg)	10 mg/kg (typically 600 mg)
		Children	10–20 mg/kg	. . .	10–20 mg/kg	. . .[b]
Rifabutin	Capsule (150 mg)	Adults[d]	5 mg/kg (typically 300 mg)	. . .	Not recommended	Not recommended
		Children	Appropriate dosing for children is unknown. Estimated at 5 mg/kg.			
Rifapentine	Tablet (150 mg film coated)	Adults		10–20 mg/kg[e]	. . .	. . .
		Children	Active tuberculosis: for children ≥12 y of age, same dosing as for adults, administered once weekly. Rifapentine is not FDA-approved for treatment of active tuberculosis in children <12 y of age.			
Pyrazinamide	Tablet (500 mg scored)	Adults	See Table 10	. . .	See Table 10	See Table 10
		Children	35 (30–40) mg/kg	. . .	50 mg/kg	. . .[b]
Ethambutol	Tablet (100 mg; 400 mg)	Adults	See Table 11	. . .	See Table 11	See Table 11
		Children[f]	20 (15–25) mg/kg	. . .	50 mg/kg	. . .[b]

Baseline Evaluations

- Collect appropriate specimens for microscopy and culture
  - 3 sputum samples, *8-24 hr apart*
  - Sputum induction or bronchoscopy
- Perform susceptibility testing for INH, Rif, EMB on an initial positive culture (each site of disease)
- Perform HIV counseling and testing for **all** patients/suspects
  - CD4,viral load if HIV-positive

Monitoring for Drug Toxicity

- At baseline
  - ALT, bilirubin, alkaline phosphatase, serum creatinine, and platelet count
  - Eye examination (V_a, color*) for all patients receiving EMB
  - Education
  - Education!
- At least MONTHLY
  - Clinical evaluations usually are sufficient, *unless* abnormal baseline values are found or other risk factors for toxicity exist
    - *e.g.,* Risk factors for hepatitis: chronic hepatitis (hep. C), use of hepatotoxic drugs (including acetaminophen, EtOH, ?lipid lowering drugs), age (>35), postpartum, young black or Hispanic women
  - Eye examinations (EMB) – monthly testing of V_a and color* is recommended for patients receiving EMB >15-20 mg/kg/d and if on drug for >2 mos.
- For second and third-line medications, seek expert consultation

* Ishihara Color Testing plates

CDC/ATS/IDSA. MMWR 6/03

Response to Treatment

- May be rapid (days)
  - Signs/symptoms
- Weight gain is an excellent early marker of effective treatment.
- Expect > 90% sputum culture conversion by 3 months
  - If slow conversion – evaluate and consider longer treatment
- Allow return to home/work environment based on individual considerations
  - Infectiousness of case
    look for clinical response, declining organisms on smear
  - Risk of others becoming infected (contacts)

Follow-up Evaluations

- For pulmonary TB
  - Sputum smear/culture *monthly* until 2 consecutive samples are culture negative
    - Repeat drug susceptibility testing, other investigations, if culture-positive still at 3 months
  - If initial culture positive - consider repeat CXR at 2 mos, and get CXR at completion of therapy
  - If initial culture negative – perform 2 mos CXR to assess response; CXR at completion of therapy
- For extrapulmonary TB
  - Frequency and types of evaluations depend on site

Clinical Hepatitis in Persons Taking INH and Rif

Drug	Studies	Patients	% Clinical Hepatitis
INH	6	38,257	0.6
INH + other drugs (*NOT* Rif)	10	2,053	1.6
INH + Rif	19	6,155	2.7
Rif + other drugs (*NOT* INH)	5	1,264	1.1

Steele, *et. al*. Chest 99: 465 – 471, 1991

Serum Drug Level Monitoring

- Useful in selected circumstances
  - *e.g.,* inadequate response to treatment, severe disease where malabsorption is questioned
- Helps determine therapeutic concentrations
  - Allows adjustments for variable drug absorptions
- Documents adherence to treatment
- May reduce toxicities

Serum Drug Level Monitoring

- Aminoglycosides
  - To reduce toxicity, achieve therapeutic levels
  - In-house (Amikacin) *vs* send-out (Kanamycin)
- Ethambutol
  - May be useful in renal insufficiency to reduce toxicity
- Rifampin
  - To determine malabsorption (*e.g.* in severe HIV)
- Cycloserine
  - To determine therapeutic levels

Legal Considerations

- Throughout the US, there are quarantine laws to protect the public
- Slight variability between states
- RI: Intention to Cure Law
  - All other measures must have been tried and have been documented to fail
- Most patients want to be well. The challenge is finding out the why of what they are doing to fix the peripheral issues that are hindering compliance.

Completion of Therapy

- Completion of treatment primarily defined by number of ingested doses within specified time frame (not solely on duration of therapy)
- For example:
    1. 6-month daily regimen (7 days/wk) = at least 182 doses of INH and RIF, and 56 doses of PZA
    2. 6-month daily regimen (5 days/wk) = at least 130 doses

Completion of Therapy

- In cases of drug toxicity or non-adherence to regimen, all specified number of doses must be administered within:
  - 3 months for initial phase
  - 6 months for 4-month continuation phase
- If the specified number of doses is not administered within the targeted time period, patient is considered to have interrupted therapy

Therapy Deviations

- Treatment interruptions: Significance varies with
  - Bacillary load at time of interruption
  - Time in course when interruption occurred (initial or continuation phase)
  - Duration and intermittency of interruption
- Split dosing of first line agents
  - Lowers peak serum concentrations – may encourage emergence of resistance

Management of Treatment interruptions

Table 6. Management of Treatment Interruptions[a]

Time Point of Interruption	Details of Interruption	Approach
During intensive phase	Lapse is <14 d in duration	Continue treatment to complete planned total number of doses (as long as all doses are completed within 3 mo)
	Lapse is ≥14 d in duration	Restart treatment from the beginning
During continuation phase	Received ≥80% of doses and sputum was AFB smear negative on initial testing	Further therapy may not be necessary
	Received ≥80% of doses and sputum was AFB smear positive on initial testing	Continue therapy until all doses are completed
	Received <80% of doses and accumulative lapse is <3 mo in duration	Continue therapy until all doses are completed (full course), unless consecutive lapse is >2 mo If treatment cannot be completed within recommended time frame for regimen, restart therapy from the beginning (ie, restart intensive phase, to be followed by continuation phase)[b]
	Received <80% of doses and lapse is ≥3 mo in duration	Restart therapy from the beginning, new intensive and continuation phases (ie, restart intensive phase, to be followed by continuation phase)

Clin Infect Dis. (2016)doi: 10.1093/cid/ciw376First published online: August 10, 2016

Renal Disease

- Consider increasing dosing interval of renally excreted anti-TB drugs (rather than lower dose) if Creatinine clearance decreased (<30ml/min)
  - EMB, PZA, Fqn, aminoglycosides, Capreo, CS
- Consult experts for dosing of patients on dialysis
  - No adjustment for INH & RIF
  - Lengthen interval for EMB & PZA (generally 3x/wk, following dialysis)

CDC: Treatment of Tuberculosis, 2016 *Table 12*

Fluoroquinolones and Drug-Resistant TB

- Use of a fluoroquinolone-class drug alone in patients with *unsuspected tuberculosis* has been shown to delay diagnosis and induce resistance to this class of drug (Wang, Thorax, 2006; Ginsberg, NEJM, 2003; Ginsberg, CID, 2003)
  - *Potential contribution to XDR*
- Up to 1/3 of patients with pulmonary TB will have "atypical" radiographic presentations
- TB risk history should be performed before empiric use of these drugs is initiated for CAP
  - *Persons at-risk for TB should not be treated with fluoroquinolone empirically*
  - *EDUCATE YOUR COLLEAGUES !!!*

IDSA / ATS: *Empirical Antibiotics for Community Acquired Pneumonia*

- Outpatient
  - 1. Previously healthy and no use of antimicrobials within the previous 3 months
    - A macrolide (strong recommendation; level I evidence)
    - Doxycycline (weak recommendation; level III evidence)
  - 2. Presence of comorbidities such as chronic heart, lung, liver or renal disease; diabetes mellitus; alcoholism; malignancies; asplenia; immunosuppressing conditions or use of immunosuppressing drugs; or use of antimicrobials withinthe previous 3 months (in which case an alternative from a different class should be selected)
    - A respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin [750 mg]) (strong recommendation; level I evidence)
    - A b-lactam **plus** a macrolide (strong recommendation; level I evidence)
- Inpatients, non-ICU
  - A respiratory fluoroquinolone (strong recommendation; level I evidence)
- Inpatients, ICU
  - b-lactam + azithromycin or respiratory fluoroquinolone

From *Table 7:* CID. 44 (suppl. 2), 2007

Summary

- Patient-centered case management is standard of care
- When prescribing treatment:
  - Use preferred regimens
  - Extend treatment for cavitation and/or + sputum cultures at 2 mos
    - Consider extension in other patient specific instances
  - Calculate # doses within prescribed time frame
  - Use DOT as a tool to ensure treatment adherence
- Special situations
  - Be mindful of additional guidelines for pregnant or breastfeeding women, HIV (+) persons, patients with renal or liver disease

Official American Thoracic Society /Center for Disease Control/IDSA Clinical Practice Guidelines for Management of Drug Susceptible TB

Clinical Infectious Disease

Advanced Access Published on web August 10,2016

http://cid.oxfordjournals.org/content/early/2016/07/20/cid.ciw376

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Will you join us?

Stop TB Partnership www.stoptb.org

The Union www.theunion.org

Join today!