

Complex TB Cases – The Triathlon



TB Nurse Case Management
Session 5
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2013



Objectives

Participants will:

- be able to identify situations that may require treatment regimens different than the standard 4-drug regimens.
- be able to state circumstances that may change the presentation of TB disease.
- recognize when additional assessment is needed for failure to clinically improve, or when clinical condition declines.
- identify when to initiate interventions utilizing options in the "TB Control Law Guidebook", based on state code and regulation.



Baby J

Case 1

Resources

MMWR
Morbidity and Mortality Weekly Report

PEDIATRIC TB
RADIOLOGY

RED BOOK

Pediatric Tuberculosis
Aron M. Loeffler, MD
Pediatric TB Consultant
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May 23 - Memorial day weekend

The phone rings, it's 1:30 PM

- A local pediatrician office calls to inform you of TB infection in an 8 month old infant. The TST is 7mm

What sort of questions you would ask?

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Discussion

- Why was the TST done?
- Is there any risk of being infected?
- Is the baby healthy? Does the baby have symptoms?
- What is the doctor's plan?
- Do you need assistance with providing treatment?
- Is this TB infection or TB disease?
- Has a CXR been done, and if so, what are the results?
- Collect demographics

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May 23 - Memorial day is this weekend

15 minutes later
The phone rings, it's 2 PM

- As soon as you hang up the phone you receive a call from the mother of baby J
- She is worried about baby J and has questions about TB

What sort of questions you would ask?
What are the teaching points?



Discussion

Emphasize the importance of asking questions and digging deeper

- Answer the mother's questions first
- How has baby J has been feeling lately?
- Why did the baby go to the doctor?
- Ask about the family. Is there anyone else in the house who is ill?
- Is the baby adopted or foreign born?
- Teach about the difference between TB and LTBI
- Plan to keep in touch



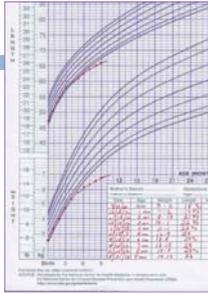
Going back in time to May 20th



Now for the rest of the story

Baby J status/ 8 mos old

- Delayed Growth
- Unable to roll over
- Lethargic/ listless
- Not interested in play
- Low grade fevers
- Persistent weak cough
- Supraclavicular adenopathy
- Lymphadenopathy is the most common clinical sign in pediatric patients



Baby J/ Visit to pediatrician/ May 20, 2013

- Inspiratory wheezing, upper and mid lung
- Initial diagnosis: r/o bacterial pneumonia
- Treatment: Bactrim pediatric
- TST placed
- CXR today, CT if indicated
- Scheduled I&D of lymph node in two days
- Atypical infections, such as *M. bovis* can look identical to *M. tb*



Findings - May 22, 2013

- CXR done – Hilar lymphadenopathy
- PPD read: 4mm (theoretically negative)
- Not feeding
- I & D: results pending, gram stain and AFB ordered
- Infant increasingly lethargic – stat head CT ordered
- Hospitalized

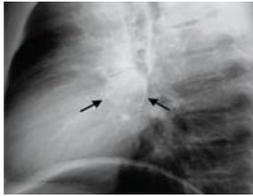


Imaging – Chest: PA and lateral

CXR: PA view
Hilar lymphadenopathy.



CXR: Lateral view
Rounded lymph node



Do a PA and lateral film for pediatric patients to get a better view of the hilar lymph node





Miliary Pattern

Imaging – Head CT or MRI

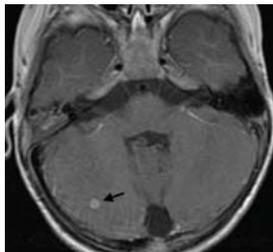
Tuberculoma is most common form of localized disease

Ring Enhancing lesions

Cerebral Hemisphere most common site

Asymmetrical Vascular Enhancement

Usually 2 – 6 months after infection and most common in children under 2 yrs of age





Would your approach be different now?

Be more aggressive and dig deeper

- Is treatment being started?
- How long has the baby been ill?
- What has the mother told you?
- Request medical records
- Do a home visit. The source of a young child's illness is likely in the home, over 75% are.

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Diagnostic Challenges

- Otherwise healthy infants
 - Known contact with an adult case of TB
 - Positive TST
 - Suggestive signs on a chest x-ray
- 'Typical' TB symptoms are often not present
 - Change in behavior
 - Failure to thrive (growth delay)
 - Unexplained lymphadenopathy (firm, nontender)
 - Shallow, weak, dry cough (children are poor TB transmitters)
 - They often do not improve long term with 'common' antibiotics
- Age is the most important risk factor for progression to disease



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Risk of progression to TB disease in untreated pediatric patients with LTBI

- The lung focus may resolve without detection in primary disease
- The CXR appearance of primary TB typically includes enlargement of regional lymph nodes
- Lymphohematogenous spread is typical and can result in disseminated disease

Age of infection	Risk of TB disease
Birth – 12 months	43 - 50%
1 – 5 years	20 – 25%
6 – 10 years	2%
11 – 15 years	16%



Proving TB disease with a + *M.tb* culture

- Sputum
 - Generally better yield than Gastric Aspirates (GA)
 - Difficult for those under 5 years, limited experience with induction
 - Induced sputum (IS) can be attempted if no active cough
 - Consider albuterol for 5 minutes
 - 15 minute induction with 5% hypertonic solution
 - Wheezing, Vomiting
 - Increased coughing, Epistaxis
- Often move forward without culture confirmation if
 - Abnormal CXR, TST +, and if reported as a known contact to TB (classic diagnostic picture for suspicion of TB in pediatric patients)



Proving TB disease with a + *M.tb* culture

- Gastric Aspirate
 - Hospitalization generally required over three days
 - Early morning
 - NG tube inserted upon waking
 - Invasive and frightening
 - Expensive
 - Study 2005 – compared yield between IS and GA
 - 3 GA = one IS (64-66%)
 - 3 IS yield much better results (87%)

Bottom Line – IS have better yield than GA



Baby J family/ Today is 5/24/13

- Born in the United States, September 13, 2012
- January 2012 - Parents arrive from Libya
 - TB evaluation upon entrance, both IGRA positive
 - Mother: CXR nodular densities LLL (stable), asymptomatic sputum X3 smear and culture negative, INH 6 months
 - Father: CXR negative, asymptomatic, INH 9 months
- Maternal grandmother arrives in U.S. late July 2012
 - No medical evaluation – Visitors visa
 - Overstays visa



From a public health perspective....

- Is this a source or contact investigation?
- What level priority is it? Not as high as a smear positive, culture positive case
- What are your first steps?
 - Thorough s/s review of immediate family
 - Always be suspicious of those you don't 'see' present at the time of the visit
 - Grandmother was the source case



Case management challenges

- Treatment regimen
- DOT
- Assessing for side effects
- Allaying fear and suspicion
- Observing and documenting improvement



Treatment Regimens and DOT

- RIPE
 - ▣ Normally well tolerated
 - ▣ May exclude EMB if resistance is not a concern
 - ▣ Give 1 hour before or 2 hours after a meal
 - ▣ Do monthly weights and adjust dosages as weight changes
 - ▣ Crush as fine as possible before mixing
 - ▣ Don't mix ahead of time
 - ▣ Expect to change strategies frequently



Rifampin and Isoniazid

- ▣ Rifampin
 - Mix thoroughly in very small amount of food
 - 150 mg capsule
 - RIF suspension is stable 4 weeks, shake before using, not refrigerated, capsules are preferred
 - 600 mg reconstituted in 10ml of sterile water for infusion
- ▣ INH
 - Rarely requires B6, unless breastfed
 - 100 mg tablet
 - INH solution, 50mg/5ml, not refrigerated; can cause gastric upset, crushed tablets are preferred
 - INH 100mg/ml for infusion



Pyrazinamide and Ethambutol

- ▣ Pyrazinamide
 - ▣ Crushed tablets only
 - ▣ Lower frequency of side effects than with adults
- ▣ Ethambutol
 - ▣ No widely standardized test available to test visual acuity
 - ▣ Weigh risk/benefit for use
 - ▣ Be alert for changes in developmentally appropriate visual response



Allaying fear and suspicion



Mr. S

Case 2

Resource



Mr. S, 32 yr., from Vietnam, IT employee

- Single, multiple sexual partners
- Past substance abuse, current alcohol use
- PCP seen for
 - Weight loss, 17 lbs. in 2 months
 - Fever, 99° to 101° F
 - Nagging cough, productive in A.M.
- Chest x-ray abnormal, not consistent with TB (RLL infiltrate)
- Treated with 10 days of levoquin
- Return in 2 1/2 weeks scheduled



Return visit to PCP 6 weeks later

- Respiratory symptoms improve x 6 weeks, then recur
- Returns to PCP
- Phlegm now blood streaked
- Repeat chest x-ray unchanged
- Respiratory culture with gram stain collected
- Azithromycin prescribed
- Told to call if symptoms don't improve



2 Weeks Later

- Cough persists
- Calls to PCP
- Office visit
 - Gram stain/respiratory culture negative
- Referred to a pulmonologist
- Appointment scheduled 1 month later



At the pulmonologist...

- Symptoms
 - Worsening cough
 - Fevers
 - Continued weight loss; 3 more lbs
 - Decreased appetite
 - Night sweats
 - Missing days at work
- MD looks at 2 prior chest x-rays and orders a CT scan
- Client refuses bronch due to fear and poor insurance
- Referral to health dept. as TB suspect



Call to refer to health department

- When do you plan to see the client? Within 3 days, or that day.
 - TB risk assessment, get medical record, sputum for AFB, explain role of the HD, discuss infection control measures
- What are the additional tests needed? HIV, TST, CXR?
- What other risk factors do you think the client might have? HIV?
- The client is worried about his poor insurance coverage; what do you tell him about potential charges? Don't worry about anything; eligibility will be done and a sliding scale applied.



Discussion

- See ASAP – this looks like TB! Contact same day; see in 1-3 business days per nursing guidelines for TB case management
- Get demographic/contact information
- Explain health department role
- Encourage to stay home
- TB risk assessment
- Arrange testing
 - Sputa x 3 for AFB and culture, etc.
 - HIV
 - TST or IGRA
 - LFTs because of current alcohol use
 - Chest x-ray (obtain prior films)
- Obtain medical records
- Who are the sexual partners?
- No charge for evaluation of TB suspects or contacts per Code of Virginia and Eligibility Guidelines



Visit with client the next day

- Take everything needed
- TST / IGRA done
- Sputa collected
- Weighed – 140 lbs
- History completed
 - Identify past heroin use
 - Identify sexual preference, MSM, name of partners unknown
 - Gay bar rendezvous weekly
- TB education done
- HIV drawn



Results – 2 days later

- 1st smear 1+
- TST negative/0 mm
- Chest x-ray with ground glass appearance throughout lung fields; RLL infiltrate resolved
- Results sent to pulmonologist and office called/message left
- Co-worker suggests an IGRA, given Hx of BCG



Discussion

- What does the 0 mm TST reveal?
 - TST might only reflect poor immune function
- Is this chest x-ray improved?
 - no
- Is this chest x-ray consistent with TB?
 - For immune suppressed, yes
- Would an IGRA be a good idea?
 - No, all signs point to immunosuppression (chest x-ray, TST, risk factors for HIV)



Additional information and orders

- Subsequent 2 sputa
 - Smear negative and +/-
- MTD positive
- Pulmonologist returns call after MTD positive results faxed
 - TB meds ordered
 - INH 300 mg po daily
 - RIF 600 mg po daily
 - PZA 1500 mg po daily
 - EMB 1000 mg po daily



Any comments?

- What should be in the discussion with the pulmonologist?



Discussion

- Dosing of EMB; EMB dosing corrected to 1200 mg po daily
- Share risk factors for HIV, and that results are pending
- Ask what the MD has told the client
- Isolation needed
- Negotiate treatment plan / who will do what?
 - Clinical evaluations
 - Labs – baseline and ongoing
 - Sputa
 - Assure HIV done if not previously performed
- Advise of HD services
 - DOT (no order needed/don't need to ask unless medical Hx → concern)
 - Vision monitoring
 - Home isolation
 - Contact investigation



HIV results positive



Resources



Section: Mycobacterium Tuberculosis Disease with HIV Coinfection; Page J 12- J 18



How will case-management change?

- What other resources would be helpful?
- How do you tell the client of HIV results?
- Is there a change needed in the TB regimen?



Discussion

- Resources
 - HIV/STD program
 - DIS
 - For visit with TB PHN to share results with client
 - For HIV contact investigation/partner notification
 - Eventually for ADAP program
- Connect to ID clinic at local teaching hospital
- No change in treatment now/not on ART



HIV management

- Client with appointment in ID clinic in 2 weeks
- CD4, viral load and other related tests planned for this week
- Because of the delay in ID appt. the PCP questions starting ART now
- All other case management activities continue



Discussion

- ART should wait until HIV labs are known; the timing of start of ART depends on client evaluation and HIV labs, especially the CD4 count



ART in the management of TB disease

- Complicated by
 - ▣ ART interactions with rifamycins, especially
 - Protease inhibitors (PI)
 - Non-nucleoside reverse transcriptase inhibitors (NNRTI)
 - ▣ Overlapping toxicities
 - ▣ Review of other medication interactions complex
- Rifabutin usually substituted for rifampin
- Review with TB Medical Consultant



IRIS - Immune Reconstitution Syndrome

- IRD – Immune Restoration Disease
- After ART is started there may be an exuberant immune system response to TB bacilli
 - ▣ Paradoxical reaction - Worsening of clinical symptoms of TB
 - ▣ Unmasking – Initial clinical symptoms related to TB
- Predictors of IRIS
 - ▣ More common with CD4 <50 and high viral load
 - ▣ Improvement of CD4 and viral load once ART is initiated
 - ▣ IF ART is initiated less than 30 days after TB treatment began
 - ▣ High burden of TB disease
- Explains the importance of ruling out TB before HIV treatment is initiated



Symptoms of IRIS



- Within 3 months of starting ART
- Initial TB symptoms worsen
 - ▣ Large adenopathies, including abdominal
 - ▣ Cold Abscess
 - ▣ Return of night sweats, fever, poor appetite
 - ▣ Worsening CXR with new or worsening respiratory symptoms, cavity formation
 - ▣ New or worsening CNS
 - ▣ Miliary TB with large nodules
 - ▣ Sputa remain negative if conversion has occurred



Treatment

Do Not Stop TB or ART meds

- Corticosteroids
- NSAIDS
- Drainage?
- Additional interventions dependent upon site involved
- Can be life threatening



Client states “you’re killing me”

- Client refuses all medication
- What do you tell the client?
- How do you discuss the refusal?
- Stops being available for DOT



Discussion

- Review Sx
- Give opportunity to vent
- Education; re: IRIS, signifies an immune system being restored
- Discuss options
 - TB drugs not negotiable
 - Encourage
 - Offer some hope; 2 TB drugs can be stopped after 8 weeks
- Work with ID clinic
 - Discuss options for side effects
 - Treatment of IRIS
 - Collaborate with HIV case manager to assure consistent message



Client no longer available for DOT

- Three doses of DOT missed
- Refuses to provide sputa
- Also not adhering to home isolation
- What can be done?



Discussion

- Talk with the client
 - ▣ Address concerns
 - ▣ Reinforce need for isolation, potential for drug resistance
 - ▣ Review agreements that were signed (DOT and Isolation)
 - ▣ Document, document, document
- Code of Virginia
- TB Law Guidebook – letter templates available
 - ▣ Counseling Order Letter
 - ▣ Examination Request Letter
 - ▣ Outpatient treatment Order
 - ▣ Emergency Detention Order
- Work with health director and TB Control Program



Contact investigation unfolds...

- IT workplace; 300 employees
- Gay bar weekly
 - ▣ Multiple partners
 - ▣ One regular weekly partner – only nickname is known
- Hookah bar weekly – the Crystal Cathedral



Discussion

- How to approach contact investigation in uncomfortable or unsafe places
 - ▣ Partnership with DIS or Community Based Organizations
 - ▣ Approach management/evaluate each setting
 - Provide education
 - Get their input on how to best reach regular customers
 - ▣ Prioritize the locations and the people at those places
 - Attempt to identify any symptomatic
- TB elimination will require reaching out to non-traditional sites of transmission



The Outcome

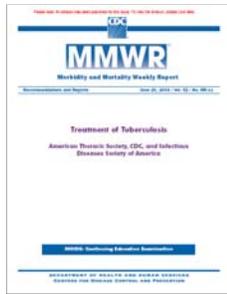
- A counseling letter is delivered
- Face to face counseling preferable, or mail to last known address
- Consider certified mail and regular delivery together
- Client returns to treatment after 1 week missed therapy
- Rest of treatment course uneventful
 - ▣ IRIS resolved
 - ▣ Treated for 26 weeks
 - ▣ Contact investigation continues 😊



Ms. K

Case 3

Resource



Ms. K, female, age 71, today is 5/31/13, 4:00 P.M.
What topics might be covered in this phone call?

- Infection Preventionist from local hospital calls with a referral on TB suspect, Ms. K
- AFB smears are 4+, and 3+ twice
- Other diagnoses
 - End-stage renal disease
 - Insulin dependent diabetes mellitus



What topics might be covered in this phone call?

- Airborne isolation (Aii), a.k.a. “negative pressure”
- Need for “TB Treatment/Discharge Plan” completion
- All pertinent information available on TB intake form
- Treatment plan for the TB drug regimen; TB drug start date
- Is the person on dialysis?
- Hx of prior TB, prior + TST or IGRA, Tx for LTBI, NTM diagnosis?
- Arrange hospital visit if possible
- Potential discharge date



This information is discovered in the call;
what is your input or concern now?

- Suspect was in airborne isolation
- HIV had not been done due to client's age
- Wt. is 52 kg
- Patient is on dialysis, and has been "for months"
- TB medication was started on 5/15/13
 - ▣ INH 300 mg. tablet, po, daily
 - ▣ Rifampin 300 mg. capsule, po, twice daily
 - ▣ Pyrazinamide 500 mg. tablet, po, twice daily
 - ▣ Ethambutol 400 mg. tablet, po, twice daily



Discussion

- What about the TB drug regimen?
 - ▣ Doses should be given once daily, all simultaneously
 - ▣ And in this case?
- Encourage HIV testing
- Was airborne isolation in place from first contact forward, or after positive AFB smears found?
- May address delay in health department notification



Renal Insufficiency Considerations, page 63-64 (1)

- Related to Toxicity:
 - ▣ Dependant on creatinine clearance of individual
 - < 30 ml/minute – dosing adjustment recommended
 - >30 ml/minute – no recommendation for dosing adjustment, but measurement of serum drug concentrations recommended to detect potential toxicity
 - ▣ INH and RIF are metabolized by the liver; no dosing adjustment needed
 - ▣ PZA also metabolized by liver, but metabolites excreted by kidneys
 - ▣ EMB cleared by kidneys
 - ▣ The recommendation is to alter the dosing interval for EMB and PZA



How should the current treatment regimen be addressed?

- The infection preventionist is reluctant to discuss the regimen with the physician prescriber
- The client has been on this TB treatment regimen daily for 11 days, with no reduction in clinical symptoms or sputum smear positivity (still 3+ and 4+)
- Hospital discharge is not expected in the near future because family says they can't care for the client at home



Discussion

- Call the prescribing physician and discuss the regimen
- Discuss with your health director or health department TB clinician
- Ask for all labs and review the creatinine clearance or glomerular filtration rate
- Call TB Control Program and ask advice
- Call TB Control Program and request to speak to a TB medical consultant



Importance of Interviewing

- This person is still in the hospital
- The interview:
 - Builds rapport
 - Opportunity for education and to gain more TB exposure and past treatment information directly
 - Elicits solid information to pursue a contact investigation in a setting with high risk persons (dialysis)
 - Provides a more complete contact list outside of dialysis
 - Provides information to assist in determining infectious period
 - Elevates the importance of health department involvement



Client progress over the next 10 days;
what might be suspected/why no improvement?

- Sputa remain at 3+
- The regimen has been changed to the recommended three times a week dosing intervals, with the recommended doses and no split dose administration
- The clinical picture is essentially unchanged after 3 weeks of treatment



Discussion

- The client has an NTM, not TB (but wouldn't growth and ID occurred by now with a rapid grower?)
- The client has drug resistance issues
- The client may have absorption issues due to the DM
- The client may have absorption issues due to food, other medications, or other clinical conditions
- Non-adherence



Interventions

- Call the lab and check culture growth
- Were serum drug levels done at 2 weeks (DM)?
If not, suggest they be done now
- Evaluate TB medication administration –
 - ▣ On empty stomach?
 - ▣ Drug interactions?
 - ▣ Calcium containing products?
- Evaluate medication administration practice (DOT?)
- Review co-morbidities, diarrhea, vomiting, etc.



What is discovered;
what should be recommended?

- Lab reports M.tb positive culture
- Nausea was an issue, so TUMS were being given immediately before each dose
- Increasing joint pain reported



Recommendations

- Stop the TUMS administration
Calcium products may interfere with absorption!
- Serum drug levels drawn
- Suggest uric acid be drawn
- Suggest use of aspirin or other NSAID for joint pain



Joint pain and PZA

- Uric acid level part of baseline TB lab panel
- Increase in uric acid expected with PZA, though usually asymptomatic
- Renal insufficiency can contribute to uric acid rise
- Allopurinol Rx an option
- May require that PZA be discontinued
- If initial phase not complete with PZA, requires treatment for 39 wks. (9 months)



Discoveries and follow-up; thrice weekly

- Pansensitive
- INH level 4.8 mcg/ml (9-18 mcg/ml expected)
 - ▣ Dose adjustment ↑INH to 1200 mg. po three x a week
- RIF level 3.0 mcg/ml (8-24 mcg/ml expected)
 - ▣ Dose adjustment ↑ RIF to 900 mg. po three x a week
- Improvement in smear positivity to 1+ within a week
- Repeat serum drug levels both within expected range
- Joint pain relieved with ibuprofen



Slow Response – 4 to 6 weeks of treatment

- Definition:
 - ▣ **Sputum smear (+) not decreasing**
 - adequate decrease is:
 - 4+ to 2+
 - 3+ to 1+ or,
 - 2+ or 1+ to smear negative
 - ▣ **No improvement in TB symptoms**
 - no weight gain
 - no reduction in cough
 - persistent fever, or
 - worsening of chest x-ray if performed



Medically ready for hospital discharge; planning for dialysis and release from isolation

- Still smear positive, but +/- and 1+
- Symptoms are improved –
 - ▣ Decreased cough
 - ▣ Weight gain of 3 lbs.
 - ▣ Resolution of fever and night sweats
- On treatment for 5 weeks
- What is the criteria for release from isolation?
- What is the plan for dialysis?
- Does the dialysis plan effect the discharge plan?



Isolation and congregate settings

- “Controlling Tuberculosis in the United States,” Nov. 4, 2005, pg. 9, Box 3
 - ▣ 3 consecutive negative AFB smears
 - ▣ Collected at least 8 hrs. apart
- Dialysis could still be arranged at the hospital with appropriate Aii until release from isolation



The course is uneventful, until.../
What's up? What to do?

- Smear conversion occurs by 6 weeks (2 weeks after dose adjustment and correction of administration practices)
- Dialysis is now at the regular dialysis center (no Aii)
- Sputa continue to be collected to document culture conversion
- One sputa in week 10 returns AFB smear 1+



Interventions and Possibilities

- Revert dialysis to hospital Aii facility
- Possibilities
 - ▣ Treatment failure
 - ▣ + smear reflects dead organisms
 - ▣ Non-tuberculous mycobacterium (NTM)
- Collect series of 3 sputa, 8 hrs. apart, HCW observed
- Would an MTD “rapid test” be helpful?



Discussion

- Have to assume the worst and move to Aii
- Evaluate clinically; is clinical progress still evident?
- Won't know if dead organisms until culture final
- NTM ID likely back much sooner
- If 3 sputa all smear negative, move to regular dialysis if clinical improvement still clear
- MTD not helpful; already know it is M.tb



Uneventful course going forward ...

- Cultures converted by day 55 of treatment
- The sample with 1+ smear was identified as *M. gordonae*, a common NTM contaminant
- Completed 26 weeks of treatment...is that right?

...the end of the story



Discussion

- Extend treatment due to absence of clinical improvement and poor serum drug levels
- In other situations, if clinical improvement has occurred, extension of treatment might not be needed



Questions?

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