

Case Presentation

Adherence Difficulties in a Child with Tuberculosis

Case History:

A 15 month old child with active pulmonary tuberculosis became a significant management challenge to his public health nursing providers because of his consistent refusal to take medications.

The child developed pulmonary tuberculosis following contact with his mother who had smear-positive cavitary tuberculosis. The mother was AFB sputum smear positive and culture positive for *Mycobacterium tuberculosis*. Her chest x-ray was abnormal with a cavitary infiltrate and her culture isolate was resistant to INH at low level but susceptible at the higher testing measurement. She was started on standard four drug therapy and was very compliant.

The child was born in Mexico with extended family there. Several family members in Mexico have had, or died from, tuberculosis. The infant's father concurrently received rifampin for latent TB infection (LTBI).

At the time of the initial contact investigation, the child was asymptomatic and had a normal physical exam. The initial chest x-ray revealed a nodular opacity in the apical segment of the upper left lobe. Because neither bronchial washings nor gastric aspirates were obtained, the child was diagnosed with active tuberculosis disease on the basis of the abnormal chest x-ray and close contact to his mother. Although his mother, the source case, had low level Isoniazid (INH)-resistant disease, the child received only INH, rifampin and PZA. Ethambutol was not included in the regimen.

The child was placed on directly observed therapy (DOT) administered five days a week for the first two weeks. During the initial two weeks of therapy, he vomited or spit out two doses. A note in the record described the child as "very difficult and stubborn when taking the TB medications." Difficulties with medication delivery intensified once the treatment dosing interval was changed to twice weekly. It took both parents to restrain the infant while the health department staff administered the TB medications. His parents were very cooperative and supportive of health department staff, but concerned with the child's ongoing struggle. Several notes by the health department nurse indicated the child was "likely ingesting no more than a quarter to half of the medication in any one dosing day."

Clinically and radiographically the child was doing well. He was playful, friendly, cheerful (when not taking medications), and performing age appropriate tasks including feeding himself and drinking from a regular cup.

Heartland National TB Center was consulted regarding the following three concerns:

1. Is the treatment regimen appropriate for this child?
2. Should the length of treatment be extended because of the number of missed doses?
3. The infant frequently spits out, vomits or refuses to take TB medications. It is necessary for the parents to restrain the infant and force him to take her medications. The behavior isn't improving and parents and HD staff are very frustrated. What recommendations do you have for administering medications to infants and toddlers?

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Recommendations:

- Adults with low level INH resistant tuberculosis are usually treated with ethambutol in addition to INH, rifampin, and PZA. The addition of ethambutol helps to prevent the development of additional resistance (high level INH resistance and/or rifampin resistance). The entire four drug regimen is continued for at least 6 months and preferably 9 months. There are no published data for this issue concerning childhood tuberculosis. In general, the same treatment regimen is recommended for children, who usually tolerate the medicines well. If the child has extensive disease, and/or is responding poorly, and has no clinical evidence of toxicity, the treatment should be for a total of nine months. Daily or thrice weekly doses are recommended over twice-weekly regimens.
- Vomited doses should be noted and added to the end of the therapy.
- Multiple strategies exist for the management of a young patient who desperately fights DOT providers and other health care workers. A main strategy is to be consistent and although pleasant, indicate the expectation that the child will take the medication. Some or more of the following may lead to successful medication delivery:
 - If a child vomits 2 doses per week (on DOT), press on with therapy continuing attempts to entice the child to cooperate with swallowing the medications.
 - If the child vomits on a consistent basis three or more times per week, consider a nasogastric tube or gastric tube placement to facilitate medication delivery.
 - Hospitalization should be strongly considered for one to three weeks to work on administration of medicine. If this is slow or unsuccessful, intravenous therapy may be given during this time period.
- **Tips for increasing cooperation with DOT in young children:**
 1. Try other staff if the current DOT provider is having difficulty.
 2. "Hawaiian Punch Concentrate" can be used to make a sweet syrup that can be mixed with medication which can then be frozen into a popsicle. NOTE: Do not include INH in this mixture; it is unstable in non-commercial sugar solutions.
 3. Rifampin can be compounded into Syrpalta, a grape syrup, and other medications can then be crushed and dissolved in the same syrup mixture.
 4. Rifampin capsules can be broken open and mixed with pixie sticks or other tangy tart substances.
 5. It is better to hide bitter or unpleasant medicines in a new food that the child has not eaten before – if it is a food they like or have had before, they will be able to tell right away the taste is off and spit it out.
 6. Infants will sometimes take medications better if given daily, in smaller doses and routinely.
 7. Children tend to stop fighting when they realize that the parents are not giving up.
 8. Provide an incentive (small toy, etc) to the child for each completed dose.
 9. It is important to try to keep the experience of giving medications as positive as possible for the child. Age appropriate incentives and enforcers should be used liberally.

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10. When medication administration does not go well, the issue is often with the adult family members. The parent may not understand or believe in the necessity of the treatment, especially if the child generally looks and acts well (as many do). The parent's and other significant adult's attitudes may need to be explored and addressed.
11. Some children, especially infants and toddlers, have trouble handling the increased volume of medications that comes from adding a 4th drug – usually ethambutol – or changing to an intermittent therapy. One should always address the need for each drug and determine if daily therapy might work better for an individual child.

“Tuberculosis Medication Delivery Tips” from Anne Loeffler, MD**Liquid:**

- INH suspension is available commercially in sorbitol. The large osmotic load is poorly tolerated by most children as it can cause diarrhea, but it may be better tolerated by babies.
- Other TB medications are not commercially available as liquids. Medications may be suspended by local pharmacies but the stability and homogeneity are not guaranteed.

Pills and capsules taken intact or in halves: This is the easiest way! Tip the head back to swallow pills and tip the head forward to swallow capsules. If the child can swallow capsules, but not tablets, crush the pills and place the powder in commercially available empty capsules

Pills fragmented (with a knife or commercial pill cutter) or crushed (by commercial pill crusher, mortar and pestle, spoon against spoon or bowl); capsules can be opened. The crushed pills have a strong flavor; small fragments of the pill taste better. Crush or fragment pills right before administering (within 30 minutes); do not prepare ahead of time.

- Put a thin layer of soft food onto a spoon. Place the pill fragments or powder on top of the food layer and top with more yummy food. Give the child the dose of medication in this “sandwich.” Teach them to swallow it without chewing by practicing without the medication in place first. Some suggested foods:
 - Chocolate frosting, sauce, pudding, fudge sauce, ice cream, etc.
 - Jelly or marmalade (the texture hides the powder granularity)
 - Apple sauce or berry-sauce (better to hide the red rifampin color)
 - Nutella or peanut butter
 - Cream cheese or chili con carne
 - Whatever the family can make work

OR

- Suspend in a SMALL AMOUNT of liquid. Water is best. (INH is not stable in sugary liquids; do not mix with other medications in sugary solutions. Only use liquid INH in the commercially mixed sorbitol.) Dispense with:
 - Syringe (it is difficult to get the pulverized INH through regular tip syringe; other drugs crush finer and dissolve better)
 - Medicine dropper with larger tip; available at many pharmacies
 - Baby bottle (may need to make hole larger)
 - Special Rx MediBottle- with internal sleeve for syringe; available at many pharmacies. Pulverized INH is very difficult to get through this syringe. I suggest giving the other meds with this bottle and then giving INH separately or by the liquid product if it is tolerated by the baby.
 - Medicine delivering pacifier; available at many pharmacies) holes will need to be enlarged)

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Teaching Points:

- Good treatment outcomes depend on the application of standard treatment regimens, support for the child and care giver to promote maximum adherence to treatment, and careful monitoring of adverse effects.
- Children and their parents, along with other family members and other care givers should be educated about TB and the importance of completing treatment.
- Directly observed therapy is essential.
- Counsel the care giver at every visit for support about adverse events and the importance of adherence to completion of treatment.
- If it is not possible to ensure good adherence and treatment outcomes as an outpatient, some children may require hospitalization for social and logistical reasons.
- Treat the child according to the drug sensitivity pattern (and using the treatment history) of the source case if the child's isolate is not available.
- Treatment duration depends on the extent of the disease.
- Ethambutol is now considered safe in children at a dose of 20 mg/kg (range 15-25 mg/kg) daily.

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