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TB in developing countries: Diagnosis and treatment

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Summary Childhood tuberculosis poses great challenges to the public health mangers as well as the pediatrician. While mycobacterial detection and isolation remain the gold standard but has a poor sensitivity for several reasons. The diagnosis of the disease is often based on indirect methods like PPD positivity, radiological features and history of contact. Serology and PCR based diagnostic methods have failed to help a clinician working at the peripheral level. The review shares and discusses the place of the various tests in the diagnosis of tuberculosis. WHO has been propagating the use of intermittent supervised treatment for all cases including children. We discuss the concerns of the pediatricians and share our experience on this therapy.

Tuberculosis, the biggest infectious killer, kills more than the dreaded diseases like plague and cholera. Its impact on the patient as well as the rest of the family due to the risk of cross infection, stigmatisation and financial drain is more real and common than with any other infectious diseases. Tuberculosis in a family has both direct and indirect implications for the children in the family or the household. While most infants who get tuberculosis suffer from lung disease, yet they are more likely to develop milliary or meningeal forms with severe morbidity and sequelae. Nearly 3.4 million children in India have the disease while 94 million are at the risk of infection. The overall prevalence of infection in the 0–14 years age group is estimated between 8.6–10%.[1]

CLINICAL SYMPTOMS AND SIGNS

Tuberculosis is suspected when an ill child has a history of chronic illness of usually more than 3 weeks of duration, that includes a cough and a fever, weight loss or failure to thrive, an inability to return to normal health after measles or whooping cough, and history of contact with an adult case of pulmonary tuberculosis. Children with primary pulmonary tuberculosis, may often be asymptomatic or have non specific sign symptoms for a short. While a few may have fever (especially at night), fatigue, malaise, anorexia and weight loss.

The pulmonary disease may often be without significant chest findings even in presence of pneumonia. Extrapulmonary disease may coexist in about one fourth to a third. Children are more likely to develop extrapulmonary disease than immunocompetent adults.[2]

On physical examination there may be one or more of the following: malnutrition, lymphadenopathy (non tender, matted and some times become fluctuant or develop overlying sinuses), chest signs, hepatomegaly and/or splenomegaly, meningeal signs, altered sensorium and neurological deficit, and/or pleural effusion or ascites.

DIAGNOSIS OF TUBERCULOSIS

The diagnosis of tuberculosis in children is extremely challenging due to inability to demonstrate the acid fast bacilli (AFB), which is the gold standard. In addition, the clinical symptoms and signs of tubercular disease are non specific

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and common symptoms of cough, fever, failure to gain weight can lead to both over and under diagnosis. Often a non response of symptoms- particularly with persistence of the radiological shadows- to potent antibiotics is used as an additional ground for suspecting tuberculosis in countries like ours where the disease is common.

Mycobacterial detection and isolation

It is important to demonstrate acid fast bacilli on smear or *Mycobacterium tuberculosis* in culture from tissue specimens for a certain diagnosis. The choice of specimen is predicated by the location of the disease. The examination of sputum-induced or spontaneous, gastric aspirates (GA), bronchial washings, and any other appropriate body fluid may be undertaken. WHO and our country program recommend obtaining a minimum of 3 samples on separate days.[3] In older children bronchial secretions can be obtained by stimulating cough with an aerosol solution of 10% saline.[4] However this method is not commonly used due to safety concerns. In younger children, gastric aspirates are used in lieu of sputum. The sample is obtained after overnight fasting, first thing in the bed for 3 consecutive days. Bronchio-alveolar lavage (BAL) can also be taken where the facilities are available. The evidence so far is balanced between G As and BAL while the ease would certainly tilt the balance in favor of GA.[5]

The body secretions or aspirates are drawn into smears over a clean slide and stained with Ziehl Neelsen Stain for detecting Acid Fast Bacilli (AFB). In our experience, nearly 28–55% of the patients with pulmonary disease are smear positive. The isolation rates were higher in children with post primary or progressive primary disease. Our AFB positivity rates are higher than the other series from the country.[6,7] In our opinion it is related to the emphasis laid on the test rather than any difference in the type of patients. Our own laboratories were reporting less than 10% positivity prior to the added emphasis on the test.

Culture of specimens containing tubercle bacilli is a much more sensitive method of detecting mycobacteria than are direct smears. Two types of solid media have traditionally been used: an egg based medium (Lowenstein Jensen) and an agar based medium (Middlebrook 7H10 and 7H11). The growth of mycobacteria takes 6–8 weeks for colonies to appear. Newer rapid diagnostic methods includes the BACTEC® (Becton and Dickinson, USA) system which is a radiometric culture method. The system uses a liquid medium containing radiometric palmitic acid labeled with radioactive carbon (^{14}C). Growth of mycobacteria within the system is measured as a daily growth index that detects the production of $^{14}CO_2$ by the metabolising organisms.

While most laboratories in India use the conventional methods, Bactec is now available in some parts. The reports on better isolation rates with Bactec method among sputum negative adults[8] raised the hopes that perhaps this method shall improve the isolation among the pediatric cases as well. We conducted a study to compare the conventional LJ media with the Bactec radiometric method in childhood TB (submitted elsewhere for publication). A similar proportion specimens were found positive with either method (74/102). Bactec method certainly was significantly faster than the conventional method (Mean detection time 17 days vs 34 days). But it had higher contamination rates with specimens specimens like gastric aspirates, higher cost and environmental issues like radioactive disposal.

Tuberculin skin test or Mantoux's test

For Mantoux's test in India, testing with 1 tuberculin unit [TU] PPD RT23 with Tween 80. A reading of more than 10 mm of induration, after 48–72 hrs, is considered positive, irrespective of the BCG status of the child. Often the laboratories use higher strengths like 5TU or 10TU are used which can give rise to higher reactions and probably more false positives. Using standard preparations is essential for the correct interpretation of this simple but useful test. The poor availability of standard preparations is a real problem. For past 2 years there is a serious crunch of 1TU standardized tuberculin. Though the pediatricians are using the same cut off of 10 mm induration irrespective of the strength of tuberculin used, it obviously is not a sound scientific practice and can lead to over diagnosis.

BCG test

In India, few centers employ BCG vaccine as a testing agent. An accelerated reaction to BCG in the form of an induration of >5 mm after 5–7 days at the site of injection is considered positive. As this test utilises a very high load of several antigen, it is prone to high false positivity. The validity of the test in countries like India, where routine BCG vaccination is undertaken, is further suspect and therefore is no more recommended.[9]

Roentgenographic examination

Chest roentgengraph is an important diagnostic tool in evaluating patients particularly for pulmonary tuberculosis. Initial studies include posteroanterior and lateral views. Lateral films can improve the accuracy of diagnosis by detecting hilar adenitis not clearly appreciated on frontal films.

Fluoroscopy of the main airways helps differentiate the presence of hilar adenopathy (which remains immobile throughout respiration) from prominent pulmonary vasculature. CT scan of the chest can aid the diagnosis[10] but is not routinely recommended in the evaluation of the symptomatic tuberculosis infected child with a normal chest radiograph due to lack of specificity and high radiation. An important thing to remember is there is no radiological appearance specific to tuberculosis.

Aspiration cytology

Fine needle aspiration of cytological fluid from the lymphnode swellings and other involved areas in the solid or solidified