*Statement*

# Consensus Statement of IAP Working Group: Status Report on Diagnosis of Childhood Tuberculosis

In consonance with the decision of the Indian Academy of Pediatrics (IAP) to standardize protocols for diagnosis and management of common childhood diseases, a meeting of IAP working group on diagnosis of childhood tuberculosis was held at Mumbai on 28th and 29th June 2003 (*Annexure*). The group deliberated in the light of presentations made based on literature reviewed by the members and concluded that at present only a statement giving the status of the commonly used or available diagnostic modalities can be evolved to help the clinician in day to day practice. Recommendations were standardized to suit most of the clinical situations met with in routine practice and to ensure reasonably accurate diagnosis. It is hoped that these recommendations will be implemented by the clinicians at all levels and will help to resolve diversities and confusion hitherto prevailing in the diagnosis of childhood tuberculosis. However special circumstances may merit deviations from the standard recommendations based on individual clinician's judgement and experience.

## Clinical setting for suspecting active tuberculosis / pulmonary TB

Fever and cough >3 weeks denote need for evaluation for diagnosis of active tuberculosis. Fever should be documented if possible to avoid erroneous reporting by parents. Recent onset of fever and cough is the common presentation. Recurrent fever and cough with normal intervening period is often due to diseases other than tuberculosis. Cough as a predominant symptom without fever is mostly due to hyper reactive airways or asthma.

In addition, recent unexplained loss of weight and appetite favors possibility of active tuberculosis. Unexplained poor weight gain in infancy is relevant but not in older children, as several other common conditions also lead to a poor weight gain. History of contact must be specifically enquired and assessed in terms of activity and infectious nature of the disease. Children in contact with an infectious case are at the greatest risk. (Contact is defined as any child .who lives in a household with an adult taking anti-TB therapy or has taken such a therapy in the past 2 years.) Household contact survey is recommended in a younger child.

Diagnosis is more likely in presence of risk factors such as age <1 year, recent history of measles / whooping cough, failure to thrive, immunocompromized state and steroid therapy. Significant superficial lymphadenopathy should be specially looked for, as it is present in 40-50% patients. (Inguninal lymph-nodes >1.5 cm and other superficial lymph-nodes >1 cm in size is considered significant.)

Failure of therapeutic response to an appropriate and adequate antibiotic trial in a symptomatic child supports probability of tuberculosis.Therapeutic trial with anti-TB drugs is not recommended and all attempts must be made to diagnose TB by proper investigations.

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*Table I* summarizes indicators for diagnosis of tuberculosis.

**Tuberculin test (Mantoux test)**

1 TU PPD with RT 23 Tween 80 (or 5 TU PPD without Tween 80) is injected intradermally and the reaction is read between 48-72 hours. Induration of 10 mm or more in largest diameter is suggestive of natural infection, irrespective of prior BCG vaccination.

Natural infection under 2 years of age is suggestive of recent infection and should be treated accordingly. Beyond 2 years of age, natural infection in association with history of contact or symptoms / signs or presence of risk factors increases the risk of disease.

In case a patient presents late but within 7 days of the test, then any reaction above 10 mm is still considered as a positive test. However, if the reaction is less than 10 mm in these latecomers, then a repeat test needs to be done on the other forearm.

In case of continued search for proper diagnosis, test may be repeated few weeks or months after the first test. Induration of 6 mms or more than previous test results may be suggestive of natural infection.

BCG test is of no value and is not recommended.

**Radiology**

Ideal chest *X*-ray is taken in upright position PA view. A well centered good exposure mid inspiratory film is a must for correct interpretation.

Lateral view is useful in case of suspicion.

CT Scan of chest is not routinely required. It is not cost and radiation effective.

Radiological lesion does not confirm etiology of tuberculosis, as there are no pathognomonc radiological signs of tuberculosis.

However, in following radiological lesions, diagnosis of tuberculosis is most likely in presence of relevant clinical setting: (*i*) Miliary lesion; (*ii*) Unilateral Pleural effusion; (*iii*) Fibrocaseous cavitory lesions; (*iv*) Pneumonia with an enlarged mediastinal lymph node; and (*v*) Caseating lymph nodes on CT Scan.

Persistent pneumonia beyond 4 weeks in a symptomatic child inspite of antibiotic therapy may suggest probable TB.

In a child with confirmed diagnosis of pulmonary tuberculosis, chest x-ray usually be repeated at the end of intensive phase (usually after 2 months of initial treatment) to assess response, unless indicated otherwise in an individual case. In case of deterioration or absence of clinical improvement, chest *X*-ray should be repeated at the end of 2-3 weeks as needed. Every child should have a final *X*-ray at the end of treatment.

USG chest is rarely required except in case of a suspected pleural effusion not evident on plain chest *X*-ray.

Right upper lobe bacterial non-tuberculous pneumonia in an infant often persists with radiological shadow for >4-6 weeks but in such situation, child is clinically normal with appropriate antibiotic therapy. Such a child does not need further evaluation for tuberculosis especially in absence of any risk factors.

**Bacteriology**

Bacteriology is possible in childhood tuberculosis and may yield positive results in 30-40% of the patients. Hence attempt at bacteriological diagnosis should be made in every patient. Gastric lavage may be used when sputum is not available. Yield increases if multiple samples are examined. Ideally, 3 sputum or gastric aspirate samples should be

**TABLE I–** *Indicators for Diagnosis of Tuberculosis*

| Symptoms | Descriptor | Exclusions | Specific points |
|---|---|---|---|
| Fever | Recent onset of persistent fever >3 weeks<br>Fever can be of any type in a child with TB | Recurrent fever | Fever should be documented as far as possible. |
| Cough | Recent onset of cough with fever is significant | Recurrent / episodic cough without fever | Recurrent cough / fever with intervening normal period is often due to diseases other than TB |
| Unexplained recent loss of weight / appetite | Recent onset of symptoms are relevant | | More relevant in infancy<br>Nonspecific symptoms due to many organic or functional disorders |
| Contact history | Any adult taking anti-TB treatment currently or in the past 2 years | | Younger the child more important is household contact survey |
| Risk factors | Age <1 year / failure to thrive / recent measles or whooping cough / immunocompormized state / steroid therapy | | In suspicious clinical settings, presence of risk factors increase the probability of disease.<br>Enlarged superficial lymphonodes must be looked for.<br>Therapeutic trial of anti-TB drugs is not recommended. |

tested in each case. Vancomycin added to the sample prevents growth of other bacteria and thus improves the yield. Bacteriological confirmation is easy in cavitory lesion and is mandatory in suspected case of multi-drug resistant tuberculosis.

Bactec can offer faster results within 7-8 days but does not increase chances of finding bacteria.

**PCR**

Results of PCR test depends upon generation of the probe used and some studies suggest that using two probes may be better. Sensitivity of PCR is variable in pulmonary tuberculosis and it may be as low as 20% in gastric aspirate. Hence at present, routine use of PCR is not recommended.

However, its sensitivity and specificity in CSF and pleural fluid may be high and thus it may be considered in suspected case of neuro-tuberculosis.

**Serology**

Due to many variable factors in host, mycobacterium and environment, serology is not useful in childhood TB. The sensitivity, specificity as well as predictive value of commercially available serological tests at present such as ELISA for TB does not justify their use in our settings.

**CBC / ESR**

CBC / ESR has no value in either diagnosis or follow up of childhood tuberculosis. ESR is a test, which is influenced by several factors including those extraneous to the patient and disease, therefore, is not recommended.

*Table II* summarizes the laboratory tests for diagnosis of tuberculosis.

**TB lymphadenitis**

Superficial lymphadenopathy is considered significant if it is >1.5 cm in size in inguinal region and >1 cm in cervical and axillary region. Matted lymphnodes favor diagnosis of tuberculosis. Failure of response to antibiotic therapy beyond 2 weeks is highly suggestive of tuberculosis in presence of other supportive features.

Generalized lymphadenopathy is pathological irrespective of size of glands. In case of suspected TB lymphadenitis, diagnosis must be confirmed by histopathology. FNAC is an easy and simple procedure of choice in lymphnode disease. It has high sensitivity and specificity. The aspirate can be stained for AFB. AFB can be demonstrated in a good proportion of aspirates particularly if the aspirate is caseous or necrotic. Excision biopsy is rarely required.

Reactive hyperplasia is not a feature of TB lymphadenopathy.

Isolated axillary lymphnode enlargement in an infant (on left side) is due to BCG vaccine and does not warrant treatment even if histopathology or bacteriology suggests TB.

**Abdominal TB**

Clinical presentation may be in the form of ascitis, subacute intestinal obstruction or pyrexia of unknown origin with or without hepatosplenomegaly.

Barium meal follow through showing pulled up caecum is suggestive of tuberculosis.

Abdominal USG may show significantly enlarged lymphnodes or peritoneal fluid. Presence of small lymphnodes and / or peritoneal fluid is often a finding that needs careful follow-up and should not be considered enough for diagnosis.

Serum albumin ascitic gradient <1.1 favors

**TABLE II–** *Laboratory Tests for Tuberculosis*

| Test | Technique | Interpretation | Specific points |
|---|---|---|---|
| Mantoux test | 1 TU PPD RT 23 with Tween 80 intradermally<br><br>Read after 48-72 hours (may be up-to 7 days if +ve)<br>previous test results is suggestive results, repeat test is required. | Induration of 10 mm or more in largest diameter is highly suggestive of natural infection irrespective of BCG vaccine status.<br>Induration of 6 mms or more than disease. In case of doubtful or inconclusive test | A MT positive in a child less than 2 years of age is highly suggestive of recent infection and must be treated. Beyond 2 years of age, a positive MT along with history of contact, symptoms and signs and presence of risk factors increase the risk of the of natural infection. |
| Repeat MT | Preferably on other forearm | | |
| BCG Test | – | – | BCG test is of no value & not recommended |
| **Radiology** | | | |
| X-ray Chest | Ideal X-ray Chest is taken in upright position PA view<br><br>Well centered good exposed mid-inspiratory film is ideal. Lateral view is useful in case of suspicion | The following radiological patterns strongly suggest a lesion diagnostic of TB:<br>1. Miliary lesion<br>2. Unilateral Pleural effusion<br>3. Fibrocaseous cavitatory lesions<br>4. Pneumonia with enlarged media-stinal lymph nodes.<br>5. Persistent pneumonia in a sympto-matic child inspite of antibiotic therapy. | Radiological lesions do not indicate etiology. |
| Repeat X-ray Chest | | Deterioration or absence of clinical improvement<br>In presence of good clinical improvement<br>In every child. | After 2-3 weeks of treatment<br><br>At the end of intensive phase- 2 months of treatment at the end of successful treatment. |
| CT Scan Chest | High resolution CT Scan is preferred | Caseating & matted Lymph nodes on CT Scan | Routine CT Scan Chest is not recommended |
| **Bacteriology** | Sputum or gastric lavage is examined<br>Multiple samples should be examined<br>Bactec method | Positive yeild in 30-40% of the patients<br>Increases yeild<br>Newer methods offer results in 7-10 days. No increase in the yeild | GOLD standard & must be attempted in all patients<br><br>Costly and not available easily |

| Test | Technique | Interpretation | Specific points |
|---|---|---|---|
| PCR | Some studies suggest use of two probes | Result depends on the type of generation of probe used. | Routine use of PCR not recommended |
| | PCR in Pulmonary TB & in gastric aspirate | Low sensitivity - as low as 20% | |
| | PCR in CSF & Pleural fluid | High sensitivity & specificity | May be useful in Neurotuberculosis |
| **Serology** | Commercially available tests at present are not ideal | Variable factors in host, mycobacterium & environment makes interpretation of these tests difficult | Serology is not recommended in childhood TB |
| **CBC/ESR** | – | These are nonspecific indicators of inflammation | They have no value in diagnosis or follow up of childhood TB |

**TABLE III–** *Localized TB & TB in Special Situations*

| Symptoms | Descriptor | Exclusions | Specific Comments |
|---|---|---|---|
| **TB Lymphadenitis** | Superficial Lymph nodes are considered significant if:<br>1. Inguinal Lymph nodes > 1.5 cm<br>2. Cervical & axilliary Lymph nodes > 1cm<br>3. Matted Lymph nodes<br>4. Generalized Lymphadenopathy<br>5. Failure to respond to antibiotic therapy for 2 weeks | Posterior Cervical Lymphadenopathy is almost always not due to TB | Histopathological diagnosis is a must<br>FNAC is procedure of choice<br>FNAC has good sensitivity & specificity<br>Biopsy is rarely required.<br>Aspirate must be stained for AFB/<br>Highly suggestive of TB in presence of other supportive features. |
| | Isolated left axillary lymphadenopathy in an infant | histopathology or bacteriology is positive | Due to BCG. Does not require treatment even if |
| **Abdominal TB** | Clinical presentations include Ascitis, subacute obstruction or pyrexia of unknown origin with or without hepatosplenomegaly | Small lymphnodes or mild ascitis on USG may not be significant | Abdominal USG shows the presence of significant Lymph nodes or peritoneal fluid<br>Barium meal follow through showing pulled up caecum is highly suggestive of TB<br>Serum albumin ascitic fluid gradient < 1.1 highly suggestive of TB |

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|---|---|---|
| **Neurotuberculosis** | | |
| TB Meningitis | Early diagnosis in Stage 1 is suggested by:<br>1. Fever without localization for more than 2 weeks and/or<br>2. Altered behavior / change in personality of recent origin<br>3. Headache, vomiting suggestive of raised ICT<br>4. Movement disorder<br>5. Focal deficits<br>6. Seizures | Global encephalopathy with focal deficits is highly suggestive of TBM<br>CSF examination is a must<br>In case of inconclusive results, repeat examination is necessary after antibiotic trial for 3-4 days<br>CSF glucose must be interpretd in conjunction with blood glucose<br>CSF smear & culture are negative in 90% of the cases<br>CSF antigen tests are useful but not ciurrently available<br>CSF antibody tests are not recommended<br>CSF ADA may suggest diagnosis<br>CSF PCR is variable<br>Mantoux test is negative in 70% of the cases.<br>CT Scan shows basal exudates & hydrocephalus in 80-100% of the patients and is a useful diagnostic modality. Normal CT Scan does not rule out TBM |
| Tuberculoma | Features to differentiate tuberculoma from NCC<br>1. Tuberculomas are larger<br>2. Tuberculomas are ususally multiple<br>3. Tuberculomas are more common in the posterior fossa while NCC are present in the gray-white junction | Differentiating Tuberculomas from NCC is difficult<br>MR spectoscropy shows lipid peaks in tuberculoma<br>Costly, not easily available and not recommended. |
| **HIV & TB** | In HIV positive but immunocompetent patient the manifestations of TB are typical<br>In HIV positive immunocompromized patient the manifestations of TB are florid, drug reactions are common & therapeutiv paradox is known<br>Mantoux test of 5mm of reaction is considered significant although it is often negative | Management of HIV with TB needs specialized expertise & hence referal to tertiary center is recommended. |

| | | |
|---|---|---|
| | Pathagnomic X-ray features are:<br>1. Confluent patchy consolidations involving more than half lung<br>2. Dense lobar / segmental collapse<br>3. Massive paratracheal / Hilar lymphadenopathy<br>4. Concomitant Bronchiectasis | |
| **MDR TB** | MDR TB considered when:<br>1. Child has contact with MDR TB<br>2. Failure of response to adequate treatment for 8-12 weeks | MDR TB is rare in in children<br>Before considering diagnosis of MDR TB, consider reviewing diagnosis of TB itself.<br><br>MDR TB must be confirmed by bacteriology<br>Ideally patient must be refered to a referral center for further management |
| **Congenital TB** | History of mother suffering from active TB during pregnancy<br>Clinical features include hepatomegaly, pulmonary or disseminated disease | |

diagnosis of tuberculosis. Liver biopsy may be helpful in case of hepatomegaly.

**Intracranial TB**

In TB meningitis, early diagnosis in stage 1 is very important and is suggested by: (*a*) Fever without localization >2 weeks And/or Altered behavior / change in personality of recent origin; (*b*) Headache, vomiting suggestive of raised intracranial tension; (*c*) Movement disorder; (*d*) Focal deficits; (*e*) Seizures.

Global encephalopathy with focal deficit is hallmark of TBM.

CSF must be examined in every such case. In case of inconclusive results, it should be repeated 48-72 hours after antibiotic therapy and if it shows no change in clinical status and CSF results, then it may favor diagnosis of TBM. CSF glucose must be interpreted in conjunction with simultaneous blood glucose level. CSF smear and culture are negative in 90% of cases. CSF antigen tests are reported to be useful but are not available. CSF antibody tests are not recommended due to poor sensitivity, specificity and predictive value. CSF ADA may suggest diagnosis of tuberculosis only in presence of other supportive tests but not *per se*. CSF PCR is also variable.

Mantoux test is negative in 70% of patients.

CT scan is useful and should be considered if possible. Hydrocephalus and basal exudates are seen in 80-100% patients. Normal CT scan does not rule out TBM.

Differentiating inflammatory granulomas such as Tuberculoma and Neurocysticercosis is difficult. However, following points may be used to differentiate the two; (*a*) Tuberculomas are larger and usually multiple. (*b*) They are more common in posterior fossa unlike cysticercus granuloma at the gray-white junction; (*c*) MR spectroscopy may be useful as it shows lipid peaks with tuberculoma.

**TB in special situations**

*HIV and TB*

In HIV serological positive but immunocompetent patients, manifestations of tuberculosis are similar to those seen in general population.

In HIV positive and immunosuprressed patients, tuberculosis is florid, drug reactions are common and therapeutic paradox is known.

Pathognomic *X*-ray findings are: (*i*) Confluent patchy consolidation involving more than half lung; (*ii*) Dense lobar / segmental collapse; (*iii*) Massive paratracheal / hilar lymphadenopathy; (*iv*) Concomitant bronchiecctasis.

Mantoux test with 5 mm of reaction is considered significant in immuno-compromised patients though it is often negative.

Management of HIV with TB needs specialized expertise and hence referral to tertiary center is recommended.

**MDR TB**

Drug resistant TB is rare in children. It should be considered when child has a contact with MDR TB or in case of failure of response to adequate treatment for 8-12 weeks. Before considering diagnosis of MDR TB, diagnosis of TB itself should be reviewed. Diagnosis of MDR should be confirmed by bacteriology and patient ideally be managed in a referral center.

**Congenital TB**

If mother is suffering from active disease during pregnancy, search for TB in a neonate is mandatory. Clinical presentation may be in

the form of hepatomegaly or pulmonary / disseminated lesion. Diagnostic criteria remain similar.

*Table III* is a summary of localised TB and TB in special situations.

**Scoring systems**

Evaluation of some available scoring systems has been found to have high sensitivity but low specificity, which may lead to over-diagnosis and unnecessary treatment of non-TB patients. These are not recommended for diagnosis currently, but further research could be undertaken to evaluate the existing scoring charts in the Indian context. *Table I* provides some helpful indicators for diagnosis of tuberculosis.

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**Annexure**

IAP Committee for framing Guidelines for the Management of Tuberculosis in Children. Following members participated in the meeting:

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**Members who could not attend:**

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