Draft minutes
Workshop on formulation of guidelines for diagnosis and treatment of Pediatric TB cases under RNTCP
6-7th August 2003, New Delhi

Objectives of the meeting:
To arrive at consensus on the following issues concerning Pediatric TB control under the Revised National Tuberculosis control programme (RNTCP):

- Diagnosis
- Treatment
- Monitoring

The participants in this evidence-based consensus meeting included National and International Pediatricians and TB experts, and TB Control Programme Managers.

Consensus Statement

- *Diagnosis of TB in children is to be based on a combination of clinical presentation, sputum examination, Chest X ray, Mantoux test and, history of contact as described in the diagnostic algorithm*
- *DOTS is the recommended strategy for treatment*
- *All Pediatric TB patients should be registered under RNTCP*
- *Pediatric formulations and administration of drugs should be linked to child's weight*
- *Pediatric-focussed monitoring should be an integral part of the programme*
- *Identified operational research should be prioritised and conducted*
- *Training modules should be developed for Pediatric tuberculosis under RNTCP for training of Pediatricians and medical officers.*
- *Representative(s) of Indian Academy of Pediatrics (IAP) should be included in the committee for monitoring implementation of these recommendations*

Next steps

- Draft consensus statement derived from group presentations to be circulated among participants for finalisation – 1 month.
- Simultaneous publication of finalised recommendations in Indian Pediatrics, Indian Journal of Tuberculosis, Journal of Indian Medical Association (after necessary approval, if required)
- Develop linkages with RNTCP wherever possible
- Formation of a joint RNTCP-IAP Committee to follow up on the recommendations for implementation.

Recommendations of the working groups on various aspects of Pediatric TB case management are summarised below.

Recommendations on modalities for diagnosis of Pediatric TB

Suspect cases of Pulmonary TB will include children presenting with:
- Fever and / or cough for more than 3 weeks, with or without;
- Loss of weight / no weight gain; and
- History of contact with a suspected or diagnosed case of active TB disease within the last 2 years.

Screening of TB suspect will be made by:
- Sputum examination wherever possible;
- Mantoux test with 1 TU PPD RT 23 Tween 80. The test will be read as positive if there is more then 10 mm induration at 48 - 72 hours; and
- Chest X ray – PA view.

Evaluation of some available scoring systems have been found to have high sensitivity but low specificity which may lead to over-diagnosis and unnecessary treatment of non-TB patients. It is not recommended for use in diagnosis of patients currently, but further research could be undertaken to evaluate scoring charts in the Indian context.

Case definitions:
Smear-positive pulmonary tuberculosis
- EITHER: a patient with at least two sputum specimens positive for acid-fast bacilli by microscopy;
- OR: a patient with at least one sputum specimen positive for acid-fast bacilli by microscopy and radiographic abnormalities consistent with pulmonary TB and a decision by a physician to treat with a full curative course of anti-TB chemotherapy;
- OR**:** a patient with at least one sputum specimen positive for acid-fast bacilli by microscopy, which is culture positive for *M. tuberculosis.*

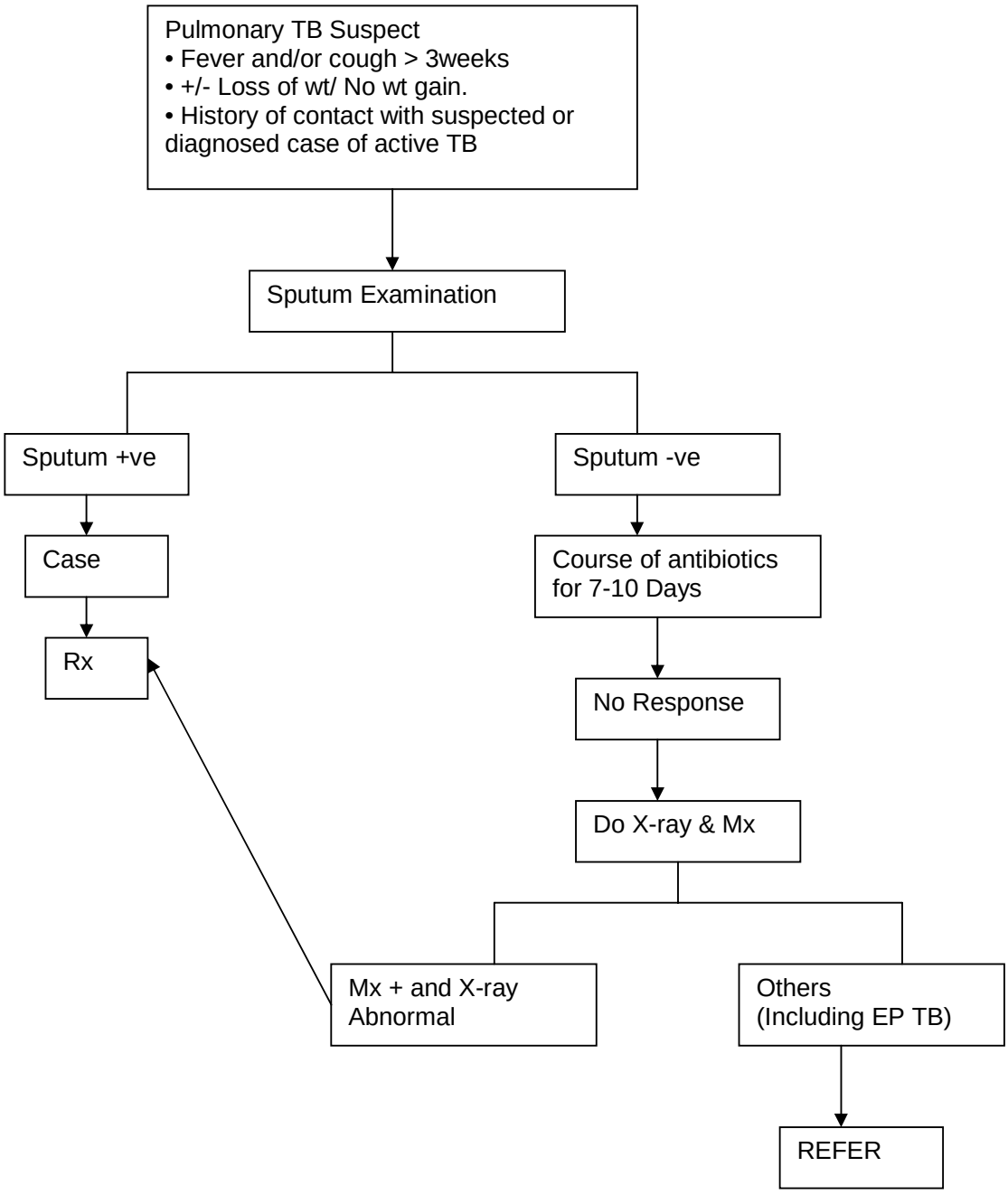
Smear-negative pulmonary tuberculosis
- EITHER: a patient with symptoms suggestive of TB with:
    - at least 3 sputum examinations negative for AFB;
    - lack of clinical response despite 7-days of a broad-spectrum antibiotic; and
    - who, when subjected to Chest X ray and Mantoux test is positive for Mantoux test and has radiographic abnormalities consistent with pulmonary TB.
- OR: a patient whose initial sputum smears were negative, who had sputum sent for culture initially, and whose subsequent sputum culture result is positive.

X-Ray findings suggestive of TB includes mediastinal / hilar lymphadenitis with or without parenchymal lesions, pleural effusion, miliary TB and fibrocaseous TB.

Children who test negative on Mantoux testing but have abnormal Chest X-ray findings, test positive on Mantoux testing but have no abnormal Chest X-ray findings, and those who test negative on Mantoux testing and have no abnormal Chest X-ray findings, should be referred to a Pediatrician for further management.

Level of Diagnosis: Diagnosis of TB in children should be made by a Medical Officer. If possible, it should be done at a facility where facilities for sputum examination, Mantoux test and Chest X-Ray are available. All referrals of children should be made to a Pediatrician. Proposed diagnostic algorithm for Paediatric TB is given at Figure 1.

Figure 1: Proposed diagnostic algorithm for Paediatric TB



Recommendations on modalities for treatment of Pediatric TB

Treatment categories and regimens

Category of treatment	Type of patients	TB treatment regimens	
		Intensive phase	Continuation phase
Category I	• New sputum smear-positive PTB • Seriously ill sputum smear-negative PTB • Seriously ill extra-pulmonary TB.	2 $H_3R_3Z_3E_3$	4 H_3R_3
Category II	• Sputum smear-positive relapse • Sputum smear-positive treatment failure • Sputum smear-positive treatment after default	2 $S_3H_3R_3Z_3E_3$/ $1H_3R_3Z_3E_3$	5 $H_3R_3E_3$
Category III	• Sputum smear-negative and extra-pulmonary TB, not seriously ill	2 $H_3R_3Z_3$	4 H_3R_3

The following recommendations are made pertaining to treatment categories and regimens:

- Seriously ill sputum smear-negative PTB will include all forms of Pulmonary TB other than primary complex
- Seriously ill extra-pulmonary TB includes TB meningitis, disseminated TB, TB pericarditis, TB peritonitis and intestinal TB, bilateral or extensive pleurisy, spinal TB with or without neurological complications, genito-urinary tract TB, bone and joint TB.
- Not-seriously ill extra-pulmonary TB includes lymph node TB and unilateral pleural effusion.
- In patients with TB meningitis on Category I treatment, the four drugs used during the intensive - HRZE should be replaced by HRZS as ethambutol does not penetrate CSF
- Continuation phase of treatment in TB meningitis and spinal TB with neurological complications should be given for 6 - 7 months, extending the total duration of treatment to 8 - 9 months.
- Steroids should be used initially to reduce inflammation in hospitalised cases of TBM and TB pericardiitis and reduced gradually over 6-8 weeks.

Formulation of drugs for children

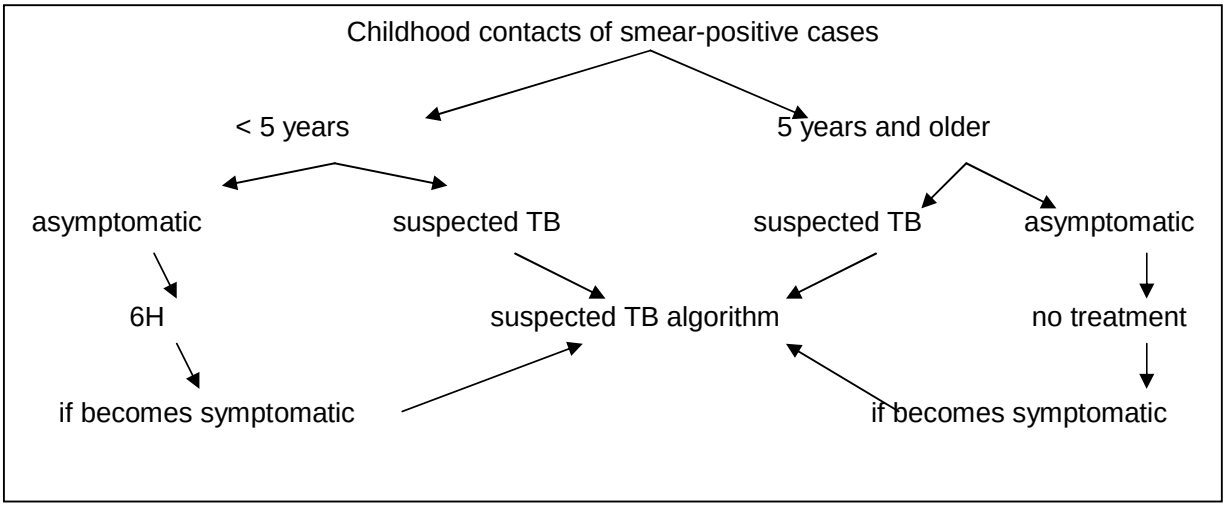
- To ease in calculation of required dosages and administering anti-TB drugs for children, anti-TB medication should be made available in the form of combipacks. Formulation of different dosage regimens for different weight groups was suggested for consideration by the RNTCP and is given at Tables 1. A committee should finalise the weight groupings and respective dosage regimens and explore the feasibility of procurement of combipacks for different weight groupings of children.
- Beam balance scales for weighing infants should be made available at all treatment centres.

Table 1: Suggested Pediatric dosage regimens

		<10kg	11-20 kg	21-30kg
Isoniazid	10mg/kg	100	200	300
Rifampicin	10mg/kg	100	200	300
Pyrazinamide	30-35mg/kg	250/300	500/600	750/900
Ethambutol	30mg/kg	200	400	600
Streptomycin	15 mg/kg			

Chemoprophylaxis

Existing RNTCP guidelines on the management of children under 6 years of age exposed to an adult with infectious (smear-positive) tuberculosis were found to be acceptable to the participants. The same is reproduced below:



Provision of treatment

- There is enough evidence, including Indian studies, demonstrating that intermittent therapy is as effective as daily therapy. Hence intermittent short course chemotherapy under direct observation as advocated in the RNTCP, should be used in children.
- All diagnosed TB patients, including indoor patients, should be initiated on Directly Observed Treatment, Short-course chemotherapy (DOTS).
- All short course chemotherapy should be administered under the direct observation of a treatment provider (DOT provider).
- If a child has not improved or deteriorated during/after treatment on intensive phase of treatment, s/he should be referred to a higher facility for assessment by a Paediatrician / TB expert. In all instances before starting a child on Category II treatment, s/he should be examined by a Paediatrician or TB expert.

Recommendations on modalities for monitoring and evaluation

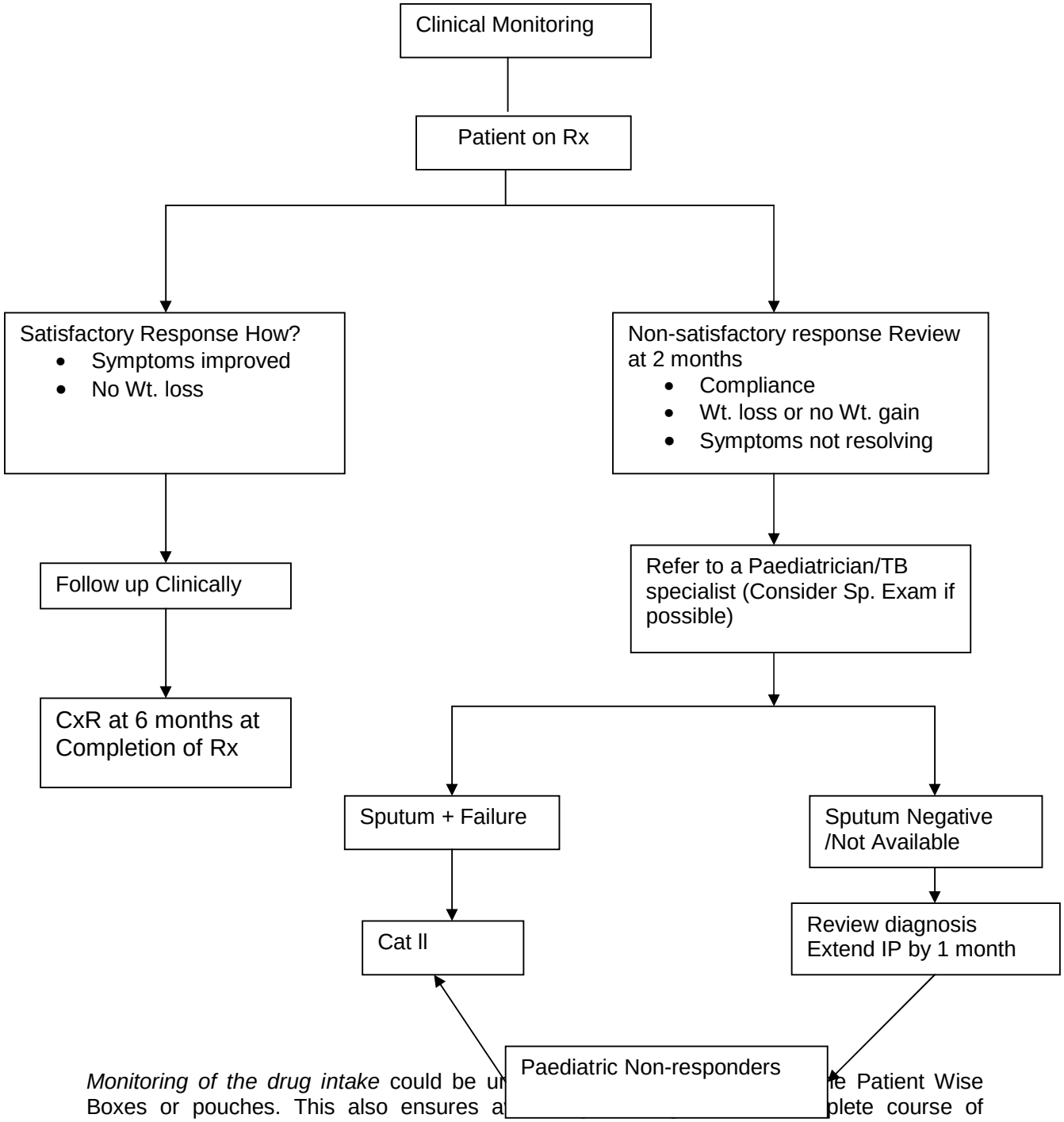
Monitoring of response to treatment in children needs to address the difficulties associated with obtaining sputum samples from children. A combination of the following is thus proposed:

- Wherever possible, follow-up sputum examinations is to be performed at the same frequency as in adults.
- Clinical or symptomatic improvement assessed at the end of the intensive phase of treatment and at the end of treatment. Improvement should be judged by lack of fever or cough, a decrease in the size of lymph node(s), weight gain etc.

- Radiological improvement assessed by Chest X-ray examination in all smear-negative pulmonary TB cases at the end of treatment.

If a patient deteriorates or fails to improve on treatment, at any time, s/he should be referred to a specialist. Proposed flow chart for clinical monitoring of paediatric TB patients is given in Figure 2.

Figure 2: Proposed flow-chart for clinical monitoring of Paediatric TB patients



Monitoring of the drug intake could be ur[illegible]e Patient Wise Boxes or pouches. This also ensures a[illegible]plete course of treatment.

Recording & reporting:

- In addition to the existing information, in relation to Paediatric TB patients the treatment card should include information on:
  - Basis for starting treatment along with categorization.
  - Documentation of clinical and radiological monitoring as described above. This information could be clubbed with the table for laboratory results in the present treatment card.
  - X rays should be retained until treatment completion, and a drawing of the X-ray picture with comments, entered in the remarks column.
  - Provision to check correct categorization and drug dosages. A dosage table based on patient's weight could be printed on the card to ensure correct dosage for the child.

  In acknowledgement of the need to include additional information in the existing treatment cards in the case of a child with TB, a committee should further examine whether to modify the existing treatment card or develop a new separate Paediatric treatment card. The advantage of modifying the existing card is that it would require minimal training and logistic burden. However, emphasis on use of X-rays for diagnosis as well as monitoring in Paediatric TB cases could create confusion in the field as the RNTCP has been stressing the role of sputum microscopy as the primary tool for diagnosis and monitoring of patients. A separate treatment card for Paediatric TB would allow for focusing on the special needs of this group of patients. However it would require training of staff and have an impact logistically on the programme.

- It was suggested that in the future, the RNTCP quarterly case finding report reflect the data for all types of TB by the age groups 0-14 and over 14 years of age as presently done for the new smear positive PTB cases. Also that Block 3 in the case finding report again presents the totals for each treatment Category, disaggregated by the age groups 0-14 and over 14 years of age.
- Further discussion is needed to define such areas as "failure/non-responder" in new smear negative PTB Paediatric cases.
- The RNTCP Quarterly and Annual bulletins should have a section / focus on Paediatric TB.

General recommendations

- In coordination with the IAP, RNTCP should organise sensitization of Paediatricians regarding the RNTCP.
- District TB Societies should include representatives from the local bodies of Paediatricians.
- All large hospitals and medical colleges should participate in the RNTCP and establish a Microscopy / DOT centre in their respective institutions.
- Teaching of RNTCP, including field visits to RNTCP diagnostic and treatment centres, should be included as a part of under-graduate teaching.
- All newly diagnosed TB cases in large hospitals/Medical colleges should be reported to the DOT centre in the hospital for arrangement of logistics to ensure that patients are started on RNTCP regimens. Similarly, before discharge of admitted patients, the DOT centre should be informed to arrange for continuation of treatment in the hospital or to organize necessary referral.
- To ensure that all diagnosed Paediatric TB cases receive DOTS, appropriate linkages need to be established between the DOT centres in the hospitals and medical colleges, and the other RNTCP diagnostic and treatment centres. The responsibility of ensuring availability of drugs and other logistics, direct observation of treatment, home visits, and

referral of patients should be overseen by the RNTCP. The Paediatricians will be consulted for any complications that arise during the course of treatment.
- Over the counter dispensing of anti-TB drugs should be stopped so that all patients are referred to the RNTCP DOT centres for treatment.
- IEC activities of the programme should include information that focuses on Paediatric TB

Research issues

Diagnosis

- Development of, and a multicentric field evaluation of a Paediatric TB diagnostic scoring system.
- Randomized Control Trial (RCT) of TB chemoprophylaxis: INH for 6 months versus INH+Rifmapicin for 3 months treatment.
- Further pharmacokinetic studies in children of the higher doses used in the intermittent regimen
- To provide additional scientific data from India, a RCT on the efficacy of daily versus intermittent short course chemotherapy treatment in specific forms of TB in children
- Should categorisation of Paediatric TB patients be determined by HIV status of the child?
- For children with TB, can mothers be used as DOT providers?
- Safety of the use of Ethambutol in children below 6 years
- Literature search on bio-availability of drugs in syrup formulations and dispersible tablets, minimum dose required for pyrazinamide /kg body weight
- Literature search on which steroid to use for TBM and Pericarditis. (Dexamethasone or Prednisolone)
- To examine yield of Paediatric TB cases if the children who have a history of contact with smear negative patients are also screened.
- Named patient based TB Register held electronically – “eTBRegister”.

Issues to be followed up

Several suggestions made by the expert group include major changes in the current RNTCP operational and technical guidelines. It is also clear that there has to be on-going discussions to incorporate these suggestions in a manner that will be applicable for use in field conditions taking into consideration operational feasibility. To follow up on the suggestions and monitor implementation, a core committee representing the RNTCP and the IAP (Joint RNTCP-IAP Committee), should be formed. Some of the issues that need further consideration include:

- Provision to make Chest X-rays and PPD available at all diagnostic centres
- Case definitions / treatment outcomes suggested for Paediatric TB cases
- Examine ways to ease administration and calculation of anti-TB drugs for Paediatric TB cases including procurement of combipacks for different weight groups of children.
- Revision / modification of current RNTCP monitoring and evaluation to address the needs of Paediatric TB cases. This could include:
  - Revision of the existing treatment card or development of a separate treatment card for children
  - Examine the need for modification in other RNTCP formats and registers in light of the suggestions by the expert group
  - Modification of the quarterly report to capture information on case finding and treatment outcomes of all types of Paediatric Tb cases
- Prioritise and conduct operational research on issues pertaining to Paediatric TB
- Revision of the RNTCP training modules to include Paediatric TB issues