



NATIONAL GUIDELINES FOR THE MANAGEMENT OF TUBERCULOSIS IN CHILDREN

2nd Edition, 2016



NATIONAL TUBERCULOSIS CONTROL PROGRAMME
DIRECTORATE GENERAL OF HEALTH SERVICES
MINISTRY OF HEALTH AND FAMILY WELFARE
DHAKA, BANGLADESH







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World Health
Organization

Country Office for Bangladesh

National Guidelines for the Management of Tuberculosis in Children

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PREFACE

Preface of the 2nd Edition

WHO, in the post-2015 strategy for tuberculosis, envisioned zero deaths, suffering and diseases by TB. Milestones were set to achieve 75% and 90% reduction of death, in comparison to deaths in 2015, by 2025 and 2035 respectively. Furthermore, targets have been set to reduce cases to 55 per 100,000 by 2025, and to 10 per 100,000 by 2035. NTP, Bangladesh has committed to attaining these goals by planning for it.

The 1st edition guideline for child TB was published in 2012, and later, reprinted in 2013, to meet the demand of pediatricians and other stakeholders. WHO has a policy to review guidelines every 3-5 years. Hence, NTP, Bangladesh has decided to publish the second edition of the guideline. To finalize it, several workshops were conducted, with pediatricians, public health experts, international child TB experts, pulmonologists, NTP officials and researchers.

In the second edition several chapters have been rewritten. The treatment chapter was updated with the addition of the latest dosage regimen and treatment as per WHO guidelines, published in 2014. Details on WHO recommended rapid diagnostic test (e.g. Xpert MTB/RIF) have also been included. Moreover a flowchart for MDR TB and the contact investigation form has been added for better understanding of the diagnosis, management and prevention of child TB. Descriptions on upcoming FDCs have also been included in this chapter. For growth monitoring, IPHN growth charts, used in the field, have been added. For active case searching, a new contact investigation form has been developed through workshops and this has been cited in the annexure.

This book, like its first edition, has not only targeted pediatricians but also doctors working in UHCs and district hospitals as GP or medical officers in both public and private sectors. It will be a helpful as a bedside reference book. Additionally, a detailed bibliography, containing 61 references to different journal articles and links to relevant documents was added.

Readers are humbly reminded that this guideline is not a replacement to a formal textbook.

PREFACE

Preface of the 1st Edition

WHO Stop TB Strategy and the launch of the Global Plan to Stop TB, 2006–2015 aims to "ensure equitable access to care of international standards for all TB patients– infectious and non-infectious, adults and children, with and without HIV [human immunodeficiency virus], with and without drug resistant TB" (Geneva, World Health Organization, 2006). The strategy thus re-emphasizes the importance of addressing management of TB in children. This guidance is therefore a timely response of the National TB Control Program, Bangladesh to the call of Stop TB Strategy to ensure equitable access to TB care for all children.

In adults, diagnosis of TB is relatively easy and mostly confirmed by examination of the sputum for acid-fast bacilli. Chest radiography plays a little role there for diagnosis of the disease. Whereas, in children suspected of having TB, diagnosis is difficult because they usually cannot cough up enough sputum to be sent for laboratory investigations, disease is paucibacillary in nature and diagnosis has to be based mostly on clinical features with a history of close contact with an infectious adult TB patient.

In diagnosing and treating pediatric TB, most countries have limited strategies in place, often guidelines for treating pediatric cases are non-existent or providers lack skills and access to available guidance and technologies.

This document is designed to complement existing WHO guidelines for managing TB in children, provides standard recommendations and evidence based best practices appropriate for the country.

The principal goal of this book is to setting national policies for managing tuberculosis in children. The further objectives are to help clinicians or other care providers improve their skills in diagnosis and management of childhood TB. The book is organized to help the reader understand the common epidemiological, pathophysiological, clinical and programmatic aspects of childhood TB and to use these to aid in the diagnosis and management of the disease in children.

The document emphasizes the needs of ensuring availability of basic tools for diagnosis including chest X-ray and tuberculin skin tests. Emphasis is also given to developing quality recording and reporting system for the effective management of child TB. Other key areas that are outlined in this book include guidance for the diagnosis and management of drug-resistant TB and TB-HIV co-infection in children. Importance of conducting contact investigations for the children who are close contacts of smear-positive TB cases are explicitly recommended in the book.

The target audiences for this guideline are the managers and health care providers of national TB control program, together with the health care professionals who provide tuberculosis care for children at the central or peripheral level health care facilities both in public and private sector.

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NB: Contributors participated in the revision workshops on 12-13 August 2015, group work during 1-5 August 2015 and 18-19 May 2015.

MESSAGE



MESSAGE

Tuberculosis services in Bangladesh are integrated under the Health, Population and Nutrition Sector Development Programme (HPNSDP), implementing through the primary health care services in the country.

In 2014, the 67th World Health Assembly (WHA) adopted WHO's "Global strategy and targets for tuberculosis prevention, care and control after 2015". The End TB Strategy aims to end the TB epidemic by early diagnosis and prompt treatment of all persons of all ages. The progress of TB control program in the country made so far, the child TB is still under detected. Nevertheless, much can be done for reducing the burden of TB among children. Revision of the guidelines on management of tuberculosis among children, following the recent WHO Guidance for national tuberculosis program, is a timely response to the National TB Control Program.

We believe that the health professionals and health managers will greatly be benefitted by this guidelines and improve their knowledge and skills in managing tuberculosis among the children in Bangladesh.

Md. Sirazul Islam
Secretary
Ministry of Health and Family Welfare
Government of the People's Republic of Bangladesh

MESSAGE



MESSAGE

Government of the People's Republic of Bangladesh has given high priority to Tuberculosis control in the country. The services for TB have been made available throughout the country. The National Tuberculosis Control Program under the Directorate General of Health Services has achieved significant success in TB Control.

Improving case finding and treatment of tuberculosis in children in one of those areas where we need to focus now. Infants and children are the most challenging to diagnose. Therefore, presumptive child TB cases should be addressed through special attention by health care professionals.

Moreover, there is an urgent need to address the lack of epidemiological data on TB in children in country, and health care workers and pediatricians in both public and private sectors should report all children diagnosed with TB to national TB programmes. The revision of the National Guidelines for the management of Tuberculosis in Children is a timely and appreciable step taken by the NTP to address issue of effective management of TB in children. We should not forget the fact that in Bangladesh, Tuberculosis in children significantly contributes to infant and child mortality in the country.

I hope this guideline will provide proper guidance to the managers and health care providers in managing TB in children.

Professor Dr. Abul Kalam Azad
Director General
Directorate General of Health Services
Ministry of Health & Family Welfare

MESSAGE



MESSAGE

The National Tuberculosis Control Program, under the Mycobacterial Disease Control (MBDC) unit of the Directorate-General of Health Service (DGHS), is working with a mission of eliminating TB from Bangladesh. The goal of NTP is to reduce morbidity, mortality and transmission of TB.

Over the last 15 years, TB case detection has steadily increased in Bangladesh, the total new cases of all forms of TB notified in 2014 were 196797 of which 6262 cases were child TB which is approximate 3%. The gaps in child TB case detection exist despite the significant TB service expansion achieved by the Bangladesh government. This is most likely due to poor detection of Tuberculosis in children throughout the country. It is estimated that with accurate diagnosis and good reporting systems children less than 15 years are likely to contribute 15-20% of the disease burden. Therefore, NTP has given high priority for early notification, management and prevention of child TB.

The National guidelines for the management of Tuberculosis in children were updated based on the recent evidence and advances in childhood TB diagnosis and treatment. This second edition aims to inform the revision of existing national guidelines and standards for managing TB, many of which include guidance on children.

I hope this revised guideline will provide appropriate guidance to the NTP managers, and health professionals with standards of preventing, diagnosing and treating childhood tuberculosis in a systemic manner with a programmatic approach.

Dr. Shahid Md. Sadiqul Islam

Director, MBDC and Line Director, TB-Leprosy
DGHS, Mohakhali, Dhaka.

MESSAGE



MESSAGE

Childhood tuberculosis (TB) affects millions of children worldwide. In 2015, an estimated 1 million children were diagnosed with TB resulting in 0.2 million deaths. TB in children is often overlooked due to non-specific symptoms and difficulties associated with its diagnosis. In that same year, 10.4 million people globally were diagnosed with this disease.

TB is a major public health problem in Bangladesh. Globally, children (aged less than 15 years) accounted for 6.3% of the new cases that were notified in 2015. The WHO South-East Asia Region was among the top three regions with 40% of TB cases in children. The burden of TB in children is likely to be higher in Bangladesh as not all cases are linked to the National Tuberculosis Control Program (NTP). Children with TB often come from poor families who lack knowledge about the disease and have limited or no access to health care services. We need to address these challenges and ensure that measures are taken so that children with TB are diagnosed and treated.

Ending the TB epidemic is part of the new agenda of the Sustainable Development Goals (SDG). In 2014, the World Health Assembly approved the End TB Strategy - a 20-year plan to end the global TB epidemic, with the vision of a world with 'zero deaths, disease, and suffering due to TB'.

WHO is committed to continue providing technical assistance to the NTP so that Bangladesh can achieve the targets of the End TB Strategy. Toward that end, WHO supported the revisions to the first national guidelines for the management of tuberculosis in children. I hope that these guidelines will be helpful for all medical professionals who manage child TB cases in health care facilities in Bangladesh.

Dr N. Paranietharan
WHO Representative to Bangladesh

MESSAGE



MESSAGE

We are at a critical juncture where Millennium Development Goal (MDG) has ended and era of Sustainable Development Goal (SDG) has begun. Bangladesh has attained significant achievement in improving child health during the period of MDG. Yet, a significant number of children are dying each year, many of them are from preventable causes. It includes both communicable and non communicable illness. Among the communicable illness, child TB is a concern of morbidity and mortality. But unfortunately case detection of child TB in Bangladesh has been low for quite a long time.

With the new WHO “The End TB Strategy”, engagement of Bangladesh Paediatric Association (BPA) with the child TB activity of National Tuberculosis Control Program (NTP) is very pertinent. To reach the target of reduction of TB incidence 90% by 2035, targeting child TB is very important where pediatrician can play vital role. BPA, since its journey in 1972, is committed for better health of the children of Bangladesh. Though WHO estimates 10% child TB cases among all cases of TB, notification in Bangladesh is just 4% indicates under-diagnosed and under-reporting. To combat this, National Guideline for The Management of Tuberculosis for Children will provide treating physician an instrument for aiding NTP, Bangladesh in the fight against TB.

Early diagnosis and screening of contacts and high risk group, the important part of the first pillar of the End TB Strategy, will prevent morbidity and mortality of children suffering from TB. Children less than 5 years of age are diagnosed less in number in Bangladesh, and clinical picture in this age group is more subtle and non-specific. Role of pediatrician in diagnosing TB in this age group is very crucial.

BPA in collaboration with USAID has been engaged, under the guidance of NTP, in capacity development program on child TB since 2013 in Dhaka and Sylhet Division. The program has increased case detection in child TB from 2.78% in 2013 to 4% in 2015, which is a definite change from last 8 years static case detection of around 3%. Further role out of the program in other divisions will play a positive role in increasing case detection of child TB cases in coming years.

In the process of development of this guideline, BPA has taken a vital role. Members of BPA from different parts of the country have taken active participation in the workshops organized by NTP and WHO. As President of BPA, I must thank NTP for involving our organization and thereby giving ownership and this will make our members morally responsible to use the guideline in their day to day practice. This cooperation will definitely fulfill the basic objective of BPA in improving child health in Bangladesh.

Professor Mohammad Shahidullah

President

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GLOSSARY OF ABBREVIATIONS

ART	Antiretroviral Therapy
BBB	Blood Brain Barrier
BCG	Bacille Calmette–Guérin
CHW	Community Health Worker
CSF	Cerebrospinal Fluid
CT	Computed Tomography
CXR	Chest X-ray
DGHS	Director General of Health Services
DOT	Directly Observed Treatment
DOTS	The Internationally recommended strategy for TB control
DST	Drug Sensitivity Test
E/ EMB	Ethambutol
EPTB	Extra-Pulmonary Tuberculosis
ELISA	Enzyme Linked Immunosorbent Assay
ESR	Erythrocyte Sedimentation Rate
FDC	Fixed Dose Combination
FNAC	Fine Needle Aspiration Cytology
GDF	Global Drug Facility
GFATM	Global Fund to fight against AIDS, TB and Malaria
H/ INH	Isoniazid
HAART	Highly Active Antiretroviral Therapy
HCW	Health Care Worker
HIV	Human Immunodeficiency Virus
icddr,b	International Center for Diarrhoeal Disease Research, Bangladesh
IGRAs	Interferon-Gamma Release Assays
IPHN	Institute of Public Health Nutrition (Bangladesh)
IPT	Isoniazid Preventive Therapy
IRIS	Immune Reconstitution Inflammatory Syndrome
LIP	Lymphocytic Interstitial Pneumonitis
LP	Lumbar Puncture
MT	Mantoux Test
MDGs	Millennium Development Goals
MDR	Multidrug-Resistant
MOH&FW	Ministry of Health and Family Welfare
MRI	Magnetic Resonance Imaging
NG	Nasogastric
NGO	Non-Governmental Organization
NIDCH	National Institute of Diseases of Chest & Hospital
NTP	National Tuberculosis Control Programme
NTRL	National TB Reference Laboratory
OFL	Ofloxacin
PJP	Pneumocystis Jiroveci Pneumonia
PCR	Polymerase Chain Reaction
PPD	Purified Protein Derivative
PTB	Pulmonary Tuberculosis
PEM	Protein Energy Malnutrition
PZA	Pyrazinamide

GLOSSARY OF ABBREVIATIONS

RMP/R	Rifampicin
RTRL	Regional Reference Laboratory
SMX	Sulfamethoxazole
SM/S	Streptomycin
TB	Tuberculosis
TBM	TB Meningitis
TMP	Trimethoprim
TST	Tuberculin Skin Test
TU	Tuberculin Unit
XDR-TB	Extensive Drug Resistance TB
WHO	World Health Organization
Z-N	Ziehl Neelsen

EPIDEMIOLOGY OF TB IN CHILDREN

GLOBAL

According to the 2016 WHO Global Tuberculosis Report, estimated new cases of tuberculosis (TB) were 10.4 million, of which about 1.0 million were children (<15 years of age)¹, 5.9 million male and 3.5 million were female. It is estimated that with accurate diagnosis and good reporting systems, children less than 15 years are likely to contribute 4-22% of the disease burden in 22 high-burden countries of the world². With excellent TB control and active provision of preventive therapy to child contacts, the burden of childhood TB can be reduced below 5%, as is the case in many developed countries. Because children acquire TB from the infectious adult cases, the incidence of pediatric TB provides an accurate measure of ongoing transmission within communities, a key indicator of epidemic control.

A common misperception used to be that children are not severely affected and that they rarely develop severe forms of disease. However, this is not the case in TB endemic areas where children often present with advanced disease and TB is a major contributor to under-5 morbidity and mortality. Global Tuberculosis Report 2015 estimates about 140,000 deaths from TB in children in 2014.

BANGLADESH

Bangladesh has a population of 158.95 million and estimated population of children <15 years is 53.7 million (33.8%)³. The incidence rate of all forms of TB for all age groups was 224/100,000 population in 2013, while the prevalence rate of the same was 402/100,000 population for the same year.

In 2015, among all forms of 199,001 total TB cases 7984 were child TB (4.01%), which was 3.35% (6262/186,968) in 2014, 2.78% (5044/181,395) in 2013 and 3% (4833/161,697) in 2012. In Dhaka division, detection of child TB cases was 3532 in 2015, 2881 in 2014, 2299 in 2013 and 2187 in 2012. The increase in Dhaka Division was 25% between 2014 and 2013 and 22% in 2015 and 2014, while the increase was only 5% between 2012 and 2013. This is most likely due to improved case detection with training of doctors and health care workers of Dhaka Division on child TB in 2013-2014⁵.

A study⁶ from 2008-09 in Madhupur upazilla in Tangail district showed an incidence of childhood TB of 52 per 100,000 among 0-14 year after a survey of all eligible children. Although this does not represent the national incidence of child TB, this figure indicates that there is a gap between the NTP-reported child TB and actual disease burden in the community. The NTP in 2007⁷ and an NGO working with TB in 2009⁸, reported detection rates of 9 and 8.6 per 100,000 0-14-year-olds, respectively.

DEFINITIONS: CONTACT

Definitions are taken from the WHO 2014 guidance⁹ include the following:

Contact screening: A systematic process for identifying contacts who have, or are at increased risk of developing TB. Contact identification and prioritization includes an interview with the index case to obtain the names and ages of contacts and an assessment of contacts' risk of having or developing TB, to determine those for whom clinical evaluation is indicated.

Contact: Any person who has been exposed to an index case.

Index Case: The initially identified case of new or recurrent TB, in a person of any age, in a specified household or other comparable setting in which others may have been exposed. An index case is the case, around which a contact investigation (section IV, page 36) is centered (but is not necessarily the source case).

Close contact: A person who is not in the household but who shared an enclosed space, such as a social gathering place, work place, or facility, with the index case for extended daytime periods during the 3 months before the start of the current treatment episode

Household contact: A person who shared the same enclosed living space as the index case for one or more nights or for frequent or extended daytime period during the 3 months before the start of current treatment episode.

THE SPECTRUM OF TB EXPOSURE, INFECTION AND DISEASE

EXPOSURE

A child is exposed to *M. tuberculosis* when he/she comes into contact with an infectious TB patient. The risk of actually inhaling the organism and becoming infected is determined by the infectiousness of the source case, as well as the proximity or closeness and duration of contact. Children are most likely to become infected if the mother or another adolescent/adult household member has sputum smear-positive TB.

INFECTION

A child becomes infected with *M. tuberculosis*, when he/she inhales the bacilli spread via tiny aerosol droplets that float in the air for prolonged periods of time. These tiny infectious droplets are mainly produced by adolescent and adult TB patients with cavities/extensive lesion into their lungs. Inhalation of infected droplets into lung leads to the development of primary parenchymal lesion (Ghon focus) into the lung with spread to regional lymph node(s). In most cases, the host immune response stops the multiplication of *M. tuberculosis* and contains the spread at this stage. However, few dormant bacilli may persist and give rise to disease later, at any stage of life, if immunity of the body becomes compromised.

Most young children become infected after household exposure to an adult with sputum smear-positive TB. In 2013, total number of sputum smear positive cases detected in Bangladesh was 108,4081 (new and relapsed case) and these patients are spreading TB infection in the community. Sputum smear-negative cases are less infectious, but may still transmit the infection if they have pulmonary TB (diagnosed on chest X-ray); especially when mother or primary caregiver of a young child have the disease. TB infection may also occur outside the household; therefore, absence of household contact does not exclude TB.

Children with *M. tuberculosis* infection are not ill and do not have symptoms of TB disease unless the disease is active. Infection without symptom/signs of disease is also known as *latent TB infection* (LTBI).

LTBI is usually indicated by a positive MT test/IGRA. However, there are many limitations to both the MT and the IGRA (see TB diagnosis section). In HIV-infected and/or malnourished children, the MT may give a false negative result. After inhalation of TB bacilli, it takes up to 3 months to give a positive MT test result. It should be noted that during this window period, infected children are asymptomatic and the MT also may not give a positive result (TB diagnosis section).

Children less than 8 years of age rarely develop lung cavities and high bacillary loads; and they are rarely infectious. However, older children (>8yrs of age) frequently develop sputum smear-positive TB and can also act as a source case.

DISEASE (active disease)

Only a small percentage of children who inhale the TB bacilli develop active disease. A child is said to have TB disease (active disease) if-

1. infected with *Mycobacterium tuberculosis*, with
2. clinical sign symptoms,
3. ± laboratory or radiologic evidence suggestive of TB

Certain groups are at far greater risk of developing active disease than others (Box-I). TB disease may manifest in many different ways, but is usually indicated by the presence of well-defined symptoms and/or radiological changes (see diagnosis section).

Risk Factors Which Influence Progression of TB Infection to Disease

The risk for developing TB disease following infection with *M. tuberculosis* is mainly determined by the following factors (Box I).

Box I: KEY RISK FACTORS FOR TB DISEASE IN CHILDREN⁹

1. Household or close contact with a smear positive or culture positive pulmonary TB (parents, siblings, close relatives, caregivers, neighbours and teachers)
2. Age <5 years: The risk of developing TB disease is highest in very young children, who is immune immature (Table-I, P-3)
3. Severe malnutrition or other Immunosuppressive conditions
 - Measles in the previous 3 months
 - Whooping cough
 - HIV infection
 - Being on drugs like steroids, immunosuppressive agents
4. The time since exposure or infection: the vast majority of children who develop TB disease do so **within the first year** after *M. tuberculosis* exposure or infection

NB: Other high risk factors are HIV/AIDS, diabetes, end-stage renal failure, cancer, connective tissue disease, silicosis, gastrectomy, solid organ transplantation and patients on prolonged steroid. Both type 1 and type 2 diabetes patient have the increased risk of having TB^{10,11}.

TABLE 1. AGE-SPECIFIC RISK OF PROGRESSION TO DISEASE AFTER PRIMARY INFECTION WITH *M. tuberculosis* IN IMMUNOCOMPETENT CHILDREN¹²

Age at Primary Infection (yr)	Risk of Progression to Disease (%)		
	Pulmonary Disease	Disseminated disease or Tubercular Meningitis	No disease
< 1 year	30-40%	10-20%	50%
1–2 years	10-20%	2-5%	75-80%
2–5 years	5%	0.5%	0.5%
5–10 years	2%	0.5%	98%
> 10 years	10-20%	0.5%	80-90%

REVISED DEFINITIONS OF TB IN CHILDREN^{9,13}

The diagnosis of TB refers to the recognition of an active case, i.e. a patient with symptomatic disease (due to *M. tuberculosis* infection). Recognition of TB is made by clinical diagnosis or by bacteriological confirmation.

Presumptive TB: a patient who presents with the symptoms or signs suggestive of TB (previously known as TB Suspect).

Bacteriologically confirmed case: is a patient from whom a biological specimen is positive by smear microscopy, culture or WHO-approved rapid diagnostics (eg. Xpert-MTB/RIF).

Clinically diagnosed TB case: is a patient who does not fulfill the criteria of bacteriological confirmation or smear not done, but diagnosed as active TB by a clinician and decided to have a full course of anti-TB treatment. These cases are diagnosed as active TB on the basis X-ray abnormalities or suggestive histology or extrapulmonary cases without laboratory confirmation.

Bacteriologically confirmed or clinically diagnosed cases of TB are also classified according to-

- i) Anatomical site of disease
- ii) Drug resistance
- iii) History of previous anti-TB treatment
- iv) HIV status. Beyond the diagnosis of TB disease, the type of TB case should be defined clearly and completely to enable appropriate treatment to be given and the outcome of treatment evaluated.

Registration/notification with NTP:

Notification of TB has been made mandatory by the Government of Bangladesh from January 30, 2014 through an official order (annex 6, page 59).

All children with TB must be registered/notified within the NTP system as smear-positive pulmonary, smear-negative pulmonary TB or extra-pulmonary TB, and as a new case or a previously treated case.

Intrathoracic TB: Bacteriologically confirmed or clinically diagnosed cases of TB involving the lungs or extrapulmonary sites should be classified as following-

TABLE 2. CLASSIFICATION OF INTRATHORACIC TB⁹

Anatomical involvement	Pulmonary TB (PTB)	Extra-pulmonary TB (EPTB)
Lung parenchyma	Yes	No
Tracheobronchial tree	Yes	No
Miliary	Yes	No
Pleural (effusion)	No	Yes
Intrathoracic lymphadenopathy (mediastinal/hilar/subcarinal)	No	Yes
Both Extra -Pulmonary and Pulmonary TB	Yes	No

PULMONARY TUBERCULOSIS (PTB) refers to any bacteriologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheobronchial tree. Miliary TB is also classified as PTB because there are lesions in the lungs too.

There are standards for the optimum number of specimens for smear microscopy¹⁴.

PTB, Smear-positive (criteria)

- One initial sputum smear examination positive for acid-fast bacilli; or
- Smear negative but culture- or Xpert-positive for *M. tuberculosis*.

PTB, Smear-negative (criteria)

A case of pulmonary TB that does not meet the above definition for smear-positive PTB. Such cases include cases without smear results/smear not done, which is frequent in children. In keeping with good clinical and public health practice, diagnostic criteria for sputum smear-negative PTB should include:

- At least two sputum specimens negative for acid-fast bacilli; and
- Have diagnostic features strongly suggestive of Pulmonary TB; and
- Decision by a clinician to treat with a full course of anti-TB chemotherapy.

EXTRA-PULMONARY TUBERCULOSIS (EPTB)

EPTB refers to any bacteriologically confirmed or clinically diagnosed case of TB involving organs outside the lung parenchyma and tracheobronchial tree (e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, joints and bones, meninges etc).

Children with tuberculosis outside lung parenchyma and tracheo bronchial tree is labelled as extra-pulmonary TB. For example, TB in pleura is regarded as EPTB. EPTB accounts for about 30% of TB in children, as seen in high burden country^{12,15}. Note that *children who have both pulmonary and extra pulmonary TB is classified under the case definition of PTB* (see Table 2, page-4).

Classification based on treatment history

New patient: Has never been treated for TB or *taken TB drugs for less than one month*. INH preventive therapy is not considered as previous treatment.

Previously treated patient: Has received 1 month or more of anti-TB drugs in the past. This group further sub-classified to relapse patient, treatment after failure patients, treatment after loss to follow-up patients and others.

Classification based on drug resistance: (details in section 3: Drug-resistant TB and TB/HIV)

DRUG-RESISTANT TB

Drug-resistant TB is a laboratory diagnosis i.e. based on drug susceptibility test (DST). Children are as susceptible to drug-resistant as to drug-sensitive TB. However, drug-resistant TB should be suspected if any of the features below are present:-

1. Features in the source case suggestive of drug-resistant TB:

- Contact with a known case of drug-resistant TB
- Remains sputum smear-positive after 3 months of treatment
- History of previously treated TB
- History of treatment interruption.

2. Features of a child suspected of having drug-resistant TB:

- Contact with a known case of drug-resistant TB
- Not responding to the anti-TB treatment regimen
- Recurrence of TB after adherence to treatment.

Diagnosis of TB in children is not straight-forward as in adult TB patient; hence it requires careful and thorough assessment of all the data derived from a careful history, clinical examination and relevant investigations, e.g. MT, chest X-ray (CXR), smear microscopy and other investigations. PTB is the common form of TB in children although bacteriological confirmation through sputum microscopy is not always possible for young children, who cannot cough up sputum for microscopic examination. Sputum induction and gastric aspirate has been documented to be an effective method for collection of specimen in younger children. Every attempt to collect sputum should be sought whenever possible; and other methods should also be tried for collection of specimen (annex 4, pages 53-55). Sputum sample collection has now being strongly pushed for the older children who are capable of producing a sputum sample.

Also, patients with fever of unknown origin, failure to thrive, significant weight loss, severe malnutrition and/or other immunosuppressive conditions such as measles in the previous 3 months, whooping cough, HIV or being on medication like steroids or unexplained lymphadenopathy should be evaluated for TB. Any child with pneumonia, pleural effusion, or a cavitary or mass lesion in the lung that does not improve with standard antibacterial therapy should also be evaluated for tuberculosis.

CHALLENGES IN THE DIAGNOSIS OF TB IN CHILDREN

Diagnosis of TB in children is often difficult for several reasons:

1. Symptoms are often non-specific particularly in young children.
2. Childhood TB is paucibacillary and a microbiological diagnosis is often not possible.
3. It is difficult to obtain sputum for bacteriological confirmation.
4. The Mantoux Test or Tuberculin Skin Test (TST) is often negative in malnourished children or overwhelming TB (see below – causes of false-negative MT). Like IGRA, MT also fails to differentiate TB disease from infection.
5. X-rays are often non specific and prone to variable interpretation.

Despite these difficulties, an accurate diagnosis can still be made in the majority of children from careful history taking, clinical examinations and relevant investigations, even in an outpatient setting of rural Bangladesh. To increase case detection rate in child TB, both active and passive case-finding strategies have to be adopted with intensified case-finding among the high risk groups (both clinical- and population-based high risk groups). In screening contact of bacteriologically-confirmed cases, all DR-TB cases and index child TB cases should be prioritized.

A trial of treatment with anti-TB medicine is not recommended as a method to diagnose or rule out TB in children.

BOX II: RECOMMENDED APPROACH TO DIAGNOSE TB IN CHILDREN^{9,14}

1. Careful history (including history of TB contact and symptoms suggestive of TB)
2. Clinical assessment (including serial weight monitoring)
3. Investigations
 - 3.1 Mantoux test
 - 3.2 Chest X-ray and other radiological evaluation
 - 3.3 Bacterial confirmation whenever possible
 - 3.4 Investigations relevant to suspected PTB/EPTB
 - 3.5 HIV testing

1. HISTORY-TAKING

1.1 DOCUMENT HISTORY OF THE INDEX CASE

History is the most important part in the diagnosis of TB in children. This includes presenting symptoms and signs, history of contact with a known case of TB and medications taken. Children usually acquire the disease from a sputum-positive, usually an adult/adolescent, source case; hence the household contact and other close contact is to be sought in all presumptive TB cases. Among children, a household contact is often positive as a source of infection; young infants, who stays at home (less mobility and remains on the lap and stays in close proximity to infectious adult/adolescent) are more likely to have contracted TB at home^{14,16}. All children below 5 years and with conditions of immunosuppression (eg. HIV, on anti-cancer medication) should be evaluated for possible TB disease or infection. Conversely if a child is diagnosed with TB, active search should be made to find household contacts/cases with active TB (reverse contact tracing)¹⁷. If a child is infectious (sputum smear +ve), other child contacts must be sought and screened.

It is also important to document whether the suspected index case is responding to TB treatment or not (cured, not cured, dead). While taking history, if an index case is found not to be responding or poorly responding to treatment, it points that it may be a case of drug-resistant TB and the child contact (if diagnosed as TB) is most likely to have drug-resistant TB. This is an important consideration in the diagnosis and treatment of the child.

Young children living in close contact/household contact with a source case are at particular risk of TB infection and disease. The risk of infection is greatest if the contact is in close proximity, exposure is prolonged and a source case has sputum smear-positive PTB. Source cases that are sputum smear-negative but culture-positive are also infectious, but to a lesser extent.

If no source case is identified, but someone else in household is found to have chronic cough upon further inquiry, assessment of that person for possible TB is warranted.

Children usually develop TB within 2 years after exposure and most of them (90%) within the first year. Therefore, history of close contact with a patient (adult or adolescent or even a child) with pulmonary TB within the recent past (last one year) is the most important clue.

Clinical assessment alone is sufficient to decide whether the contact is well or symptomatic. Routine clinical assessment of exposed contacts will not require CXR or MT. This approach applies to contacts of smear-positive pulmonary TB cases, but screening should also be available for contacts of smear-negative pulmonary TB cases. If the contact of a source case with smear-negative pulmonary TB is symptomatic, then the diagnosis of TB needs to be investigated as above, whatever the contact's age is.

Objectives of contact management:

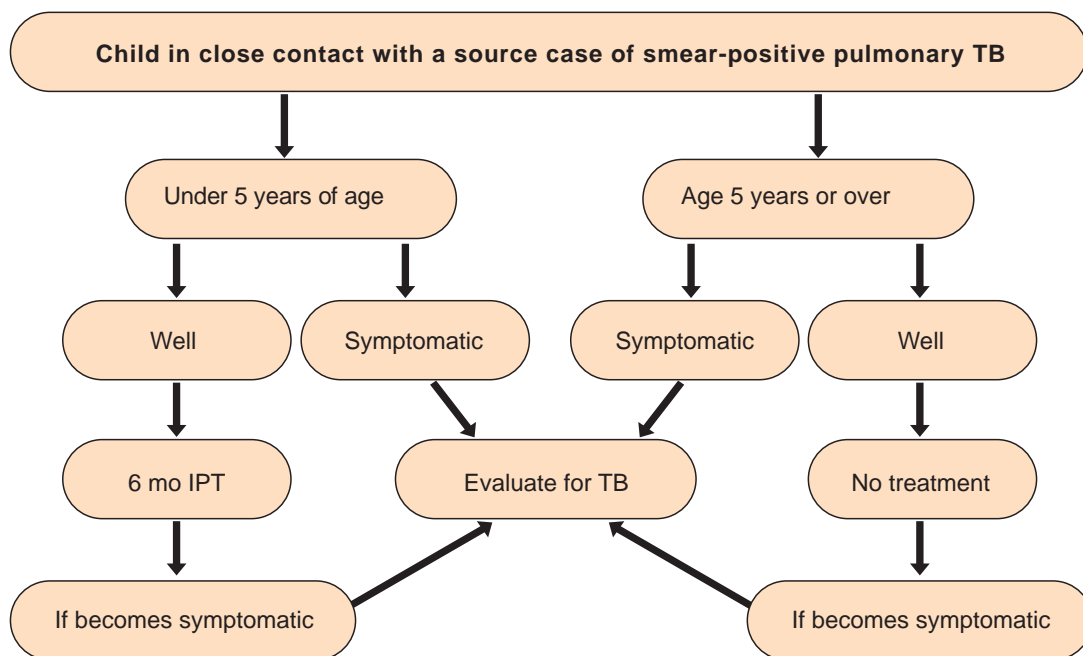
1. to diagnose undetected case in household and community
2. to initiate Isoniazid Prophylaxis Therapy (IPT)

APPROACH TO CONTACT MANAGEMENT

To increase case detection, all children with close contacts or household contacts should be asked/checked for common TB sign-symptoms. Although the best way to detect TB infection is the TST; and a CXR can suggest PTB. Symptom-based screening has been found to be a good tool in case detection in resource-limited countries^{16,17,18,19}. These tests should be done where they are available to screen exposed contacts.

A simple approach is outlined on the next page.

FIGURE 1: APPROACH TO CONTACT MANAGEMENT WHEN CHEST X-RAY AND MT ARE NOT READILY AVAILABLE



2. APPROPRIATE CLINICAL ASSESMENT

2.1 IDENTIFY SYMPTOMS SUGGESTIVE OF TB

TB in children commonly presents with fever and failure to thrive, but these are non-specific²⁰. In most cases, children with symptomatic TB develop chronic unremitting symptoms (symptoms persisting for >2 weeks even after appropriate treatment). Haemoptysis or coughing up of blood (a common symptom in adults) is rare in children with TB, but may occur in adolescents. Malnutrition has been recognized as an important risk factor for TB in children and enough evidence has been generated¹¹. TB disease can be more severe and of rapid onset in infants and young children. For EPTB, symptoms depend on the organ involved (enlarged lymphnode with/without sinus formation, spinal deformity and seizures). Children particularly those <3 yrs of age, severely malnourished and living with HIV pose the greatest challenge for clinical diagnosis.

In severely malnourished under-five children cough and/or fever of <2 weeks duration has been demonstrated to be symptoms of TB in children many parts of the world like in Bangladesh and Africa. This high-risk group of children, presenting with severe pneumonia, accounted for 23% TB cases in Bangladesh²¹.

In general, TB is a slowly-developing chronic disease, but it may present acutely in young and HIV-infected children. However, TB in children can manifest in various ways in different age groups: (annex-1, page 45)

- Infants (<1 year): primarily pneumonia-like
- Children (1-9 years): usually with a chronic cough
- Adolescents (10-19 years): as in adults

2.1.1 SYMPTOM CRITERIA FOR PTB (See Box III):

BOX III- SYMPTOM CRITERIA FOR PTB

- Persistent, non-remitting cough for >2 weeks not responding to conventional antibiotics (amoxicillin, co-trimoxazole or cephalosporins) and/or bronchodilators
and/or
- Persistent documented fever (>38°C/100.4°F) for >2 weeks after common causes such as typhoid, malaria or pneumonia have been excluded
and/or
- Documented weight loss or not gaining weight during the past 3 months (especially if not responding to de-worming together with food and/or micronutrient supplementation) OR severe malnutrition
and/or
- Fatigue, reduced playfulness, decreased activity

NB: Any one of the above symptom criteria in a child (<15 years) in close contact with a known bacteriologically confirmed TB or clinically confirmed TB should be regarded as presumptive TB case and referred to a physician for evaluation.

TABLE-3 SYMPTOMS AND SIGNS SUGGESTIVE OF EXTRA-PULMONARY TB

Symptoms and Signs	Extra-pulmonary TB
A painless enlarged mass of matted lymph nodes (>2x2 cm), usually in the neck, not fixed to the underlying tissues, initially firm and fluctuant later, that may present with sinus, not responding to a course of antibiotics	TB lymphadenitis (commonly cervical)
Cough and shortness of breath	Pleural TB, Pericardial TB
Reduced playfulness, irritability, weight loss, headache, vomiting without diarrhea, drowsiness, lethargy, convulsions, unconsciousness; and meningitis of acute or sub-acute onset and not responding to antibiotic	TB meningitis, Tuberculoma
Abdominal pain, altered bowel habit, mass or ascites	Abdominal TB
Gibbus (acute angulation of vertebrae)	Spinal TB
Chronic pain and swelling of joint(s), usually single	TB arthritis

** If any of the above symptoms are associated with a history of contact, possibility of TB is high.

TB LYMPHADENITIS

The most common extra-thoracic manifestation of TB is cervical lymphadenitis; sometimes it can also involve axillary and inguinal lymph nodes. Generalized lymphadenopathy is an uncommon presentation of TB in children, unless associated with disseminated TB or AIDS. In cervical region this presents as a painless visible neck mass, usually composed of matted lymph nodes, not fixed to the underlying tissues. Suppuration and spontaneous drainage of the lymph nodes may occur with the development of sinus. Fever, weight loss, fatigue, and malaise are usually absent or minimal.



The axillary lymph node can also enlarge after BCG vaccination. In such case, ask for recent BCG vaccination and look for a BCG scar. It usually occurs on the left axilla (BCG given over left deltoid). The differential diagnosis includes; acute suppurative lymphadenitis (usually tender and hot, that can be associated with scalp and ear infection), reactive hyperplasia (usually with a viral episode) and malignancy (look for other nodes and spleen).

PLEURAL AND PERICARDIAL TB

Pleural effusion is infrequent in children <6 years and rare before 2 years of age. The typical history of tuberculous pleurisy reveals intermittent fever, chest pain that increases in intensity on deep inspiration, and shortness of breath. Chest pain is localized to one side of the chest associated with stony dull percussion note on the same side with diminished breath sounds. Other signs include increased respiratory rate, respiratory distress and fullness of chest. Restricted movement of the chest and intercostal fullness are highly suggestive of a tuberculous pleural effusion. The child with tuberculous pleural effusion is not sick-looking in contrast to post-pneumonic pleural effusion or empyema.

Cardiac involvement in tuberculosis is rare (0.5 to 4%) and mainly affects the pericardium. Clinical features are due to the presence of the pericardial fluid and those due to pericardial constriction. Pericardial effusion is the most common presenting feature of the cardiac involvement of tuberculosis; presenting symptoms are often non-specific with low-grade fever, malaise and weight loss. Though chest pain is unusual in children, yet tightness of chest and respiratory distress can occur. On examination distant heart sounds, pericardial friction rub, raised jugular venous pressure (JVP) and pulsus paradoxus may be appreciated. The disease most commonly spreads to the pericardium by direct extension from the lungs and also from the mediastinal/ hilar or subcarinal lymph nodes, the sternum or the spine.



Right-sided TB pleural effusion



Pericardial TB: Enlarged cardiac shadow

MILIARY TB

It is a disseminated form of TB, a serious complication of primary TB in young children; and children <3 years of age are at highest risk. Miliary TB may manifest with low-grade fever, malaise, weight loss, and fatigue. A rapid onset of fever and associated symptoms may also be observed. History of cough and respiratory distress may be obtained.



Miliary TB

Physical examination findings include enlarged lymph nodes, liver and spleen. Systemic signs include fever, increased respiratory rate, cyanosis, and respiratory distress. Other signs, which are subtle and should be carefully sought in the physical examination, include papular, necrotic, or purpuric lesions on the skin or choroid tubercles in the retina of the eye. A miliary or millet-seed-like pattern, seen on chest radiography can be helpful in the recognition of disseminated TB manifesting in the lungs.

TB MENINGITIS

The most severe manifestation of TB is TB meningitis (TBM) and commonly occurs in children <4 years^{12,15}. Presentation can be acute or chronic. More commonly, signs and symptoms occur slowly over weeks. Rapid progression tends to occur in infants and young children, where it is frequently fatal. Presenting clinical features in children with TBM starts with fever, headache, vomiting and malaise which evolve over 1-2 week to signs of meningeal irritation, cranial nerve palsies, convulsions, deterioration of mental status, hemiplegia-paraplegia, coma, and death. Treatment in early stage results in full recovery; and poor sequelae if treated in the later stages. Treatment should be started immediately in a child with signs of TBM with history close contact. Most important diagnostic test in TBM is CSF study. Current recommendations also include Xpert MTB/RIF as an initial investigation when available, for prompt recognition and treatment^{9,14}.



TB meningitis

ABDOMINAL TB

Abdominal TB presents with non-specific, often deceptive and mimics symptoms of different gastrointestinal (GI) disorder; hence the diagnosis is frequently delayed by clinicians, more so in children. Tuberculosis can involve any part of the GI tract from the mouth to the anus, the most common site of involvement being the ileocaecal region. The spectrum of abdominal TB disease in children is different from adults, in whom adhesive peritoneal and lymph nodal involvement is more common than GI disease. Most children have constitutional symptoms of fever, abdominal pain, constipation, alternating constipation and diarrhoea, weight loss, anorexia and malaise. It can also present with pain and attacks of intestinal obstruction. Abdominal distention due to ascites is the presenting feature of TB peritonitis. Other clinical features depend upon the site, nature and extent of involvement eg. hepatosplenomegaly, doughy abdominal mass, enterocutaneous fistula. Children are often malnourished.



Abdominal TB

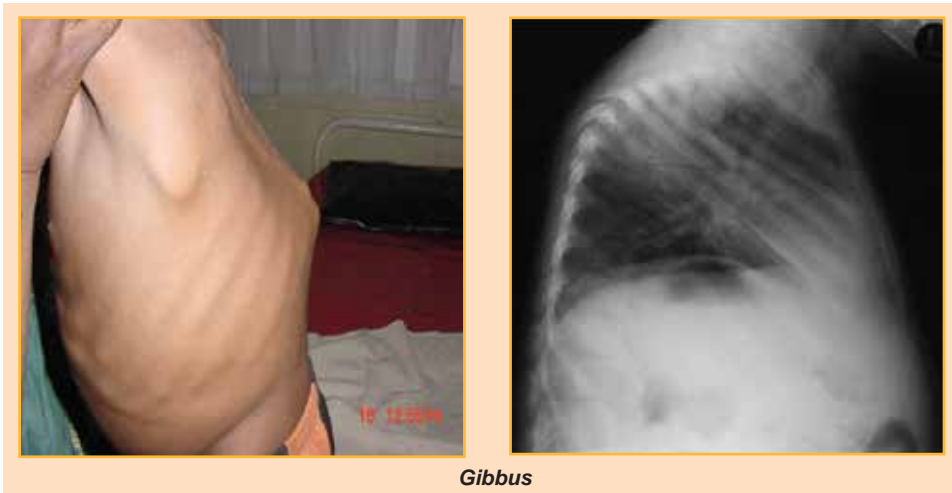
OSSEOARTICULAR TB: TB SPINE AND TB ARTHRITIS

Osteoarticular Tuberculosis can involve any bone and joint, but the spine is affected commonly (50% of all osteoarticular TB)²². Other common areas of involvements are hip, knee and short long bones of the hand and feet. In growing children, the disease can destroy areas responsible for their spinal growth (growth plates in vertebra). This may cause permanent deformity of spine or neurological complications in growing children if not treated properly.

TB bacteria do not directly affect bones and joints. The primary focus of infection is generally in the lungs or lymph nodes. It starts insidiously, usually as a monoarticular involvement. Child complaints of pain in the joint which is aggravated by movement and often wakes up at night- classic “night cries”. In later stages all movements become more restricted due to erosion of articular cartilage.

In spinal TB common clinical features are back pain for few weeks, more at night with tenderness in the affected area; angulation of the spine called “gibbus” deformity a feature of Pott’s disease (severe kyphosis with destruction of the vertebral bodies). It may also present acutely as cord compression, leading to paraplegia or quadriplegia resulting difficulty in walking and voiding of urine/stool. Cold abscess over the femoral triangle, anterior or posterior triangle of the neck or gluteal region may be seen according to involvement of region of vertebrae.

Any child with local pain and tenderness over the spine must be suspected of having spinal tuberculosis. **A rapid onset of a gibbus (‘hump back’) is almost always due to tuberculosis.**



Gibbus

CONGENITAL TB

Despite TB being a common disease, congenital TB is rare. At birth there may be no symptoms except LBW. Symptoms usually manifest at 2nd-3rd week of life. It should be suspected in neonates with nonspecific symptoms (respiratory distress, pallor, fever, growth failure, ear discharge, lethargy, irritability) born to a mother suffering from tuberculosis or, if any newborn suffering from persistent pneumonia or fever and hepatosplenomegaly and peripheral lymphadenopathy (seen in one third of cases).

It usually occurs in two ways-

- (1) trans-placental through umbilical vein causing primary complex in liver and
- (2) aspiration/swallowing of infected amniotic material during birth process or in utero²³. A diagnostic criteria has been laid by Cantwell (1994) can be followed²⁴.

2.2 DANGER SIGNS REQUIRING URGENT HOSPITAL REFERRAL²⁵

Although TB is usually a chronic disease, there are certain danger signs that require urgent hospital referral.

BOX-IV: DANGER SIGNS REQUIRING URGENT HOSPITALIZATION

- Severe respiratory distress (TB pneumonia with/without bacterial super infection, Pleural effusion)
- Severe wheezing not responding to bronchodilators (signs of severe airway compression)
- Headache (especially if accompanied by vomiting), irritability, drowsiness, neck stiffness and convulsions (signs of TB meningitis)
- Acutely ill with hepatosplenomegaly and ascites (signs of disseminated TB)
- Breathlessness and peripheral oedema (signs of pericardial effusion)
- Acute angulation (bending) of the spine with/without paraplegia (sign of TB spine - "gibbus")
- Other co-morbidities e.g. severe anaemia, severe malnutrition

NB: Hospital referral should also be considered with diagnostic uncertainty requiring further investigations.

2.3 UNCOMMON SIGNS INDICATIVE OF RECENT TB INFECTION

- Phlyctenular conjunctivitis - raised red nodule at the junction of the sclera and cornea surrounded by a red area of conjunctivitis. Occurs due to allergic response by cornea & conjunctival epithelium to mycobacterial & some bacterial proteins.
- Erythema nodosum - raised, tender, purple patches on the shin.

2.4 GROWTH ASSESSMENT

Documented weight loss or failure to gain weight, especially after being treated in a nutritional rehabilitation programme, is a good indicator of chronic disease in children, of which TB may be the cause.

To assess children's nutritional status, the Institute of Public Health Nutrition (IPHN), Bangladesh have developed growth chart to be used for the boys and girls of Bangladesh. These charts can be used to assess growth of child with TB (annex 2A to 2F, pages 46-51).

3. DIAGNOSTIC TESTS

In children except adolescent, usually demonstration of TB bacilli in sputum smear or culture is often not possible as children can not expectorate sputum and the disease itself is usually paucibacillary.

3.1 MANTOUX TEST (MT)/ Tuberculin Skin Test (TST)

Tuberculin Skin Test (TST) measures the delayed type hypersensitivity response to tuberculin Purified Protein Derivative (PPD). There are a number of TSTs available, but the Mantoux Test (MT) method is the most validated one.

A positive MT only indicates infection with M. Tuberculosis and does not always indicate active disease (TB). However, the MT can also be used in conjunction with other tests in diagnosing TB in children at

risk with signs and symptoms suggestive of TB. Health-care workers must be trained in performing and reading a MT.

MT is carried out⁹ by injecting 5 TU of tuberculin PPD-S or 2 TU of tuberculin PPD RT23 into the skin (intra-dermal) on the inner aspect of the left forearm. (annex 3, page- 52). The MT should be regarded as positive when the induration is:

1. >10 mm diameter
2. >5 mm diameter in children with PEM, HIV infection and immunosuppression.

Interpretation of MT should be done irrespective of previous BCG vaccination. It should also to be noted that, a **negative MT does not exclude TB exposure, infection or disease.**

False negative MT may occur in:

- Severe malnutrition
- Immunosuppressive conditions:
 - Measles in last 3 months
 - Whooping cough
 - HIV infection
 - Drugs like steroids, anti-cancer agents
- Disseminated and miliary TB and/or TB meningitis (TBM)
- Very recent TB exposure (within last 3 months)

3.2 CHEST X-RAY (CXR)

Chest radiography is useful in the diagnosis of TB in children along with other criteria (signs/symptoms, history of exposure, MT, suggestive diagnostics). In the majority of cases, children with pulmonary TB have CXR changes suggestive of TB. Good-quality CXRs (annex-5, pages 56-58) are essential for proper evaluation. CXRs should preferably be read by a radiologist or a health-care provider trained in reading X-ray films/image. A lateral chest X-ray is helpful to evaluate hilar lymphadenopathy. **CXR should always be done in all forms of TB.**

Chest X-ray changes are often non-specific. Different CXR changes suggestive of TB are summarised below.

3.2.1 COMMONEST RADIOLOGICAL PATTERN OF TB IN CHILDREN

- Increased density in the hilar region due to enlarged hilar lymph nodes; and/or a broad mediastinum due to enlarged mediastinal lymph nodes.
- Persistent opacity in the lung: Persistent opacification which does not improve after a course of antibiotics should be investigated for TB.

3.2.2 LESS COMMON RADIOLOGICAL SIGNS

- Compression of the airways due to enlarged lymph nodes; partial occlusion may lead to **segmental or lobar hyperinflation**, complete airway occlusion may cause **collapse of a lung segment or lobe.**
- Miliary pattern of opacification (highly suggestive in HIV-negative children)
- Unilateral pleural effusions (usually in children > 5 years old)

Adolescent patients with TB often have CXR changes similar to adult patients- pleural effusions, apical infiltrates with cavity formation being the most common forms of presentation.

3.2.3 RADIOLOGICAL FEATURES THAT REQUIRE URGENT HOSPITAL REFERRAL

- Widespread fine millet-sized (1-2 mm) lesions indicative of disseminated or miliary TB
- Severe airway obstruction (always evaluate the airways)
- Severe parenchymal involvement
- Acute angulation of the spine (TB spine, gibbus)

NB: CXR is less useful in HIV-infected children due to overlap with other HIV-related lung disease eg. Interstitial pneumonia.

3.3 BACTERIOLOGICAL CONFIRMATION

Bacteriological confirmation is done by smear microscopy from appropriate clinical samples to demonstrate AFB followed by culture and other recommended diagnostics.

It is always advisable to confirm diagnosis of TB in a child using whatever specimens and laboratory facilities are available. Appropriate clinical samples include sputum, gastric aspirates and other relevant material (e.g. lymph node for biopsy, CSF). Samples should be collected properly and sent for microscopy and culture where facilities are available.

Bacteriological confirmation is especially important for children who have:

- Suspected drug-resistant TB
- Severe immunosuppression including HIV infection
- Complicated or severe cases of disease
- Uncertain diagnosis

3.3.1 SMEAR MICROSCOPY (annex 4, pages - 53-55)

Common ways of obtaining samples for smear microscopy include the followings:

- a) EXPECTORATION
- b) GASTRIC ASPIRATION
- c) SPUTUM INDUCTION
- d) FINE NEEDLE ASPIRATION CYTOLOGY (FNAC)

3.3.2 CULTURE

Collection of specimens for culture should be considered where facilities are available. TB culture is of particular value in complicated cases or when there is a concern regarding drug resistance. Probability of obtaining a positive TB culture improves when more than one sample is taken; with at least 2 samples.

Facilities for culture are available at present in:

- NTRL, National Institute of Diseases of Chest & Hospital (NIDCH), Mohakhali, Dhaka;
- RTRL, Chest Disease Hospital, Rajshahi;
- RTRL, Chest Disease Hospital, Khulna;
- RTRL, General Hospital, Chittagong;
- ICDDR,B;
- TB-Leprosy Project Hospitals, Netrokona, Mymensingh & Tangail; Damien Foundation.

3.4 INVESTIGATIONS RELEVANT FOR SUSPECTED EXTRA-PULMONARY TB

In most of the cases, TB will be suspected from the clinical picture and confirmed by histopathology or other special investigations. The table next page shows the investigations that are used to diagnose the common forms of extra pulmonary TB.

TABLE: 4 SITES AND DIAGNOSTIC APPROACH FOR COMMON FORMS OF EPTB IN CHILDREN

Site	Practical approach to diagnosis
Peripheral lymph nodes	Lymph node biopsy or FNAC
Miliary TB /disseminated TB	CXR and CSF study (routine & Gene-xpert) (to exclude meningitis)
Tubercular meningitis	CSF study (and CT scan where available)
Tuberculoma of brain	CT scan/MRI
Pleural effusion	CXR; pleural tap; pleural biopsy and histopathology.
Abdominal TB	Abdominal ultrasound; ascitic fluid study
TB arthritis or Osteoarticular TB	X-ray; joint fluid study or synovial biopsy
Pericardial TB	CXR; echocardiography and pericardial tap; pericardial biopsy and histopathology
TB, all forms	MT and CXR

3.5 Xpert MTB/RIF^{9,14}

This WHO-approved technique, also called Gene-Xpert is a cartridge-based, automated diagnostic test that can identify *Mycobacterium tuberculosis (Mtb)* DNA and also detect resistance to rifampicin (RIF) by Polymerase Chain Reaction (PCR). It can optimally provide rapid result (turnover time) in 2 hours versus 4-6 weeks by culture. The process purifies and concentrates Mtb, subsequently amplifies the genomic DNA by PCR. Aside from sputum (expectorated or induced) and aspirates by gastric lavage, this test can also use samples from other biologic fluids (e.g. CSF) and tissues (e.g. lymph node by FNAC). It may be used rather than conventional microscopy and culture as the initial diagnostic test in children suspected of having DR-TB, HIV-associated TB. WHO recommends it should be used in preference to smear and culture as the initial test in suspected TBM. So far 39 Xpert machines has been installed in different hospitals of Bangladesh.

3.6 HIV TESTING

Most HIV infections in children are passed from mother to child. Other associated risk factors are, blood transfusions using infected blood or injections, injecting drug use and needle sharing among young people. Although sexual transmission is not a main cause of HIV/AIDS among children but may also become infected through sexual abuse or rape.

In areas with lower HIV prevalence like Bangladesh, HIV counseling and testing is indicated for TB patients with symptoms and/or signs of HIV-related conditions, and in TB patients having a history suggestive of high risk HIV-exposure.

In areas with a high prevalence of HIV infection, where TB and HIV infection are likely to coexist, and in populations at high risk for HIV infection (sex workers, IV drug users), WHO advocates HIV counseling and testing for all TB patients as part of their routine management.

3.7 OTHER TESTS

A complete blood count may be indicated in a seriously ill patient but is not useful for the diagnosis of TB. **ESR is a non specific test for inflammation and has no role in confirming or excluding TB in children²⁶.** A baseline liver function test is indicated if there is an underlying liver disease, history of taking other hepatotoxic drugs or in severe forms of TB^{27,28}.

Newer tests like novel T-cell activation marker or interferon-gamma release assays (IGRAs) provide essentially the same information as MT and offer little additional diagnostic benefit. This should not replace routine MT test in Bangladesh. Also IGRAs should not be used for the diagnosis of TB disease.

Similarly, commercial serodiagnostic tests (ALS and other Anti-TB Immunoglobulin tests) should not be used for the diagnosis of TB^{27,28}.

Other specialized tests, such as CT scan and bronchoscopy are not recommended for the routine diagnosis of TB in children. But these tests (such as brain CT scan to delineate basal thickening in TB meningitis) can be performed in higher centers, if specialist opines.

ESTABLISHING DIAGNOSIS OF TB IN CHILDREN

It can be a challenge to confirm diagnosis of TB in children; however, in a great number of children it is not very difficult to establish a fairly accurate presumptive diagnosis, even in the absence of sophisticated tests (Box-V).

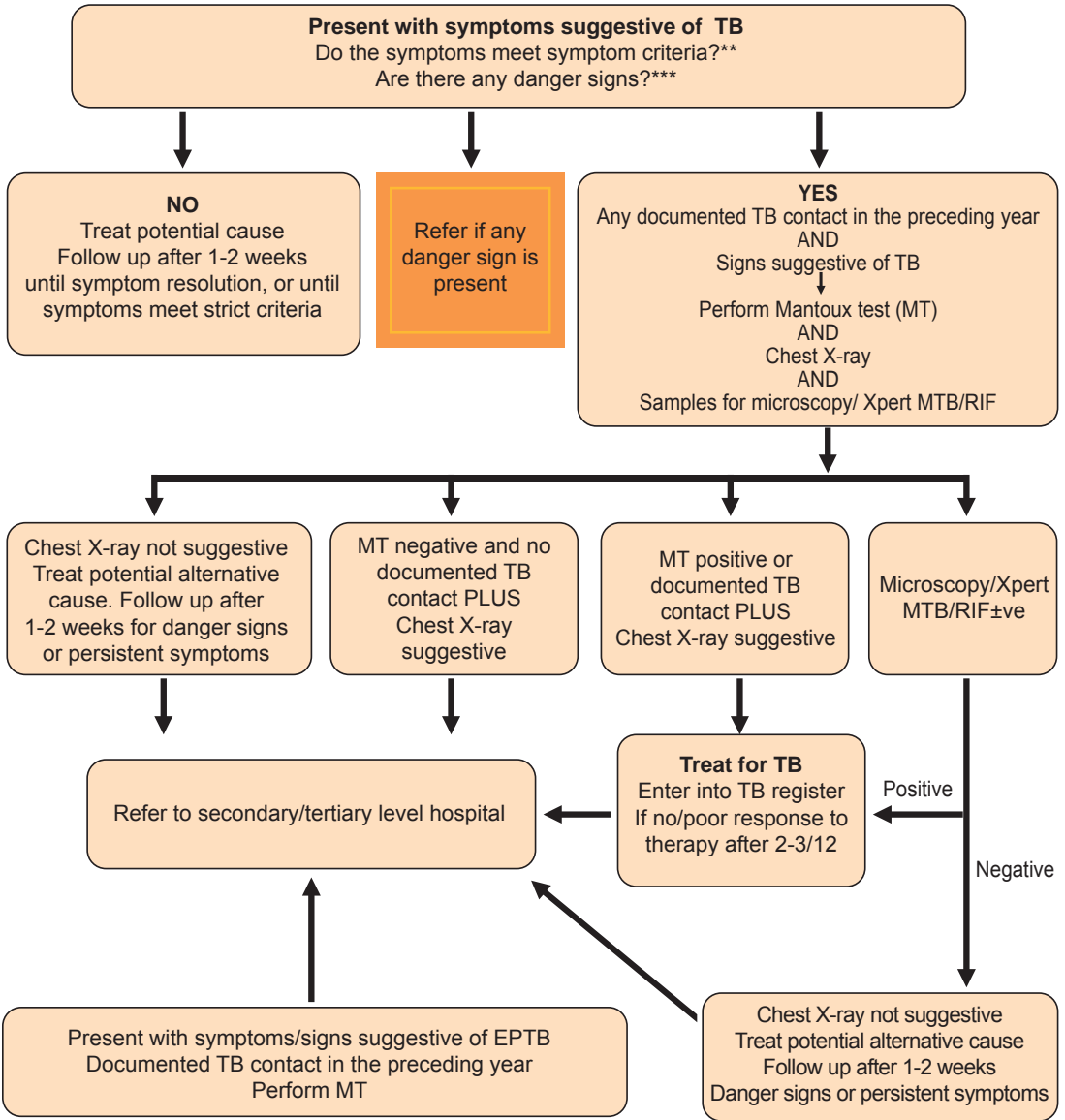
BOX-V: CLINICAL CRITERIA FOR DIAGNOSIS OF TB IN CHILDREN

The presence of 3 or more of the following features suggests a diagnosis of TB:

- Symptom criteria suggestive of TB
- A history of recent close contact (within the past 12 months)
- Physical signs highly suggestive of TB
- A positive Mantoux test
- Chest X-ray suggestive of TB
- Special laboratory test- CSF, Histopathology

NB. If a child has only 2 features, and other criteria (see Box II - recommended approach to diagnose TB in children) are not helpful in diagnosis, expert opinion can be sought before proceeding further.

Figure: 2 ALGORITHM FOR THE DIAGNOSIS OF CHILDREN <8 YRS* OF AGE WHO PRESENT WITH SYMPTOMS SUGGESTIVE OF TB



*Children ≥8 years of age should be managed as an adult.

**Symptoms (3/4) suggestive of TB (Section 2.1.1) plus at least 2 other positive tests (eg. MT and X-ray) suggest a diagnosis of TB.

***See text (Box IV) for the danger signs require urgent referral

TABLE: 5 APPROPRIATE LEVEL OF CARE FOR THE DIAGNOSIS OF TB IN CHILDREN

TB Disease	Practical approach to diagnosis	Level of diagnosis and initiation of treatment
Screen child contacts for TB disease	Symptom-based screening	DOTS centre/Field level
Uncomplicated intra-thoracic TB	Symptom-based referral	UHC
	Chest X-ray based diagnosis	Primary level hospital (UHC)
Complicated intra-thoracic TB	Symptom-based referral	UHC, CDC, District Hospital
	Chest X-ray-based referral	CDC, CDH, Secondary/Tertiary referral hospital
Cervical lymphadenitis (rarely other sites)	Symptom-based referral	Primary level hospital (UHC)
	Fine needle aspiration cytology(FNAC) or Lymph node excision biopsy	Secondary/Tertiary referral hospital
Miliary /disseminated TB	Symptom-based referral	CDC, CDH, UHC
	Chest X-ray based referral	Secondary/Tertiary referral hospital
TB meningitis (TBM)	Symptom-based referral Lumbar puncture Chest X-ray Cranial CT (where available)	Secondary and Tertiary referral hospital
Pleural effusion	Symptom-based referral Chest X-ray, pleural tap	Primary /Secondary level hospital, CDC
Abdominal TB	Symptom-based referral Chest X-ray Abdominal ultrasound, Ascitic tap	Secondary or Tertiary referral hospital
Osteo-articular TB	Symptom-based referral X-ray of bone/joint Joint tap or synovial biopsy CT where available	Tertiary referral hospital
Pericardial TB	Symptom-based referral Ultrasound and pericardial tap	Tertiary referral hospital

Children usually have paucibacillary pulmonary disease as cavitation is rare in the young with early TB. In contrast, children develop EPTB more often than adults. Severe and disseminated TB (e.g. TB meningitis and miliary TB) occur more commonly especially in young children aged less than 3 years. All children who have been diagnosed with TB disease must receive directly observed treatment (DOT) with the appropriate regimen and this must be recorded in the TB treatment register. Once TB treatment is started, it should be continued until completion, unless an alternative diagnosis has been confirmed. Treatment outcomes in children are generally good, even in young and immunocompromised children who are at higher risk of disease progression and disseminated disease. Children with TB respond to treatment and tolerate anti-TB drugs well.

OBJECTIVES OF ANTI-TB TREATMENT

Cure a patient who has TB with optimal use of drugs by:

1. killing the causative agent, *Mycobacterium tuberculosis*
2. preventing complications of disease progression, reducing morbidity and mortality
3. preventing relapse of TB (by eliminating the dormant bacilli)
4. reducing transmission by reducing reservoir
5. preventing the development of drug resistance
6. reducing adverse drug reactions

EFFECTIVE USE OF ANTI-TB DRUGS

Rapid reduction in the organism load is important since it limits disease progression, tissue damage and systemic effects with clinical improvement, terminates transmission and protects against random drug resistance to drugs. This is achieved by bactericidal drugs that kill actively metabolizing organisms. However, there are multiple sub-populations of organisms, some extra- and others intra-cellular, with highly variable rates of metabolism- require use of a combination of drugs to target these specific bacillary populations. Permanent cure requires effective eradication of all organisms, including hypometabolic bacilli, at effective drug concentrations for a prolonged duration (at least 6 months).

TABLE: 6 ANTI-TB DRUGS: MODE OF ACTION AND ACTIVITY OVER BACTERIAL POPULATION

Drug	Anti-bacterial action	Mycobacteria population	Remark
INH	Bactericidal	Rapidly metabolizing extra-cellular bacilli	Most potent. Kills vast majority within first few days; good CSF levels.
Rifampicin	Bactericidal	Intracellular organism	Effective killer; limited penetration of blood-brain- barrier/CSF levels.
Ethambutol	Bacteriostatic/ bactericidal in higher concentration	Actively growing bacilli	Reduces RMP resistance in high bacillary load; limited penetration of BBB, CSF levels.
Pyrazinamide	Bactericidal	Extracellular bacilli within acidic centers of caseating granuloma	Effective against dormant intracellular bacteria; good CSF levels.

The main variables that influence the success of chemotherapy, apart from drug resistance, are the bacillary load and its anatomical distribution. Sputum smear-negative disease is usually paucibacillary and therefore the risk of acquired drug resistance is low even in previously-treated children. Drug penetration into the anatomical sites involved is good and the success of 3 drugs (INH, RMP, PZA) during the 2-month intensive phase and 2-drugs (INH, RMP) during the 4-month continuation phase, is well established. In the presence of extensive disease (excluding TB meningitis), HIV co-infection and/or suspicion of INH resistance, the addition of EMB as a fourth drug during the intensive phase is recommended in order to improve outcome and reduce the risk of acquiring drug resistance. Sputum smear-positive disease implies a high bacillary load and an increased risk for random drug resistance. Once the bacillary load is sufficiently reduced, daily therapy with INH and RMP during the 4-month continuation phase is sufficient to ensure organism eradication.

It is essential to consider the cerebrospinal fluid (CSF) penetration of drugs used in the treatment of TB meningitis. INH and PZA easily penetrate the CSF, while RMP only achieve therapeutic levels in the presence of meningeal inflammation. **EMB also penetrates the CSF in the presence of meningeal inflammation, CSF penetration of SM is unpredictable²⁹ which explains why EMB replaces SM in the treatment of TBM³⁰.** Oral availability of EMB also assures better compliance and completion of treatment.

RECOMMENDED TREATMENT REGIMENS

Anti-TB treatment is divided into two phases: **an intensive phase and a continuation phase.**

The purpose of the intensive phase is to rapidly eliminate the majority of organisms and to prevent the emergence of drug resistance. This phase uses a greater number of drugs than the continuation phase. The purpose of the continuation phase is to eradicate the dormant organisms. Fewer drugs are generally used in this phase because the risk of acquiring drug resistant is low, as most of the organisms have already been eliminated.

Regular weight-based dose adjustment is important, particularly in young and/or malnourished children during the intensive phase of treatment, when weight gain may be accelerated.

TABLE:7 RECOMMENDED DAILY DOAGES OF FIRST-LINE ANTI-TB DRUGS FOR CHILDREN³¹

Drug	Daily dose and range (mg/kg body weight)	
Isoniazid (H)	10 (7-15)	[maximum 300mg]
Rifampicin (R)	15 (10-20)	[maximum 600mg]
Pyrazinamide (Z)	35 (30-40)	[maximum 2000mg]
Ethambutol (E)	20 (15-25)	[maximum 1200mg]

NB: Higher dosage (mg/kg) are required for young children to achieve effective bactericidal activity, as these age group influences drug metabolism. Moreover, systematic review also shows an excellent safety profile of revised dosages and are not associated with an increased risk of toxicity (no increased risk of drug-related hepatotoxicity due to INH or PZA, or of optic neuritis due to ethambutol).

FIXED-DOSE-COMBINATIONS (FDCs) FOR CHILDREN

Child-friendly formulations are ideal for use to ensure adequate therapeutic blood levels and compliance to treatment regimen. These are dispersible tablets and currently available formulations contain 60 mg of Rifampicin, 30 mg of INH and 150 mg of Pyrazinamide per tablet. As there is a need to break these tablets for some weight bands (see Table 9), which pose uncertainty in reaching the desired levels and also cumbersome to use. The WHO, along with the Global Alliance for TB Drug

Development, has taken the initiative for a new FDC. It contains 75 mg of Rifampicin, 50 mg of INH and 150 mg of Pyrazinamide per tablet³², which is child-friendly and in line with the higher WHO recommended dosage from the Rapid Advice 2010 (see table 7). The weight band table below is provided for ease of instruction. This new FDC will be available in Bangladesh by 2017 in one flavour (mango/orange).

TABLE: 8 FORMULATIONS AVAILABLE:

FDC tablet	Current FDC	Upcoming FDC*
3-FDC	R60, H30, Z150	R75, H50, Z150
2-FDC	R60, H30	R75, H50

*In 3 flavours- mango, strawberry and orange

TABLE: 9 WEIGHT BAND TABLE WITH THE CURRENTLY AVAILABLE FDC

Body weight Kg	Intensive Phase (2 months) Number of Tablets RHZ* 60,30,150	Continuation phase (4 months) Number of Tablets RH 60,30
2-2.9	½	½
3-5.9	1	1
6-8.9	1½	1½
9-11.9	2	2
12-14.9	2½	2½
15-19.9	3	3
20-24.9	4	4
25-29.9	5	5
30-35.9	6	6

TABLE: 10 WEIGHT BAND TABLE FOR “NEW”/UPCOMING FDCs

Weight Bands (Kg)	Number of Tablets		
	Intensive Phase		Continuation Phase
	RHZ (mg)	E (mg)	RH (mg)
	75/50/150 per tablet	100 per tablet	75/50 per tablet
4-7	1	1	1
8-11	2	2	2
12-15	3	3	3
16-24	4	4	4
25+	Use adult dosages and preparations		

TREATMENT REGIMENS:

- Children with clinically diagnosed or confirmed pulmonary tuberculosis or tuberculous peripheral lymphadenitis who live in settings with low HIV prevalence or low resistance to isoniazid and children who are HIV-negative can be treated with a three-drug regimen (HRZ) for 2 months followed by a two-drug (HR) regimen for 4 months.
- Children with extensive pulmonary disease (cavitary lesion, military TB, smear positive TB) and severe EPTB (disseminated TB) in any settings or children with TB living in settings of high HIV prevalence or high INH resistance should be treated with a four-drug regimen (HRZE) for 2 months followed by a two-drug regimen (HR) for 4 months. Ethambutol is considered to be safe in children at a dose of 20 mg/kg (range 15-25 mg/kg) daily.
- Children ≥ 8 years and/or ≥ 25 Kg are routinely treated as adults regimen.

TABLE:11 TREATMENT REGIMENS FOR CHILDREN IN EACH TB DIAGNOSTIC CATEGORY⁹

TB cases	Regimen	
	Intensive phase	Continuation phase
<ul style="list-style-type: none"> ■ Smear negative pulmonary TB (without extensive involvement) ■ TB lymph node (intrathoracic/extrathoracic) 	2(HRZ)	4(HR)
<ul style="list-style-type: none"> ■ Smear positive pulmonary TB ■ Smear-negative PTB with extensive involvement ■ Severe EPTB (except TBM and Osteoarticular) ■ Previously treated cases** ■ All forms of TB in HIV+ve cases (except TBM and Osteoarticular) 	2(HRZE)	4(HR)
<ul style="list-style-type: none"> ■ TB meningitis/CNS TB* ■ Osteoarticular TB* 	2(HRZE)	10(HR)
<ul style="list-style-type: none"> ■ MDR TB ■ XDR TB 	Specially designed standardized treatment (2nd line anti TB drugs)	

*For children with TB meningitis and osteoarticular TB, treatment may be extended up to 12 months based on clinical judgment.

**INH resistance is 35.8% among previously treated cases in Bangladesh (DRS-2011)³³

NB: Where treatment failure is in doubt, DR-TB should be considered and worked upon.

CORTICOSTEROIDS

Corticosteroids may be used for the management of some complicated forms of TB.

BOX-VI: INDICATIONS FOR ORAL STEROIDS IN CHILDREN WITH TB

- CNS TB including TB meningitis
- TB pericarditis (reduces the risk of restrictive pericarditis)

In cases of advanced TB meningitis, corticosteroids have been shown to improve survival and decrease morbidity, and thus recommended in all cases of TB meningitis. As rifampicin is a powerful inducer of prednisolone metabolism hence high dose of prednisolone is required³⁴; sudden withdrawal can cause serious side effects such as adrenal crisis. The following dosage schedule is recommended:-

Prednisolone - 2-4 mg /kg/day (max. 60mg) for 4 weeks
- then tapered over 1-2 weeks

DIRECTLY OBSERVED TREATMENT, SHORT COURSE (DOTS)

DOTS is a very important component of internationally recommended policy package for TB control-DOTS strategy. DOTS means that an observer watches the patient swallowing their drugs, which is essential for completion of treatment and recovery from TB. This ensures that a patient takes right anti-TB drugs, in the right doses, at the right interval and for the right period of time.

Treatment of TB should always be directly observed and drugs are used as a fixed-dose combination. Ethambutol needs to be added additionally with the FDC when indicated. Drug dosages, depending on the body weight of the child, are given daily. **The dose should be adjusted as the weight changes during the course of treatment.** Children should therefore be weighed at least after 1, 2, 3 (or at a lesser interval when necessary) and 6 months of therapy; their weight should be documented on the TB treatment card. If there is poor response to therapy (no weight gain, persistent symptoms after 2-3 months of treatment) they should be referred for urgent assessment by a competent physician.

Parents and caregivers should be counseled about TB and the importance of treatment adherence.

REFERRALS

The following children should be referred for expert opinion and management to pediatricians/CDC/CDH/District Hospital/Tertiary Hospital:

- All children with severe forms of TB (TB meningitis, tuberculoma, cavitary PTB, miliary TB, TB peritonitis, spinal or osteoarticular TB);
- Children with presumptive MDR-TB, XDR-TB (or in contact with MDR-TB, XDR-TB case and not responding to first-line therapy)
- If there is poor response to therapy (no weight gain, persistent symptoms after 2-3 months of treatment)

FOLLOW UP OF CHILDREN DURING TREATMENT

Children should be followed up on a monthly basis for the first 3 months. Children responding to treatment should experience improvement or resolution of symptoms and gain weight within 2-3 months. It is important to accurately document the child's weight on the IPHN growth chart (annex- 2A-2F, pages 46-51) at each follow-up and adjust the drug dosages accordingly. Children with sputum smear-positive TB should be followed as adult clients with repeat sputum examinations done after 2, 5 and at 6 months of treatment.

Chest X-ray is a poor indicator of treatment response and lymph nodes may initially enlarge as a result of an improvement in the child's immune response. Routine follow-up chest X-rays are not required in children. Follow-up X-rays are only recommended in children with persistent symptoms or poor response to treatment, or if new symptoms develop on treatment.

CAUSES OF DETERIORATION DURING TB TREATMENT

Children may sometimes deteriorate or experience a worsening of symptoms despite adequate therapy. The most important questions to answer are:

- Is the drug dosage correct?
- Is the child taking the drugs as prescribed (good adherence)?
- Is the child HIV-infected?
- Is the child severely malnourished?
- Is there a reason to suspect drug-resistant TB (the index case has drug resistant TB or is a re-treatment case or is also not responding to therapy)?
- Is there another reason for the child's illness other than TB?

Severely malnourished children, children following nutritional rehabilitation or HIV-infected children on highly active antiretroviral therapy may sometimes develop a temporary worsening of symptoms due to the recovery of their immune responses. This is referred to as *immune reconstitution inflammatory syndrome (IRIS)*. Any child with severe persistent symptoms should be referred for assessment.

TABLE: 12 THE TOXICITIES RELATED TO DOSE AND REGIMENS OF TB DRUGS

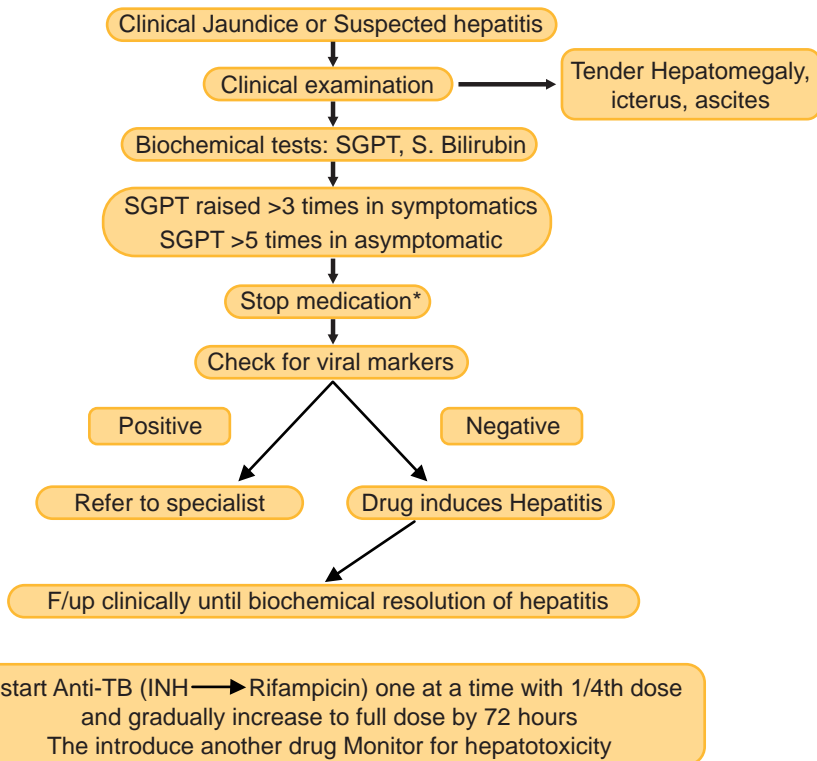
Anti-TB Drugs	Mode & mechanism of action	Main toxicities	Single daily dose mg/kg (range); [maximum dose, mg]
1st line Drugs			
Isoniazid	Bactericidal	Hepatitis Peripheral neuropathy	10 (7-15) [300]
Rifampicin	Bactericidal	Hepatitis Orange discolouration of secretions Drug interactions	15 (10-20) [600]
Pyrazinamide	Sterilizing	Hepatitis Arthralgia	35 (30-40) [2000]
Ethambutol	Bacteriostatic	Visual disturbance (acuity, color vision)	20 (15-25) [1200]
2nd line Drugs			
Aminoglycosides- Kanamycin Amikacin Streptomycin	Bactericidal	Ototoxic & nephrotoxic	15-30 [1000] 12-18 [1000]
Fluoroquinolones- Ofloxacin Levofloxacin Moxifloxacin	Bactericidal	Arthralgia (rare) Insomnia, confusion	15-20 [800] 7.5-10 [750] 7.5-10 [400]
Ethionamide	Bactericidal	Vomiting Hypothyroidism Hepatitis	15-20 [1000]
Polipeptides Capreomycin	Bacteriostatic	Oto & nephrotoxic	15-30 [1000]
Cycloserine derivative- Terizidone	Bacteriostatic	Psychosis, depression, convulsions	10-20 [1000]
Para-aminosalicylic acid (PAS)	Bacteriostatic	Diarrhoea & vomiting Hypothyroidism	150-200 [12gm] Divided in 2-3 doses/day

Note:

1. Hypersensitivity reactions and drug rashes may occur with any drug;
2. WHO endorsed new recommendations for dosing of first-line TB drugs in children;
3. Streptomycin is rarely used;
4. Ciprofloxacin has the weakest activity and is no longer indicated for TB treatment.

Adverse events caused by TB drugs are uncommon in children than in adults³⁵. The most serious adverse event is the development of hepatotoxicity, which can be caused by PZA>INH>RMP. It is not required to monitor liver enzyme routinely, as asymptomatic mild elevation of serum liver enzymes (<5 times normal values) is common and is not an indication to stop TB treatment. However, the occurrence of liver tenderness, hepatomegaly or jaundice should lead to further investigation (urgent referral). Hepatic involvement is found to be more common in severe form of TB disease among Indian children (1% vs. 2%)³⁶.

FIGURE: 3 MANAGEMENT OF DRUG INDUCED HEPATITIS



*In TBM, Disseminated TB and military TB: After withdrawal of the suspected offending drugs, continue medication with streptomycin, ethambutol and fluoroquinolones till restarting first line drugs after resolution of drug induced hepatitis.

However, the occurrence of liver tenderness, hepatomegaly or jaundice should lead to further investigation (urgent referral). Perform serum liver enzyme levels and stop all potentially hepatotoxic drugs. Children should be evaluated for other causes of hepatitis (e.g. Hepatitis A), and no attempt should be made to reintroduce these drugs until the liver functions have normalized. When the liver function becomes normal, previous anti-TB drugs should be restarted one by one with full dose in an interval of 48 to 72 hours and started with less hepatotoxic drugs such as INH then rifampicin but not pyrazinamide. An expert should be involved in the further management of these cases.

INH may cause peripheral neuropathy (symptomatic pyridoxine deficiency), particularly in severely malnourished, HIV-infected children on HAART, chronic liver disease and renal failure. Supplemental pyridoxine (12.5-25 mg = ½ - 1 tablet/day) is recommended in older children and multi-vitamin syrup in infants. Pyridoxine is not routinely prescribed other than the group mentioned above.

RETREATMENT

Failure of treatment in children is not expected but its cause has to be sought for better care; it is managed in the same way that failure in adults is managed. The most likely cause for treatment failure or relapse within 6 months of treatment completion is failure of adherence to treatment instructions. In children when anti-TB treatment fails or a relapse occurs, every effort should be made to find the most likely cause for the failure or relapse. There are multiple (psychosocial, economic and practical) reasons why people are non-adherent.

Mycobacterial culture and drug susceptibility testing should be performed for all re-treatment cases before starting treatment, depending on what is known about the risk of MDR-TB in this group of patients. If an adult source case with drug-resistant TB is identified, the child should be treated according to the drug susceptibility pattern of the source case's strain, in case isolate from the child is not available. *Two or more new drugs should be added to any re-treatment regimen in case of genuine failure of treatment and the duration of treatment should be not less than 9 months.*

Management of drug-resistant cases is discussed further in section III.

DRUG RESISTANT TB (DR-TB) IN CHILDREN**INTRODUCTION**

According to the First National Drug Resistance Survey (2010-2011), MDR-TB in Bangladesh is estimated at 1.4% and 28.5% among new and previously treated TB cases respectively³³. It is evident that current control efforts are not adequately containing the spread of the drug-resistant TB epidemic. Children with paucibacillary TB are unlikely to acquire drug resistance and contribute little to the creation and/or transmission of drug-resistant strains. Children with DR-TB provide an accurate estimation of transmitted (primary) drug resistance within communities. MDR-TB in children is mainly newly transmitted drug resistance. Contact tracing and follow-up of children exposed to MDR/XDR-TB should receive high priority. Extrapolating MDR-TB (1.4% in new cases), among 8104 cases diagnosed in 2015, there should be 113 cases of MDR TB in children in Bangladesh, but the number is much less.

TYPES OF DRUG RESISTANT TB IN CHILDREN⁹**1. MONO DRUG RESISTANCE**

Mono drug resistance means *M. tuberculosis* is resistant to only one first-line anti-TB drug for example E or H or S resistance. Resistance to H is usually the first step to the development of MDR-TB. The risk of acquiring MDR-TB is increased in patients with high bacillary loads.

TABLE: 13 PATTERN OF RESISTANCE TO 1ST LINE ANTI-TB DRUG IN BANGLADESH³³

Drug Resistance pattern (Any drug resistance)	New (%)	Previously treated (%)	Total (%)
Resistance to INH	5.3	35.8	11.6
Resistant to RIF	1.6	28.9	7.3
Resistance to Ethambutol	0.9	17.8	4.4
Resistance to Streptomycin	9.9	33.1	14.7

2. POLY DRUG RESISTANCE

When *M. tuberculosis* develops resistance to more than one first line anti-TB drugs, organism is then called poly drug resistant. Examples of poly drug resistance are H-E or E-S or S-R-E resistance.

3. MULTI DRUG RESISTANCE (MDR)

MDR-TB implies when TB bacilli are resistant to Isoniazid and Rifampicin, the two most potent first line anti-TB drugs, with or without resistance to others.

4. PRE-XDR³⁷

TB bacilli are resistant to Isoniazid and Rifampicin and with either a Fluoroquinolone or second line injectable agent (amikacin, capreomycin or kanamycin) but not both.

5. EXTENSIVE DRUG RESISTANCE (XDR) TB

Extensively drug-resistant TB or XDR-TB, a sub-set of MDR-TB, can be defined as MDR-TB that is also resistant to any fluoroquinolone and to at least one of three injectable second line anti-TB drugs (amikacin, capreomycin or kanamycin). XDR-TB develops when second-line drugs are misused or mismanaged.

6. RIFAMPICIN RESISTANCE (RR)

Resistance to Rifampicin is detected by using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs. It includes resistance to Rifampicin, whether mono-resistance, polydrug resistance, MDR or XDR.

Is drug resistant TB infectious?

Drug-resistant TB is as infectious as drug-susceptible TB. Children usually become infected from adult or adolescent MDR-TB contact.

How to recognize a presumptive drug-resistant patient?

Drug-resistant TB is a laboratory diagnosis, but should be presumed if any of the following features are present in a child:

- **Features in a child suggestive of having drug resistant TB**
 - Contact with a known case of MDR-TB
 - Child not responding to adhered standard TB treatment
 - Child with TB recurrence after completing TB treatment
- **Features in the index case suggestive of drug-resistant TB**
 - Index case remaining smear-positive after 3 months of treatment
 - History of previous TB treatment interruption or recurrence after completion of TB treatment

CASE-FINDING STRATEGIES³⁹

According to National Guidelines and Operational Manual for Programmatic Management of Resistant TB the following groups should be targeted as risk groups for culture and DST:

High Risk:

- Failure: remains SS+ve at 5 mo / SS-ve becomes SS+ve at month 2
- Close contact of a MDR-TB patient with symptoms

Medium Risk:

- Non-converters (remain SS+ve at month 2-3)
- All relapses
- All treatment after lost to follow-up
- Any smear negative or EPTB patient doing clinically poorly on TB Therapy

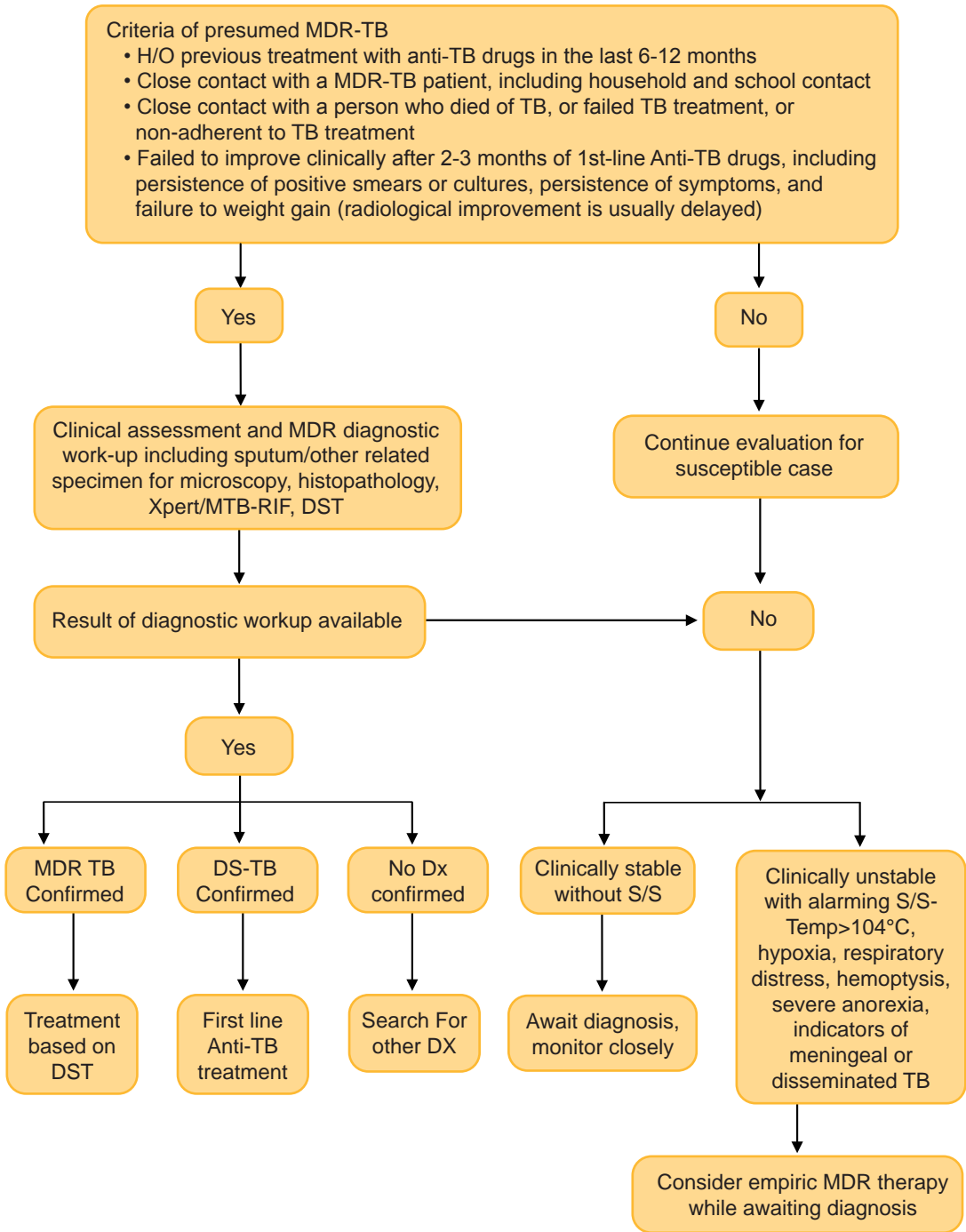
Low Risk:

- All TB/HIV patient at the start of therapy

DIAGNOSIS OF MDR-TB IN CHILDREN

In younger children bacteriological confirmation may not be possible for unavailability of sample, yet diagnosis of MDR-TB can be made on clinical and radiological data in most cases. A child over 8 years can expectorate sputum for bacteriology and DST. In younger children who are unable to provide specimen, a high index of suspicion is needed to initiate empiric therapy. An algorithm of presumed child MDR-TB is given below (see figure 4, page-31).

FIGURE: 4 ALGORITHM FOR PRESUMED MDR-TB IN A CHILD⁴⁰
 (Adapted from Management of Multidrug Resistance Tuberculosis in Children: A Field Guide)



PRINCIPLES OF MANAGEMENT OF MDR-TB IN CHILDREN⁴¹

- Manage in a specialized MDR-TB treatment facility (NIDCH/CDH).
- Directly Observed Treatment (DOT) is essential.
- Be aware of drug groups / cross-resistance.
- NEVER add one drug to a failing regimen.
- Use standard drug regimen where 3-4 or more drugs are to be susceptible to the patient's isolate.
- Counsel the patient/parents at every visit for support, about adverse events, and importance of adherence.
- Do Drug Susceptibility Testing (DST) for 2nd-line drugs when indicated.
- Follow-up is essential- done clinically and by cultures (monthly in the intensive phase and then quarterly in the continuation phase). Radiological follow-up may be done 6-monthly and when indicated.

THE STANDARD MDR-TB REGIMEN IN CHILDREN

Children with confirmed MDR-TB is managed as per current National Child TB Guideline. The standard MDR-TB regimen should be given for a minimum of 20 months and at least 18 months past sustained culture conversion.

The recommended standard MDR-TB regimen is:

- Intensive phase regimen includes: **8 (Z-Km-Lfx-Eto-Cs)**
- Regimen in continuation phase includes: **12 (Z-Lfx-Eto-Cs)**

The numbers in front of the drug abbreviations represent the average number of months the drugs are given. In the intensive phase five drugs are used; four of them are second-line anti-TB drugs of which one is an injectable (Km). Although pyrazinamide is a first-line drug, it is also added, because the probability of drug sensitivity is still high.

If kanamycin is not available, amikacin can be substituted. Prothionamide can be substituted for ethionamide.

TREATMENT SUCCESS

Treatment outcomes in child with MDR TB is encouraging, in a meta-analysis by Ettehad et al reported treatment success in 81.67% with 5.9% death among non-HIV cohorts⁴². Again a recent met-analysis in multidrug resistant tuberculosis in HIV infected child is found to have better outcome than adult (83.4% vs. 49.9%)⁴³. Side effects reported to occur among 39.1%, most common were nausea and vomiting while most serious side effects were hearing loss, hypothyroidism and psychiatric effects.

TABLE: 14 PAEDIATRIC DOSING OF SECOND-LINE ANTI-TB DRUGS

Drug	Daily dose (mg/kg)	Frequency	Maximum daily dose
Pyrazinamide 400mg, 500mg	35 (30-40)	Once daily	2000mg
Kanamycin (Km) (1 g vial)	15–30	Once daily	1 g
Amikacin (Amk) (1 g vial)	15-22.5	Once daily	1 g
Streptomycin (1gm)	20-40	Once daily	1g
Capreomycin (Cm) (1 g vial)	15–30	Once daily	1 g
Ofloxacin (Ofx) (200 mg)	15–20	Once daily	1000 mg
Levofloxacin (Lfx) (250 mg, 500 mg)	15-20 < 5 years 10 > 5 years	Once daily	1000 mg
Moxifloxacin (Mfx) (400 mg)	7.5–10	Once daily	400 mg
Ethionamide (Eto) (250 mg)	15–20	Once daily	1 g
Prothionamide	15-20	Once daily	1 g
Cycloserine (Cs) (250 mg)	10–20	Once or twice daily	1 g
PAS (4 g sachets)	300	Twice or thrice daily	12 g
Clofazimine (50 and 100 mg)	2-3	Twice daily	200 mg
Amoxicillin/Clavulanate (500/125) –dosing is base on Amoxicillin component.	30 < 3 months 45 > 3 months and <40 kg	Thrice daily	2000 mg of Amoxicillin

NB: For children all drugs, including the fluoroquinolones, are dosed at the higher end of the recommended ranges.

DURATION OF TREATMENT

Most patients on the standard MDR-TB regimen will convert to negative smear and culture between month 0 and 2 and will need only 20 months of treatment. Nine month regimen for MDR-TB used for adult has yet not established for children.

FOLLOW UP OF DR-TB IN CHILDREN

In the management of MDR-TB patient, follow-up is given for 2 years after completion of treatment and is done 6-monthly by sputum microscopy, culture and rapid diagnostic tests like Xpert MTB/RIF.

TB-HIV CO-INFECTION

HIV is the most potent risk factor for TB. HIV-infection increases the risk of TB-disease by 20-fold compared with HIV-seronegative in high HIV prevalence countries⁴⁴. This increased risk of TB is for two reasons, firstly because they are likely to be exposed to TB as their HIV-infected parents are more likely to have TB. Secondly, the risk of developing TB disease following TB exposure/infection is greatly increased in HIV-infected children due to decreased immunity. Among HIV-infected children TB-coinfection is found to be 19.5%, with 59% being pulmonary TB in high HIV-burden country⁴⁵. HIV-infected children may develop multiple episodes of TB and a previous TB episode disease does not exclude future TB.

To further complicate diagnosis of TB, HIV-infected children often have other lung disease related to HIV infection, including Pneumocystis jiroveci pneumonia (PJP)-previously known as PCP, lymphocytic interstitial pneumonitis (LIP) and viral or bacterial pneumonia. In addition, there may be multiple and concurrent opportunistic infections, hence presence of one disease does not exclude other causes of illness.

WHOM TO INVESTIGATE FOR HIV INFECTION?

The following children should be tested for HIV infection:

- Mother known to be HIV-infected
- Mother with high-risk behaviour (injectable drug user, commercial sex worker etc.)
- Children with recurrent TB or presumptive drug resistant TB.

Presumptive children should be referred to a facility where HIV counselling and testing services are available.

DIAGNOSING TB IN HIV-INFECTED CHILDREN

In HIV-infected children the diagnosis of TB disease is more complex because:

- The symptoms and signs of TB and those of other HIV-related lung diseases could be indistinguishable. Symptoms such as chronic cough, weight loss, lymphadenopathy and persistent fever are common to both HIV related lung diseases and TB.
- The MT test is frequently negative even though the child may be infected with TB or has TB disease.
- The radiological features are usually similar to that found in HIV-negative children, but the picture could also be atypical. Radiological changes of HIV-related lung diseases are often confused with TB, e.g. LIP may look very similar to miliary TB.
- The differential diagnosis of pulmonary disease is much broader and includes; bacterial or viral pneumonia, fungal infections, Pneumocystis jiroveci pneumonia, pulmonary lymphoma and Kaposi's sarcoma.

There is a risk that TB may be over-diagnosed, resulting in unnecessary TB treatment. TB may also be missed, resulting in increased morbidity and mortality. LIP is the most difficult condition to distinguish from TB, due to radiological similarities, although it is usually associated with typical clinical signs, such as clubbing and/or parotid enlargement. However, TB can occur in children with an underlying diagnosis of LIP, bronchiectasis, or any other lung infection. In spite of these difficulties TB can be diagnosed with a fair degree of accuracy in the majority of HIV-infected children. Severe weight loss has been found to have a fairly good sensitivity (88.9%) and specificity (88.6%) with positive predictive value of 23% for TB in HIV-co-infected children²⁵. **The diagnostic approach for TB among HIV-infected children is essentially the same as for HIV-uninfected children.** Since the symptoms of TB can be confused with the symptoms of HIV disease and the chest X-ray is more difficult to interpret, if possible every effort should be made to try and establish a bacteriological diagnosis.

TREATMENT OF TB IN HIV-INFECTED CHILDREN

Due to the risk of relapse in severely immunocompromised children, prolonged treatment may be considered in HIV-infected children. Possible causes for treatment failure, such as non-adherence to therapy, poor drug absorption, drug resistance, and alternative diagnoses should be investigated in children who are not improving on TB treatment. A trial of TB treatment is not recommended in HIV-infected children. A decision to treat for TB should be carefully considered, and once this is done, the child should receive a full course of treatment and be notified, unless an alternative diagnosis is confirmed.

GENERAL HIV CARE FOR CO-INFECTED CHILDREN

Once a child with TB has been diagnosed with HIV-infection, it is the responsibility of TB staff to communicate and refer the child to HIV staff/program to ensure that the child and family receive appropriate HIV-related care.

CO-TRIMOXAZOLE PROPHYLAXIS AND IPT

Daily co-trimoxazole prophylaxis prolongs survival in HIV-infected children and reduces the incidence of respiratory infections and hospitalization. All HIV-infected children should be treated with co-trimoxazole. All patients living with HIV should also receive IPT for at least 6 months.

TABLE: 15 CO-TRIMOXAZOLE DOSAGE FOR CHILDREN³³

Body weight (Kg)	Once daily dose
	Oral suspension (200+40=240mg); Tablet (400+80=480mg) mL oral suspension or Tablet
<5	2.5 mL
5-14.9	5 mL or 1/2 tablet
15-29.9	10 mL or 1 tablet
≥30	2 tablets

ANTIRETROVIRAL THERAPY (ART)

Appropriate arrangements for access to ART should be made. All children with TB disease and HIV infection requires ART. In HIV-infected children with confirmed or presumptive TB disease, initiation of TB treatment is the priority. The decision on when to initiate ART after starting TB treatment should consider the child's immune status and clinical severity of disease, the child's age, pill burden, potential drug interactions, overlapping toxicities and possible IRIS. This should be weighed up against the risk of further HIV disease progression and immune suppression with associated increase in mortality and morbidity in the absence of ART. **Recommendations are to try and initiate ART within 2-8 weeks after starting TB treatment.** Early initiation is of particular importance in the severely immune compromised child.

Rifampicin causes liver enzyme induction, resulting in reduced serum drug levels of protease inhibitors, especially lopinavir. Therefore, the doses need to be adjusted during concurrent TB and HIV treatment. Liver enzyme induction persists for 1-2 weeks after rifampicin is stopped. Given the complexity of co-administration of TB treatment and ART; it is important to refer to the latest national HIV guidelines for current recommendations regarding the co-treatment of TB and HIV in children.

WHO has adopted a global strategy framework (The End TB Strategy) to achieve its vision of a world free of tuberculosis and the end the global tuberculosis epidemic as post-2015 strategy with some targets. Besides other targets, WHO envisioned to reduce TB incidence by 50% (of 2015) by 2025 and 90% (of 2015) by 2035⁴⁶. To achieve this important pillars are early diagnosis and preventive treatment of peoples at risk.

Preventive measures can be taken through-

1. Intensified Case Finding (ICF)
2. Contact tracing and investigation
3. Preventive measures-
 - 3.1. INH preventive therapy (IPT)
 - 3.2. BCG vaccination
4. TB infection control

1. INTENSIFIED CASE FINDING (ICF)

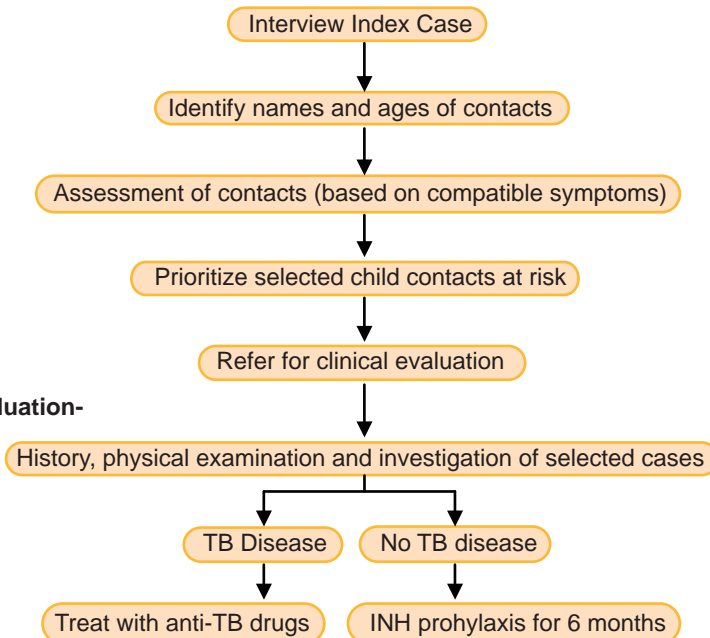
Finding and treating adults with TB is an important step to prevent disease transmission to child but is not enough in preventing disease; all close contacts and family members, including children, should be screened and provided appropriate diagnosis and treatment. Children are 50% less likely to be infected with TB when this strategy is adopted⁴⁷. Bangladesh's National Guidelines and Operational Manual for Tuberculosis Control (5th Ed, 2013) is a good tool to achieve this.

2. CONTACT TRACING AND INVESTIGATION

This is a systematic process intended to identify previously undiagnosed cases of TB among the contacts of an index case. It consists of two components:

2.1. Identification and prioritization-

Systematic approach for identifying contacts who have or, are at risk of developing TB disease.



2.2. Clinical evaluation-

Clinical evaluation should also be done in children-

1. with suggestive symptoms of TB disease
2. with age <5 years
3. with immunocompromised conditions (eg. those living with HIV, anti-cancer medication) of any age
4. index case is considered MDR-TB or Pre-XDR-TB or XDR-TB

Through contact screening, a TB case could be identified early and treated, thereby reducing not only the risk of developing serious disease but also preventing transmission. Young children (< 5 years) are immune-immature and if they are in close/household contact with a sputum-positive case, the chance of getting the disease is very high (5-50%)¹². Besides, a child with HIV is 20 times more likely to get TB than with immunocompetent children⁴⁸.

3.1 INH PREVENTIVE THERAPY (IPT)

IPT is providing INH (for 6 months) to children less than 5 years of age, who do not have TB disease to prevent risk of developing TB disease in the near future. These children are household contacts or close contacts with a TB index case, and highly likely to be infected with the *Mycobacterium tuberculosis*. IPT should also be provided to all immunocompromised children with a history of contact, regardless of age. IPT is safe and effective; side effects in children is rare and minor; efficacy is over 65% when taken correctly^{49,50,51}. It reduces TB incidence by 37% among HIV-infected persons when taken along with ART.

NTP, Bangladesh has issued a circular to initiate IPT to all illegible children with contact of infectious TB patient (annex 6, page 59).

WHO SHOULD RECEIVE PREVENTIVE THERAPY?

Due to limited resources, preventive therapy is only given to the most vulnerable children (those at highest risk to develop TB disease in the near future) following documented TB exposure and/or infection, after active disease has been ruled out.

The following should receive IPT:

- Very young (immune immature) children (<5 years of age)
- Immune compromised children (e.g. severely malnourished or HIV-infected, or on steroids/ immunosuppressive drugs), irrespective of their age
- Baby born to infected mother

Previous TB preventive therapy or treatment does not protect the child against subsequent TB exposure/infection. Therefore highly vulnerable children (as defined above) should receive preventive therapy after each episode of documented TB exposure, unless the child is currently receiving TB prophylaxis or treatment. **Always exclude TB disease before providing preventive therapy** (eg. Prophylaxis with Isoniazid).

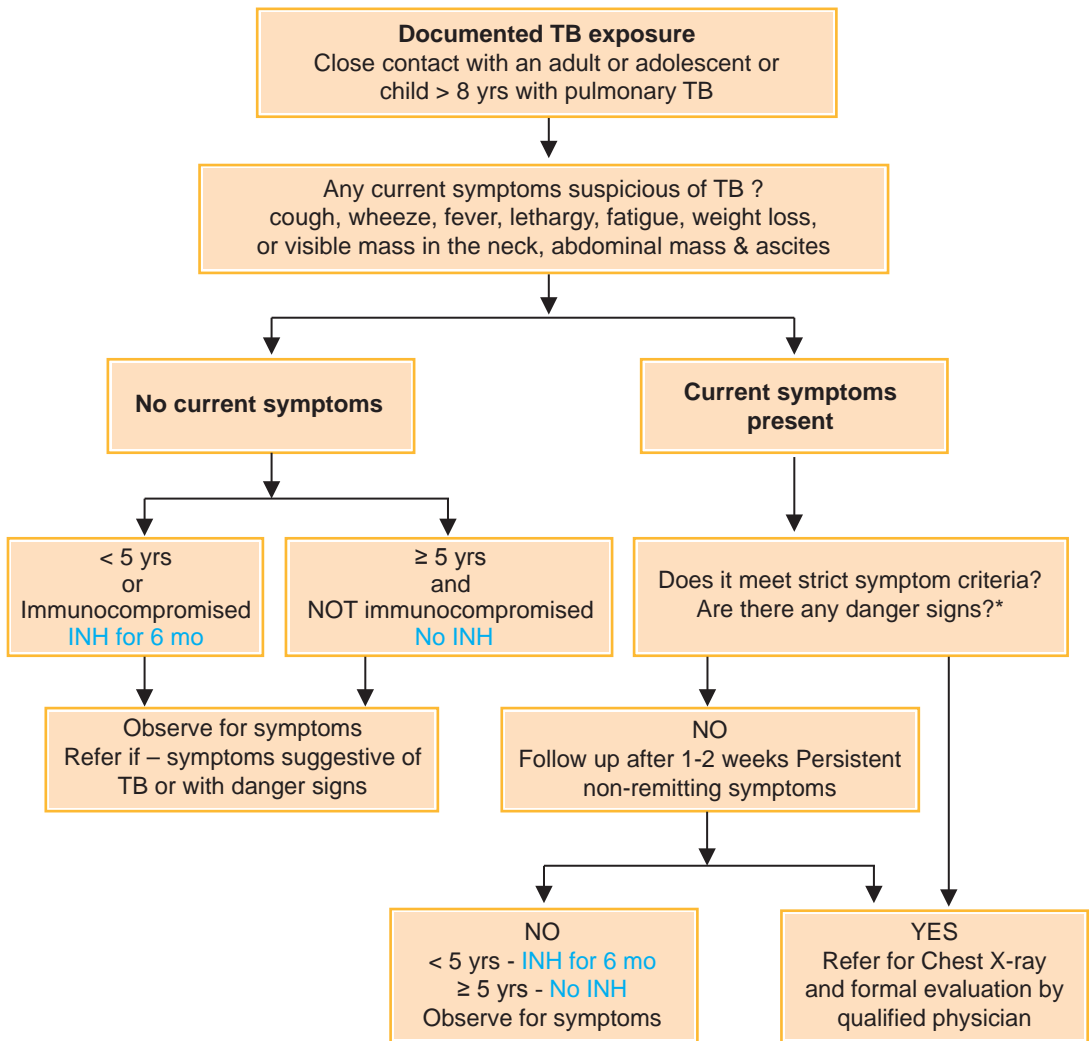
Evaluation of Children with contact history-

1. Asymptomatic children
2. Symptomatic children-

1. Asymptomatic children (playful and thriving, no cough or wheeze, no fever, no unusual fatigue or lethargy, no visible neck mass or gibbus) do not require additional tests to exclude TB disease, before providing preventive therapy^{12,51}. Children <5 years of age or immunocompromised children of any age in close contact with an adult or adolescent with pulmonary TB, should receive a course of INH prophylaxis to prevent the development TB⁵². Adherence to IPT is a major issue, which varies from 15-28% in South Africa to 57-74% in Australia and 26% in Indonesia⁵³. If a child aged <5 years and have a positive MT, s/he should also receive IPT even in the absence of contact history.

2. Symptomatic children should be evaluated to exclude TB disease. A symptom-based approach is sufficient to exclude TB disease in settings where Mantoux tuberculin skin testing (MT) and/or chest X-ray are not readily available⁵³.

FIGURE:5 ALGORITHM FOR THE SCREENING OF CHILDREN IN CLOSE/HOUSEHOLD CONTACT WITH ADOLESCENT OR ADULT PULMONARY TB



* Refer if – symptoms suggestive of TB of danger signs

HOW IS PREVENTIVE THERAPY GIVEN?

Preventive therapy comprises of isoniazid mono-therapy for 6 months. This is usually not given as directly observed therapy (DOT), but poor adherence is a serious concern and parents/caregivers must be adequately counseled to explain why the medicine is given and to encourage good adherence. Parents/caregivers should also be counseled to recognize the symptoms of TB disease, such as a persistent non-remitting cough or fever, unusual fatigue or lethargy and/or weight loss, which should prompt them to bring the children back to the hospital for further evaluation. Follow-up should be carried every 2 (two) months after initiation of IPT. Cases should be recorded in IPT register (annex-9, page-62).

CHANCE OF DEVELOPING INH RESISTANCE WITH IPT

There is little or no risk of isoniazid resistance developing in children receiving IPT, even if the diagnosis of active TB is missed. A meta-analysis since 1951 of studies on IPT did not show any increased risk of developing INH resistance^{55,56}.

TABLE:16 GUIDANCE FOR THE CORRECT DOSING OF INH PREVENTIVE THERAPY

Dose recommendations for INH preventive therapy in children	
Body weight (kg)	Isoniazid (INH) 100mg /tablet*
2-4.9	1/2
5-9.9	1
10-19.9	1 1/2
20-29.9	2 1/2
>30	3

* NB. INH 10 mg/kg/day, single dose; there is concern regarding bioavailability of crushing the appropriate fraction and dissolving in water or multi-vitamin syrup, thus the need for the new dispersible tablet. (See section on Treatment)

3.2. BCG VACCINATION

BCG (Bacille Calmette-Guerin) is a live attenuated (weakened) bacilli form of the cow TB organism (*M. bovis*). BCG is not fully protective against TB disease in children but it provides some protection against severe forms of TB (73% in TB meningitis and 77% in miliary TB)⁵⁷. Many children continue to get TB despite routine BCG vaccination and the youngest remain the most vulnerable, nevertheless, the BCG vaccination is recommended to avoid life threatening TB diseases.



ADVERSE EVENTS FOLLOWING BCG IMMUNIZATION

These are adenitis, local BCG abscess, lymphadenopathy, wart-like nodules, large ulcers, osteomyelitis, local bacterial infections and lupoid reactions. The commonest complication is **BCG adenitis**⁵⁸. Clinically two forms of BCG adenitis are present.

1. Non-suppurative- is a benign condition
2. Suppurative- afebrile axillary (rarely cervical and supra-clavicular) lymphadenopathy with no identifiable cause of adenitis. It develops abruptly within 2-5 months of vaccination ipsilateral to the site of vaccination, size 1-5 cm with absent or minimal tenderness⁵⁹.



Management:

1. Non-suppurative BCG adenitis is best left alone.
2. Suppurative and fluctuating adenitis: Needle aspiration or total excision is necessary to reduce scar from spontaneous rupture
3. If there is a high risk of disseminated disease (e.g. in HIV positive children), then treatment is with multiple drugs. BCG is resistant to PZA and may be intermediately resistant to INH, depending on strain used.

WHAT SHOULD BE DONE WHEN THERE IS NO BCG SCAR?

According to the current EPI policy of Bangladesh, give BCG again with the 3rd dose of pentavalent vaccine (annex: 8, page-61)

HOW SHOULD A BABY BORN TO A MOTHER OR OTHER CLOSE CONTACT WITH TB BE MANAGED?

A baby born to a mother diagnosed with TB in the last two months of pregnancy (or who has no documented sputum smear-conversion) needs to be carefully managed.

If the baby is symptomatic (difficulty breathing, feeding problems or poor weight gain, abdominal distension, enlarged liver or spleen, or jaundice):

- The baby needs to be referred to hospital for evaluation to exclude TB
- If the baby has TB, the baby should receive a full course of TB treatment.

TB treatment should be started in a referral centre to ensure correct dosages.

If the baby is asymptomatic:

- Withhold BCG at birth and give BCG after completion of 6 months INH therapy
- Give IPT for 6 months
- If symptoms develop, the baby needs to be referred to hospital for evaluation to exclude TB. (Symptoms of congenital TB usually develop at 2-3 wks)

The mother should be encouraged to breastfeed. Anti-TB drugs are secreted in breast milk, but the concentrations are very low and do not affect the baby. The drug levels in breast milk are too low to protect the baby and therefore the baby must receive INH preventive therapy as indicated.

Because the TB drugs are likely to kill the live BCG vaccine strain, BCG should not be given at birth in patients receiving IPT or TB treatment. BCG should be given after completion of 6 months IPT or TB treatment. BCG is contra-indicated if the infant is known to be HIV-infected.

4. TB INFECTION CONTROL

Prevention of TB transmission and infection in the household and health facilities are important components of control and management of TB in children, as children are found to be spending prolonged time with adults in overcrowded and underventilated waiting room (wherein adults are coughing). The following simple procedures are effective in TB infection control at home and clinics:

1. Early diagnosis and treatment of adult TB cases in the household
2. At the clinic promptly identify potential and known infectious cases of TB; separate and treat them with minimal delay by conducting triage and screening. Place posters in all patient and staff areas containing TB (Infection and Environment Control) IEC messages.
3. Provide health education about TB transmission without stigmatizing TB patients
4. Encourage proper cough hygiene both at home and at health facilities-
 - Cover nose and mouth with back of the hand (s), arm (sleeve), tissue, cloth or face mask when coughing or sneezing;
 - Turn head away from others when coughing or sneezing;
 - Use in the nearest waste bin to dispose of the tissue, cloth etc. after use;
 - Spit in a cloth or container with lid;
 - Perform hand hygiene (e.g. hand washing with soap and water, antiseptic hand wash) after having contact with respiratory secretions;

5. Ensure natural ventilation and sunlight:
 - Keep doors and windows open on opposite sides of the TB clinic and other clinics for effective ventilation- air circulation and changing.
 - Segregate children from adult TB patients if possible. Where children and adults stay together, keep windows open with ventilation fans.
 - Advise TB patients to do the same at home.
 - Apply the same in the hospitals.
6. HCWs/ care givers should be screened out if symptomatic
7. Personal protection of health care workers, by use of respirator device (eg. N-95 mask or FFP-2 mask) when appropriate (eg. sputum induction, bronchoscopy, BAL etc)
8. Prompt recognition and treatment of TB patients at community settings will act as the most effective measure of decreasing nosocomial transmission of TB.

The NTP has a well structured recording and reporting system consists of standardized cards, registers and reports which also includes specific areas for recording and reporting of TB cases for children. The National Tuberculosis Control Program recommends to use those cards, registers and reporting formats supplied from the program and expects that the areas specific for the children should be carefully filled up and reported. The methods on how to use the cards, registers and reporting formats are elaborately described in the National Guidelines and Operational Manual for Tuberculosis Control (Fifth Edition, 2013). The recording and reporting TB forms are attached in the guideline as annex.

SECTION VI

SUPERVISION, MONITORING AND EVALUATION

Supervision is the key element of TB control and a cornerstone for sustainability of the program. Effective supervision, monitoring and evaluation ensures sustaining achievements and improves performance of the health care professionals. The policy, process, tools, documentation and reporting of supervision, monitoring and evaluation are elaborately narrated in the National Guidelines and Operational Manual for Tuberculosis Control (Fifth Edition, 2013) in the section-8. This chapter covers all aspects of supervision, monitoring and evaluation of Child TB Management. NTP advises to follow the guidance described in the National Guidelines for Child TB Management as well.

SECTION VII

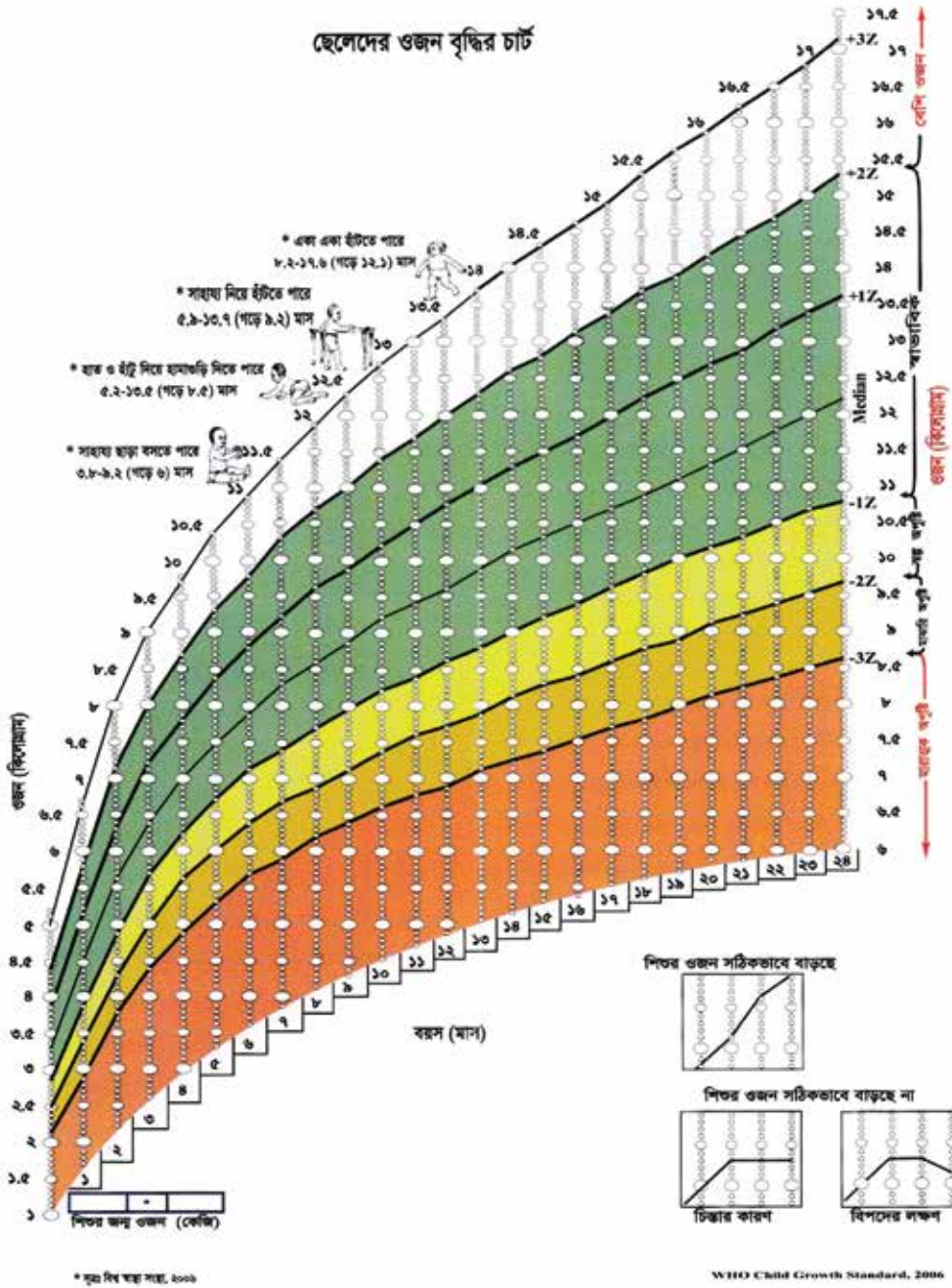
SUPPLY OF DRUGS, LABORATORY CONSUMABLES AND DOCUMENTATION MATERIALS

NTP ensures uninterrupted supply of quality drugs, laboratory consumables and documentation materials for Paediatric TB care to all health facilities throughout the country and provides diagnostics and drugs for case detection and management of registered child TB cases free of charge. Please see National Guidelines for detail.

ANNEX 1: FREQUENCY OF SYMPTOMS AND SIGNS OF PULMONARY TB STRATIFIED BY PATIENT AGE

Clinical features	Infants (0-11 mo)	Children (1-9 yr)	Adolescents (10-19 yr)
Symptom			
Fever	Common	Uncommon	Common
Night sweats	Rare	Rare	Uncommon
Cough	Common	Common	Common
Productive cough	Rare	Rare	Common
Haemoptysis	Never	Rare	Rare
Dyspnoea	Common	Rare	Rare
Sign			
Crepitations	Common	Uncommon	Rare
Wheezing	Common	Uncommon	Uncommon
Fremitus	Rare	Rare	Uncommon
Dullness to percussion	Rare	Rare	Uncommon
Decreased breath sounds	Common	Rare	Uncommon

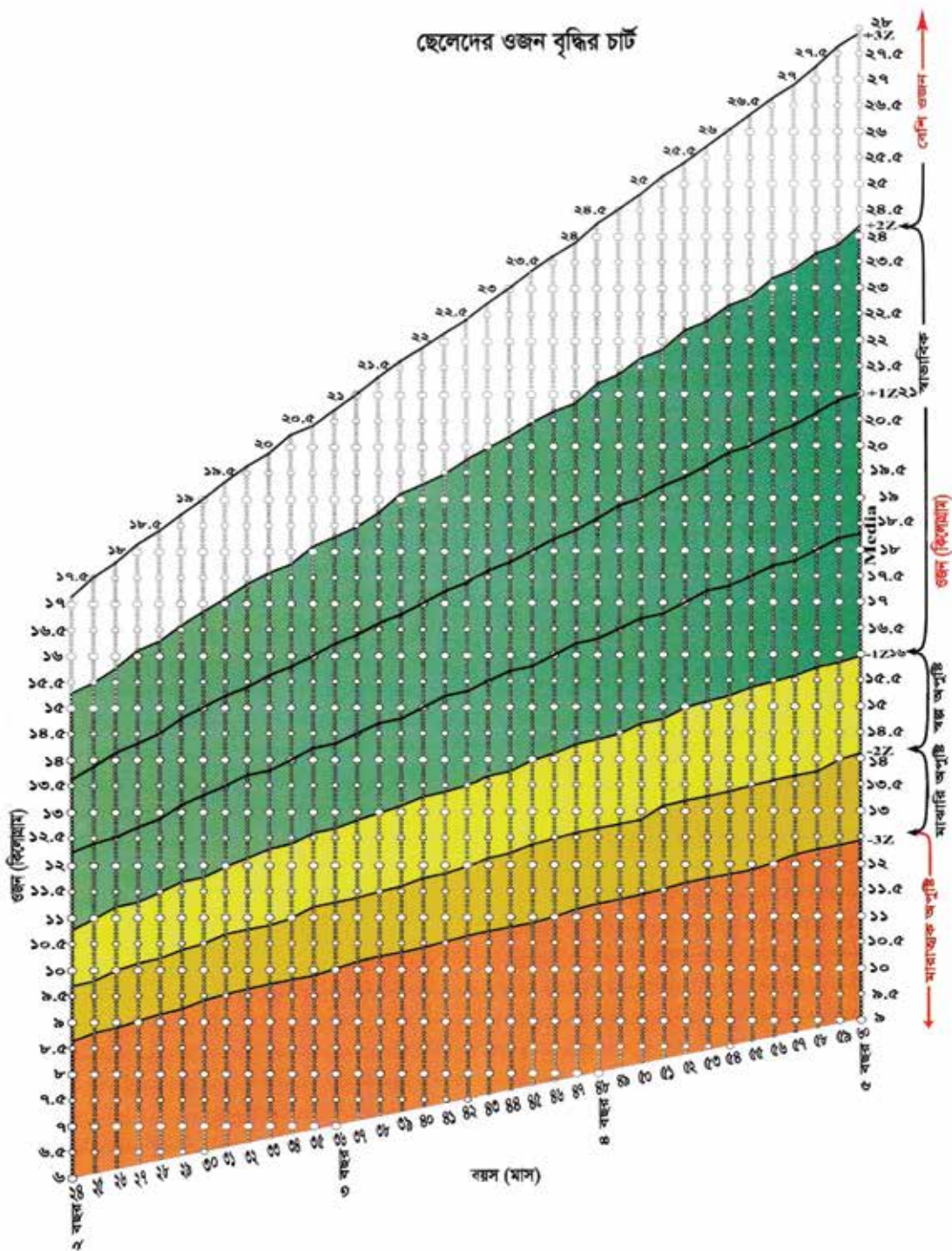
ANNEX 2A: IPHN GROWTH CHARTS: BOYS (Upto 24 months)



ANNEX 2

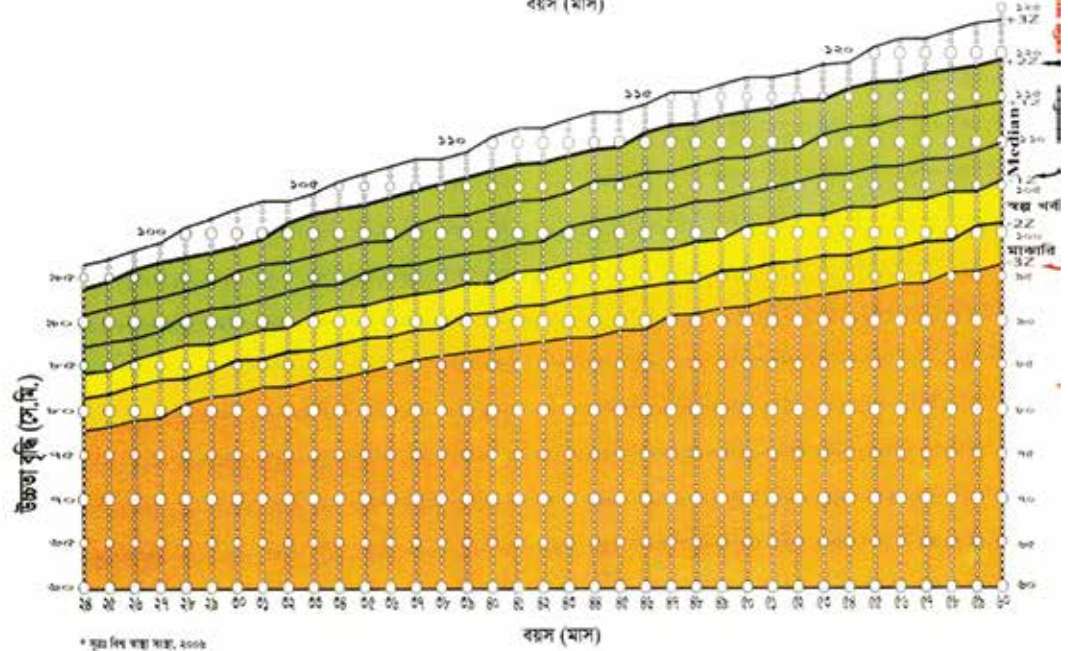
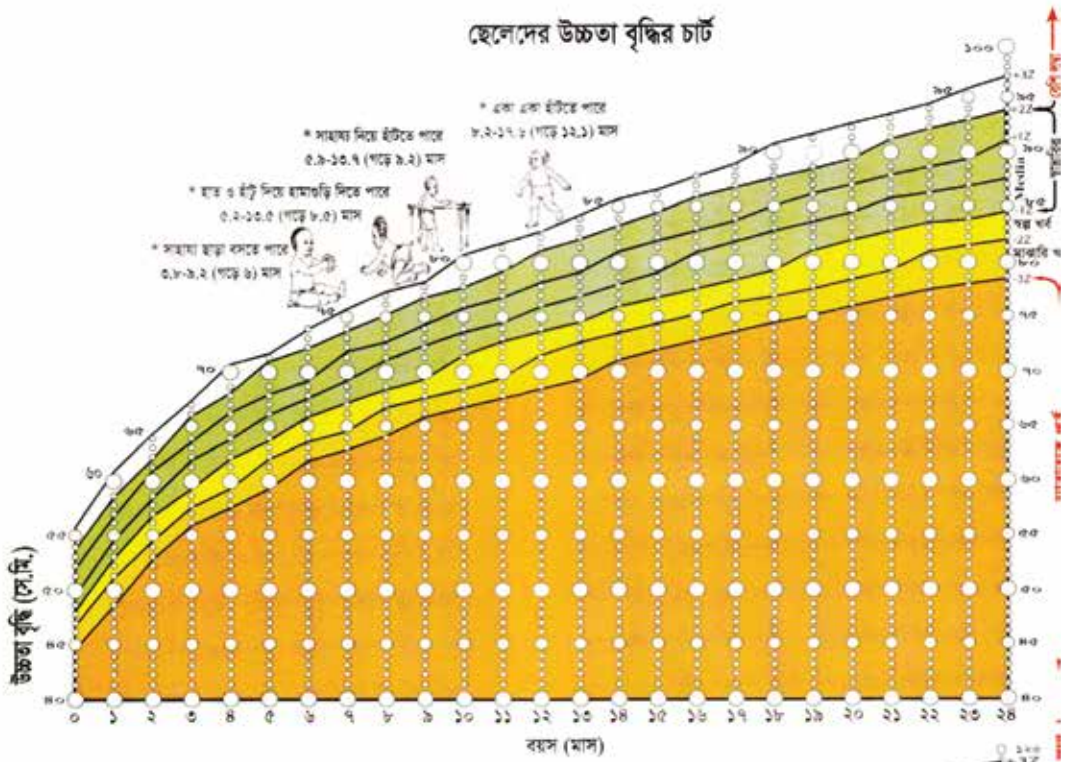
ANNEX 2B: IPHN GROWTH CHART FOR BOYS (24-59 Months)

ছেলেদের ওজন বৃদ্ধির চার্ট



ANNEX 2C: IPHN GROWTH CHART FOR BOYS-HEIGHT (0-59 Months)

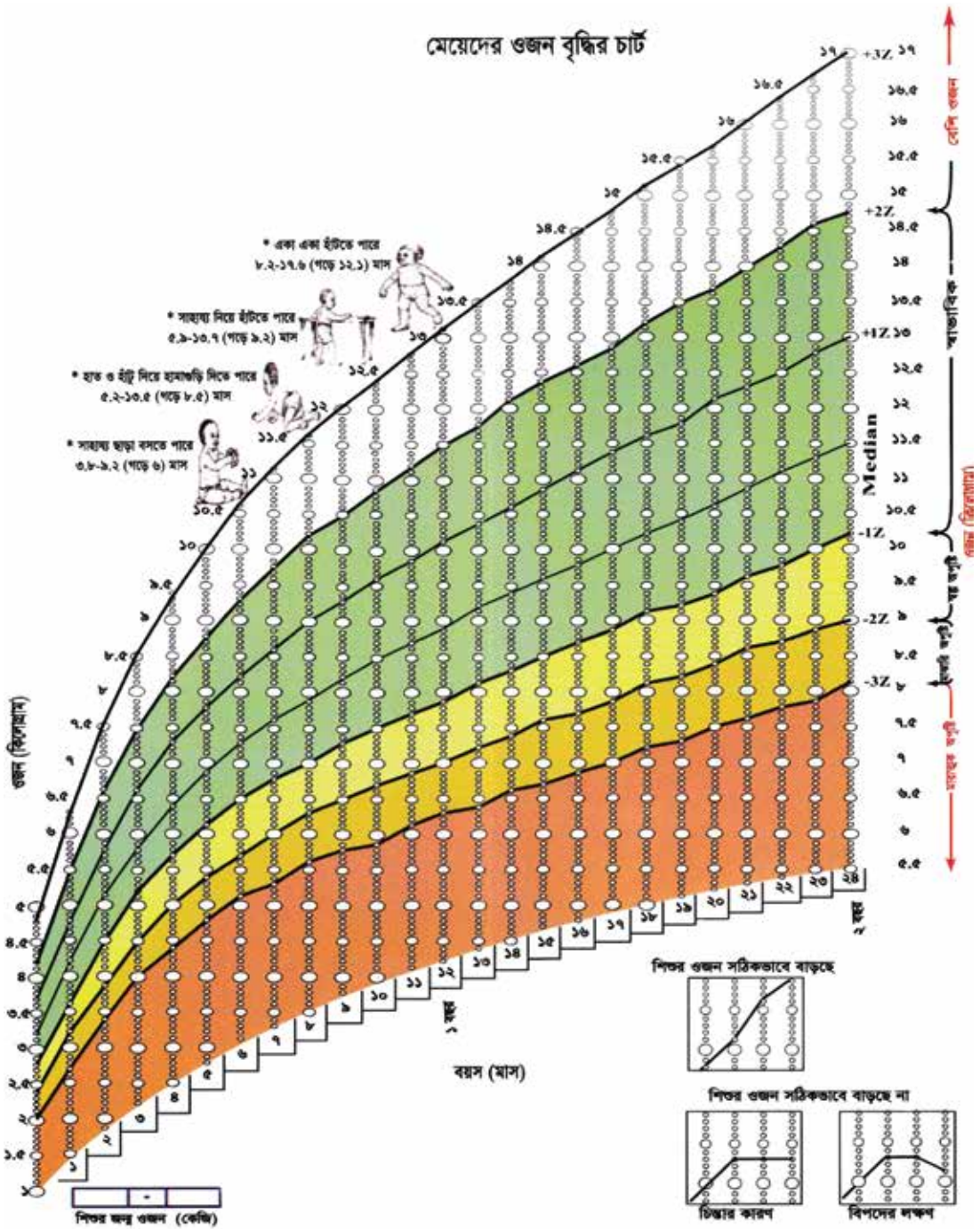
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ANNEX 2

ANNEX 2D: IPHN GROWTH CHART: GIRLS WEIGHT (0-24 Months)

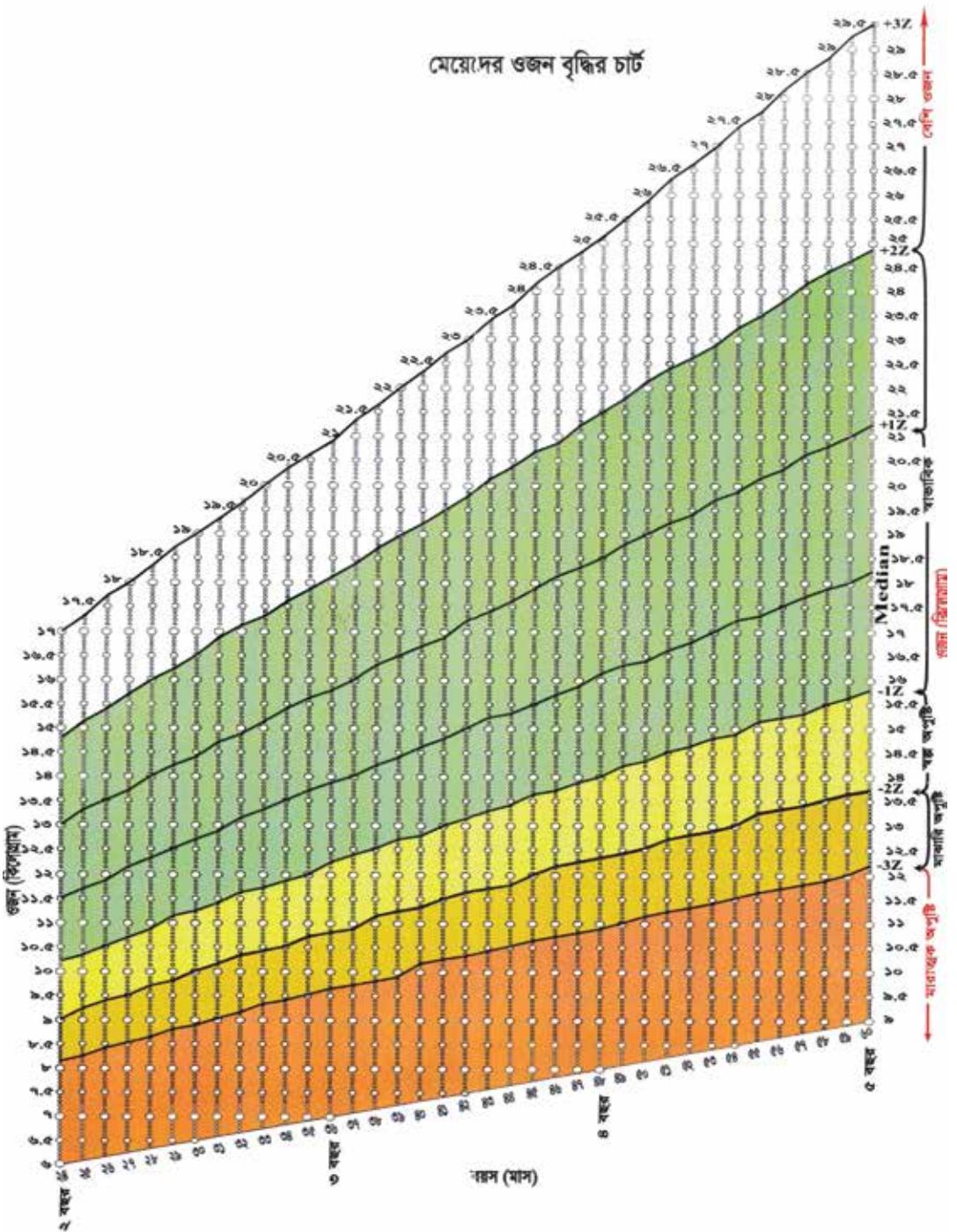
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ANNEX 2

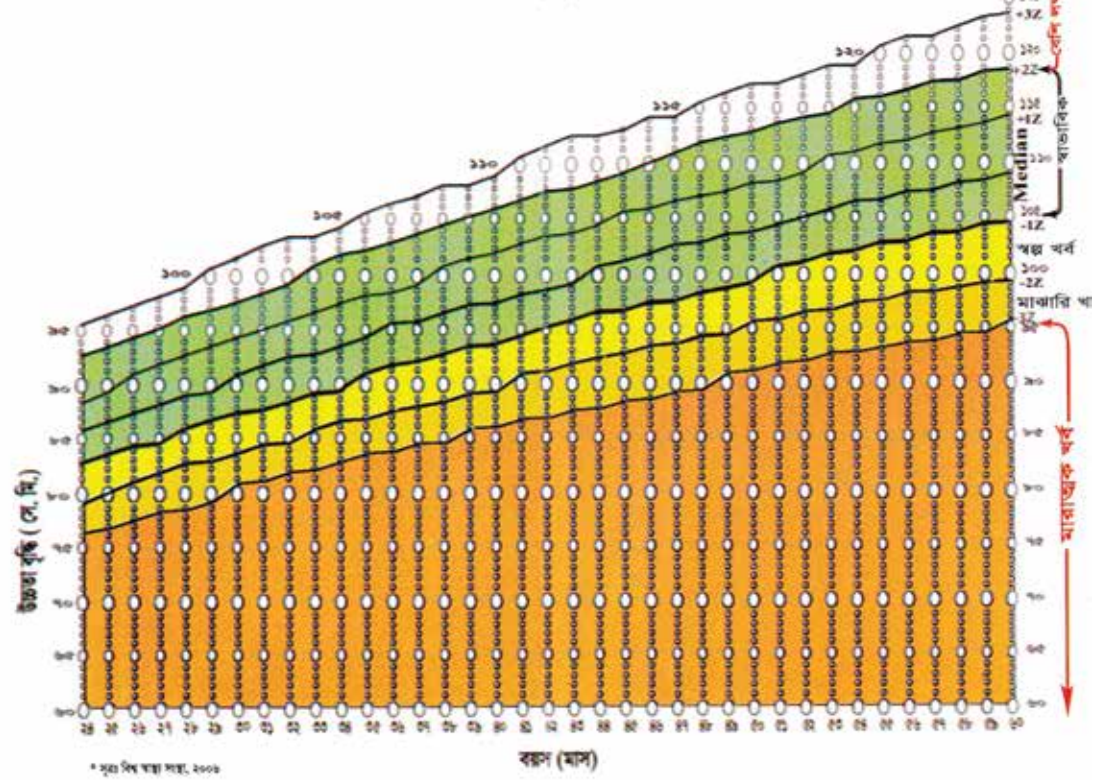
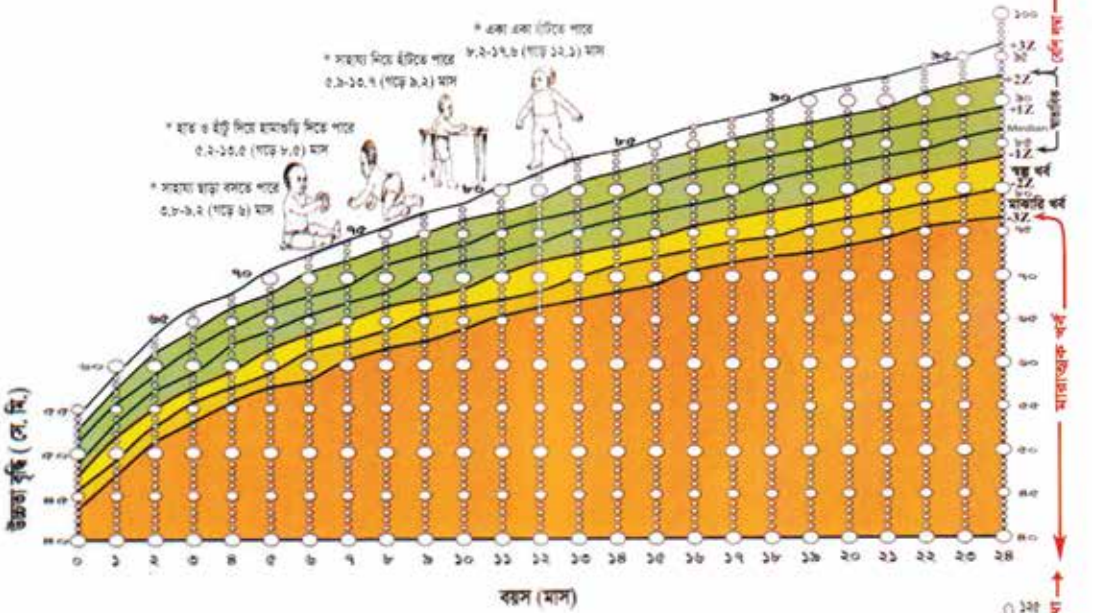
ANNEX 2E: IPHN GROWTH CHART GIRLS WEIGHT (24-59 Months)

মেয়েদের ওজন বৃদ্ধির চার্ট



ANNEX 2F: IPHN GROWTH CHART GIRLS HEIGHT (0-59 Months)

মেয়েদের উচ্চতা বৃদ্ধির চার্ট










* সূত্র বিশ্ব স্বাস্থ্য সংস্থা, ২০০৬

ANNEX 2

A MT is the intradermal injection of a combination of mycobacterial antigens which elicit an immune response (delayed-type hypersensitivity), represented by induration, measured in millimeters. The TST using the Mantoux method is the standard method of identifying people infected with *M. tuberculosis*.

Details of how to administer, read and interpret a TST are given below, using 5 tuberculin units (TU) of tuberculin PPD-S. An alternative to 5 TU of tuberculin PPD-S is 2 TU of tuberculin PPD.

MANTOUX TEST (MT)

ADMINISTERING MT	READING MT						
<p>a) Locate and the clean injection site</p> <ul style="list-style-type: none"> Place forearm palm-side up on a firm, well-lit surface Select an area 5–10 cm (2–4 inches) below elbow joint free of scars or sores Clean the area with an alcohol swab, allow to dry 	<p>The skin test must be read 48 to 72 hours after administration. If this window period is missed, the MT test may have to be re-administered.</p> <p>a) Inspect</p> <ul style="list-style-type: none"> Inspect the skin test site under good lighting  <p>Palpate Use your fingertips to determine if any induration is present</p>  <p>b) Mark</p> <ul style="list-style-type: none"> Mark the edges of induration (hard, dense, raised area, NOT the erythema/red area) across the forearm with a pen held at a 45° angle  <p>Measure Place "0" of ruler line on the inside-left edge of the induration</p> <ul style="list-style-type: none"> Read ruler line on the inside-right edge of the induration  <p>c) Record induration in millimetre (mm)</p> <ul style="list-style-type: none"> DO NOT record as "positive" or "negative". If there is no induration, record as 0 mm. 						
<p>b) Prepare the syringe</p> <ul style="list-style-type: none"> Check expiration date on vial and ensure vial contains tuberculin PPD-S (5 TU per 0.1 ml). Use a single-dose tuberculin syringe with a short (¼- to ½-inch) 27-gauge needle with a short bevel. Fill the syringe with 0.1 ml tuberculin. 							
<p>c) Inject tuberculin</p> <ul style="list-style-type: none"> Insert the needle slowly, bevel up, at an angle of 5–15°, almost parallel with the skin surface (see pictures below) Needle bevel should be visible just below skin surface.  							
<p>d) Check injection site</p> <ul style="list-style-type: none"> Ensure 8–10 mm wheal appears Repeat test 5 cm (2 inches) away from the original site if wheal doesn't appear or is not more 5 mm Do not cover with band aid 							
<p>e) Record information including:</p> <ul style="list-style-type: none"> Location (Left or Right arm) Tuberculin lot number Tuberculin Expiration date Date and Time test administered Signature of the health professional 							
<p>Interpretation of results:</p> <table border="1"> <thead> <tr> <th>MT reaction size</th> <th>Setting in which reaction is considered positive</th> </tr> </thead> <tbody> <tr> <td>≥5 mm</td> <td>Severely malnourished children (with clinical evidence of marasmus or kwashiorkor). HIV-infected children</td> </tr> <tr> <td>≥10 mm</td> <td>All other children</td> </tr> </tbody> </table>		MT reaction size	Setting in which reaction is considered positive	≥5 mm	Severely malnourished children (with clinical evidence of marasmus or kwashiorkor). HIV-infected children	≥10 mm	All other children
MT reaction size	Setting in which reaction is considered positive						
≥5 mm	Severely malnourished children (with clinical evidence of marasmus or kwashiorkor). HIV-infected children						
≥10 mm	All other children						

This annex reviews the basic procedures for the more common methods of obtaining clinical samples from children for smear microscopy: expectoration, gastric aspiration and sputum induction.

A. Expectoration

Background

1. The sputum smear remains a valuable test to perform in any child who is able to produce a sputum specimen. Sputum should always be obtained in older children who are pulmonary TB suspects. All sputum specimens produced by children should be sent for smear microscopy and, where available, mycobacterial culture. Children who can produce a sputum specimen may be infectious, so, as with adults, they should be asked to do this outside and not in enclosed spaces (such as toilets) unless there is a room especially equipped for this purpose. Three sputum specimens should be obtained: an on-the-spot specimen (at first evaluation), an early morning specimen and a second on-the-spot specimen (at follow up visit)

Procedure (adapted from Laboratory services in tuberculosis control. Part II. Microscopy (1))

2. Give the child confidence by explaining to him or her (and any family members) the reason for sputum collection.
3. Instruct the child to rinse his or her mouth with water before producing the specimen. This will help to remove food and any contaminating bacteria in the mouth.
4. Instruct the child to take two deep breaths, holding the breath for a few seconds after each inhalation and then exhaling slowly. Ask him or her to breathe in a third time and then forcefully blow the air out. Ask him or her to breathe in again and then cough. This should produce sputum from deep in the lungs. Ask the child to hold the sputum container close to the lips and to spit into it gently after a productive cough.
5. If the amount of sputum is insufficient, encourage the patient to cough again until a satisfactory specimen is obtained. Remember that many patients cannot produce sputum from deep in the respiratory track in only a few minutes. Give the child sufficient time to produce an expectoration which he or she feels is produced by a deep cough.
6. If there is no expectoration, consider the container used and dispose of it in the appropriate manner.

B. Gastric aspiration

Background

Children with TB may swallow mucus which contains *M. tuberculosis*. Gastric aspiration is a technique used to collect gastric contents to try to confirm the diagnosis of TB by microscopy and mycobacterial culture. Because of the distress caused to the child, and the generally low yield of smear-positivity on microscopy, this procedure should only be used where culture is available as well as microscopy.

Microscopy can sometimes give false-positive results (especially in HIV-infected children who are at risk of having non tuberculous mycobacteria). Culture enables the determination of the susceptibility of the organism to anti-TB drugs.

Gastric aspirates are used for collection of samples for microscopy and mycobacterial cultures in young children when sputa cannot be spontaneously expectorated nor induced using hypertonic saline. It is most useful for young hospitalized children. The diagnostic yield (positive culture) of a set of three gastric aspirates is only about (25-30%) but the specificity is very high (90-99%) with active TB. However, a negative smear or culture never excludes TB in a child. Gastric aspirates are collected from young children suspected of having pulmonary TB. During sleep, the lung's mucociliary system beats mucus up into the throat. The mucus is swallowed and remains in the stomach until the stomach empties. Therefore, the highest-yield specimens are obtained first thing in the morning.

Gastric aspiration on each of three consecutive mornings should be performed for each patient. This is the number that seems to maximize yield of smear-positivity. Of note, the first gastric aspirate has the highest yield. Performing the test properly usually requires two people (one doing the test and an assistant). Children not fasting for at least 4 hours (3 hours for infants) prior to the procedure and children with a low platelet count or bleeding tendency should not undergo the procedure.

The following equipment is needed:

- Gloves
- Nasogastric tube (usually 10 French or larger)
- 5, 10, 20 or 30 cm³ syringe, with appropriate connector for the nasogastric tube
- Litmus paper
- Specimen container
- Pen (to label specimens)
- Laboratory requisition forms
- Sterile water or normal saline (0.9% NaCl)
- Sodium bicarbonate solution (8%)
- Alcohol/chlorhexidine.

Procedure

The procedure can be carried out as an inpatient first thing in the morning when the child wakes up, at the child's bedside or in a procedure room on the ward (if one is available), or as an outpatient (provided that the facility is properly equipped). The child should have fasted for at least 4 hours (infants for 3 hours) before the procedure.

1. Find an assistant to help.
2. Prepare all equipment before starting the procedure.
3. Position the child on his or her back or side. The assistant should help to hold the child.
4. Measure the distance between the nose and stomach, to estimate distance that will be required to insert the tube into the stomach.
5. Attach a syringe to the nasogastric tube.
6. Gently insert the nasogastric tube through the nose and advance it into the stomach
7. Withdraw (aspirate) gastric contents (2–5 ml) using the syringe attached to the nasogastric tube.
8. To check that the position of the tube is correct, test the gastric contents with litmus paper: blue litmus turns red (in response to the acidic stomach contents). (This can also be checked by pushing some air (e.g. 3–5 ml) from the syringe into the stomach and listening with a stethoscope over the stomach.)
9. If no fluid is aspirated, insert 5–10 ml sterile water or normal saline and attempt to aspirate again. If still unsuccessful, attempt this again (even if the nasogastric tube is in an incorrect position and water or normal saline is inserted into the airways, the risk of adverse events is still very small). Do not repeat more than three times.
10. Withdraw the gastric contents (ideally at least 5–10 ml)
11. Transfer gastric fluid from the syringe into a sterile container (sputum collection cup).
12. Add an equal volume of sodium bicarbonate solution to the specimen (in order to neutralize the acidic gastric contents and so prevent destruction of tubercle bacilli).

After the procedure

1. Wipe the specimen container with alcohol/chlorhexidine to prevent cross-infection and label the container.
2. Fill out the laboratory requisition forms.
3. Transport the specimen (in a cool box) to the laboratory for processing as soon as possible (within 4 hours).
4. If it is likely to take more than 4 hours for the specimens to be transported, place them in the refrigerator (4–8 °C) and store until transported.
5. Give the child his or her usual food.

Safety

Gastric aspiration is generally not an aerosol-generating procedure. As young children are also at low risk of transmitting infection, gastric aspiration can be considered a low risk procedure for TB transmission and can safely be performed at the child's bedside or in a routine procedure room.

C. Sputum induction

Note that, unlike gastric aspiration, sputum induction is an aerosol-generating procedure. Where possible, therefore, this procedure should be performed in an isolation room that has adequate infection control precautions (negative pressure, ultraviolet light (turned on when room is not in use) and extractor fan).

Sputum induction is regarded as a low-risk procedure. Very few adverse events have been reported, and they include coughing spells, mild wheezing and nosebleeds. Recent studies have shown that this procedure can safely be performed even in young infants (2), though staff will need to have specialized training and equipment to perform this procedure in such patients.

General approach

Examine children before the procedure to ensure they are well enough to undergo the procedure. Children with the following characteristics should not undergo sputum induction.

- **Inadequate fasting:** if a child has not been fasting for at least 3 hours, postpone the procedure until the appropriate time
- Severe respiratory distress (including rapid breathing, wheezing, hypoxia)
- Intubated
- **Bleeding:** low platelet count, bleeding tendency, severe nosebleeds (symptomatic or platelet count <50/ml blood)
- Reduced level of consciousness
- History of significant asthma (diagnosed and treated by a clinician)

Procedure

1. Administer a bronchodilator (e.g. salbutamol) to reduce the risk of wheezing.
2. Administer nebulized hypertonic saline (3% NaCl) for 15 minutes or until 5 cm³ of solution have been fully administered.
3. Give chest physiotherapy if necessary; this is useful to mobilize secretions.
4. For older children now able to expectorate, follow procedures as described in section A above to collect expectorated sputum.
5. For children unable to expectorate (e.g. young children), carry out either: (i) suction of the nasal passages to remove nasal secretions; or (ii) nasopharyngeal aspiration to collect a suitable specimen.

Any equipment that will be reused will need to be disinfected and sterilized before use for a subsequent patient.

D. Fine needle aspiration cytology (FNAC)

In children with palpable peripheral lymph node masses, FNAC is the diagnostic modality of choice. It also assists to rule out malignancy as a possible alternative diagnosis. If FNAC is not available, a provisional TB diagnosis may be made if other likely causes have been ruled out and response to treatment is carefully monitored.

Chest radiography is the cornerstone of the diagnosis of intrathoracic tuberculosis. The great danger is that the chest radiograph is seen in isolation, without taking into account the clinical history, examination and tuberculin skin test. A balanced view is needed to ensure that there is not over- or under diagnosis.

The following basic conditions must be met:

1. Full-size chest radiographs must be taken. If possible, a lateral chest radiograph should also be taken, as this increases the diagnostic yield in childhood TB.
2. All previous chest radiographs should be available for accurate interpretation.
3. A good viewing box makes the examination easier.
4. The chest radiograph should be examined in a systematic manner.

Basic approach to the chest radiograph (Figs. 1, 2):

1. First check the identity of the patient and the date of the chest radiograph.
2. Now look at three aspects concerning the quality of the chest radiograph:

Rotation

Check rotation by looking at the clavicle head ends or by ensuring that the rib ends are equidistant from the chest edge. The position of the patient is also important as lordotic views are difficult to evaluate.

Penetration

Correct penetration is ensured when the intervertebral spaces can just be distinguished through the heart shadow.

Inspiration

Adequate inspiration is when the 8th/9th posterior rib, or the 6th anterior rib, is visible.

3. The next step is to look at the three structures that are white:

Soft tissue

Examine the soft tissue of the chest for swelling or lumps.

Bony structures

Examine the bony tissue for fractures, signs of rickets or areas of infiltration.

Heart shadow

Examine the cardiac shadow for position, size and shape.

4. The next step is to look at the three structures that are black:

The trachea and the bronchi

Follow the trachea and bronchi carefully, look for displacement or narrowing.

The right and left lung

Stomach bell

Look to ensure that the gas shadow in the stomach does not extend into the chest (hernia).

1. When looking at the lung always follow these three steps:
 - a. Compare the sizes of the two lungs.
 - b. Compare the vascularity of the two lungs.
 - c. Compare the two hilar shadows for:
 - a. Position
 - b. Size
 - c. Shape

2. Check three aspects of the diaphragm and pleura:
 - a. The position of the left and right diaphragms
 - b. The two costophrenic angles
 - c. The pleura on both sides

Quality Features

Rotation is absent when the clavicle ends are equidistant from the midline. This is often difficult to see in small children. A useful technique is to measure the ribs ends projecting over the lung fields and compare the two sides, which should be similar (Fig. 1). **Inspiration** is adequate if 8th/9th posterior ribs or 6th anterior ribs are visible. In young children, counting the posterior ribs is more accurate as their ribs are more horizontal, making counting anterior ribs inaccurate. Penetration is adequate if the intervertebral spaces are just visible through the heart shadow. Ensure that the radiographs are not lordotic as this can make interpretation difficult.

One of the normal structures that often causes considerable difficulty in deciding if the mediastinum is wider than usual and therefore containing enlarged lymph glands is the thymic shadow in a young child. The thymus is normally not visible in children older than four years. The classic sign of the thymic shadow is the sail sign (Fig. 3).

It is important to ensure that the chest radiograph is of acceptable quality, as a poor quality chest radiograph can lead to an incorrect diagnosis. Included is an example of a chest radiograph of unacceptable quality.



Normal chest radiograph. Note the good inspiration, lack of rotation, and good penetration. The rib ends are marked to aid in evaluating absence of rotation.



The normal lateral chest radiograph. It is a common mistake to interpret pulmonary artery as enlarged lymph glands.

Common cause for a widened mediastinum in a young child is a large thymus which causes the sail sign on the chest radiograph.



This is a poor-quality chest radiograph. The radiograph is of insufficient penetration, of poor inspiration, and is rotated, leading to the possible misinterpretation of hilar lymph glands.

Annex 6: NTP OFFICE ORDER ON IPT

গণপ্রজাতন্ত্রী বাংলাদেশ সরকার
জাতীয় যক্ষ্মা নিয়ন্ত্রন কর্মসূচি
স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা-১২১২

স্মারক নং: ০৫-৩৪/টিবি-লেপ্র/জিএফএটিএম/০৯(অংশ)/৪৮৯

তারিখ: ০৯/০৫/২০১২

সিভিল সার্জন (সকল)

বিষয়: **অনূর্ব ৫ বছরের শিশুদের “Isoniazid Preventive Therapy” (IPT) প্রয়োগ প্রসংগে।**

আপনি অবগত আছেন যে, জাতীয় যক্ষ্মা নিয়ন্ত্রন কর্মসূচি (NTP) ১৯৯৩ সনে “DOTS Strategy” এর মাধ্যমে যক্ষ্মা নিয়ন্ত্রন কার্যক্রম শুরু করে এবং আপনার আন্তরিক সহযোগিতায় উল্লেখযোগ্য সাফল্য অর্জন করেছে। আপনি আরও অবগত আছেন যে, NTP ২০০৬ সাগ থেকে STOP TB-Strategy কার্যক্রম বাস্তবায়ন করছে যার উল্লেখযোগ্য অংশ হ'ল শিশুদের যক্ষ্মা নিয়ন্ত্রন। শিশুদের যক্ষ্মা নিয়ন্ত্রনকল্পে NTP ইতিমধ্যে “National Guidelines for the Management of Tuberculosis in Children” প্রকাশ করেছে এবং তদানুযায়ী প্রশিক্ষণ প্রদান ও যন্ত্রপাতি সরবরাহের পদক্ষেপ নিয়েছে।

এ ছাড়াও শিশুদের যক্ষ্মা রোগ প্রতিরোধকল্পে NTP অনূর্ব ৫ বছরের শিশুদের “Isoniazid Preventive Therapy (IPT)” প্রয়োগের সিদ্ধান্ত নিয়েছে। IPT-প্রয়োগের নীতিমালা “National Guidelines for the Management of Tuberculosis in Children” এর ৩৭-৩৯ এবং (৬-৮) পৃষ্ঠায় উল্লেখ আছে।

নীতিমালা উল্লেখযোগ্য অংশ সংক্ষেপে নিম্নে প্রদত্ত হ'ল:

ক) যে সকল শিশুকে IPT প্রয়োগ করতে হবে:

- শিশুর কোন Pulmonary TB রোগীর সাথে close contact এর প্রমাণ থাকতে হবে;
- শিশুর বয়স ৫ বছরের নীচে হতে হবে;
- শিশু “যক্ষ্মা রোগে ভুগছে না” এ মর্মে নিশ্চিত হতে হবে;
- IPT চলাকালীন সময়ে যক্ষ্মার লক্ষণ দেখা দিলে প্রয়োজনীয় ব্যবস্থা গ্রহণের জন্য শিশুকে সংশ্লিষ্ট চিকিৎসক/স্বাস্থ্য কেন্দ্র/ হাসপাতাল এ প্রেরণ করতে হবে;

খ) IPT প্রয়োগের পদ্ধতি:

- প্রতি দিন নির্ধারিত মাত্রায় Isoniazid বড়ি খাওয়াতে হবে;
- নির্ধারিত মাত্রার বড়ি বুকের দুধ(প্রয়োজ্য ক্ষেত্রে)/ পানি/ভিটামিন সিরাপের সাথে মিশিয়ে খাওয়াতে হবে;
- INH বড়ি মোট ৬ মাস এক নাগাড়ে খাওয়াতে হবে;
- সঠিক মাত্রায় নিয়মিত Isoniazid বড়ি খাওয়ানোর বিষয়ে শিশুর অভিভাবক ও নিকটস্থ আত্মীয়স্বজনদের ভালভাবে বুঝাতে হবে;
- যথাযথ ভাবে IPT প্রয়োগ নিশ্চিতকল্পে সংশ্লিষ্ট স্বাস্থ্য কর্মীগণ নিয়মিত তদারকী করবেন এবং এ সংক্রান্ত তথ্য রেকর্ড রিপোর্ট নিশ্চিত করবেন।

অতএব, আপনার জেলাগার আওতাধীন অনূর্ব ৫ বছরের সকল শিশুদের “National Guidelines for the Management of Tuberculosis in Children” অনুসরণ পূর্বক “INH Preventive Therapy” প্রয়োগের ব্যাপারে যথাযথ পদক্ষেপ গ্রহণের জন্য আপনাকে অনুরোধ করা হ'ল।

ডাঃ মোঃ আশেক হোসেন
পরিচালক, এমবিডিসি ও লাইন ডাইরেক্টর, টিবি/লেপ্র
স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা-১২১২

রেজিস্টার্ড নং ডি এ-১

২০১৪ সনের ৫ নং

বাংলাদেশ



গেজেট

কর্তৃপক্ষ কর্তৃক প্রকাশিত

মুহূর্ত্তস্বাক্ষর, জানুয়ারি ৩০, ২০১৪

স্বাস্থ্য ও পরিবার কল্যাণ মন্ত্রণালয়

বিশ্ব স্বাস্থ্য-২ শাখা

বিজ্ঞপ্তি

তারিখ: ২২ জানুয়ারি ২০১৪

নং স্বাপকম/বিশ্বস্বাস্থ্য-২/Pro-1/GFATM-TB/2008(Pt-1)/৮০—
বাংলাদেশে যক্ষ্মারোগ একটি প্রধান জনস্বাস্থ্য সমস্যা। উল্লেখযোগ্য সংখ্যক নারী, পুরুষ ও শিশু প্রতি বছর এ রোগে আক্রান্ত হন এবং কিছু সংখ্যক মৃত্যুবরণ করেন। সময়মত রোগ নির্ণয় ও নির্দিষ্ট মেয়াদের চিকিৎসায় এ রোগ সম্পূর্ণ নিরাময় করা যায়। কিন্তু ভুল রোগ নির্ণয় এবং অসম্পূর্ণ চিকিৎসার ফলে এ রোগ জটিল আকার ধারণ করে এবং বিস্তার লাভ করে। যথাযথ রোগ নির্ণয় ও ব্যবস্থাপনার জন্য বাংলাদেশের সকল যক্ষ্মারোগীর তথ্য জাতীয় যক্ষ্মা নিয়ন্ত্রণ কর্মসূচীর গোচরীভূত থাকা আবশ্যিক। সুতরাং সরকার এ মর্মে সিদ্ধান্ত গ্রহণ করেছে যে, সরকারি এবং বেসরকারি সকল স্বাস্থ্য সেবা প্রদানকারী যক্ষ্মারোগীর তথ্য নিকটস্থ সরকারি স্বাস্থ্য কর্মকর্তার নিকট অবহিত করবেন।

কেস নোটিফিকেশনের জন্য যক্ষ্মারোগকে নিম্নোক্তভাবে সংজ্ঞায়িত করা হল :

- Any patient diagnosed with sputum specimen positive for acid fast bacilli, or culture-positive for Mycobacterium tuberculosis, or NTP endorsed rapid molecular diagnostic test positive for TB

Or

- Any patient diagnosed clinically as a case Tuberculosis, without microbiological confirmation, and initiated on anti-TB drugs.

বিস্তারিত তথ্য ও ব্যাখ্যার জন্য জাতীয় যক্ষ্মা নিয়ন্ত্রণ কর্মসূচি, স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা-১২১২ বরাবর যোগাযোগ করা যেতে পারে।

২। এই বিজ্ঞপ্তি জারীর ফলে বাংলাদেশে যক্ষ্মারোগ আবশ্যিকভাবে Notifiable Disease হিসেবে গণ্য হবে।

রাষ্ট্রপতির আদেশক্রমে

নাসীমা হোসেন

সিনিয়র সহকারী সচিব।

Government Gazette
on mandatory notification

বিসিজি টিকা

বিসিজি টিকা যক্ষ্মা রোগ থেকে রক্ষা করে।

এটি জমানো শুষ্ক পাউডার আকারে থাকে যা ডাইলুয়েন্টের সাহায্যে তরল করলে হয়। বিসিজি ডাইলুয়েন্ট, এমআর এবং হামের ডাইলুয়েন্ট থেকে ভিন্ন। লেবেল পড়ে বিসিজি, এমআর এবং হামের ডাইলুয়েন্টের পার্থক্য বোঝা যায়।

বিসিজি টিকা ও ডাইলুয়েন্ট একই প্রস্তুতকারকের হতে হবে। অন্য প্রস্তুতকারকের ডাইলুয়েন্ট ব্যবহার করা যাবে না।

সংমিশ্রণের পর টিকার কার্যকারিতা দ্রুত নষ্ট হয় বিধায় সংমিশ্রণের পর ৬ ঘন্টা পর্যন্ত এই টিকা ব্যবহার করা যায়।

সংমিশ্রণের ৬ ঘন্টা পর টিকা ব্যবহার করলে শিশুর মারাত্মক পার্শ্ব-প্রতিক্রিয়া হবে এমনকি মৃত্যুও হতে পারে।

বিসিজি টিকার কার্যক্ষমতা আলোতে দ্রুত নষ্ট হয়ে যায়, সেজন্য গ্র্যাম্পুল/ভায়ালের রং বাদামি রঙের হয়।

বিসিজি টিকা + ২ ডিগ্রী সেলসিয়াস থেকে +৮ ডিগ্রী সেলসিয়াস তাপমাত্রায় সংরক্ষণ করতে হয়।

জন্মের পর যত শীঘ্র সম্ভব বিসিজি টিকা দেয়া উচিত। বাম বাহুর উপরের অংশে, চামড়ার মধ্যে ইনজেকশনের মাধ্যমে ০.০৫ এম এল সংমিশ্রিত টিকার এক ডোজ দিতে হয়।

বিসিজি টিকা দেওয়ার পর স্বাভাবিক প্রতিক্রিয়া কী হয় তা অভিভাবককে অবশ্যই জানাতে হবে। অর্থাৎ টিকা দেওয়ার

২ সপ্তাহ পর টিকার স্থান লাল হয়ে ফুলে যাবে এবং আরো ২/৩ সপ্তাহ পরে শক্ত দানা, ক্ষত বা ঘা হতে পারে। ধীরে ধীরে এই ক্ষত বা ঘা শুকিয়ে যাবে এবং দাগ (Scar) থাকবে। কোনো গুণ্ড বা তেল ক্ষতে দেয়া যাবে না। নিজ থেকেই ক্ষত শুকিয়ে যাবে।

বিসিজি টিকা অনেক গভীরে প্রবেশ করলে এবং টিকা বেশি পরিমাণে দেয়া হলে বিসিজি টিকার জায়গায় পার্শ্ব-প্রতিক্রিয়া, প্রদাহ বা গভীর ফোঁড়া হতে পারে।

শিশু বিসিজি টিকা নিয়েছে কিনা তা দাগ দেখে পরীক্ষ করা যায়। যে শিশুকে বিসিজি টিকা দেয়া হয়েছে পরবর্তী সাক্ষাতে সাধারণ প্রতিক্রিয়াজনিত দাগ হয়েছে কিনা তা দেখা উচিত। অস্বাভাবিক প্রতিক্রিয়া হলে, মেডিকেল অফিসারের নিকট পাঠাতে হবে। কোনো প্রতিক্রিয়া না হলে অর্থাৎ টিকার দাগ (Scar) অর্থাৎ টিকার দাগ (Scar) না উঠলে ডিপটি/পেন্টাভ্যালেন্ট টিকার ৩য় ডোজের সময় আবার বিসিজি টিকা দিতে হবে।

বিসিজি টিকা ২০ ডোজের ভায়াল ব্যবহার করা হয়।

Annex 9: IPT REGISTER

National Tuberculosis Control Programme Directorate General of Health Service, Bangladesh Isoniazid Preventive Therapy (IPT) Register

Date	Name of *Eligible child	Age		Sex M/F	Name and address of parents	TB Registration no. of source case	Relation with source case	**IPT Registration no.	IPT Registration date	IPT Starting date	IPT Completion date	***Outcomes	Remarks
		Year	Month										

* Eligible child: A Child is defined eligible if following criteria are met: - 1 Child who was in close contact with pulmonary smear positive patient. 2. Age between 0-5 years. 3. Asymptomatic as declared by a graduate doctor.

** IPT registration number: This number will be given to the child who has been selected as a candidate for IPT among all eligible children.

***Outcomes:

1. Treatment Completed: Full Course of 6 month's IPT completed.
2. Defaulted: Treatment interruption for 2 consecutive months or more. Need to be re-registered for 6 month's IPT.
3. Transferred out: child who has been transferred to another center. Name of the center where the child was transferred should be written in the remarks column & feedbacks recorded.
4. Died: child known to have died during the course of IPT.
5. Developed active TB: child who has developed active TB diseases during the course of IPT.

Note: List of all transferred in Children should be maintained separately, feedbacks to be given to referring center and all these information should be mentioned in Remarks column.

Annex 10: CONTACT INVESTIGATION FORM

NTP Government of Bangladesh Contact Investigation (CI) for TB/ DR TB



(Block A:)Information of index patient		Name of the DOTS Corner:	
Name:		Treatment initiation centre:	
Village/Ward:		TB /DR TB Reg. no:	
Union:		Name of the contact investigator :	
Upazilla:		designation of the contact investigator :	
District		Phone number of contact investigator:	
		Name of the DOT provider:	
		designation of the DOT provider:	
Phone number:		Phone number of the DOT provider:	

(Block B)	Date	Contact name	Age (yrs/mo)	Sex (M/F)	Relation (code)	Symptoms* (Yes/No)	Refer (Yes/No)	Date entered in CI register	Remarks
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									

*যক্ষ্মার উপসর্গ ১. Three weeks (for adult) দুই সপ্তাহের (for child) বেশি লাগাতার কাশি ২. ওজন না বাড়া** বা কমে যাওয়া ৩. নিশ্বাস হয়ে যাওয়া বা খোলাখুলা কমা করা** ৪. জ্বর
৫. কাশি antibiotic এ ভাল না হওয়া ৬. কাশির সাথে রক্ত যাওয়া
Code: Contact 1. Household member, 2. Workplace, 3. Neighbour, 4. Other
**for Child

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