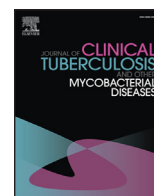




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How to manage children who have come into contact with patients affected by tuberculosis



Laura Lancella^a, Andrea Lo Vecchio^b, Elena Chiappini^c, Marina Tadolini^d, Daniela Cirillo^e, Enrico Tortoli^e, Maurizio de Martino^c, Alfredo Guarino^b, Nicola Principi^f, Alberto Villani^a, Susanna Esposito^{f,*}, Luisa Galli^c, for the Italian Pediatric TB Study Group¹

^a Unit of General Pediatrics and Pediatric Infectious Diseases, IRCCS Bambino Gesù Hospital, Rome, Italy

^b Section of Pediatrics, Department of Translational Medical Science, Federico II University of Naples, Naples, Italy

^c Pediatric Clinic, Meyer Hospital, University of Florence, Florence, Italy

^d Section of Infectious Diseases, Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy

^e Microbiology Unit, IRCCS San Raffaele Hospital, Milan, Italy

^f Pediatric Highly Intensive Care Unit, Department of Pathophysiology and Transplantation, University of Milan, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

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ABSTRACT

Childhood tuberculosis (TB) indicates a recent infection, particularly in children aged < 5 years, and therefore is considered a sentinel event insofar as it highlights the presence of an undiagnosed or untreated source case. The risk of acquiring TB is directly proportional to the number of bacilli to which a subject is exposed and the environment in which the contact occurred. This document contains the recommendations of a group of Italian scientific societies for managing a child exposed to a case of TB based on an analysis of the risk factors for acquiring latent tuberculous infection (LTBI) and developing the disease, and the particular aspects TB transmission during the first years of life. The guidance includes a detailed description of the methods used to identify the index case, the tests that the exposed child should receive and the possibilities of preventive chemoprophylaxis depending on the patient's age and immune status, the chemotherapy and monitoring methods indicated in the case of LTBI, the management of a child who has come into contact with a case of multidrug-resistant or extensively drug-resistant TB, and the use of molecular typing in the analysis of epidemics. The group of experts identified risk factors for tuberculous infection and disease in pediatric age as well as gave recommendation on management of contacts of cases of TB according to their age, risk factors and exposure to multidrug-resistant or extensively drug-resistant TB.

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* Corresponding author. Tel.: +39 02 55032498; fax: +39 02 50320206.

E-mail address: susanna.esposito@unimi.it (S. Esposito).

¹ The Italian Pediatric TB Study Group also includes: Samantha Bosis, Claudia Tagliabue, Laura Senatore, Beatrice Ascolese (Pediatric Highly Intensive Care Unit, University of Milan, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy); Laura Cursi, Annalisa Grandin, Caterina Marabotto (Unit of General Pediatrics and Pediatric Infectious Diseases, IRCCS Bambino Gesù Hospital, Rome, Italy); Carlotta Montagnani, Daniele Ciofi, Filippo Festini, Martina Anziati, Sabrina Becciani, Giulia Remaschi, Sara Sollai, Chiara Tersigni, Elisabetta Venturini (Pediatric Clinic, Meyer Hospital, University of Florence, Florence, Italy); Riccardo Scotto (Section of Pediatrics, Department of Translational Medical Science, Federico II University of Naples, Naples, Italy); Filippo Bernardi (Pediatric Emergency Unit, University of Bologna, Bologna, Italy); Elisa Bertazzoni (Pharmacology Unit, University of Verona, Verona, Italy); Francesco Blasi (Pneumology Unit, University of Milan, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy); Marialuisa Bocchino, Luca Assante (Pneumology Unit, Federico II University of Naples, Naples, Italy); Elio Castagnola, Giuseppe Losurdo (Infectious Diseases Unit, IRCCS Giannina Gaslini, Genoa, Italy); Luigi

Codeca (Referral Center for Tuberculosis, Lombardy Region, Milan, Italy); Giuseppe Di Mauro (primary care pediatrician, Caserta, Italy); Marino Faccini (Prevention Department, ASL Milano, Milan, Italy); Clara Gabiano, Silvia Garazzino, Daniele Le Serre, Irene Raffaldi (Pediatric Infectious Diseases Unit, Regina Margherita Hospital, University of Turin, Turin, Italy); Gianluigi Marseglia, Amelia Mascolo (Pediatric Clinic, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy); Amelia Di Comite, Mauro Stronati (Neonatology and Neonatal Intensive Care Unit, Fondazione IRCCS Policlinico San Matteo, Pavia); Italy Alberto Matteelli (World Health Organization, Global Tuberculosis Programme, Geneva, Switzerland); Giovanni Battista Migliori, Rossella Centis, Lia D'Ambrosio (World Health Organization Collaborating Centre for Tuberculosis and Lung Diseases, Fondazione S. Maugeri, Care and Research Institute, Tradate, Italy); Angela Pasinato (primary care pediatrician, Vicenza, Italy); Cristina Russo (Microbiology Unit, IRCCS Bambino Gesù Hospital, Rome, Italy); Franco Scaglione (Pharmacology Section, University of Milan, Milan, Italy); Elisabetta Scala (MOIGE Association, Rome, Italy); Paolo Tomà (Radiology Unit, IRCCS Bambino Gesù Hospital, Rome, Italy) Scientific Societies involved in the Italian Pediatric TB Study Group: Società Italiana di Neonatologia (SIN), represented by Amelia Di Comite and Mauro Stronati; Società

Introduction

Childhood tuberculosis (TB) indicates a recent infection, particularly in children aged <5 years, and therefore is considered a sentinel event insofar as it highlights the presence of an undiagnosed or untreated source case [1]. The transmission of *Mycobacterium tuberculosis* is usually due to the inhalation of airborne particles or droplets containing 2–3 micro-organisms spread by the sneezing or coughing of an adolescent or adult with bacilleferous pulmonary or laryngeal TB.

It is now universally accepted that the risk of acquiring TB is directly proportional to the number of bacilli to which a subject is exposed [2]. In the first place, it depends on the characteristics of the source case: contagiousness is generally limited to subjects with lung disease, and is greater among the patients with bacilleferous forms (i.e. those with positive microscopic test results), in whom the estimated transmission rate is about 35% as against the 17% observed among those with non-bacilleferous forms [3,4]. It is also known that subjects with cavitating TB and frequent cough are more bacilleferous and contagious than those with other pulmonary pictures or who cough less frequently [5]. Furthermore, any manoeuvre capable of stimulating coughing can lead to more aerosolised respiratory secretions and consequently increase contagiousness. The subjects with extra-pulmonary disease (meningitis or abdominal, renal or bone TB) are generally considered not to be contagious, but the absence of pulmonary involvement must be documented before this can be declared [5]. Children with TB who are less than 10 years old are less frequently contagious because their pulmonary lesions are usually small and paucibacillary, and their cough is often unproductive [3,6].

The number of bacilli to which a subject is exposed is strictly related to the environment in which the contact takes place. Enclosed and poorly ventilated places favour the concentration of tubercular bacilli in the air and increase the likelihood of transmission, whereas contacts in the open air or well-ventilated environments decrease it [7]. Similarly, it is important to evaluate the time spent in an enclosed space with the source case. The effect of the combination of these two variables has been clearly shown in studies of the contacts arising during air flights [8]. Living together gives rise to the greatest exposure to TB: this has been documented in studies such as that of Singh et al. who evaluated the prevalence of TB in children living with adults with active TB and found a significant difference between those living with adults with microscopic positive or negative expectorate (respectively 68.4 and 31.6%) [6].

Only few, highly variable and conflicting data are available concerning transmission by pediatric source cases, all of which come from individual case reports: the rate of transmission when a child or

Table 1

Quality of evidence and strength of recommendation.

Quality of evidence	
I	Evidence from more than one properly designed, randomised, controlled study and/or systematic review of randomised studies
II	Evidence from one properly designed, randomised, controlled study
III	Evidence from cohort studies or their meta-analysis
IV	Evidence from retrospective case-controlled studies or their meta-analysis
V	Evidence from case series without control group
VI	Evidence from opinions of respected authorities, based on clinical experience
Strength of recommendation	
A	The panel strongly supports a recommendation for use
B	The panel moderately supports a recommendation for use
C	The panel marginally supports a recommendation for use

adolescent has microscopic positive expectorate or gastric aspirate ranges from 0.5 to 39.3% [5], whereas the only two reported cases of children with microscopic negative expectorate/gastric aspirate transmitted TB to 29.8 [9] and 72.4% [10] of their contacts. However, the exiguous number of described cases and the lack of information concerning the presence of other risk factors for the acquisition of TB in the contacts does not allow any conclusions to be drawn concerning the real rate of transmission when the source case is a child.

This document contains the recommendations of a group of Italian scientific societies for managing a child exposed to a case of TB based on an analysis of the risk factors for acquiring latent tuberculous infection (LTBI) and developing the disease, as well as the particular evolution of TB during the first years of life.

Methodology

The Consensus Conference method was used, following the National Institutes of Health and the National Plan Guidelines as previously reported (Table 1) [11,12]. Relevant publications in English were identified through a systematic review of MEDLINE and the Cochrane Database of Systematic Reviews from their inception through December 31, 2014. Search strategy: "children[Title/Abstract] OR pediatric[Title/Abstract] OR paediatric[Title/Abstract] AND tuberculosis[Title/Abstract] AND English[lang]". The Working Group agreed on a list of clinical problems relevant to the management of children at risk of, or exposed to TB. The evidence review procedures focused on patients aged 0–18 years and included section-specific targeted searches as well as formal systematic reviews on selected topics. In addition, the clinical recommendations reported in relevant and updated international guidelines have been reviewed and critically compared in case of debated issues. All the data were included in tables of evidence for each topic. Trained personnel performed the critical appraisal of the acquired literature using the Scottish Intercollegiate Guidelines Network methodological checklists [13]. Subsequently, the bibliographical material and a preliminary draft of the document were provided to the panel members. In the various meetings, literature evidence was reported and discussed and the Delphi method was used to reach a consensus when the evidence did not provide consistent and unambiguous recommendations [13]. The final text was revised on the basis of these discussions and submitted by e-mail to participants at the Consensus Conference for final approval. The multidisciplinary panel of clinicians and experts in evidence-based medicine were identified with the help of the participating scientific societies. Specifically, the panel included experts in the fields of general pediatrics, pediatric infectious diseases, infectious diseases, pneumology, microbiology, radiology and methodologists and was coordinated by the Italian Society of Pediatric Infectious Diseases (SITIP). No panel member declared any

Italiana di Infettivologia Pediatrica (SITIP), represented by Susanna Esposito, Maurizio de Martino, Luisa Galli, Alfredo Guarino, Laura Lancella, Andrea Lo Vecchio, Nicola Principi, Samantha Bosis, Elio Castagnola, Clara Gabiano, Silvia Garazzino, Giuseppe Losurdo, Carlotta Montagnani, Martina Anziati, Beatrice Ascolese, Sabrina Becciani, Laura Cursi, Annalisa Grandin, Daniele Le Serre, Caterina Marabotto, Irene Raffaldi, Giulia Remaschi, Riccardo Scotto, Laura Senatore, Sara Sollai, Claudia Tagliabue, Chiara Tergisni and Elisabetta Venturini; Società Italiana di Pediatria (SIP), represented by Alberto Villani, Cristina Russo and Paolo Tomà; Società Italiana di Malattie Respiratorie Infantili (SIMRI), represented by Filippo Bernardi; Società Italiana di Immunologia e Allergologia Pediatrica (SIAIP) represented by Gianluigi Marseglia and Amelia Mascolo; Società Italiana di Pediatria Preventiva e Sociale (SIPPS), represented by Giuseppe Di Mauro and Elena Chiappini; Società Italiana per le Cure Primarie Pediatriche (SiCUPP), represented by Angela Pasinato; Società Italiana di Malattie Respiratorie (SIMER), represented by Francesco Blasi, Marialuisa Bocchino and Luca Assante; Associazione Italiana Pneumologi Ospedalieri (AIPO), represented by Luigi Codecasa; Società Italiana di Malattie Infettive e Tropicali (SIMIT), represented by Alberto Matteelli; Associazione Microbiologi Clinici Italiani (AMCLI), represented by Enrico Tortoli; Società Italiana di Chemioterapia (SIC), represented by Elisa Bertazzoni; Società Italiana di Farmacologia (SIF), represented by Francesco Scaglione; STOP TB, represented by Daniela Cirillo, Marino Faccini, Giovanni Battista Migliori, Marina Tadolini, Rossella Centis and Lia D'Ambrosio; Società Italiana di Scienze Infermieristiche Pediatriche (SISIP), represented by Filippo Festini and Daniele Ciofi; MOIGE, represented by Elisabetta Scala.

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