

# The “Titi” study

Transmission Investiguée de la Tuberculose Infantile

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*Childhood TB working group meeting*

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# Background

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- A **workshop** was organized by The Union in January 2014 in Benin with NTP (managers/childhood TB focal points) and paediatricians from 8 countries in francophone Africa: Benin, Burkina Faso, Cameroon, Central African Republic, Côte d'Ivoire, DRC, Madagascar, Niger
- The objective of the workshop was to identify **key actions** to improve the control of childhood TB
- Among the major conclusions of the workshop : systematic **investigation and preventive therapy** for children <5 years who are contacts of contagious TB cases, although internationally and nationally recommended, remain partially implemented and are not fully documented

# Workshop recommendations

On operational research :

- To conduct a study on how to implement and document systematic investigation and preventive therapy for contact children < 5 years within the NTP framework
- To conduct a study on how to implement a shorter RH regimen for preventive therapy in children < 5 years

The Union together with 4 country teams (Benin, Burkina Faso, Cameroon, CAR) decided to write a protocol of an implementation research study combining these 2 objectives and to submit it to Expertise-France for funding  
Research grant obtained in 2015

# National research teams

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- 1 PI and 1 co-investigator
  - 1 NTP
  - 1 pediatrician or pneumologist
- 1 research assistant (social worker or anthropologist)
- Nurses
- Data managers

# Study objectives

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- Primary objective is to demonstrate the feasibility of conducting contact investigation and preventive therapy within the framework of the NTP
- Specific objectives
  - Estimate the number of children < 5 years who are close contacts of sputum smear positive (SS+) cases
  - Determine the prevalence and analyse risk factors for active TB among contact children (at inclusion)
  - Determine the incidence of active TB in children during and after preventive therapy using 6H or 3 RH75/50
  - Assess children adherence to preventive therapy
  - Develop standardised simple recording & reporting tools

# Sites - Population

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- **Study sites**

- Major city of each country: Cotonou, Ouagadougou, Douala, Bangui,
- 13 Basic Management Units (BMUs)

- **Study population**

- 2 000 children : 500 per country
- Recruitment : screening of all adult SS+TB cases diagnosed in each BMU
  - Residence > 3 months
  - Home < 5 km of BMU
  - With children < 5 years living at home
  - Accepting to participate

# Inclusion (1)

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- **Step 1 : Basic Management Unit (BMU)**
  - As part of consultation of each new SS+ adult TB case
  - Questionnaire : minimal information – eligibility criteria
  - Informed consent signed by parents of children
- **Step 2 : Home visit**
  - Performed < 3 days of initial adult consultation
  - Nurse and social worker/anthropologist
  - Questionnaire on family structure and contacts
  - Questionnaire for each child < 5 : contacts, symptoms & physical examination
  - (Tuberculin Skin Test in some countries)
  - BMU appointment







# Inclusion (2)

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- **Step 3 : clinical evaluation of child at BMU (nurse)**
  - TST (read 48 - 72 h)
  - Chest X-ray : all read by a doctor using a standard form
  - Physical examination (height, weight, T° , RR)
  - Child referred to pediatrician if signs/symptoms suggestive of TB (cough, fever, weight loss, reduced playfulness) and/or abnormal X-Ray
  - If child not referred, or later found free of TB by pediatrician, preventive chemotherapy is initiated
    - RH 75/50 mg during 3 months (CAR, BF, CMR)
    - H 100 mg during 6 months in BEN

# Dosages

**Table 4a.** *H50 or H100 tablets daily for 6 months duration (IPT – 6H)*

<i>Weight bands</i>	<i>Isoniazid (mgs)</i>	<i>H50 tablet</i>	<i>H100 tablet</i>
4-7 kg	50	1	1/2
8-11 kg	100	2	1
12-15 kg	150	3	1 1/2
16-24 kg	200	4	2

**Table 4b.** *RH 75/50 FDC daily for 3 months (3RH)*

<i>Weight bands</i>	<i>RH 75/50 tabs</i>
4-7 kg	1
8-11 kg	2
12-15 kg	3
16-24 kg	4

For children that are 25 kg and above, use adult preparations: one tablet of H300mg or two RH150/75.



# Follow-up

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- **Monthly during preventive chemotherapy**
  - 4 TB symptoms
  - Physical examination
  - Adherence to treatment
  - Adverse reactions (AR)
- **Quarterly after preventive chemotherapy**
  - Up to 12 months after termination of therapy
  - 4 TB symptoms
  - Physical examination
- If any sign/symptom suggestive of TB or suspected AR, nurse refers the child to the pediatrician

# Chest X-Ray form

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- Based on the « template chest X-Ray review tool » (*Graham S et al. JID 2012*)
  1. Airway compression or tracheal displacement
  2. Image suggestive of lymphadenopathy
  3. Air space opacification
  4. Nodular picture
  5. Pleural effusion
  6. Cavity
  7. Calcified parenchyma
  8. Vertebral spondylitis
- Conclusion : normal/abnormal suggestive of TB/abnormal suggestive of other disorder

# Register for preventive Tt

Month 0 Date		Month 1 Date		Month 2 Date		Month 3 Date		Result
Poids	Dose	Poids	Dose	Poids	Dose	Poids	Dose	TT (Treatment completed) A (Treatment stopped for adverse reaction) PDV (lost to follow-up) DCD (death) F (transferred out) TB (tuberculosis )



# Progress

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- The study has started successfully
  - Authorizations from the ethical committees (national, The Union) were obtained at the end of 2015
  - Inclusion started 01/04/16 and will last ~18 months.
  - Already > 500 children started on preventive therapy.
- No major problem encountered in conducting home visits, BMU visits, doctor visits and monthly follow-up
- Good participation of families, children happy to take RH75/50 (good taste!)
- Tools appear useful

# Challenges and perspectives

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- Procurement of tuberculin has been a headache
- Quality and interpretation of chest X-rays appear heterogeneous between countries : NTPs lack experience in doing chest X-rays in young children
- The study highlights the needs for training NTP staff in children clinical evaluation and in obtaining specimen (gastric aspiration) for TB diagnosis
- Final results expected for end-2018, but lessons could be learned from preliminary results next year

**Thank you for your  
attention**

