

Preventive Chemotherapy against Leprosy: Results to Date, Challenges and Solutions

Session Date & Time:	Monday, November 18; 1:00 PM to 4:00 PM
Session Location:	Beau Rivage
Session Description:	The session will address the major challenges in implementing preventive chemotherapy against leprosy under program conditions. Who should be targeted, how to implement and monitor, and how many are at risk?
Session Chairs:	Epcó Hasker and Jan Hendrik Richardus
Session Rapporteur:	Ashley Souza

KEY DISCUSSION POINTS

The session opened with a series of presentations summarizing key research projects focusing on preventive chemotherapy against leprosy. The following table summarizes the studies presented, the objectives, and the key findings or status of each study.

Study	Outcome or status
PEP with rifampicin Indonesia study	<ul style="list-style-type: none"> Blanket administration of two doses rifampicin post-exposure prophylaxis (PEP) resulted in 75% reduction in incidence No significant difference between control arm and contact-only arm
COLEP	<ul style="list-style-type: none"> Resulted in 57% reduction in leprosy incidence after PEP provided to household, neighbor and social contacts. Contacts who had received bacillus Calmette-Guérin (BCG) vaccine previously as neonatal vaccination (evidenced by BCG scar) had a comparable protective effect. Among those with a BCG scar who received single dose rifampicin (SDR), 80% reduction in risk was observed No rebound effect was observed at 6-year follow-up indicating that the intervention prevented rather than postponed leprosy
LPEP	<ul style="list-style-type: none"> SDR-PEP demonstrated to be safe, feasible, and acceptable Intervention had overall positive affect on leprosy programs outside of the intended benefits of the intervention
MALTALEP	<ul style="list-style-type: none"> A 40% (but statistically not-significant) reduction observed in paucibacillary (PB) cases among contacts after one year when SDR was given 8-12 weeks after BCG (thought to be due to sample size)

	<ul style="list-style-type: none"> BCG resulted in identification of new cases within 8-12 weeks suggesting that BCG may have an effect on pre-clinical cases by altering the incubation period or encouraging manifestation of disease that may have otherwise been self-limiting
PEP++	<ul style="list-style-type: none"> Ethical approval obtained in Brazil, India and Indonesia Household level mapping and cluster identification completed in study areas in India and Indonesia Project launch planned in Q1 2020 in all three countries
Leprosy perception study – India (part of PEP++)	<ul style="list-style-type: none"> Messaging should focus on transmission and cause rather than curable nature of disease which is already well understood Most accepted communication methods: loudspeaker announcements, community meetings, and posters
Population at risk estimation study (part of PEP++)	<ul style="list-style-type: none"> The number of people needing treatment with SDR PEP as proxy for population at risk SIMCOLEP modelling used to predict the relationship between the number of people treated and the effect on the new case detection rate. 20 million contacts need to receive SDR PEP over 5 years to achieve a 50% reduction in incidence at the global level; a 70% reduction will be achieved after 10 years, and to achieve a 90% reduction, this figure is 40 million over 22 years
PEP4LEP	<ul style="list-style-type: none"> Ethical approval obtained in Mozambique and Tanzania; Ethiopia pending Training already done in Tanzania; launch expected in January 2020
PEOPLE trial	<ul style="list-style-type: none"> Baseline survey indicates that door to door active case detection resulted in a major increase in detection rate Door to door survey not feasible in programmatic setting

DISCUSSION TOPICS

In the second part of the session there was discussion on a number of issues related to PEP, the main points discussed are listed below:

- Could PEP implementation have unintended consequences such as stigma?
- Is active case finding which is required for PEP implementation feasible outside study contexts?
- Effective PEP interventions require an understanding of who to screen and how to do it. Without standardization in methodology and training, results cannot be relied upon.
- It is understood that only 30% of new cases arise from known close contacts, while 70% arise from more distant individuals in the population. Screening the entire population is not feasible. In high endemic settings, is it possible/acceptable to focus screening only on close contacts, but extend SDR administration to the entire population?

KNOWLEDGE GAPS IDENTIFIED

- How can PEP interventions be expanded to prevent the 70% of cases that arise from individuals with no known contact with index cases?
 - Can a blanket approach be used to target the 70%? In which programmatic settings is the blanket approach appropriate and feasible?
- Is it possible to identify and address “super spreaders” that may pose an increased risk of transmission?
- How can PEP interventions be tailored to overcome the need for disclosure?
- How can contact-based case finding through PEP interventions complement other active case finding efforts and vice versa?
- What is the most effective and efficient active case finding methodology to identify new cases, especially in non-contact populations?
 - Evidence base needed in order to provide guidance and recommendations on methodology tailored to each programmatic setting
- Need to understand where to implement PEP interventions. Can criteria from existing data be developed to guide decision making? Can alternative strategies such as sero-surveillance be used to decide on the need for PEP?

RECOMMENDED NEXT STEPS

- Design a study to develop and explore an alternative approach to PEP in which active screening of contacts with provision of PEP is reinforced with blanket PEP distribution among those who are not direct contacts but do belong to the same high incidence communities
- Conduct modelling, costing and other analyses of existing data to provide programs with a decision-making tool for PEP implementation.
- Conduct follow-up studies in areas where PEP implementation did not go well to understand what went wrong and what can be improved for better results
- Develop and test alternative implementation strategies that avoid the risk of disclosure when targeting neighbor and social contacts.
- Explore feasibility of sero-surveys as a surveillance tool for leprosy, preferably combined with other neglected tropical diseases.