Innovations in Leprosy Prophylaxis: Current Evidence and Upcoming Trials

Session Date: Friday, October 26

Session Time: 1:00pm – 4:00pm

Session Location: Conde, 3rd Floor

Session Description: Contacts of leprosy patients have an elevated risk of developing leprosy themselves. A number of innovative approaches to improve the efficacy of chemo- and immunoprophylaxis are being explored. The risk reduction conferred by the administration of a single dose of rifampicin to the contacts of newly diagnosed leprosy patients has been established beyond doubt. Strong evidence also suggests a lower risk of leprosy in BCG vaccinees. However, the operationalization of this intervention in the face of weak and diverse health systems has only recently been approached. The Leprosy Post-Exposure Prophylaxis (LPEP) program has been designed to establish the feasibility of integrating chemoprophylaxis with a single dose of rifampicin for household, neighbour and social contacts of newly diagnosed leprosy patients across eight different countries and their health systems on three continents. While the intervention has been demonstrated to be well accepted by most leprosy patients and their contacts, and has invigorated contact tracing and leprosy control at local level, considerable logistical challenges have been identified, particularly with regard to BCG vaccination of adults and the tracing of social contacts. Also, reservations persist to integrate the intervention into leprosy control program routines. Innovations with regard to the definition, tracing and selection of contacts, and the prophylactic regimen, will soon be explored in three large trials. The focus is on the identification of contacts at particular risk of developing leprosy, more potent chemoprophylactic regimens than single-dose rifampicin, and the combination of chemo- with immunoprophylaxis, either using BCG or a newly developed defined leprosy vaccine. Studies focusing on leprosy prophylaxis tend to be long-term, expensive and logistically challenging, with related issues faced by different designs but different experience depending on the study setting. Hence, there is considerable scope for exchange between sites and studies to improve the quality of ongoing and future studies based available experience.

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KEY DISCUSSION POINTS

The following key findings, data, and issues were identified by the group via presentations and subsequent discussions.

Key findings

1. Post-exposure prophylaxis (PEP) has emerged as an exciting new tool for leprosy control. It represents a potential new strategy to reduce the number of new cases of leprosy by at least 50%.
2. The Leprosy Post-Exposure Prophylaxis (LPEP) program, conducted in eight countries, demonstrated that PEP with single-dose rifampicin (SDR) is feasible and well-accepted, and that it improves contact tracing and leprosy control at local level.
3. Two large-scale studies are planned to optimize the effectiveness of PEP: a) PEP++, which will use multiple doses of rifampicin and Moxifloxacin, as well as a "blanket" approach; and b) the PEOPLE trial, a cluster-randomized trial in the Comoros and Madagascar, which will compare three approaches to PEP, and assess cost, effectiveness, feasibility, and geospatial clustering.
4. Advances have been made in immune-prophylaxis, with the completion of Phase I trials of a recombinant leprosy vaccine, LepVax.
5. Epidemiologic models suggest that the time required to achieve goal of zero leprosy can be significantly shortened using a "blanket" approach to PEP, perhaps reaching <10,000 cases worldwide by 2040.

Issues raised in discussions

1. Optimization of PEP will require advances in mapping of leprosy.
2. Application of molecular and genomic tools will be essential to understanding transmission of leprosy.
3. Leprosy programs can be further integrated with programs for other NTDs, including visceral leishmaniasis.
4. Research studies on PEP should include genomic and molecular tools to maximize knowledge gained regarding transmission.
5. Without a better understanding of transmission, the leprosy community will be in "a weak position" to argue for funding for zero leprosy (said an official representing a major donor).
6. The quality of data being collected in many programs is sub-optimal.
7. Surveillance requires staff trained in skin diseases; an integrated skin disease program may be cost-effective.
8. Some donors consider leprosy to have been eliminated (as was claimed) – they will find it hard to understand a request for new funding.

KNOWLEDGE GAPS IDENTIFIED

What data and tools need to be generated to address the issues raised by the group?

1. Better diagnostic tests are essential – not only for leprosy but for other NTDs as well.
2. Molecular and genomic tools need to be refined and applied to understand networks of transmission – which will be essential for achieving zero leprosy.
3. Optimization of the PEP platform is essential to maximize its impact.
4. An effective vaccine is needed, and it needs to be evaluated as part of PEP (e.g., combined immunoprophylaxis and chemoprophylaxis of contacts.
5. A new cadre of health workers needs to be trained to recognize and diagnose leprosy; those who had these skills previously are retiring or are no longer in the work force.
6. Epidemiologic models need to be further developed to guide interventions and support advocacy efforts.

RECOMMENDED NEXT STEPS

1. Optimizing PEP: data from LPEP need to be fully analyzed; and PEP++ and PEOPLE studies should move forward in a coordinated fashion.
2. Vaccine development: Phase II trials for LepVax should be initiated soon and further collaboration explored with investigators in India on the MIP vaccine.
3. Diagnostics: PCR diagnostics need to be assessed across multiple laboratories to identify the best approaches and methods and develop standardized best practices.
4. Diagnostics: Cadres of health workers need to be trained to diagnose leprosy.
5. Diagnostics: Use of digital technology to facilitate diagnosis should be pursued.
6. Mapping: Improved approaches to mapping to identify foci of transmission need to be developed and deployed (also a hot issue for other NTDs – coordinated approaches would be ideal).
7. Epidemiologic models need to be further developed to guide interventions and support advocacy efforts.