Innovations in Interrupting Leprosy Transmission

Session Date: Saturday, November 4

Session Time: 1:00pm – 4:00pm

Session Location: Severn I

Session Description: This session will discuss recent innovations in Leprosy that may also be applied to other neglected tropical disease (NTD) operational strategies. Talks will feature the development of a new leprosy vaccine, leveraging digital tools for Leprosy surveillance, reviewing current protocols and emerging evidence for Leprosy Post Exposure Prophylaxis and understanding the progress made towards reaching Leprosy elimination in Latin America. Goals for the session include: 1) Review recent evidence based innovations in Leprosy control and understand how best to accelerate operational strategies to reach zero transmission; 2) Seek collaborative opportunities on leprosy diagnosis and interrupting transmission amongst the NTD community; 3) Share new initiatives towards leprosy elimination (and elimination of other NTDs) and to introduce digital health as a potential enabler to a Leprosy elimination toolkit.

Session Chairs: David Addiss, Task Force for Global Health
                              Santiago Nicholls, Pan American Health Organization

Session Rapporteur: Joanna Pritchard, Task Force for Global Health

KEY DISCUSSION POINTS

The new global strategy: advocacy urgently needed

Dr. Santiago Nicholls of PAHO provided an overview of the 2016-2020 Global Leprosy Strategy on behalf of Dr. Erwin Cooreman of WHO. The new strategy envisions zero disease, zero transmission, zero disability and zero stigma and discrimination, and identifies three pillars: first, strengthening government ownership, coordination and partnership; second, stopping leprosy and its complications; and third, stopping discrimination and promoting inclusion. WHO has published an Operational Manual and M&E Guide to support implementation of the new strategy.

Discussion focused on the challenge arising from pursuing and achieving, elimination "as a public health problem" as a prior strategy, and the fact that this definition is widely used in NTD programs today. National leprosy programs now face an uphill battle to reach the new goals due to the perception among politicians and the public that leprosy has been eliminated. The strategy was successful in galvanizing action and reducing prevalence but there is an urgent need now to refocus political attention on leprosy, especially interrupting transmission and addressing the immense burden of disability. There is strong awareness in the leprosy community that the task is unfinished and that the next step is to communicate this effectively to politicians and the wider community.

Discussion in the broader NTD community may provide support to other NTDs in anticipating and mitigating this risk as they approach elimination targets.

Leprosy vaccine now in phase 1 clinical trials

Development of a leprosy vaccine began in 2004 following the synthesis of the *M. leprae* genome. The research aimed for a product that would be safe in uninfected and infected individuals, that would induce *M. leprae*-specific immune responses and long-lasting anti-*M. leprae* immunity, and that would be used in contacts together with single dose rifampicin (SDR) to inhibit transmission and disease progression. IDRI initiated Phase 1a clinical trials for the vaccine ("LepVAX") in the US in September 2017. Preliminary safety data indicates no safety concern post 1st or 2nd injection. Phase two clinical studies are expected to be completed by 2021 and phase three by 2025. Preclinical data from animal studies were very encouraging, demonstrating safety, a strong reduction in mycobacterial burden and protection of progressive nerve damage.

Digital health can dramatically accelerate diagnosis and treatment

Early diagnosis and treatment are vital in reaching zero transmission. A digital health project in partnership with Novartis Foundation and the Philippines Department of Health tested whether a mobile phone-based surveillance system could accelerate diagnosis and treatment in a difficult programmatic setting. The "Leprosy Alert Response Network and Surveillance System" (LEARNS) aims to improve case finding and reduce delays in diagnosis by linking front line health care workers with leprosy specialists. Challenges faced by the national leprosy program include extreme geographic isolation of communities, limited access to health services, underutilization of information and communications technology (ICT) in the health system, and a lack of leprosy specialists.

More than 6,000 healthcare workers have been trained using LEARNS to send an SMS with a photo upon first evaluation of the patient, notifying a rural physician and leprosy specialist. The specialist replies with a diagnosis and the rural physician provides treatment within two weeks. Evaluation results from Ateneo de Manila University, Philippines, showed a high diagnostic concordance between LEARNS and in-person diagnosis of leprosy, and a dramatically shorter time-to-diagnosis: 2.3 days in the LEARNS arm compared with 92.2 days in the control arm.

The project represents remarkable opportunities to speed up diagnosis and treatment and is easy to scale up. The discussion noted that the current standard of care diagnosis is alarmingly slow. The approach has potential to make a strategic contribution to leprosy elimination programs through early diagnosis and prompt treatment, and should be embraced broadly. The next steps are building the approach into a toolkit, disseminating the results and regional scale-up. Novartis Foundation is also assessing opportunities for other disease indications and evaluating the feasibility of using machine-based learning algorithms.

The Philippines department of health is also implementing a NTD management information system (presented at the COR-NTD Innovation Lab) and is exploring how to link with LEARNS.

PEP able to reverse rising trends in incidence rates

Focusing on patient contacts may provide another effective new tool in interrupting transmission. The Leprosy Post Exposure Prophylaxis (LPEP) Program launched in 2015 to evaluate the impact on leprosy incidence and the feasibility of contact tracing and SDR under routine program conditions. Eight countries have participated in the program. The rationale for the program was the efficacy of SDR for leprosy prevention in contacts of patients: previous trials had demonstrated a risk reduction of about 50-60%.

In terms of feasibility, the program integrated well into existing programs and communities were interested and willing to participate. Ninety-two percent of the 123,311 contacts accepted treatment with SDR. Of those not receiving SDR, the majority were ineligible, and only 427 refused.

The program invigorated local leprosy control efforts: the new tool, the ability to offer treatment, and the training and supervision motivated health care workers.

In terms of the impact on incidence rates, the results for India, Myanmar and Nepal were presented. Of these, both India and Nepal saw their previously rising incidence rates change to a downward trend after LPEP was implemented. Myanmar already had a downward trend and did not see a strong impact. The positive impact provided solid evidence for policymakers to adopt as policy. Integration and expansion are already underway or planned.

There was discussion at the breakout session on defining the most effective target group for treatment. One option might be to treat all second tier contacts, such as the entire village or school. In the LPEP program, the definition of contacts varies from country to country. The program provided a basic definition of contacts in the generic protocol, which included household members, neighbours and social contacts. National programs tailored the definition to their context, with stigma playing an important role, and only two of the eight limited the list to household members. Modeling studies suggest that treating a wider proportion of the population at risk will have a significant impact on incidence rates. Treating a larger population would also protect the identity of the index patient. Further research to identify the most effective target group is needed.

Leprosy in the Americas
The Americas region achieved elimination as a public health problem in 2002 and saw a 29.2% reduction in new cases from 2011 to 2016. Brazil, with 92% of new cases, is the only country that has not achieved elimination as a public health problem at the national level. Concerns in the region include the increase in percent of MB and G2D in new cases from 2015 to 2016, although the increase in the percentage of MB cases could also be a sign of the end game, where MB cases eventually become 100% of all cases.

Challenges for the national programs include maintaining political, public and financial support for leprosy programs. Strengthening program quality at the primary level is also critical, especially maintaining expertise in active case finding, care services and disability management as case numbers decrease.

The regional program aims to interrupt transmission in countries with less than ten new cases per year by enhancing interventions, providing proof of concept for other countries.

KNOWLEDGE GAPS

Increasing political and public will for a leprosy-free world
How does the global leprosy community overcome the widespread perception among politicians and the public that leprosy is no longer a problem? Work is needed to identify an appropriate and coordinated advocacy plan for leprosy to support implementation of the new global strategy. There is a need to build on the success story of MDT while including a powerful call to action to interrupt transmission and address the immense morbidity burden.

Interrupting transmission: PEP or MDA?
While PEP demonstrates that treating contacts is highly effective in reducing incidence, there is no consensus on how far to go in treating communities with leprosy patients. What is the most effective target population to interrupt transmission? More evidence is needed, including understanding basic biology and mode(s) of transmission, in order to generate global recommendations on preventive treatment of communities with leprosy patients.

Mapping

Spatial analysis of leprosy cases to date has been very limited, but more work in this area may provide new disease insights and would leverage collaborative opportunities in the NTD community. Several knowledge gaps for mapping exist:

- How might existing leprosy mapping efforts be linked, such as WHO DHIS2 mapping functions, AIM's leprosy geolocation, GIS mapping in Brazil, and case confirmation surveys that identified unexpected sub-district variations in spatial disease distribution?
- What might we learn from micro-mapping the new cases? The relatively small number and current technologies make this feasible; it may identify new insights into the disease and the causes of the persistent appearance of new cases each year. In addition, micro-mapping may aid in tracking outcomes of enhanced interventions in regional elimination scenarios.
- What lessons can be learned from other NTD disease mapping exercises (e.g. GTMP)?

Diagnostic test

Expertise in clinical diagnosis is diminishing partly as a result of the success in reducing the caseload by >90% over the last 30 years. This makes a diagnostic tool more important and Novartis Foundation is currently researching a molecular diagnostic based approach, but it is not yet field-tested.

Animal reservoirs

There is limited knowledge to date on the role of animals as leprosy reservoirs. More research is needed to understand to potentially develop a strategy for interrupting transmission from animals to humans.

Stigma reduction

Zero transmission requires significant reduction in stigma. Much progress has been made but additional work is needed to understand how to reduce stigma in communities, how to address stigma in healthcare workers, and how and why stigma differs from country to country. More funding and research are needed to gather evidence and translate it into policy and practice.

RECOMMENDED NEXT STEPS

Global partnership for leprosy

There was a strong sense that increased global alignment, planning and resourcing is essential to follow up adequately on knowledge gaps. Steps have already been taken to discuss and take the research priorities and issues forward for the end game via a global leprosy partnership. Functions of a global partnership might include:

- Achieving global alignment on the priority needs and knowledge gaps (including but not limited to those discussed today)
- Presenting the priorities cogently for advocacy purposes
- Coordinating on resource mobilization
- Translating evidence from research into policy and practice
- Increasing knowledge exchange with the broader NTD community
  - Share lessons from leprosy with the broader NTD community
    - The challenges of pursuing – and achieving - elimination as a public health problem
    - Morbidity management

- Dismantling discriminatory legislation
- Mental health care
  o Learning from other NTDs
    - Defining target populations for preventive treatment
    - Mapping
    - Advocacy and resource mobilization
  o It was suggested that a session be proposed on the intersections between leprosy and other NTDs at the next COR-NTD meeting

Next steps on research priorities to reach zero transmission

- Invest in research on effectiveness of different approaches to post exposure prophylaxis (PEP), with or without vaccines
- Invest in real-time surveillance now & in diagnostics for early detection
- Leverage, embrace and strengthen digital solutions for rapid data collection and analysis
- Update WHO guidance as research and tools evolve (e.g. enhanced PEP)
- Increase and prioritize funding to research and implement new approaches
- Continue basic research on transmission and disease markers