Leprosy post-exposure prophylaxis: innovation and precision public health

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Eradicating leprosy as a public health issue has been hindered by difficulties. Since the 1980s, an effective multidrug therapy (MDT) has been available, curing more than six million people. When treatment is correctly delivered, the rates of relapse, including those due to resistance, are low. So why has the rate of new cases been stagnant at more than 200 000 patients worldwide every year for the past 10 years?

Firstly, leprosy is a disease of neglected populations affecting the poorest people. Populations affected tend to have lower levels of education and live in areas in which we typically find primary care units with poorer infrastructure,[1] attended by patients who are often neglected by health systems. Adding to that, leprosy is a chronic disease with a long incubation period in which patients have a myriad of clinical forms that are difficult to diagnose. No clear markers can discriminate infection from active disease. Finally, delayed diagnosis is very common, thereby maintaining the transmission cycle, which generally occurs before patient treatment.

Large-scale novel public policies are needed to assist leprosy control and reduce the number of new cases. The population at risk is concentrated to households, neighbours, or social contacts of patients who have clinical forms of leprosy with higher bacterial load.[2] Control, therefore, must be focused on two pillars—contact tracing and dermatoneurological evaluation of contacts for early detection of new cases. The epidemiological features of patients who are newly diagnosed by contact surveillance show that these individuals have lower levels of disability and immunological reactions, as well as lower bacterial loads.[3]

Once a contact is identified as a new case, they can be treated adequately, but the management and follow-up of healthy contacts is more difficult.[4] Cohort studies and, in the past 10 years, randomised controlled trials have suggested prophylaxis for the healthy population who are at risk. Observational studies have indicated that BCG given at birth or revaccination as a booster for healthy household contacts of people with leprosy confers up to 56% protection.[5,6] Among different protocols for chemoprophylaxis, single-dose rifampicin (SDR) has also been shown to be effective. A seminal randomised controlled trial (COLEP),[7] provided evidence that SDR has an overall efficacy of 57% in reducing the risk of leprosy during the first 2 years of follow-up after administration. Furthermore, the combination of SDR with BCG at birth increases the protective effect to 80%, although blood-related contacts show lower protective rates.[2] SDR can decrease the incidence of leprosy, thus WHO guidelines from 2018 recommended SDR as prophylaxis for contacts.[7] An extension of the strategy has also been evaluating multidose and multidrug leprosy post-exposure prophylaxis (LPEP) initiatives.[8,9]

In *The Lancet Global Health*, the biggest multinational strategy implemented thus far is presented by Jan Hendrik Richardus and colleagues,[10] describing the long endeavour to assess the feasibility of an LPEP programme using SDR; the results are encouraging. Chemoprophylaxis is safe, affordable, and well accepted. LPEP enrolled 9170 index patients and listed 179 769 contacts. 174 782 (97·2%) were successfully traced and screened. SDR was subsequently administered to 151 928 (86·9%) screened contacts. The data suggest that LPEP could empower health systems, overcoming potential contact screening failures. LPEP can facilitate and promote the training of field workers. Then, health professionals can either detect leprosy early and treat the patient with MDT, or give SDR to healthy contacts. However, there are challenges ahead. Differences in the detection of new cases during the screening of contacts are expected in different countries. In Brazil, for example, a higher number of patients with leprosy have been observed among contacts at intake. Precision public health strategies need to be defined by country or region according to the local epidemiological situation, such as endemicity, multibacillary to paucibacillary ratio, and household size, while respecting cultural, political, and social conditions of different countries. The specifics of the national leprosy programmes must also be considered, such as whether chemoprophylaxis is combined with BCG vaccination, since SDR, by definition, provides only temporary protection. Bacterial load reduction with use of antimicrobial

agents could last longer if a subsequent immunological booster with BCG is used in combination.

With the challenges of controlling leprosy in mind, a multidisciplinary approach combining translational and operational research is essential. At present, the priorities include the need to create precise methods to detect individuals who are at risk (subclinical infection) and correctly diagnose new cases, especially at the early stages of the disease; provide continuous professional health training; use mapping and geographical information systems tools to expand epidemiological assessment of highly endemic areas; and generate communication campaigns to bring awareness towards the disease and reduce stigma. Nevertheless, LPEP provides hope and indicates that we are moving forward. Innovative and feasible public policies, such as SDR, along with the priorities listed above could be, at least in part, a step towards leprosy control, providing patients and their families with a better future.

We declare no competing interests.

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