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Editorial

Single-Dose Rifampicin Prophylaxis for Leprosy Contacts: Aligning with Antimicrobial Stewardship Principles

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Dear Editor,

Despite notable declines in prevalence over the past few decades, leprosy remains a public health concern. In 2024, the World Health Organisation (WHO) reported over 172,717 new cases worldwide, with South East Asia 124 295 and India bearing about 100957 of the burden [1]. In addition to achieving elimination objectives, creative approaches are needed to ensure that interventions align with broader public health principles, such as antimicrobial stewardship (AMS). One such measure recommended by WHO in its Global Leprosy Strategy is single-dose rifampicin (SDR, 600mg) chemoprophylaxis for contacts of leprosy patients [2, 3]. The WHO definition for a contact (having spent time with an untreated patient for 20 h per week or more in the past 3 months) is no longer applies when everyone in the community is considered a contact. The 'close-contact' approach targets approximately 20 household, neighbor, and social contacts of an index leprosy case, whereas 'blanket post-exposure prophylaxis (PEP)' involves community-wide screening within a defined geographic area and provision of PEP to all eligible individuals without clinical evidence of leprosy. When all types of leprosy are considered together, a protective effect of single-dose rifampicin (SDR) is observed. The Chemoprophylaxis of Leprosy (COLEP) experiment in Bangladesh [4], which randomly assigned 21,711 contacts of newly diagnosed patients to SDR or placebo, is the main source of evidence supporting SDR chemoprophylaxis.

While a protective effect was noted among more distant relationships, the study found no statistically significant protection among home contacts. SDR decreased the incidence of paucibacillary and single-lesion leprosy but did not appreciably prevent multibacillary leprosy. Significantly, the protective benefit lasted for about two years, indicating that SDR is only beneficial for people with low mycobacterial burdens. SDR was added to national programs' post-exposure prophylactic toolset as a result of this strong evidence. SDR offers a practical, scalable solution, but in the context of AMS, it raises serious issues. A key antibiotic in the treatment of tuberculosis (TB), rifampicin is also used in combination regimens for a number of bacterial infections. Theoretically, rifampicin-resistant strains of Mycobacterium TB could be selected for in large prophylactic campaigns if rifampicin is used unrestrictedly or with inadequate monitoring [5]. This danger is highlighted by the few reports of rifampicin resistance resulting from improper usage in non-TB diseases [6].

With a pooled resistance prevalence of 11% (95% CI: 7%–15%), a meta-analysis shows a significant worldwide burden of rifampicin resistance in *Mycobacterium leprae*. Patients who experienced a

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leprosy relapse exhibited resistance that was almost twice as high as that of freshly diagnosed cases. The risk of rifampicin resistance was alarmingly more than four times higher in nonresponsive and intractable leprosy cases compared to new patients. In order to maintain the efficacy of rifampicin-based multidrug therapy, these results stress the growing problem of antimicrobial resistance in leprosy and emphasize the critical need for enhanced surveillance, early molecular detection of resistance, and tailored treatment options [7]. To balance the long-term risk of resistance with the clinical benefits of antibiotics, AMS programs place strong emphasis on prudent antibiotic use [8]. The following would be involved in implementing SDR using AMS principles:

1. Careful selection of eligible contacts (apart from those with active TB symptoms).

2. Integration with surveillance and screening systems for tuberculosis to prevent unintentional monotherapy in patients who have not yet been diagnosed.

3. Increasing molecular surveillance and pharmacovigilance for indicators of rifampicin resistance.

4. Education of the public and healthcare professionals on the two-pronged objectives of preventing antibiotic resistance and controlling leprosy.

Additionally, unlike long-term rifampicin regimens used in TB or other chronic infections, SDR is a one-time intervention, which must be considered in the risk-benefit calculation. Theoretically, resistance is less likely due to the brief exposure and low selective pressure [9]. However, stringent programmatic protections are needed to scale up SDR to millions of contacts across endemic nations. Under the National Leprosy Eradication Programme, India, which has the highest number of leprosy cases, has begun SDR deployment. This offers an opportunity to incorporate AMS frameworks into the design, ensuring rifampicin remains effective against tuberculosis while advancing the lofty objective of "Zero Leprosy." SDR prophylaxis represents a targeted public health intervention with modest, time-limited effectiveness, primarily in preventing paucibacillary leprosy among contacts with low mycobacterial burden. However, the global AMS agenda should not be separated from its widespread implementation. It is the right moment to initiate these agenda organized under the following subheadings: 1) Policy for AMR containment, 2) Resource integration for Integrated Antimicrobial Stewardship practice, 3) Education to different cadres of healthcare providers, 4) Surveillance of practices, 5) right Culture of sending and acting upon diagnostics, 6) Rational antimicrobial use, 7) Information updates through AMR dashboards, 8) attention to right Behavioral interventions driving appropriate practices, 9) Engagement with multiple sections and cadres, and 10) Sustainability plans and actions [10]. We can preserve rifampicin's effectiveness for future generations and hasten the eradication of leprosy by combining contact prophylaxis with TB screening, surveillance, and these 10 PRESCRIBES stewardship principles.

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