Since 1981, worldwide leprosy prevalence has declined sharply due to the implementation of multidrug therapy (MDT) conducted by the World Health Organization (WHO). The national prevalence of leprosy finally decreased to 0.05 per 10,000 population in 1998, which meant the WHO threshold of leprosy elimination (below 1 per 10,000 population) was reached in China through a well-organized control network and through the implementation of MDT (1). However, the number of newly registered leprosy cases each year, the grade 2 disability (G2D) rate, as well as the rate of fatal adverse drug reactions (ADR) had not significantly changed since 1998 (2–3), so leprosy is still seen as a public health problem in China. In addition, dermatological clinics rather than leprosy control stations became the main source for leprosy case finding at every level. Delayed diagnosis was common due to a general lack of awareness and adequately precise techniques among dermatologists to detect Mycobacterium leprae (M. leprae) that results in leprosy.

In order to eliminate the harm of leprosy, Ministry of Health of the People’s Republic of China published a national leprosy-control plan (2011–2020) in 2011. Since then, both the number of newly detected leprosy patients and newly diagnosed cases with G2D each year have been reduced compared to 2009. The rate of life-threatening condition – dapsone hypersensitivity syndrome (DHS) was reduced to 0.0% in all pre-screened populations in 2018. According to the WHO, the number of new cases and reported new cases with G2D globally only slightly decreased from 2009 to 2018 (4). China’s progress in leprosy control is due largely to the efforts of the government, leprosy control institutions, doctors, and scientists. These stakeholders have made tremendous contributions in setting up effective strategies to monitor leprosy patients, developing accurate techniques to measure infections, and finding useful ways to prevent adverse events from occurring during treatment. This report summarizes progress towards leprosy harm elimination in China.
rifampicin or conducting long-term follow-ups have been given to contacts of newly diagnosed leprosy patients to at least partially interrupt transmission of leprosy. However, epidemiological studies suggest that 95% of individuals exposed to M. leprae will not be infected. Among those 5% infected individuals, only 20% would develop leprosy, indicating that chemoprophylaxis or long-term follow-ups might protect only a small proportion of leprosy contacts and that a host’s genetic factors played a major role in the pathogenesis of the disease.

Since 2009, thirty-one independent susceptibility loci of leprosy have been discovered through genome-wide association studies (GWASs) and candidate-gene studies conducted by the research group of the Shandong Provincial Institute of Dermatology and Venereology (SPIDV) (6–12). Based on the genetic variants associated with leprosy in the Chinese population, SPIDV made a risk prediction model through a weighted genetic risk score (GRS) with an area under the curve (AUC) of 0.743 (13). When using 22.38 as GRS cut-off value, the sensitivity and specificity were 67.1% and 69.7%, respectively. In order to prevent 64.9% people affected by leprosy, 39.31% of contact subject should receive post-exposure prophylaxis or be followed up with according to the model. The risk prediction model might be a more effective and economical tool to detect higher-risk groups among all leprosy contacts.

**Early Diagnosis**

Early diagnosis of leprosy is a crucial step for preventing disability. Traditional laboratory techniques such as acid-fast bacilli staining showed low sensitivity and specificity. In the past few years, efforts have been made to establish more efficient and accurate diagnostic methods. Paucibacillary (PB) patients were more prone to be misdiagnosed compared to multibacillary (MB) leprosy patients, so early diagnostic methods, especially for early diagnosis of PB patients, were needed. There were mainly two strategies for the development of new early diagnostic methods.

Serological analysis could be a convenient and useful tool for diagnosis of MB leprosy. The Beijing Tropical Medicine Research Institute (BTMRI) evaluated the ability of M. leprae antigen specific immune responses to support the leprosy diagnosis (14–17). In addition, BTMRI tested a panel of M. leprae-stimulated host markers in an overnight whole-blood assay and found that M. leprae-induced CXCL8/IL-8 showed potential diagnostic and discriminatory value for PB patients (18). These simple tools could be set up in endemic areas without clinical molecular laboratories.

Furthermore, detection of M. leprae-specific DNA could be more sensitive. New primer sets for the M. leprae-specific repetitive element (RLEP) gene were designed by BTMRI and single tube nested PCR (STNPCR) and SYBR Green PCR assays were performed to test M. leprae for PB patients (19). SPIDV developed the droplet digital polymerase chain reaction (ddPCR) assay using primers for M. leprae–specific RLEP and groEL genes to detect M. leprae in PB patients with a high sensitivity of 79.5% (20). All diagnostic approaches assisted with earlier diagnosis of leprosy and reduced the rate of disability in new leprosy patients.

**Precision Treatment**

Since MDT was introduced for leprosy in 1981 by the WHO, the number of leprosy patients has been reduced dramatically. Even though leprosy transmission could be quickly stopped by administration of MDT, the occurrence of DHS among some leprosy patients raised another problem. In China, the incidence of DHS was 1.0% and the mortality was 11.1% among all patients with DHS between 2006 and 2009 (3), so preventing the occurrence of DHS was prioritized. In 2013, HLA-B*13:01 (odds ratio, 20.53; p=6.84×10^{-3}) was discovered as a strong risk factor for DHS by both the SPIDV and the National Center for STD and Leprosy Control independently in the Chinese population (21–22), which has been validated in Indonesia, India (23), Thailand (24), Malaysia, and Republic of Korea. SPIDV developed an HLA-B*13:01 kit with both a sensitivity and a specificity of 100%. Since 2015, SPIDV has carried out a nationwide clinical trial to evaluate the efficacy of HLA-B*13:01 screening to prevent DHS. A total of 1,512 patients were genotyped for HLA-B*13:01, and 1,251 patients were HLA-B*13:01-negative. These leprosy patients were treated with dapsone, and none of the 1,251 patients developed DHS. Therefore, screening for HLA-B*13:01 prior to dapsone administration could decrease the incidence of DHS in Chinese population (25).

**Discussion**

Based on the national strategy, there has been significant progress towards the harm of leprosy in China. Prevalence, incidence, rate of grade 2 disability,
and the incidence of DHS reached historically low levels. The strategy depends on several pillars including all levels of government, the China Leprosy Association, and leprosy-related research institutes. Full government support and well-organized surveillance were crucial for the detection and treatment of leprosy patients. Also, instead of applying chemoprophylaxis or long-term follow-ups to all contacts of leprosy patients, precision prophylactic measures based on genetic factors would be a more cost-efficient way to prevent infection transmission to high-risk contacts. In addition, laboratory-supported diagnostic methods can significantly reduce the number of misdiagnosis or delayed diagnosis patients. Finally, DHS has been eliminated by pre-screening for HLA-B^*13:01 in China.

In 2016, the WHO carried out “The Global Leprosy Strategy 2016–2020: accelerating towards a leprosy-free world”, and significant strides have been made in China for controlling leprosy. However, more than 20 countries are still considered high-burden countries for leprosy. In order to share new clinical and research progress with other countries that are facing challenges for leprosy control, the First International Training Program on Leprosy For Developing Countries was held in China from June 23 to July 7, 2019. The training program was funded by the Ministry of Science and Technology (MOST) of China and organized by SPIDV. In this two-week program, 22 trainees from 10 countries with high-leprosy burdens were trained and received certification from the MOST of China. The aim of the training course was to improve the capacities of leprosy control institutions and for individuals to recognize early symptoms and provide technical assistance for leprosy prevention, diagnosis, and treatment. The collaborative platform has been established and further efforts can be collected to continue progress towards a leprosy-free world.

The findings above are subject to some limitations. First, samples involved in the genetic studies were all from Chinese participants. The efficacy of the risk model based on genetic variants should be tested via clinic and the model’s ability to be extended to other countries needs to be investigated because of population heterogeneity. Second, more studies should be done to evaluate the diagnostic approaches mentioned before using these methods in routine clinical practice. Third, the allele frequency of HLA-B^*13:01 differs between populations. Moreover, for some HLA-B^*13:01 carriers, dapsone has been removed from the MDT regimen to prevent DHS. The modified MDT regimen with only two drugs, rifampicin and clofazimine, needs to be investigated for possible increased relapse risk of the disease and risk of failed treatment. Therefore, many barriers still exist in achieving global elimination of leprosy.

In conclusion, China has made significant progress in controlling leprosy, and more international cooperation between China and other countries would accelerate leprosy elimination. Efforts to achieve zero disability, zero death, and zero discrimination in leprosy nationwide need to be sustained.

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