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PERSPECTIVES

Latent infection treatment to prevent TB transmission in school settings

Pin-Hui Lee*, Feng-Yee Chang

Centers for Disease Control, Department of Health, Taiwan

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With 8.8 million incident cases and 1.4 million deaths worldwide in 2010, tuberculosis (TB) has remained a global public health challenge.¹ An estimated one-third of the global population has been infected with TB, and latent tuberculosis infection (LTBI) represents a great reservoir of potential TB disease. Taiwan has a moderate burden of tuberculosis with incidence of 55 cases per 100,000 population in 2011, and this incidence fell by 25% compared with 2005 since implementation of the Mobilization Plan to Halve Tuberculosis in Ten Years (2006-2015).^{2,3}

Although TB is a curable disease, its characteristics of airborne transmission, delayed diagnosis, and lack of effective vaccine to prevent infection or disease together influence the performance of TB control programs. More than 50% of Taiwan's TB cases had been elderly people, but the incidence among over-65s declined over the last 5 years. However, the incidence among younger populations has not changed greatly, with age-specific incidence ranging from 2.6/100,000 at childhood to 17.7/100,000 among adolescents in 2010 (Fig. 1). The majority of daily activities of younger populations are at schools, and threats of school outbreaks would occur if poor ventilation precipitated TB transmission.

Taiwan's Centers for Disease Control (TCDC) established a surveillance system for TB outbreaks that defined

a suspect cluster as two confirmed TB cases with epidemiological link occurring in the same institution within 1 year. Isolates for genotyping methods are used to confirm transmission. A cross-section study of 19 suspect school outbreaks during 2006 to 2009 conducted by Feng et al⁴ revealed 35% of TB cases with positive acid fast smear in suspect outbreaks, and 30% had cavitation lesion at time of TB diagnosis. In the five (26.3%) confirmed outbreaks proven by genotyping methods, most of the index cases had a 6-month or longer infectious period. Overall, 5544 contacts were followed, or 64 contacts per index case needing to be traced by public health staff. An additional 38 newly confirmed cases were found through contact tracing; the incidence among close contacts in school outbreaks was 685.4/100,000, which was 32.7 times the TB incidence among the general population aged 10 to 34 years. According to TCDC statistics for 2007 to 2011, the proportion of confirmed TB clusters (46%) was highest in school settings, followed by 15% among health care workers and 11.1% in long-term care facilities. In 2010 and 2011, two large-scale school outbreaks occurred in northern Taiwan. In the outbreaks at Schools L and A, subsequently four (8.5%) and 10 (10.5%) confirmed cases were found respectively among contacts in the same class within 1 year after the index case in each school was notified.⁵ The other 11 confirmed cases were found among contacts in school buses, after-school classes and clubs. Challenges encountered during school outbreaks included media pressure, stigmatization of TB disease, human resources issues, and difficulty in tracing contacts postgraduation.

Since 2008, LTBI treatment has targeted contagious index cases' close contacts with age younger than 13

Abbreviations: BCG, bacillus Calmette-Guérin; LTBI, latent tuberculosis infection; TB, tuberculosis; TST, tuberculin skin test.

* Corresponding author. Taiwan Centers for Disease Control, 6 Linsen South Road, Taipei 100, Taiwan.

E-mail address: leepinhui@cdc.gov.tw (P.-H. Lee).

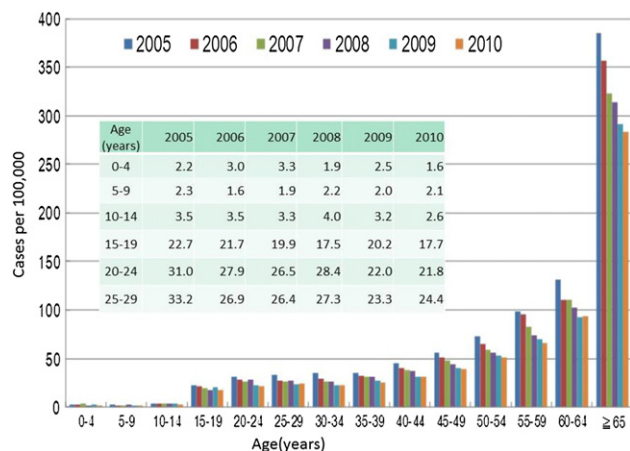


Figure 1 Age-specific incidence of newly confirmed tuberculosis cases in Taiwan, 2005–2010.

years.⁶ LTBI with 9 months of isoniazid therapy for the contacts followed until September 2011 reduced the risk of developing TB by 96%.⁷ Evaluating diagnostic tools such as the tuberculin skin test (TST) and interferon gamma release assay is difficult due to the lack of a standard for LTBI. The sensitivity of TST was less optimal in populations receiving prior bacillus Calmette-Guérin (BCG) vaccination due to antigenic cross-reactivity of purified protein derivative with nontuberculous mycobacteria or BCG. In Taiwan, the program of boosting BCG at sixth grade has been stopped since 1997; therefore the birth cohort since 1986 only received one shot of BCG. Longitudinal studies support that greater size of TST among contacts with very high coverage of BCG immunization still correlates with future risk of developing active TB.⁸ As the positive predictive value of TST for diagnosis of LTBI is up to 80% used in high-prevalence situations of TB infection among close contacts (approximately 30%),⁹ TST is still recommended for diagnosis of LTBI in selected Taiwan populations. Since April 2012, LTBI treatment program has been expanded for contacts aged 13 to 25 years in household, school and congregate settings if the index case is smear- and culture-positive for TB. Both TST and isoniazid therapy with directly observed treatment have also been provided to identify infection and help contacts complete treatment and monitor adverse events.

In Taiwan, hepatotoxicity was 1.3/1000 among childhood contacts receiving isoniazid treatment (hepatotoxicity defined as symptomatically 3 times elevation of glutamic pyruvic transaminase, or 5 times elevation without symptoms).⁷ For a study conducted in inmates by Chan et al,¹⁰ we observed 8% of the isoniazid therapy group experienced GPT elevation ≥ 120 U/L, but all cases recovered after discontinuation of treatment. After the

expansion of LTBI treatment to those aged 13 to 25 years, 394 (62%) eligible contacts from this January to April have started LTBI treatment after clinical evaluation from referral physicians. TCDC will continue to monitor effectiveness, adverse events, and isoniazid-resistant strains' impact after program expansion.

In conclusion, early detection of active TB cases is the priority for TB control, but highly contagious and socio-active characteristics among younger populations may cause TB transmission in crowded environments such as schools. Therefore expansion of LTBI treatment among close contacts of highly contagious index cases in school settings could prevent TB disease and further transmission among younger population. While the incidence of TB has gradually declined and directly observed treatment coverage has reached more than 90% to increase treatment successes against active TB, Taiwan will also scale up LTBI treatment for TB control in the future.

References

1. World health organization: *global TB control report 2011*. Geneva: World Health Organization; 2011.
2. Centers for Disease Control, Taiwan: *Taiwan Tuberculosis Control Report 2011*. Centers for disease control, Department of Health, R.O.C. (Taiwan). Available from: <http://www2.cdc.gov.tw/ct.aspx?Item=36891&ctNode=1947&mp=1>; 2011 [accessed 20.07.12].
3. Lo HY, Chou P, Yang SL, Lee CY, Kuo HS. Trends in tuberculosis in Taiwan, 2002-2008. *J Formos Med Assoc* 2011;110:501–10.
4. Feng CF, Chan PC, Yang CH, Huang YF. *Tuberculosis outbreaks among students in school settings in Taiwan, 2006–2009*. Presented at the 40th World Conference on Lung Health of the International Union against Tuberculosis and Lung Disease, Cancun, Mexico, December 3-7, 2009.
5. Chan PC, Su Chia-Ping, Wan-Chin Chen, Sung-Hsi Wei, Ping-Hui Lee, Tsai-Wu Wang, et al. *Tuberculosis outbreak investigations in school settings in Taiwan, 2009–2011*. Presented at the 2011 Annual Meeting of Taiwan Society of Pulmonary and Critical Care Medicine, Taipei, Taiwan, December 10, 2011.
6. Chan PC, Yang CH, Chang FY. Scaling up of latent tuberculosis infection treatment for close contacts of tuberculosis in Taiwan. *J Formos Med Assoc* 2011;110:733–6.
7. Chan PC, Chiou MY, Hsieh MC, Wang KF, Chang LY, Yang CH, et al. *Safety of latent TB infection treatment in children contacts*. Presented at the 2011 Taiwan Pediatric Association annual conference, Taipei, Taiwan, April 23, 2011.
8. Ling DL, Liaw YP, Lee CY, Lo HY, Yang HL, Chan PC, et al. Contact investigation for tuberculosis in Taiwan contacts aged under 20 years in 2005. *Int J Tuberc Lung Dis* 2011;15:50–5.
9. Small PM, Fujiwara PI. Management of tuberculosis in the United States. *N Engl J Med* 2001;345:189–200.
10. Chan PC, Yang CH, Chang LY, Wang KF, Lu BY, Lu CY, et al. Latent tuberculosis infection treatment for prison inmates: a randomised controlled trial. *Int J Tuberc Lung Dis* 2012;16: 633–8.