

Countermeasures against tuberculosis in the elderly in Japan

Introduction

In this issue, I will describe about TB control and QFT-Plus in the elderly.

Tuberculosis control in the elderly in Japan

The Japanese government has set a target for tuberculosis prevalence of 10 per 100,000 or less by 2020, and is taking various measures to prevent the spread of tuberculosis and reduce the prevalence. The Ministry of Health, Labor and Welfare (the MHLW) is focusing on elderly people over the age of 80 to promote the early detection of tuberculosis-causing patients in the elderly efficiently through the accelerate countermeasures to more effectively prevent the spread of tuberculosis infection and reduce the TB prevalence in Japan. (1).

In addition, the MHLW has notified that “Special Promotion Program for Infectious Disease Control” to deepen their understanding of tuberculosis through awareness raising and training for elderly people over 80 years old who account for a large percentage of newly registered TB patients. The government has

instructed prefecture local governments to further strengthen tuberculosis measures by early detection of tuberculosis patients (2).

Number of registered active tuberculosis and latent tuberculosis infections patients in Japan 2018 (3)

The total number of newly registered tuberculosis patients in Japan in 2018 is 15,590, and the tuberculosis prevalence proportion is 12.3 per 100,000, which has been decreasing for the past several years, but it is still high compared to the Western countries. Tuberculosis patients are aging more and more, and newly registered tuberculosis patients over 70 years old account for 59.9% of the total. The tuberculosis prevalence proportion per 100,000 by age group is higher in older age groups: 19.7 for 70-79 years, 51.2 for 80-89 years, and 82.8 for 90 years and older. Among TB patients in Japan,

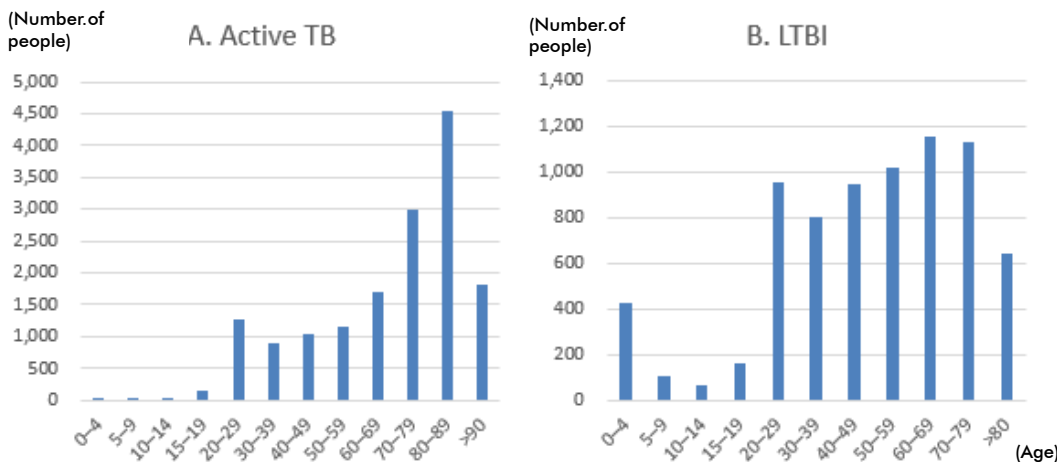


Figure. Number of newly registered active TB and LTBI in Japan 2018 (Modified data of “Statistics of B 2018”)

67% of patients are over 80 years old, and the highest proportion is among 80-89 years old with 29.1%.

On the other hand, the newly registered number of latent tuberculosis infection (LTBI) in 2018 was 7,414, an increase of 159 persons from the previous year. By age group, there is a decrease in each age group of children under 14 years of age and each age group of between 30 and 69 years of age, but 15-19 years old, 20-29 years old youths and over 70 years old It is increasing in the elderly. In particular, the increase was 159 for the 20-29 year old age group, and 137 for the 70-79 year old age group.

TB reinfection of the elderly and contact investigation

Seto et al. found that a half of the 60s, a third of the 70s, and one 4th of the 80s and older of close contacts was estimated as a recent tuberculosis infection by statistically analysis on 1,420 of people who were observed by TB contact investigation in Yamagata Prefecture (4).

In addition, the same authors showed that reinfection of elderly people occurred by VNTR analysis in the contact examination for elderly people (5). A report of Iwamoto et al. on a TB contact investigation after TB outbreak at in elderly nursing facility, showed that VNTR and drug susceptibility test results were the same pattern in 15 TB active cases with culture positive. Eight cases were found to be 81 years old or older. The authors suggested these elderly people had exogenous reinfection (6).

It has been considered generally that many elderly tuberculosis patients are thought to have been infected with *M. tuberculosis* during adolescence, when Japan had been under high TB prevalence, and then became elderly and developed active TB. However these reports above suggest the need for tuberculosis countermeasures that are conscious of the fact that the elderly group also develop TB and LTBI from reinfection.

Detection of TB and LTBI in the elderly

It has been pointed out that age increase false negative rates of IGRAs in elderly with active TB (7). However, Fukushima et al., conducted head-to-head comparison study between QuantiFERON TB Gold (QFT-3G) and demonstrated that QFT-Plus was less more sensitive (lower false negative rate) than QFT-3G in the elderly (8). This report also showed that in active tuberculosis patients over 80 years of age, the proportion of patients with CD4+ T cell (CD4) cell counts of less than 200/ μ L was as high as 40.4% (23/57). Reduction of immune function correlated with reduced reactivity of all IGRAs but the least impact on QFT-Plus. QFT-3G's immune response signal is only from CD4, while the immune response to QFT-Plus is due to CD4 and also CD8+ T cells (CD8), which suggests that the higher sensitivity of QFT-Plus in the elderly is due the addition of CD8 antigens to the latest generation IGRA, QFT-Plus.(4). As already described in and earlier Mr. QFT communication (9), Chien et al. conducted head-to-head comparison study between QFT-3G and QFT-Plus in 229 elderly people (median 80 years old, 60 to 102 years old) whowere in long-term care facilities pf Taiwan. The study showed that the positive rate of QFT-Plus in elderly people over 75 years old is significantly higher than that of QFT-3G, and the number of positive cases of TB2 value is higher than TB1 value. Additionally, the calculated sensitivity for LTBI was statistically superior to QFT-GIT with equal specificity. In effect, the negative predictive value was 100% (10).

Conclusion

These research studies together suggest that QFT-plus may be more effective compared to QFT in the diagnosis of active and latent tuberculosis infections in high-risk groups, such as the elderly.

Mr. QFT



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QFT-Plus is an in vitro diagnostic aid for detection of *Mycobacterium tuberculosis* infection (including disease) and is intended for use in conjunction with risk assessment, radiography, and other medical and diagnostic evaluations. QFT-Plus results alone cannot distinguish active TB disease from latent infection. QFT-Plus Package Inserts, available in multiple languages, as well as up-to-date licensing information and product-specific disclaimers can be found at www.QuantiFERON.com.

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