The window period of IGRA and the timing of IGRA measurement at contact investigation

In this article I will describe about window period of Interferon gamma release assay (IGRA) and timing of IGRA measurement at contact investigation based on previous reports.

One of purpose of TB contact investigation is detection of contact with latent TB infection (LTBI) and treatment[1], and so on. Currently IGRA is mainly used to detect LTBI. Therefore, it is important for service providers to understand the window period of IGRA.

Window period of IGRA, interval between TB infection and detectable of IGRA reactivity, is estimated to be 2-3 months[2] through the experience of Tuberculin Skin Test (TST) of which test principle such as cell mediated immune-response to Mycobacterium tuberculosis is the same as IGRA[3].

According to a report[4] on TB contact investigation used by QFT-2G, one year after exposed to active TB patient (index patient) 28% of contacts converted into QFT® positive, first 2 months its 67% converted, 2-6 months later its 26%, 6-12 months later its 7% converted. The other report[5] of contact investigation used by QFT-3G showed that 9 of 10 contacts converted into QFT-3G positive until 14 weeks after exposure to index cases and one of contact kept negative until 18 weeks. Timing of IGRA measurement at TB contact investigation is described in "Seshokusha kenshin no tebiki" (the Japanese guideline of contact investigation 2015)[6] considering to IGRA window period based on the results mentioned below.

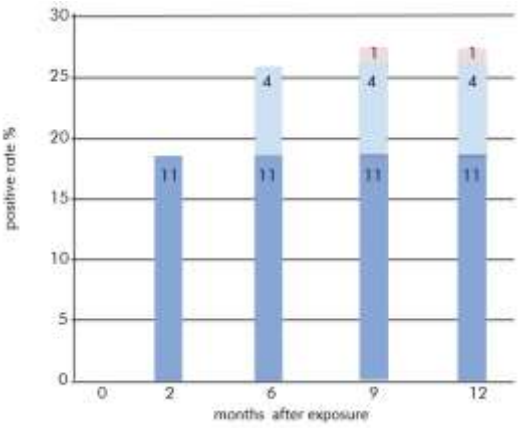

Fig. Number of positive converted cases of QFT-2G at contact investigation (n=59) Modified figure of the article of Kazama, et al.

" <Timing of implementation of IGRA> ····· Basically IGRA of contacts should be implemented at time of 2-3 months passed since last exposer to index case (the exposure). However, if there are contacts who are high risk, for example long-time exposure to Mycobacterium tuberculosis, the secondary TB developed patients are found, or target are the most prioritized contacts, IGRA of those contacts should be implemented just after the exposure, then 2-3 months later the 2nd IGRA should be implemented."

And if high rate of IGRA positivity of contacts (>15%) or more than one of TB developed patients are found at time of 2-3 months passed since the exposure, IGRA measurement should be implemented again for those contacts at time of 6 months passed since the exposure.

Recently study result on contact investigations used by QFT-3G was reported[7]. Totally 13 groups and 108 of contacts with the index cases (all of positive acid-fast bacillus (AFB) sputum-smear results) were checked by QFT-3G at time of 3 months pass since the exposure, and high positivity of QFT-3G of those contacts was found: ranged from 50.0 to 66.7%, total 59.3%. The rest of QFT negative contacts (Total n=27; negative n= 26, gray zone n= 1) were checked by QFT-3G again at time of six months passed since the exposure, the QFT results of each contact were the same as those at time of 3 months. The same study group also reported on results of different TB contact investigations[8]. The contacts (n=2063) who were QFT-3G negative at time of 2-3 months passed since the exposure and then did not receive LTBI treatment were followed up for two years. There were two cases who developed active TB (one case was other TB outbreak) within 2 years. These reports do not mean that 6 months as timing of IGRA measurement, which the guideline recommends, might not be necessary. Because risk assessment in terms of negative impact of missing LTBI case should be considered and these reports were based on the results used only by QFT. Two IGRAs (another IGRA as well as QFT-3G) have been used generally for contact investigations in Japan, therefore more data of field site by another IGRA in Japan (not oversea) will be needed thought there is one report[9].

The more accumulated data regarding windows period of two IGRAs will contribute to the more accurate timing of IGRA measurement to avoid missing a patient with LTBI at contact investigation in Japan.

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