



## Letter to the Editor

**Comment on: Clinical features and outcomes of Bacille Calmette-Guérin (BCG)-induced diseases following neonatal BCG Tokyo-172 strain immunization**


Dear Dr. Poland:

We read with great interest the article by Dr. Rattanachai Rermruay and colleagues on the clinical features and outcomes of BCG-induced diseases following neonatal BCG Tokyo-172 strain immunization [1]. They described that overall, 92% of children had regional lymphadenitis corresponding to the BCG site, 5% had osteitis, and 3% had disseminated BCG. They concluded that the BCG Tokyo-172 strain may be more virulent than expected, even it has been reported to be less reactogenic than the Pasteur and Danish strains. However, their conclusion seems to require further investigation. In this study, as the parent population of vaccinated infants in Thailand was not known, the frequencies of adverse events/BCG-induced diseases (BCG-IDs) in Thailand and Japan could not be compared. The authors suggested that the severe adverse events following BCG vaccination were influenced by factors such as the injection technique, dose and strain, and manufacturing process, as well as host immune defects. We agree with their suggestion.

However, we believe that the BCG strain used by the authors was not the BCG Tokyo-172 strain, owing to the following reasons. First, the Thai Red Cross Society (TRCS) analyzed the genetic characteristics of the BCG TRCS strain, and found that there were considerable differences in genomic profiles between the BCG TRCS and BCG Tokyo-172 strains [2]. Second, the culture method for the BCG Thai strain is different from that for the BCG Tokyo-172 strain. The BCG Tokyo-172 strain has been prepared as a freeze-dried product from the culture of the 172nd passage, in the exact same manner as that used in the original technique developed by Calmette and Guérin, on potato slices cooked in beef bile supplemented with glycerol [3]. However, the BCG TRCS strain has been developed using potato culture without beef bile [4].

Furthermore, the authors also mentioned that the BCG vaccine used in Thailand has been manufactured by the TRCS using the BCG Tokyo-172 strain since 1953. However, there is no formal record that the BCG Tokyo-172 strain was donated to Thailand at

that time. According to the related records of the Queen Saovabha Memorial Institute of Thailand, the BCG Danish 1331 was provided from the Statens Serum Institute of Denmark in 1953 [4]. It should be made clear whether the authors simply misreported the year in which the BCG Tokyo-172 strain was introduced into Thailand, and whether the Danish strain has been maintained as a seed lot to prepare BCG vaccines in Thailand.

### Competing interests

The authors are the employees of Japan BCG Laboratory.

### References

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