

MADRAC *Bulletin*

For healthcare professionals only

Volume 61 | Issue 04/2026

In this issue

The MADRAC Bulletin is a bi-monthly publication that provides a selection of local safety signals and articles discussing local individual case safety reports (ICSRs) meant to raise awareness among health care professionals. Information contained in this publication is not comprehensive but rather represents a selection of clinically relevant items warranting enhanced dissemination.

The MADRAC Bulletin also features pharmacovigilance-related activities conducted by the National Pharmaceutical Regulatory Agency (NPRA) and contains a list of directives based on safety issues advised by the Malaysian Adverse Drug Reactions Advisory Committee (MADRAC) and endorsed by the Drug Control Authority (DCA) as well as safety alerts that have been published on the NPRA website.



To receive each new issue of this bulletin, complete the [subscription form](#) available on the NPRA website.

Articles Based on Case Reports

- **Osteomyelitis as a Rare Complication of BCG Vaccination** ... 2

Features

- **Training** ... 5
 - **Lunch and Learn: Pharmacovigilance Webinar on Strengthening Medicine Safety in Malaysia**

What's New

- **List of Safety Alerts/Directives Related to Drug Safety Issues** ... 6

DISCLAIMER

The MADRAC Bulletin is published by the National Pharmaceutical Regulatory Agency (NPRA), Ministry of Health (MOH), Malaysia. This publication is meant to provide updates on medication safety issues to health care professionals, and not as a substitute for clinical judgement. While reasonable care has been taken to verify the accuracy of the information at the time of publication, the NPRA shall not be held liable for any loss of whatsoever arising from the use or reliance on this publication. The opinions expressed in all articles are the authors' own and do not necessarily reflect the view of NPRA.

We would like to thank the Director General of Health, Malaysia for his permission to publish the signal and case report articles.

Articles Based on Case Reports

This section discusses local individual case safety reports of suspected adverse events recorded in the Malaysian Pharmacovigilance Database (QUEST).¹ The case reports presented in this section are intended to serve as a reminder of potential adverse events that health care providers should be aware of in day-to-day clinical practice, take account of, and report to the NPRA if any relevant events occur. Information contained in these articles is not exhaustive but rather represents a selection of clinically relevant items that warrants dissemination.

Osteomyelitis as a Rare Complication of BCG Vaccination

By Chang Lina

Case Report¹

A one-year-old boy with no known family history of immunodeficiency received the Bacillus Calmette–Guérin (BCG) vaccine at birth for prophylaxis against tuberculosis. Approximately one year following the immunisation, he presented to the hospital with left ankle swelling for two weeks, followed by redness for one week. Physical examination revealed a 3 × 3 cm erythematous, fluctuant mass over the left posterior medial ankle, although he was still able to bear weight. Diagnostic workup revealed caseating material extending into the intramedullary canal of the distal tibia. Histopathological examination revealed chronic necrotising changes with positive acid-fast bacilli (AFB) staining, while molecular testing detected *Mycobacterium tuberculosis* complex. Tissue culture subsequently confirmed the presence of the BCG strain of *Mycobacterium bovis*. The patient was diagnosed with **BCG-induced osteomyelitis** of the left tibia. He underwent surgery including incision, drainage and curettage of the distal tibia. At the time of reporting, the patient was stable and the postoperative wound was clean with no discharge. The event was assessed as having a consistent causal association with the BCG vaccine.

Discussion

The **BCG vaccine** is a live, freeze dried vaccine derived from attenuated strains of *Mycobacterium bovis*, consisting of live bacteria of Calmette and Guérin.² It is primarily used for the prevention of tuberculosis and is routinely administered to infants, ideally soon after birth. In Malaysia, only one BCG vaccine product is currently registered and available in freeze-dried formulation.³ Before administration, the BCG vaccine is reconstituted with saline diluent and administered as an intradermal injection on the outer part of the upper arm.²

Although the BCG vaccine has a well-established safety profile, rare adverse events can still occur.² One such complication is **BCG-induced osteomyelitis**, a form of disseminated BCG infection involving the bone.⁴⁻⁶ This condition is documented as a very rare adverse reaction in local BCG product information, with an incidence of approximately one in 80,000 to 100,000 vaccinations.^{2,4} The clinical manifestations of BCG-induced osteomyelitis are often gradual and non-specific, making early diagnosis challenging and frequently delaying diagnosis.^{5,6} In contrast to acute bacterial osteomyelitis, systemic symptoms like high fever and abrupt bone pain are usually absent.⁵⁻⁸ Children commonly present with localised swelling, mild pain or tenderness over the affected bone and surrounding soft tissue.⁶⁻⁹ Functional impairment such as limping, antalgic gait or reduced range of motion may occur when the infection affects the lower extremities.⁶⁻⁹

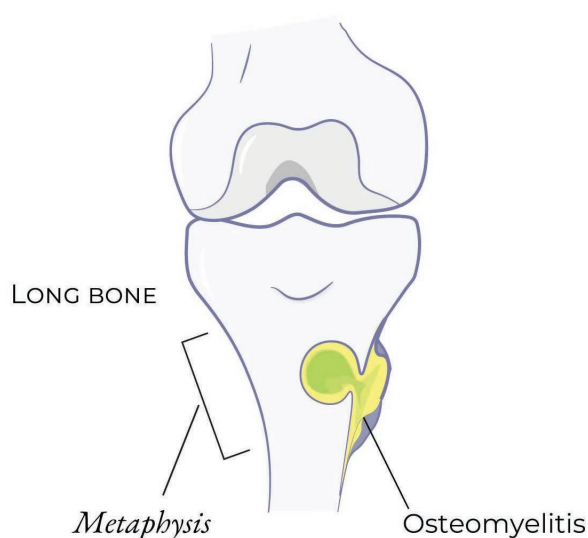


Figure 1. Osteomyelitis.¹⁴

While the precise pathophysiology of BCG-induced osteomyelitis remains unclear, the primary mechanism involves the hematogenous dissemination of live attenuated BCG bacteria from the vaccination site to the bones, particularly the metaphysis and epiphysis of long bones.^{4-6,10,11} In infants, specific anatomical features such as transphyseal blood vessels and localised microtrauma from increased physical activity facilitate the spread of the bacteria.^{9,11} Once the bacteria is established within the bone tissue, they will trigger a chronic granulomatous inflammatory response that may lead to localised bone necrosis and destruction.^{10,11}

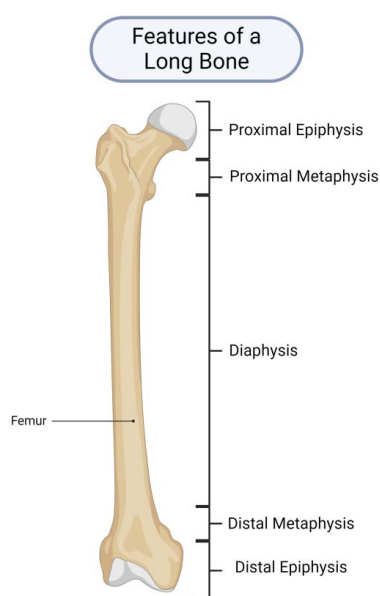


Figure 2. Features of a long bone structure: Epiphysis, Metaphysis and Diaphysis.¹⁵

Although BCG-induced osteomyelitis is a well-documented complication that can affect immunocompetent children, it is significantly more likely to occur in infants with primary or secondary immunodeficiencies.² High-risk groups include infants with severe combined immunodeficiency (SCID), IL-12/IFN- γ pathway defects, HIV infection or extreme preterm infants (those born before 30 weeks of gestation or weighing less than 1.5kg).¹² BCG-induced osteomyelitis typically develops after a prolonged latency period with symptoms usually appearing between four to 24 months post-vaccination, with the average onset occurring between 11 and 17 months.^{6,7,9}

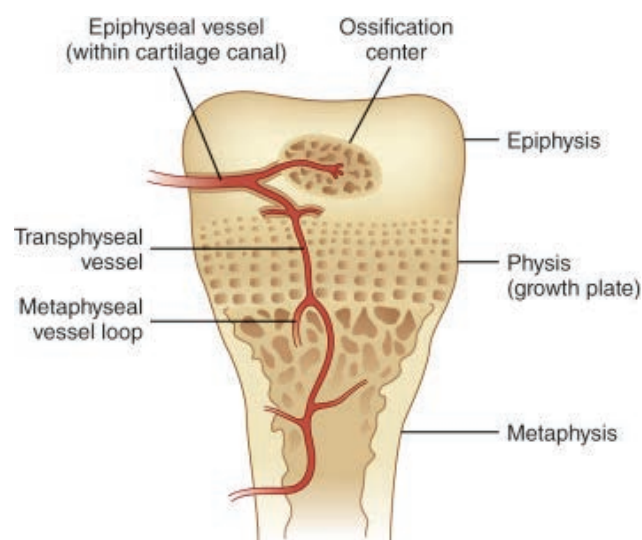
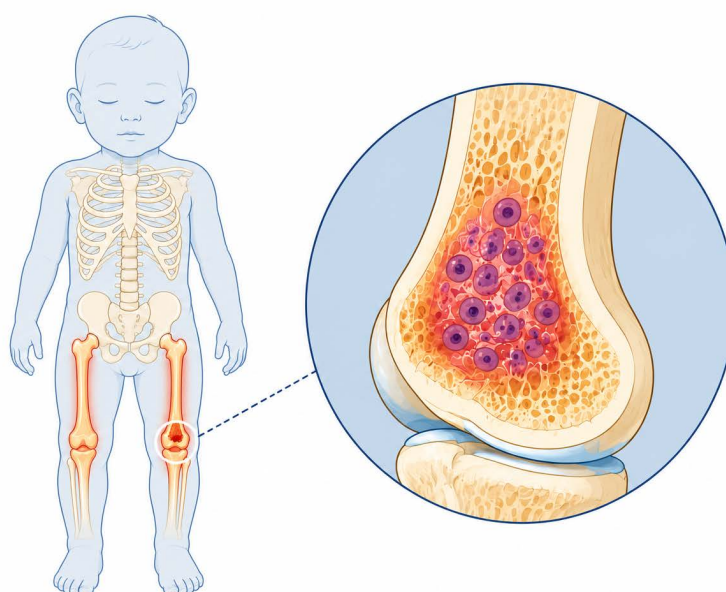


Figure 3. Vascular anatomy of the long bone of infants.¹⁶



**AI-generated image*

Management of BCG-induced osteomyelitis primarily involves a combination of prolonged antituberculous chemotherapy and limited surgical intervention when necessary.^{6,10,11} Antituberculous treatment typically consists of a six to 12-month course of oral isoniazid and rifampicin.^{4,6,7,11} Pyrazinamide must be excluded from the treatment regimen, as *Mycobacterium bovis* BCG strains are intrinsically resistant to this drug. Surgical management should remain conservative, prioritising minimally invasive approaches such as image-guided biopsy, debridement to remove necrotic tissue and polymerase chain reaction (PCR) studies to establish a definitive diagnosis.^{2,7,8,9}

As of June 2026, NPRA has received 123 reports with 171 adverse events following immunisation (AEFI) suspected to be related to the BCG vaccine. The most frequently reported AEFIs were lymphadenitis (30 reports), axillary lymphadenitis (21) and injection site swelling (18).¹ To date, there have been five cases of osteomyelitis involving the BCG vaccine in Malaysia, including the one discussed in this article. Globally, the World Health Organisation (WHO) database of individual case safety reports recorded a total of 137 cases of osteomyelitis suspected to be associated with the BCG vaccine.¹³

*DISCLAIMER

VigiBase is the WHO global database of reported potential adverse effects of medicinal products, developed and maintained by Uppsala Monitoring Centre (UMC). This information comes from a variety of sources, and the likelihood that the suspected adverse effect is drug-related is not the same in all cases. This information does not represent the opinion of the UMC or the WHO.

References:

1. National Pharmaceutical Regulatory Agency (NPRA). The Malaysian National ADR Database (QUEST) [Internet]. 2026 [cited 2026 June 22]. Available from: <https://www.npra.gov.my> (access restricted).
2. National Pharmaceutical Regulatory Agency (NPRA). Freeze Dried Glutamate BCG Vaccine [Package Insert]. QUEST3+ Product Search. 2026 [cited 2026 June 22]. Available from: <http://www.npra.gov.my>
3. National Pharmaceutical Regulatory Agency (NPRA). QUEST3+ Product Search [Internet]. 2026 [2026 June 22]. Available from: <https://www.npra.gov.my>
4. Chan PK, Ng BK, Wong CY. Bacille Calmette-Guérin osteomyelitis of the proximal femur. Hong Kong Med J. 2010;16(3):223-226. Available from: <https://pubmed.ncbi.nlm.nih.gov/20519760/>
5. Kwon HJ, Chung BH, Choi BM, Park KU, Kim YK. Severe osteomyelitis as a complication of Tokyo-172 BCG vaccination. J Korean Med Sci. 2012;27(2):221-224. Available from: <https://doi.org/10.3346/jkms.2012.27.2.221>
6. Alawfi A. Bacillus Calmette-Guérin vaccine-related osteomyelitis in immunocompetent children in Saudi Arabia: A narrative review. Cureus. 2022;14(12):e32762. Available from: <https://doi.org/10.7759/cureus.32762>
7. Tsai YL, Chen YJ, Lai YC. Long-term follow-up of osteomyelitis caused by Bacille Calmette-Guérin vaccination in immunocompetent children. Sci Rep. 2020;10(1):4072. Available from: <https://doi.org/10.1038/s41598-020-61152-6>
8. Kim JY, Jeon JI, Chang H. Bacille Calmette-Guérin osteomyelitis of the distal radius in a toddler. Arch Hand Microsurg. 2020;25(2):134-139. Available from: <https://doi.org/10.12790/ahm.20.0017>
9. Low YY, Hsu YL, Chen JA, Wei HM, Lai HC, Chiu YT, et al. Bacillus Calmette-Guérin (BCG) osteomyelitis among children: Experience in a single tertiary center in central Taiwan. J Microbiol Immunol Infect. 2022;55(6):965-972. Available from: <https://doi.org/10.1016/j.jmii.2021.09.007>
10. Al-Azri MS, Manarang J, Al-Mufargi Y. Bacille Calmette-Guérin vaccine-induced tuberculous hip osteomyelitis in an infant. Sultan Qaboos Univ Med J. 2017;17(3):e358-362. Available from: <https://doi.org/10.18295/squmj.2017.17.03.019>
11. Abe S, Sasaki Y, Matsukura K, Ito H. Long-term outcomes of BCG osteomyelitis in infants: Epiphyseal regeneration and minimal leg-length discrepancy after 10 years. JOS Case Rep. 2024;3(2):111-116. Available from: <https://doi.org/10.1016/j.joscr.2024.01.003>
12. Starshinova A, Kudryavtsev I, Rubinstein A, Dovgalyuk I, Kulpina A, Churilov LP, et al. BCG vaccination: historical role, modern applications, and future perspectives in tuberculosis and beyond. Front Pediatr. 2025;13:1603732. Available from: <https://doi.org/10.3389/fped.2025.1603732>
13. Uppsala Monitoring Centre (UMC). The WHO Global ICSR Database (Vigilyze) [Internet]. 2026 [cited 2026 June 22]. Available from: <https://www.vigilyze.who-umc.org> (access restricted)
14. Osteomyelitis. In: Clinical Medicine for Medical Students. ditki; 2026 [cited 2026 June 26]. Available from: <https://tinyurl.com/398b3fmr>
15. Price T, Hutchins J, Burr J, Johnston M, Silberman P, Speth J, et al. Bone features and formation. In: Integrated human anatomy and physiology [Internet]. UEN Digital Press; [cited 2026 Jul 16]. Available from: <https://tinyurl.com/39wrndn9c>
16. Cassat J. Bacterial infections of the bones and joints. In: Maldonado Y, Nizet V, Barnett ED, Edwards KM, Malley R, editors. Remington and Klein's Infectious Diseases of the Fetus and Newborn Infant. 9th ed. London: Elsevier; 2025 [cited 2026 June 26]. p. 263-273. Available from: <https://doi.org/10.1016/B978-0-323-79525-8.00018-4>

Advice for Health Care Professionals

- **Screen** children for underlying immunodeficiency risk or prior BCG complications and **consider** delaying BCG vaccination in high-risk infants, in particular those born prematurely, and those with known with SCID, IL-12/IFN- γ pathway defects, or HIV infection.
- **Monitor** infants and young children (≤ 5 years) with a history of BCG vaccination for mild localised swelling, tenderness, limited range of motion, antalgic posture or a limping gait, if these symptoms develop four to 24 months after vaccination.
- **Utilise** advanced imaging and diagnostics such as Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) to detect any bone destruction or deformities in symptomatic patients. **Obtain** tissue biopsy for histology, culture and **conduct** PCR testing to identify the *Mycobacterium bovis* BCG strain.
- **Report** any suspected AEFIs associated with BCG vaccine to NPRA.

Features

Training

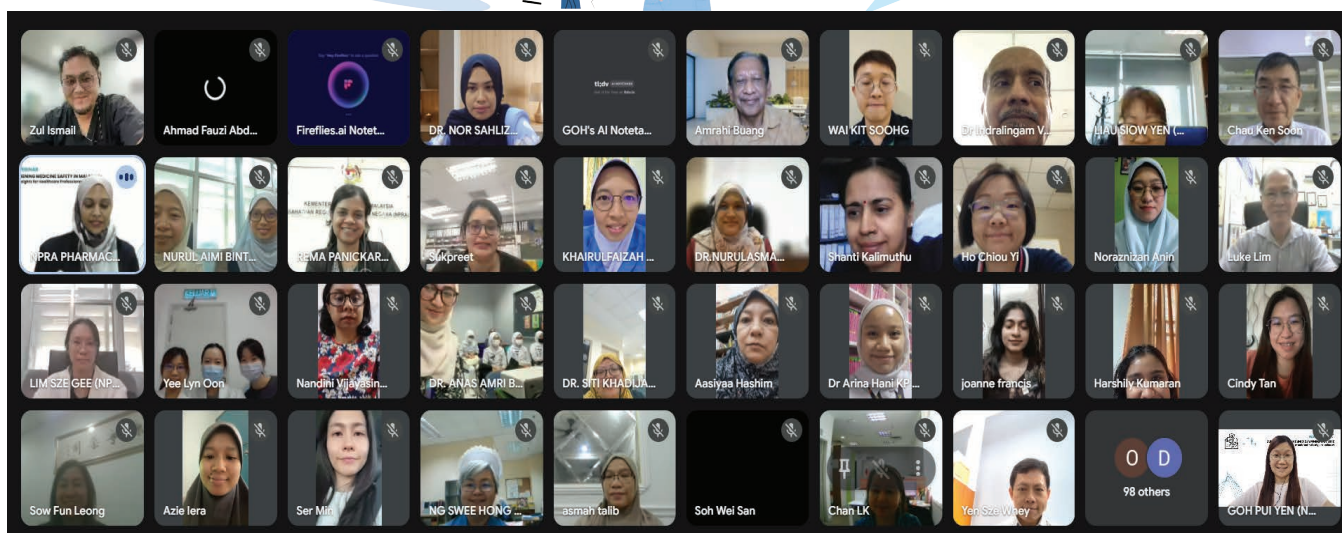
Lunch & Learn - Pharmacovigilance Webinar on Strengthening Medicine Safety in Malaysia

On 9 June 2026, the NPRA Pharmacovigilance Section hosted a lunchtime webinar titled Strengthening Medicine Safety in Malaysia: Practical Insights for Healthcare Professionals. Designed to accommodate busy healthcare professionals, the lunchtime session was well received by participants, as reflected in the following feedback:

"The lunchtime webinar was very suitable for those of us who are busy with our clinical duties during working hours."



"The topics and knowledge shared were highly valuable and applicable to daily practice. Thank you and congratulations to the organisers for this initiative."



This webinar aimed to strengthen medicine safety awareness among healthcare professionals and provide practical guidance on adverse event reporting as well as the utilisation of allergy cards in clinical practice. More than 600 doctors, dentists, pharmacists, nurses, and allied health professionals from both the public and private healthcare sectors nationwide tuned in for the session.

Key takeaways:

When in Doubt, Report! – Attendees received a comprehensive refresher on adverse drug reaction (ADR) and adverse event following immunisation (AEFI) reporting. The session emphasised how timely, high-quality reports drive signal detection and post-marketing surveillance. Importantly, attendees were assured that reports remain strictly anonymous and are used solely for safety, fostering a culture of learning rather than blaming.

Demystifying Drug Allergies – Our guest speaker from the Pharmacy Practice and Development Division led a vital segment on allergy cards and hypersensitivity assessments. Through real-world case studies, attendees learned to pinpoint true drug allergies, ensuring accurate documentation so patients aren't unnecessarily deprived of essential medications.

Participant Feedback & Impact: Feedback from the 173 post-webinar evaluation responses showed highly positive results. Participants indicated that the session provided them with useful knowledge for their daily work:

- **High Satisfaction: 98.3%** of respondents reported that the webinar met or exceeded their expectations.
- **Practical Confidence: 96.5%** felt confident or very confident in applying the information learned to their daily clinical practice.
- **Future Interest: 92.5%** expressed interest in attending future webinars organised by the NPRA Pharmacovigilance Section.

What's New

List of Safety Alerts/Directives Related to Drug Safety Issues

NPRA reviews and presents drug safety issues at meetings of the Malaysian Adverse Drug Reactions Advisory Committee (MADRAC) to determine the appropriate risk minimisation measures. Regulatory actions are proposed to the Drug Control Authority (DCA), resulting in DCA directives issued to ensure local package inserts and consumer medication information leaflets (RiMUP) for all products containing the affected active ingredients are updated with the required safety information. The table below shows the safety alerts/DCA directives that were recently issued, which are available on the NPRA website.

	Active Ingredients	Safety Alerts		Directive Ref. No. [Date]
		Title	Date	
1	Aciclovir and Valaciclovir	Risk of Acute Generalised Exanthematous Pustulosis (AGEP)	6-Jul-2026	
2	Cefazolin	Risk of Kounis Syndrome	6-Jul-2026	
3	Lamotrigine	Risk of Photosensitivity Reactions	6-Jul-2026	NPRA.600-1/9/13 (6) Jld. 2 [14-Apr-2026]
4	GLP-1 and Dual GLP-1/GIP Receptor Agonists	Risk of Severe Acute Pancreatitis	22-Jul-2026	

How to report adverse events?

NPRA encourages all healthcare professionals to report all suspected adverse drug reactions (ADR) to medicines, including pharmaceutical products, over-the-counter medicines, traditional medicines, and health supplements, as well as adverse events following immunisation (AEFI) with vaccines.

To report ADR/AEFI:

1. Visit www.npra.gov.my
2. Report ADR as **Healthcare Professional**
 - a) Choose **ADR / AEFI Google Form**; or
 - b) Download the **ADR manual form** and submit the completed form via email or post:



fv@npra.gov.my



Pharmacovigilance Section,
National Pharmaceutical Regulatory Agency (NPRA),
Ministry of Health, Malaysia.
Lot 36, Jalan Prof Diraja Ungku Aziz (Jalan Universiti),
46200 Petaling Jaya, Selangor, Malaysia.

NPRA Safety Information Mailing List

To join the mailing list:



- a) scan the QR code to complete the [subscription form](#) available on the NPRA website, or



- b) send an email with your details to fv@npra.gov.my

Editorial Board

Advisors

Rosliza Lajis
Saleha Abd Rahman @ Ngah

Chief Editor

Norleen Mohamed Ali

Editors

Dr. Rema Panickar
Goh Pui Yen