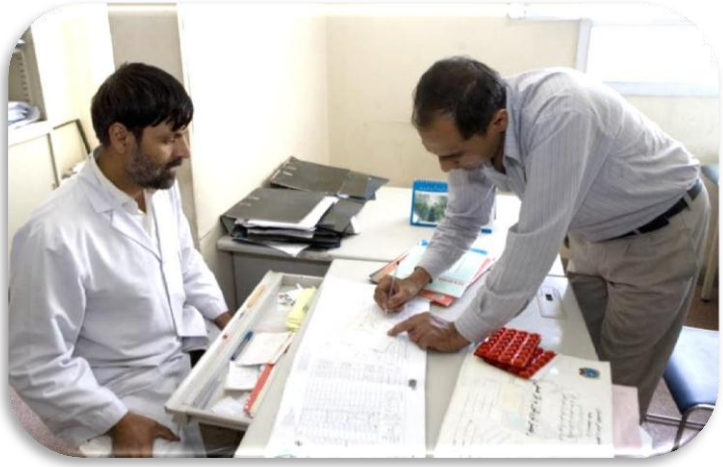
WHO Informations Sheets on Observed Rates of Vaccine Reactions

World Health Organization

http://www.who.int/vaccine_safety/initiative/tools/vaccinfosheets/en/index.html



Supporting vaccine introduction

To strengthen the capacity of entities introducing vaccines in Member States WHO publishes information sheets that provide details on vaccine reaction rates of selected vaccines – whether single antigen or combined in a single product.

The papers are primarily designed for use by national public health officials and immunization programme managers but may appeal to others interested in such information.

Data from these sheets can be used in the evaluation of Adverse Events Following Immunization (AEFI) reported during national immunization programmes, but also in preparing communication materials about specific vaccines.

The WHO information sheets have been developed and reviewed in collaboration with the Global Advisory Committee on Vaccine Safety (GACVS).

Information sheet structure

Designed for practical use in the field, the information sheets follow a simple, modular pattern.

They usually include a short summary of the vaccine specifics and adverse events.

The section on Adverse events usually includes passages on:

- mild adverse events;
- serious adverse events;
- other safety issues
- summary table for quick overview

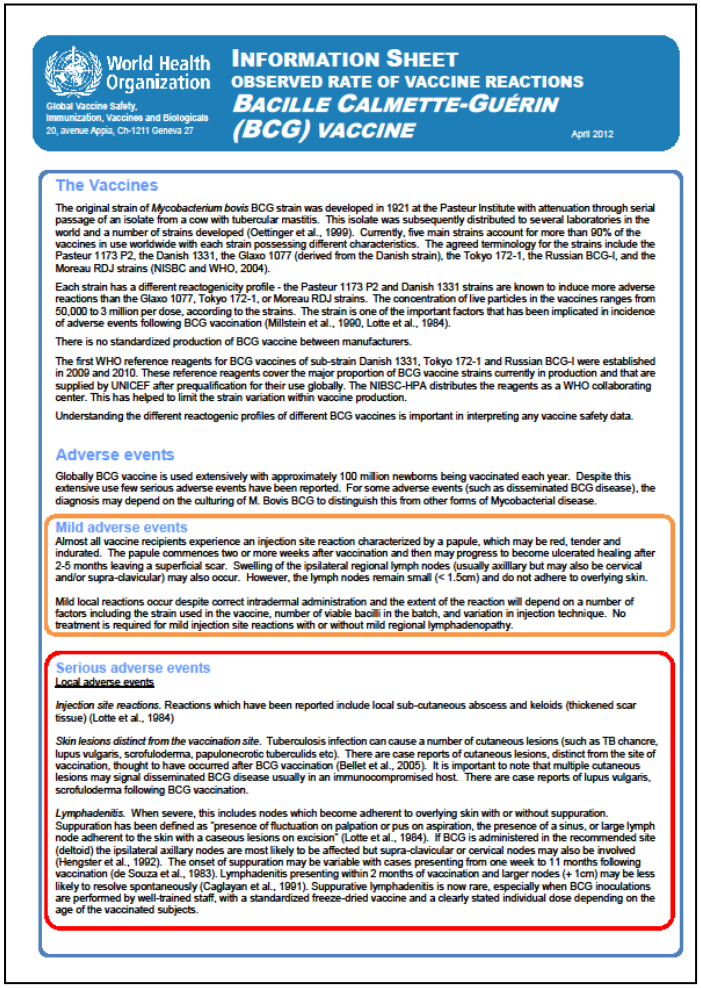
To satisfy potential further research needs, all information sheets include a detailed list of source material.

Online availability

Please check the following web-link for the first information sheets available:

http://www.who.int/vaccine_safety/initiative/tools/vaccinfosheets/en/index.html

Further information sheets are currently being drafted. If you would like to be notified of the next information sheets that will become available, please subscribe at: vaccsafety@who.int



World Health Organization

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INFORMATION SHEET
OBSERVED RATE OF VACCINE REACTIONS
BACILLE CALMETTE-GUÉRIN (BCG) VACCINE

April 2012

The Vaccines

The original strain of *Mycobacterium bovis* BCG strain was developed in 1921 at the Pasteur Institute with attenuation through serial passage of an isolate from a cow with tubercular mastitis. This isolate was subsequently distributed to several laboratories in the world and a number of strains developed (Oettinger et al., 1999). Currently, five main strains account for more than 90% of the vaccines in use worldwide with each strain possessing different characteristics. The agreed terminology for the strains include the Pasteur 1173 P2, the Danish 1331, the Glaxo 1077 (derived from the Danish strain), the Tokyo 172-1, the Russian BCG-I, and the Moreau RDJ strains (NISBC and WHO, 2004).

Each strain has a different reactogenicity profile - the Pasteur 1173 P2 and Danish 1331 strains are known to induce more adverse reactions than the Glaxo 1077, Tokyo 172-1, or Moreau RDJ strains. The concentration of live particles in the vaccines ranges from 50,000 to 3 million per dose, according to the strains. The strain is one of the important factors that has been implicated in incidence of adverse events following BCG vaccination (Millstein et al., 1990, Lotte et al., 1984).

There is no standardized production of BCG vaccine between manufacturers.

The first WHO reference reagents for BCG vaccines of sub-strain Danish 1331, Tokyo 172-1 and Russian BCG-I were established in 2009 and 2010. These reference reagents cover the major proportion of BCG vaccine strains currently in production and that are supplied by UNICEF after prequalification for their use globally. The NIBSC-HPA distributes the reagents as a WHO collaborating center. This has helped to limit the strain variation within vaccine production.

Understanding the different reactogenic profiles of different BCG vaccines is important in interpreting any vaccine safety data.

Adverse events

Globally BCG vaccine is used extensively with approximately 100 million newborns being vaccinated each year. Despite this extensive use few serious adverse events have been reported. For some adverse events (such as disseminated BCG disease), the diagnosis may depend on the culturing of M. Bovis BCG to distinguish this from other forms of Mycobacterial disease.

Mild adverse events

Almost all vaccine recipients experience an injection site reaction characterized by a papule, which may be red, tender and indurated. The papule commences two or more weeks after vaccination and then may progress to become ulcerated healing after 2-5 months leaving a superficial scar. Swelling of the ipsilateral regional lymph nodes (usually axillary but may also be cervical and/or supra-clavicular) may also occur. However, the lymph nodes remain small (< 1.5cm) and do not adhere to overlying skin.

Mild local reactions occur despite correct intradermal administration and the extent of the reaction will depend on a number of factors including the strain used in the vaccine, number of viable bacilli in the batch, and variation in injection technique. No treatment is required for mild injection site reactions with or without mild regional lymphadenopathy.

Serious adverse events

Local adverse events

Injection site reactions. Reactions which have been reported include local sub-cutaneous abscess and keloids (thickened scar tissue) (Lotte et al., 1984)

Skin lesions distinct from the vaccination site. Tuberculosis infection can cause a number of cutaneous lesions (such as TB chancre, lupus vulgaris, scrofuloderma, papulonecrotic tuberculids etc). There are case reports of cutaneous lesions, distinct from the site of vaccination, thought to have occurred after BCG vaccination (Bellet et al., 2005). It is important to note that multiple cutaneous lesions may signal disseminated BCG disease usually in an immunocompromised host. There are case reports of lupus vulgaris, scrofuloderma following BCG vaccination.

Lymphadenitis. When severe, this includes nodes which become adherent to overlying skin with or without suppuration. Suppuration has been defined as "presence of fluctuation on palpation or pus on aspiration, the presence of a sinus, or large lymph node adherent to the skin with a caseous lesions on excision" (Lotte et al., 1984). If BCG is administered in the recommended site (deltoid) the ipsilateral axillary nodes are most likely to be affected but supra-clavicular or cervical nodes may also be involved (Hengster et al., 1992). The onset of suppuration may be variable with cases presenting from one week to 11 months following vaccination (de Souza et al., 1983). Lymphadenitis presenting within 2 months of vaccination and larger nodes (+ 1cm) may be less likely to resolve spontaneously (Caglayan et al., 1991). Suppurative lymphadenitis is now rare, especially when BCG inoculations are performed by well-trained staff, with a standardized freeze-dried vaccine and a clearly stated individual dose depending on the age of the vaccinated subjects.

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