BCG vaccine in Australia

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SYNOPSIS

Australia has low rates of tuberculosis, but there are still high rates in immigrants and indigenous people. BCG vaccination is indicated in high-risk groups, particularly children who may be exposed to tuberculosis, and possibly in healthcare workers. The vaccine reduces the risks of invasive tuberculosis and death from tuberculosis by about 70%. The degree of protection against pulmonary tuberculosis is uncertain. Adverse effects are uncommon and can usually be managed conservatively.

Index words: tuberculosis, Mantoux test.

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Introduction

Tuberculosis is a global emergency. One third of the world's population is infected and there are eight million new clinical cases and three million deaths each year. Australia currently enjoys one of the lowest notification rates for tuberculosis in the world at fewer than four cases per 100 000 population per annum. This annual rate declined from 48 per 100 000 in the late 1940s as a result of a highly successful national tuberculosis control program involving active case finding, standardised treatment, mass X-ray surveys and widespread BCG vaccination.[1] Most of these strategies were abandoned in the mid-1980s with the decline in tuberculosis, but there are worrying signs that the decline has halted and that rates of infection in Australia may be rising. Three quarters of all cases of tuberculosis in Australia now arise in people born overseas, usually in high-risk countries, but the Aboriginal population also has much higher risks of tuberculosis than other people born in Australia.

BCG vaccine

BCG (Bacillus Calmette-Guérin) is a living attenuated strain of *Mycobacterium bovis* which stimulates cell-mediated immunity by producing a localised and self-limiting infection. The vaccine is given intradermally, normally in the arm, but in parts of northern Europe often in the thigh or buttock (an important consideration if looking for a scar to prove previous vaccination). Vaccination should be given around the site of the insertion of the deltoid muscle, slightly posteriorly (Fig.1). This minimises keloid scar formation and also ensures that the lymphatic drainage of the site is to the axilla, rather than to the neck glands. The cosmetic effects of persistent lymphadenopathy or scars from suppurating lymph nodes are thus minimised. Normally one to three weeks after vaccination a small red papule appears. This usually vesicates and a scab forms. The site should be kept clean and dry and exposed to air as much as possible. It can be washed with clean warm water, but should be dabbed dry and kept open. Antiseptics, creams and other local applications should not be used. Normally the vaccination site heals leaving a small, depressed scar over a three to four month period. The duration of immunity is thought to be 10–15 years, but usually patients are not revaccinated.

Indications for BCG

BCG should be used in the following circumstances:

- newborn Aboriginal and Torres Strait Islander babies in areas where tuberculosis is prevalent
- neonates and children who are likely to travel to or live in countries where tuberculosis is common
- newborn babies, if either parent has leprosy
- children and adults who have been in contact with tuberculosis and remain Mantoux negative three months after last contact.

BCG may also be considered in the following circumstances:

- healthcare workers in frequent contact with patients with tuberculosis, especially multi-drug resistant tuberculosis
- adults who will spend prolonged periods in countries where tuberculosis is common
- newborn babies living in households where they may be exposed to migrants or visitors from overseas countries with high tuberculosis rates

Fig. 1

Intradermal injection of BCG vaccine

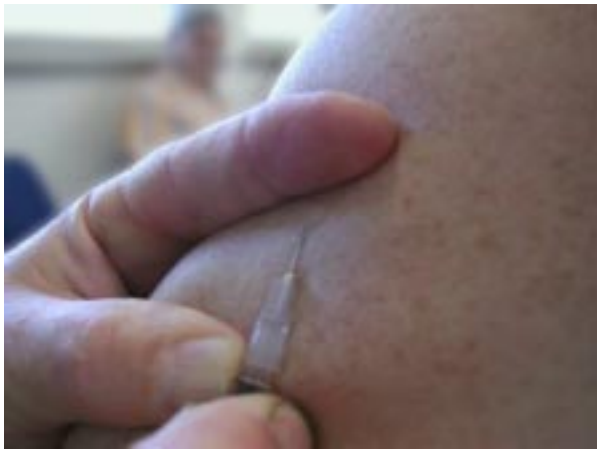

Photo courtesy of the author

- children under 16 years who are in contact with a patient with tuberculosis where the infection is resistant to treatment or where the child cannot take prophylactic antituberculosis treatment.

Healthcare workers

Healthcare workers represent a special group and there are two quite different views on how they should be managed with respect to potential tuberculous infection. The American view is that BCG should not be given and that healthcare workers should be monitored with regular Mantoux tests to detect tuberculous infection which can then be treated appropriately. This is expensive and labour intensive.

In parts of Australia where exposure to environmental mycobacteria is high and where many healthcare workers have had prior BCG, Mantoux tests may prove difficult to interpret. The alternative view, that new staff should be screened by Mantoux testing and then offered BCG vaccination if the result is negative, has become less popular and has been abandoned in some states which have adopted the American policy. Nevertheless, this approach is a viable option for staff likely to be exposed to tuberculosis regularly and certainly for those exposed to multi-drug resistant tuberculosis, although this is still uncommon in Australia.

The role of Mantoux testing

Over a century after the Mantoux test was introduced, it remains the standard test for detecting prior tuberculous infection. Guidelines recommend that it precede BCG vaccination in all but those under six months of age. Mantoux testing involves the intradermal injection of mycobacterial proteins (purified protein derivative – PPD) into the volar aspect of the forearm. Contraindications include a previous strongly positive test, past history of tuberculosis and recent vaccination with live vaccines.

The test is read by measuring the transverse diameter of induration (**not** erythema) at the injection site after 72 hours. Unfortunately, the interpretation of the result is highly complex and dependent on many factors including the patient's age, prior BCG vaccination, other medical conditions and geographical location – this last probably representing exposure to environmental mycobacteria. In general, reactions of less than 5 mm can be considered negative (though Mantoux conversion may not occur for 6 to 12 weeks after primary infection as it represents a cell-mediated response). Larger reactions however do not necessarily indicate tuberculous infection and expert advice from the local chest clinic should be sought.

Contraindications to BCG vaccination

BCG should not be given to:

- patients with current or previous tuberculosis
- patients with a current febrile illness
- patients with skin conditions such as eczema or dermatitis
- patients who have had a previous live vaccination within the past four weeks
- patients with a history of a positive reaction to a Mantoux test
- people who are HIV positive, or are in a high risk group for HIV and have not been tested
- patients receiving immunosuppressive medication such as corticosteroids or cancer chemotherapy or with other conditions likely to suppress immunity.

Adverse effects of BCG

Immediate adverse effects include vasovagal attacks or, extremely rarely, anaphylaxis. These should be managed conventionally.

The amount of inflammation at the injection site varies considerably. There may be a localised erythematous rash which settles within three days and there may be a low-grade fever for the first 24 hours. Inadvertent subcutaneous inoculation can result in localised abscess formation. Large local reactions are usually accompanied by more prominent lymphadenopathy, but usually settle without treatment.

Lymphadenopathy, which if the vaccination site is correct should be in the axilla, is common and usually settles without treatment. If the lymph nodes are not tethered to the skin and are not fluctuant, observation is the best policy. Minor enlargement of the lymph nodes may be permanent. If there is skin tethering and erythema and it looks as if an abscess may be forming, drug treatment is indicated. Isoniazid 5–10 mg/kg daily for three months is usually adequate. Surgery is rarely necessary. Isoniazid treatment would also be appropriate if secondary spread to other sites occurred. This is only really seen if patients with eczema or other skin conditions are inadvertently vaccinated. Should disseminated infection occur because of vaccination of an immunosuppressed person multi-drug therapy with rifampicin, isoniazid and ethambutol will be needed. Pyrazinamide is of no use as BCG is resistant to this drug.

Does BCG work?

The precise efficacy of BCG vaccine has been contentious for many years and there seems to have been a recent tendency to underestimate its effectiveness. A widely quoted meta-analysis estimates an overall reduction in the risk of developing tuberculosis of 50%.[2] The true protective effect, however, may be higher. The meta-analysis was considerably skewed by one very large trial in South India which showed no protection whatsoever. Other studies in more temperate climates have found protection rates of up to 80%. The explanation for the widely different results remains obscure but exposure to environmental mycobacteria and subsequent modification of the immune response has been suggested.

The protection rates refer to protection against pulmonary tuberculosis. There is strong evidence that BCG offers very good protection against the disseminated forms of tuberculous infection. Miliary and meningeal tuberculosis and also deaths related to tuberculosis are reduced by about 70%. Although it is far from perfect, BCG clearly provides significant and worthwhile protection against tuberculosis. If Australia does not manage to avoid the worldwide epidemic of multi-drug resistant tuberculosis then the protective effects of BCG may be of increasing value.

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Conflict of interest: none declared

Self-test questions

The following statements are either true or false (answers on page 151)

11. Eczema is a contraindication to BCG vaccine.
12. With the exception of babies under six months of age, Mantoux testing is recommended before patients are given BCG vaccine.

Tuberculosis testing and immunisation in the Australian Defence Force

Prepared by Air Vice-Marshal Bruce Short, Surgeon General, Australian Defence Force

In the course of peacetime service in Australia, the exposure of Australian Defence Force personnel to tuberculosis, and hence risk of infection, is similar to that of the general population. However, when operationally deployed, particularly in Australia's region of interest, personnel may be exposed to infected people. This risk is heightened during humanitarian or peace-keeping operations.

In the past, the mainstay of prevention was immunisation with BCG vaccine. In recent times the widespread use of BCG vaccination has been shown to prevent few cases in regions with low incidence rates. The vaccine may also cause false positives in Mantoux tests and this may increase the difficulty in diagnosing tuberculosis infection.

The Australian Defence Force has followed the guidelines of the US Centers for Disease Control and Prevention and, therefore, does not recommend routine BCG vaccination.[1]

Within the Australian Defence Force, screening for tuberculosis is undertaken by skin testing all personnel on entry, using 10 units of tuberculin purified protein derivative. Tuberculin skin testing may also be performed in two steps if the initial induration is less than 15 mm diameter. It is not performed by using multiple puncture tests (Heaf test).[2]

The tuberculin skin test is also used to screen personnel after redeployment or removal from a country with a high incidence of tuberculosis, provided that the period of redeployment has been at least three months. This testing is performed three months after the personnel return to Australia. A high incidence country is one in which the annual tuberculosis incidence is at least 49 per 100 000. For people visiting and residing in such an area for at least 3–12 months, incidence rates for tuberculosis infection have been reported as 1.8%.[3]

Personnel who have been exposed to high risk situations are also tested. This latter group includes those people who have spent a total of eight or more hours with an infected person in a confined environment, as well as healthcare workers who have had regular close contact with an index case.

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New drugs

Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may have been little experience in Australia of their safety or efficacy. However, the Editorial Committee believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained either from the manufacturer's approved product information, a drug information centre or some other appropriate source.

Eptifibatide

Integrilin (Schering Plough)

10 mL vial containing 2 mg/mL

100 mL vial containing 0.75 mg/mL

Approved indications: unstable angina, myocardial infarction, intracoronary stenting

Australian Medicines Handbook section 7.2.1

Eptifibatide is the latest of several glycoprotein IIb/IIIa receptor antagonists such as tirofiban and abciximab, to be marketed in Australia. These drugs work in acute coronary syndromes by inhibiting platelet aggregation.[1]

Patients with unstable angina or non-Q wave myocardial infarction are given an intravenous bolus of eptifibatide. This is followed by an infusion which continues, for up to 72 hours, until the patient has a coronary bypass or leaves hospital. In