The BCG vaccine: information and recommendations for use in Australia

National Tuberculosis Advisory Committee

Executive summary

The Bacille Calmette-Guérin (BCG) vaccine since its first use in 1921 has been the subject of much controversy as to its effectiveness and applicability. BCG vaccination is still considered an important strategy in the National Tuberculosis Programs of countries with a high burden of tuberculosis (TB) because of its benefit to infants but its effect on the control of TB has been limited. By contrast, in countries with a low prevalence of TB, significant policy differences exist both within and between countries.

BCG vaccination does not prevent transmission of infection to the individual. In immune-competent neonates and infants it is accepted that BCG reduces the likelihood of TB infection progressing to disease or if disease occurs, substantially lessens the chance of a severe outcome. The benefit in older age groups is less clear.

In the Australian health worker, the BCG strategy is no longer recommended as the primary means of health care worker (HCW) protection. The preferred strategy is appropriate infection control measures, staff education and a tuberculin skin testing program that identifies and treats the at-risk infected HCW. The emergence of multi-drug resistant strains has however renewed interest in BCG in the HCW.

This document provides recommendations for use of the BCG vaccine in the Australian community based on the best available evidence and consensus opinion. State and Territory TB Control Units should be consulted with regard to their BCG vaccination guidelines.

Recommendations

BCG vaccination is not recommended for general use in the Australian population.

BCG is recommended for:

1. Aboriginal neonates in areas of high incidence of TB (e.g. Northern Territory, Far North Queensland, northern areas of Western Australia and South Australia);
2. neonates and children 5 years and under who will be travelling or living in countries or areas with a high prevalence of TB for extended periods;
3. neonates born to parents with leprosy or a family history of leprosy;

In addition to these recommendations BCG may be considered in the following:

4. children over 5 years who will be travelling or living in countries or areas with a high prevalence of TB for extended periods;
5. HCWs who may be at high risk of exposure to drug resistant cases.

Introduction

Mass BCG vaccination in populations with a low prevalence of tuberculosis disease is no longer considered necessary.[1] Rather, such an intervention should be directed at well -defined, high-risk groups principally because of its direct effect in reducing the serious consequences from primary infection. The indirect population effect of mass vaccination in terms of reducing the number of infectious cases and hence limiting future transmission to the uninfected population is considered minimal in low prevalence countries.[2]

In Australia, the broad-based BCG vaccination program originated at a time when the epidemiological circumstances of tuberculosis (TB) were quite different. Initially in 1948, vaccination targeted health workers, Aboriginal people and close contacts of active cases, especially children. In the 1950s the program was expanded to include all Australian school children except those from New South Wales and the Australian Capital Territory. This policy was discontinued in the mid-1980s (1991 in the Northern Territory) in favour of a more selective approach. The change occurred because of the low prevalence of TB in our community and concerns about the balance between the benefits and the risks.

Sweden, which prior to 1975 vaccinated all newborns, is one of the few countries to have closely studied the implications of this. The observed incidence of TB in unvaccinated Swedish children from a low risk background remains low, and importantly, the risk of serious TB is still rare.[3]

Further, the similarities in TB disease trends between Australia and countries where universal BCG vaccination has never been practised (USA, Netherlands) suggest that the incidence of TB in a community is determined by the combined effect of all TB control measures rather than BCG vaccination alone.

BCG vaccination does not prevent the transmission of infection to an individual. Its direct effect for which it was introduced appears to be in limiting the spread of primary infection in an infected individual. Varying reports suggest levels of protection anywhere from 0 to 80 per cent.[4,5,6,7] The differences possibly relate to use of different BCG strains, methodological factors, the influence of environmental mycobacteria and age, immune or genetic factors.[8]

Recent meta-analyses have been helpful in summarising the variable findings from several studies on BCG efficacy. The key conclusions were that it is about 50 per cent effective in preventing disease and that the most important protective benefits are in minimising the risk of death, meningitis and miliary disease in neonates and young children.[9,10]

Although the use of BCG in health workers has waned considerably there has been renewed interest related to multi-drug resistant TB.[7] The benefit of BCG vaccination over TST screening may be enhanced for the health worker in such a setting.[11,12,13] It offers some protection irrespective of drug susceptibility status, whereas the benefit of preventive therapy is unproven in those infected with an MDR strain.[14,15] This dilemma highlights the importance of appropriate infection control measures in health care settings.

Risk groups

For the majority of Australian born now, the risk of acquiring TB infection and developing disease is very low. However certain groups in our community are considered at increased risk.[16–18]

The National Health and Medical Research Council (NHMRC) consensus statement has defined high risk as referring to those subgroups of the population who have an annual notification rate above 25 cases per 100,000 population.[19] This provides a useful criterion for determining groups who may benefit from a BCG policy.

The following groups have been assessed as falling into the high-risk category but significant debate continues as to how extensive BCG vaccination programs should be within them.

Aboriginals

Aboriginal people are at greater risk for developing active TB than non-Aboriginal Australian born and this likely reflects socioeconomic, nutritional and health factors.[20–22] While the number of cases of active TB recorded is small, their rate of disease is estimated to be about 15–20 times higher than for the non-Aboriginal Australian born.[16–18] The rate appears to be higher in the rural and traditional communities compared to the urban groups.

The recommendation that at risk Aboriginal neonates be BCG vaccinated shortly after birth is based on the premise that in high risk populations, infants and children have a greater potential for exposure to an active case of tuberculosis. Infection in this age group has a significantly higher risk for producing the severe manifestations of TB, including meningitis, rapid dissemination and death.

Migrants

The most important factor contributing to the change in the epidemiology of TB in Australia has been the increased migration from countries with a high incidence of TB. Their rates of TB remain similar to those of their country of origin, particularly in the first 5 years after arrival.[16–18]

The rate of TB in children, particularly those aged less than 5 years, is an important indicator of TB control. The overall rates of TB for non-Indigenous children born in Australia remain very low. While the rates are higher in overseas-born children the actual numbers reported are small.[16–18] Further, data from Australian prevalence surveys indicate that the rate of TB infection in children born in Australia of overseas-born parents is as low as that of children of Australian-born parents.[23–26]

Hence it is now recommended that BCG vaccination in neonates and infants of migrant parents should be based on a careful assessment of the individual situation.

Health care workers

Health care workers are at variable risk of being exposed to patients with active TB. This will be dependent on the specific occupation and likelihood of contact with certain groups.

Two strategies have been advocated to control TB in HCWs. Namely, BCG vaccination or regular tuberculin skin testing (TST) and the use of preventive therapy in ‘converters’. The role of BCG vaccination in HCWs is unclear and the uncertainty has led to divergent policies in the States and Territories and overseas. The main issues are the lack of evidence

supporting a protective benefit from BCG in the adult and the fact that it renders future interpretation of the post-exposure TST imprecise.[7]

The TST policy is theoretically sound but weakened by the reluctance of many HCWs to comply with the recommended measures. Further, with the emergence of multi-drug resistant disease, the benefit of preventive treatment for infected contacts is uncertain.[14,15] Although the number of cases reported to date in Australia is small, multi-drug resistant TB is nevertheless a major concern because of the poor cure rate, high mortality and potential implications for exposed HCWs.

In addition, irrespective of the HCW strategy, it is important to ensure that both the individual and the institution in which they are working are adequately informed about TB and that appropriate infection control measures are in place to minimise the risk of transmission.

HCWs who are at significant risk of exposure to TB cases or potentially infected laboratory material should be recommended to have regular TST screening. This includes:

- medical and nursing staff working in Respiratory Units and at Chest Clinics;
- bronchoscopy theatre staff;
- laboratory personnel involved in handling tuberculous material; and
- staff involved in post-mortems.

BCG should not be recommended as the primary means of HCW protection. The use of BCG vaccination should be assessed according to individual circumstances. It should be considered in those who may be at high risk of exposure to drug resistant cases e.g. the HCW moving to an overseas country to work in an area with a known or suspected drug resistance problem.

The use of BCG vaccination for HCWs in low risk settings is not recommended.

Overseas travel

The number of cases of TB reported in Australians who have travelled or lived overseas for significant periods is small.

Vaccination is not considered necessary in those undertaking brief holidays to well known tourist destinations. However in neonates and children 5 years and under who will be staying in countries where the incidence of TB is high for extended periods, vaccination is recommended. Each individual's situation needs to be carefully assessed. The protective benefit of vaccination in older age groups is less certain.[7] BCG should be given 2 to 3 months prior to departure.

Other groups

There are additional groups in our community based on overseas experience that may be at increased risk of TB and these include the homeless, prison residents and injecting drug users. BCG vaccination is not recommended for these persons.

Recommendations

BCG vaccination is not recommended for general use in the Australian population based on the low incidence of tuberculosis.

BCG is recommended for:

1. Aboriginal neonates in areas of high incidence of TB (e.g. the Northern Territory, Far North Queensland, northern areas of Western Australia and South Australia);
2. neonates and children 5 years and under who will be travelling or living in countries or areas with a high prevalence of TB for extended periods;
3. neonates born to parents with leprosy or a family history of leprosy;

In addition to these recommendations BCG may be considered in the following:

4. children over 5 years who will be travelling or living in countries or areas with a high prevalence of TB for extended periods;
5. HCWs who may be at high risk of exposure to drug resistant cases.

State and Territory TB Control Units should be consulted with regard to their BCG vaccination guidelines.

Important notes

All individuals should be tuberculin skin-tested prior to BCG vaccination except in infants less than 6 months of age where a history of TB contact has been excluded.

BCG should not be given to an individual with a tuberculin reading of 5 mm or more.

BCG vaccine should not be administered unless consent has been obtained following a full explanation of the benefits and risks associated with the vaccination.

No more than one BCG is to be given, regardless of TST reaction.

Contraindications

The use of BCG vaccine is contraindicated in the following:

- persons immuno-compromised by HIV infection, corticosteroids or other immuno-suppressive agents and malignancies involving bone marrow or lymphoid systems (because of the risk of disseminated BCG infection);
- individuals with a high risk of HIV infection where HIV antibody status is unknown;
- individuals with any serious illness including the malnourished;
- individuals with generalised septic skin diseases and skin conditions such as eczema, dermatitis and psoriasis;
- pregnant women—BCG has not been shown to cause foetal damage but the use of a live vaccine in pregnancy is generally contraindicated;
- individuals who have previously had tuberculosis or a large tuberculin (Mantoux) reaction.

BCG should be deferred in the following:

- individuals with a significant febrile illness (administer 1 month from the time of recovery);
- neonates with a birth weight less than 2.5 kg or in those who may be relatively undernourished. It should not be offered to neonates of mothers who are HIV positive;
- a 4 week interval should be allowed following administration of another live vaccine unless given concurrently e.g. MMR, yellow fever (although there is no evidence that the immune response could be impaired).

NB: Care should be taken in those with a history of keloid scarring or an increased risk of developing it e.g. Aboriginals, Melanesians. The likelihood of this occurring can be minimised if the injection is given into the skin over the region of the deltoid muscle insertion.

It is recommended that a list of exclusion criteria be given to the patient to allow self-exclusion with complete anonymity regarding the specific risk factor.

Vaccination

The vaccine

- The BCG (Bacille Calmette-Guérin) vaccine[1] is a suspension of living organisms of an attenuated strain of *Mycobacterium bovis*. It is available as a freeze-dried powder for intradermal use in a 10-dose vial and should be stored at 2–8° C with protection from light. Exposure to heat and light both before and after reconstitution may result in a loss of potency. The expiry date should be checked prior to administration.
- The vaccine is reconstituted using 1.5 ml of the sterile saline supplied. It should be gently and thoroughly mixed then used strictly within a 4–6 hour period. Store at 2–8° C.
- As the vaccine does not contain a bacteriostatic agent, extreme care is required to avoid contamination. A new 26–27-gauge needle and 1 ml syringe should be used for each dose and the remaining vaccine discarded as per procedures recommended for biohazardous substances.
- Providing a strictly aseptic technique is adhered to in accordance with approved infection control guidelines, the use of a multi-dose vial is an accepted practice.

Vaccination procedure

The NHMRC recommends that administration of the BCG vaccine be carried out by an accredited health-worker to limit the risk of adverse events.

The BCG dose is:

- Adults and children over 12 months – 0.1 ml
- Infants 12 months and under – 0.05 ml

Vaccination should be deferred in premature or small-for-dates babies less than 2.5 kg.

- A tuberculin skin test (Mantoux) should be done prior to vaccination except in infants less than 6 months (exclude history of TB contact). BCG can be administered to those with a reaction size less than 5 mm providing no contraindications exist.

1 The manufacture of BCG vaccine in Australia has been discontinued. The Aventis Pasteur BCG vaccine (Toronto, Ontario, Canada) has been approved for use by the Therapeutic Goods Administration and is distributed by CSL Limited (Parkville, Victoria).

- The site of injection into the skin is very important in order to minimise the risk of keloid formation. The position normally recommended is at the level of insertion of the deltoid muscle into the humerus. While it can be given into the middle third of the antero-lateral aspect of the thigh, many prefer not to for cosmetic reasons.
- The injection must be given strictly intradermally—needle bevel uppermost, until its opening is just visible through the epidermis.
- A blanched weal should be raised. If little resistance is felt, then this may mean that the needle is in the subcutaneous tissue and therefore should be withdrawn. The injection should then be given at an alternative site. Inadvertent subcutaneous injection is likely to cause an excessive reaction.

BCG reaction

Initially a small red papule forms within a 2–3 week period followed by softening and ulceration. Healing usually occurs after several weeks with a resultant small scar. An accelerated reaction begins within 24–48 hours with induration followed by pustule formation in 5–7 days and healing within 10–15 days.

BCG aftercare

Information both verbal and written should be provided to the vaccinee or carer on what to expect and how to care for the resultant local reaction. The importance of reporting promptly any suspected problems should be stressed.

Adverse effects

Serious complications from BCG vaccination including anaphylactoid reactions are rare.[27–29]

Adverse effects include:

- regional lymphadenitis – this is the commonest adverse reaction;
- subcutaneous abscess;
- accelerated local reactions;
- osteitis;
- keloid scarring;
- disseminated infection.

Correct assessment and technique is essential to minimise these risks.

Immuno-compromised individuals can develop disseminated infection from BCG, e.g. malnourished children and the HIV positive person.

Reactions of an untoward nature may require antituberculous treatment.

Adverse events following vaccination should be notified to the relevant State Health Authority.

BCG revaccination

In many developing countries systematic revaccination has been accepted practice because of doubts about the persistence capacity of the vaccine when given in the early neonatal period.[30] However, such an approach is not supported by scientific evidence.

The effectiveness of repeat BCG to the individual remains in question.[31,32,33] Previously, the finding of a negative tuberculin skin test response was considered to indicate the need for revaccination. It was argued that revaccination may increase the rate of tuberculin conversion and result in more sustained reactivity over time. However the tuberculin response is not a correlate of the protective benefit derived from BCG vaccination and there is no evidence that a waning of tuberculin sensitivity with time equates to a loss of TB specific immunity.[7, 34]

Based on the information available, BCG revaccination is not recommended in any person.[34]

BCG alternative

BCG remains the only available vaccine against TB. However it only offers partial and variable protection to the uninfected for a relatively short period.

Several new vaccine candidates are under investigation. These include recombinant vaccines, sub-unit vaccines and DNA-based vaccines. Novel adjuvants are also currently being tested with experimental sub-unit vaccines.[35–37] The improved safety of the latter over live-attenuated vaccines offers potential benefit to HIV- infected persons.

The relatively short-lived efficacy of BCG for only 10–20 years appears accepted.[38] A vaccine that both has the ability to boost immunity in those vaccinated in childhood to protect against the risk from primary infection or if already infected prevent reactivation of latent infection would be a substantial advance in the control of TB globally. Despite significant ongoing research the prospect of such a vaccine remains distant.[37]

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