Policy and guidelines

The BCG vaccine: information and recommendations for use in Australia

National Tuberculosis Advisory Committee Update October 2012

Summary points

The *BCG vaccine: information and recommendations for use in Australia* (March 2006) has been updated to incorporate the most recent trends in annual national tuberculosis (TB) surveillance data.

Australia continues to meet international epidemiological criteria that limit Bacille Calmette Guérin (BCG) vaccination to selected high risk groups in countries with a low incidence of TB.

No significant change has been made to existing recommendations for BCG vaccination in Australia.

Key recommendations

BCG vaccination is not recommended for general use in the Australian population or for most health care workers (HCWs).

BCG vaccination is contraindicated in HIV infected persons.

BCG vaccination is recommended for:

1. Aboriginal and Torres Strait Islander neonates in communities with a high incidence of TB;
2. Neonates and children 5 years of age and under who will be travelling to 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.

BCG vaccination may be considered in the following:

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

State and territory TB control units should be consulted with regard to their BCG vaccination guidelines.

Executive summary

This report provides an update on the role of Bacille Calmette Guérin (BCG) vaccination in tuberculosis (TB) control and prevention in Australia. While no significant change has been made to current recommendations it was considered important to review the 2006 document in the context of the ongoing epidemiological situation and concerns about benefit versus risk.

Annual TB surveillance data for Australia in the past decade confirm ongoing low rates of disease in the general population. Most disease (80%–90%) is limited to people from high prevalence countries. In the Australian-born population, rates remain very low, particularly in children less than 5 years of age, who are an important marker of good TB control. While TB rates are higher in some Aboriginal and Torres Strait Islander communities than for non-Indigenous Australian-born people, actual case numbers are still small. Drug resistant TB is being carefully monitored based on international concerns, but the rate remains low with cases predominantly 'imported'. The impact on disease rates from HIV infection remains minimal.

The control of TB in all countries primarily relies on early detection and treatment of infectious cases to minimise transmission to the community. In Australia, this is supported by the secondary strategy of targeting those most at risk from latent TB infection for preventive therapy. BCG vaccination has a very limited role in the control and prevention of TB in low prevalence settings. Its use is limited to neonates and infants considered at high risk of exposure to TB for whom access to early detection and treatment of TB is potentially problematic. The benefit of vaccination in older age groups is less clear and it is no longer recommended as a routine measure in most health care workers (HCWs).

The National TB Advisory Committee recognises the different BCG vaccination policies that exist within and between countries and this reflects the controversial history of BCG vaccine in terms of its effectiveness. The advice provided aims to enhance uniformity between the states and territories based on the best available evidence and guiding principles for the use of BCG vaccine in low prevalence countries.

Introduction

Mass BCG vaccination in populations with a low prevalence of tuberculosis 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 to be minimal in low prevalence countries.[2]

In Australia, the broad-based BCG vaccination program originated at a time when the epidemiology of TB was quite different. Initially in 1948, vaccination targeted health care 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.

Prior to 1975, Sweden vaccinated all newborns and is one of the few countries to have closely studied the implications of this policy. TB notification data from 1975 to 2004 indicate that 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.[3,4]

Further, the similarities in TB disease trends between Australia and countries where universal BCG vaccination has never been practised (United States of America, Netherlands)[5] 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 TB to an individual. The direct effect of the vaccine (for which it was introduced) appears to be in limiting the spread of primary infection from an infected individual. Varying reports suggest levels of protection anywhere from 0% to 80%.[6–9] The differences possibly relate to the use of different BCG vaccine strains, methodological factors, the influence of environmental mycobacteria and age, and immune or genetic factors.[10]

Two meta-analyses have been helpful in summarising the variable findings from several studies on BCG vaccine efficacy.[11,12] The key conclusions were that it is about 50% effective in preventing TB disease and that the most important protective benefits are in minimising the risk of death, meningitis and disseminated disease in neonates and young children.

Although the use of BCG vaccine in health workers has declined considerably, there has been renewed interest related to multi-drug resistant (MDR) TB.[9] The benefit of BCG vaccination over tuberculin skin testing (TST) screening may be enhanced for the health worker in such a setting.[13–15] It offers some protection irrespective of antimicrobial susceptibility of the infecting organism, whereas the benefit of preventive therapy is unproven in those infected with an MDR strain.[16,17] This dilemma highlights the importance of appropriate infection control measures in health care settings.

Epidemiology

The annual incidence of TB in Australia has remained relatively stable since the mid-1980s. From 2005 to 2009 there was little change, with rates between 5.28 and 5.95 cases per 100,000 population.[18] These low rates have been maintained despite the increased level of immigration from high TB burden countries.

Overseas-born persons account for approximately 85% of notifications in Australia. Over the last decade overall incidence rates in this group have increased from 15.5 to 21.0 per 100,000. By contrast, the overall rate in Australian-born people is approximately 1 per 100,000. In 2008, the rate for Aboriginal and

Torres Strait Islander peoples was 5.9 per 100,000 with the highest rates detected in the Northern Territory (25 per 100,000) and Queensland (6.2 per 100,000). However, case numbers are low.[18]

Review of data from 2005 to 2009 shows that pulmonary cases represented an average of 57% of all cases. Sputum microscopy positive cases, which are the main source of transmission in a community, accounted for 22.8% (expected 40%–60%) of the total pulmonary cases.[18] Even if this is an underestimate due to notification factors, the rate is still very low at approximately 1 per 100,000.

Children under 5 years of age are a key indicator of the level of transmission of infection in the community. From 2005 to 2009 the proportion of cases in this age group was an average of 1.8% of the total compared with 1.97% in the preceding 5 years. The rate remains steady at about 1 per million. Of the serious forms of TB in this age group, for the same period there were only 5 cases of TB meningitis notified in Australia, equivalent to less than 1 per 20 million general population per year.[18]

These outcomes meet the International Union Against TB and Lung Disease (IUATLD) criteria for low prevalence countries, in determining BCG policy, which are:

- average annual notification rate of pulmonary sputum smear positive cases of 5 per 100,000 or less in the preceding 3 years; or
- average annual notification rate of TB meningitis in children under 5 years of less than 1 case per 10 million general population; or
- an average annual risk of TB infection of 0.1% or less.[1]

Risk groups

Significant debate continues on the role of BCG vaccination within certain groups that are classified as high risk. The Canadian and United States of America guidelines recommend that the use of BCG vaccine be limited to neonates and infants considered at high risk of exposure to TB, in whom access to early detection and treatment of TB infection is problematic, or where TB control efforts have had limited impact.[9,19] A recent Dutch study highlighted the high numbers of neonates in a low prevalence setting who would need to be vaccinated to prevent one case, and safety data in Canadian First Nations Children cautioned that the risk of BCG disseminated infection should be carefully considered.[19,20]

Aboriginal and Torres Strait Islander peoples

Aboriginal and Torres Strait Islander peoples from some communities are at greater risk of developing active TB than non-Indigenous Australian-born people. This likely reflects socioeconomic, nutritional and health factors.[21–23] Rates of TB in Aboriginal and Torres Strait Islander peoples remain higher than in non-Indigenous Australians but these rates have decreased and are not uniform. In 2007 there were only 35 notifications of TB in Ingidenous Australians, 60% of these being from the Northern Territory and 20% from Queensland.[18]

The recommendation that at-risk Aboriginal and Torres Strait Islander neonates be vaccinated with BCG 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 TB. Infection in this age group has a significantly higher risk for producing severe manifestations of TB, including meningitis, rapid dissemination and death. However with such low numbers, the safety of BCG vaccine is a key consideration. Data from vaccinated Canadian First Nations children suggest that they are at higher risk of disseminated BCG infection than children elsewhere, in turn suggesting that they may be less immunocompetent.[19] This risk needs to be carefully considered in the BCG vaccination of Aboriginal and Torres Strait Islander neonates from communities deemed to be at high risk of infection.

Migrants

The most important factor contributing to the epidemiology of TB in Australia has been the increased migration from countries with a high incidence of TB. Rates of TB in these people remain similar to those of their country of origin, particularly in the first 5 years after arrival.[24]

The overall rate of TB for non-Indigenous children born in Australia remains very low. While the rates are higher in overseas-born children the actual numbers reported are small.[18] Further, data from Australian prevalence surveys indicate that the rate of TB infection in children born in Australia to overseas-born parents is as low as that of children of Australian-born parents.[25–28]

Hence, BCG vaccination is not routinely recommended in neonates and infants of migrant parents but rather should be based on a careful assessment of the individual situation. For example, neonates of parents from high incidence countries staying for extended periods in their parents' country of origin should be considered for BCG vaccination. The optimal approach is to advise a TST after such travel if household exposure is suspected or known

and recommend preventive treatment as appropriate. If close contact with an infectious case did occur, current World Health Organization policy recommends the use of preventive therapy in those less than 5 years of age, even if vaccinated.[29]

Health care workers

HCWs in Australia are at low risk of being exposed to patients with active TB. As such, the use of BCG vaccination for HCWs is no longer recommended as the primary means of protection.

The role of BCG vaccination in HCWs is unclear and the uncertainty has led to divergent policies in the Australian states and territories and overseas. The main issues are the lack of evidence supporting a protective benefit from BCG in adults and the fact that it renders future interpretation of the post-exposure TST imprecise.[9]

For most HCWs, BCG vaccination is not indicated but should be considered in those who may be at high risk of exposure to drug resistant organisms, e.g. the HCW moving to an overseas country to work in an area with a known or suspected drug resistance problem.

The preferred strategy advocated to control TB in HCWs is TST to identify new infection and the use of preventive therapy.

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 resistance, the benefit of preventive treatment for infected contacts is uncertain.[16,17] Although the number of cases reported to date in Australia is small, multi-drug resistant TB is nevertheless a major concern because of the lower cure rate, higher mortality and potential implications for exposed HCWs.

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.

Overseas travel

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

Vaccination is not considered necessary for those undertaking brief holidays to well known tourist destinations. However, for neonates and children 5 years of age and under who will be staying for an extended period in countries where the incidence of TB is high, vaccination is recommended. Each individual's situation needs to be carefully assessed. The protective benefit of vaccination in older age groups is less certain.[9] BCG should be given 2 to 3 months prior to departure.

Other groups

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

Although BCG vaccine is considered a TB vaccine, it may also be effective against leprosy and is still recommended in some countries for neonates of leprosy patients.[10,30] In Australia, occasional cases of leprosy are reported, mainly in migrants from leprosy endemic countries but also sporadically in Indigenous communities.[31]

Recommendations

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

BCG vaccination is contraindicated in HIV infected persons.

BCG is recommended for:

1. Aboriginal and Torres Strait Islander neonates in communities with a high incidence of TB;
2. Neonates and children 5 years of age and under who will be travelling to or living in countries or areas with a high prevalence of TB for extended periods; and
3. Neonates born to parents with leprosy or a family history of leprosy.

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

1. Children over 5 years of age who will be travelling to or living in countries or areas with a high prevalence of TB for extended periods; and
2. 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 have a TST prior to BCG vaccination except infants less than 6 months of age with no history of TB contact.

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 vaccination.

BCG revaccination is not recommended, regardless of TST reaction (TST reaction size is not a correlate of BCG vaccine efficacy).

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 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; and
- individuals who have previously had tuberculosis or a large tuberculin (TST) reaction.

BCG vaccination should be deferred for 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;
- individuals with a high risk of HIV infection until HIV infection is excluded; and
- a 4 week interval should be allowed following administration of another live parenteral (injectable) vaccine unless given concurrently e.g. measles-mumps-rubella, yellow fever, varicella. There are no restrictions on the timing of BCG vaccine in relation to oral live vaccines, e.g. rotavirus, oral typhoid vaccines.

NB: Care should be taken in those with a history of keloid scarring or an increased risk of developing it e.g. Aboriginal and Torres Strait Islander peoples, and 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

BCG vaccine

- BCG vaccine* 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 100-dose vial and should be stored at 2°C to 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.
- BCG vaccine is reconstituted using 1.0 ml of the Diluted Sauton SSI (solvent) supplied. It should be gently and thoroughly mixed then used strictly within a 4–6 hour period. Store at 2°C–8°C.
- As BCG 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.

BCG vaccination procedure

The National Health and Medical Research Council recommends that administration of BCG vaccine be carried out by an accredited health care 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 TST should be done prior to vaccination except in infants less than 6 months (exclude history of

* The manufacture of BCG vaccine in Australia has been discontinued. The Sanofi Pasteur BCG vaccine (Toronto, Ontario, Canada) has been approved for use in Australia by the Therapeutic Goods Administration, however, was recalled in June 2012. Sanofi Pasteur is supplying BCG vaccine SSI, manutactured by Statens Serum Institut in Denmark, as a substitute. Product information provided above relates to BCG vaccine SSI. The indication and dosage of the BCG vaccine. Supply of the Sanofi Pasteur BCG vaccine is expected to resume by early 2014.

TB contact). BCG can be administered to those with a reaction size less than 5 mm providing no contraindications exist.

- 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 vaccination 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 vaccination aftercare

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

Adverse effects

Serious complications from BCG vaccination including anaphylactoid reactions are rare.[32–34]

Adverse effects include:

- regional lymphadenitis – this is the most common adverse reaction;
- subcutaneous abscess;
- accelerated local reactions;
- osteitis;
- keloid scarring; and
- 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 HIV positive persons.

Some adverse reactions may require anti-tuberculous 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.[35] However, such an approach is not supported by scientific evidence.

The effectiveness of repeat BCG to the individual remains in question.[36–38] Previously, the finding of a negative TST 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.[9,39]

Based on the information available, BCG revaccination is not recommended for any person.[39]

BCG vaccine alternative

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

Several new vaccine candidates (pre and post exposure) are under investigation. These include recombinant vaccines, sub-unit vaccines and DNA-based vaccines. Novel T-cell adjuvants are also being tested with experimental sub-unit vaccines.[38–42] The improved safety of the latter over live-attenuated vaccines offers a potential benefit to HIV-infected persons.

The relatively short-lived efficacy of BCG for only 10–20 years appears accepted.[43] 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.

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Recommended composition of the northern hemisphere influenza vaccine for the 2013-14 season

On 21 February 2013, the World Health Organization (WHO) recommended that vaccines for the 2013-14 northern hemisphere influenza season contain the following:

A (H1N1): an A/California/7/2009 - like virus.

A (H3N2): a virus antigenically like the cell-propagated prototype virus A/Victoria/361/2011. It is recommended that A/Texas/50/2012 is used as the A(H3N2) vaccine component because of antigenic changes in earlier A/Victoria/361/2011-like vaccine viruses resulting from adaptation to propagation in eggs.

B: a B/Massachusetts/2/2012 - like virus (Yamagata lineage)

It is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses plus a B/Brisbane/60/2008-like virus (Victoria lineage).

For further information please see the WHO web site.

The composition of the Australian 2013 influenza vaccine was announced in October 2012. For further information please see the TGA web site.