

# Quiz

## Immunization and BCG

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### ● What is immunization?

A. Immunization is the process of increasing specific antibodies in the tissues.

### ● What is active immunization?

Active immunization is the process by which bacterial or viral antigens are introduced into the subject in order to stimulate the individual's own tissues to produce antibodies and immunologically competent lymphocytes<sup>(1)</sup>.

### ● What is passive immunization?

Passive immunization is the process by which preformed antibodies derived from human or animal sera are injected into the individual providing instant umbrella of protection against the disease. The immunity obtained through passive immunization is short-lived<sup>(1)</sup>.

### ● A Woman of Child Bearing Age (CBA) has received primary series of immunization, How many doses of tetanus toxoid (TT) should be given.

The Primary series of immunization should be counted as having received two doses. She should then be given 3 additional doses of TT, at 0, 1, 6 months<sup>(2)</sup>.

### ● What are the recommendations for children who have missed their subsequent doses of vaccines?

The doses should not be repeated and the schedule should not be interrupted<sup>(3)</sup>.

### ● What is the route of administration of BCG?

The recommended route of administration is intradermal<sup>(4)</sup>.

### ● What is the dose of BCG?

0.05 ml for infants less than one year old and 0.1 ml for older children and adults<sup>(4)</sup>.

### ● Earlier dosage recommendation was 0.1 ml irrespective of age. Does the reduction in the dose have any effect on the immune response to the vaccine?

Data gathered from numerous studies has not demonstrated reduced immune response to reduced dose of the vaccine. In fact the local adverse reaction to the vaccine has declined in infants receiving lower dose<sup>(5)</sup>.

### ● What is the site of BCG Inoculation?

BCG should be given on outer left arm or shoulder<sup>(4)</sup>.

### ● At what temperature is BCG vaccine stored?

It is stored between +2 C and +8 C (4). At temperature it maintains adequate potency for 24 months.

### ● After reconstituting the BCG vaccine, how soon should it be used?

Once the vaccine has been reconstituted, any remaining reconstituted vaccine must be discarded after 6 hours or at the end of the immunization

session, whichever comes first<sup>(4)</sup>.

### ● What is the normal course of a BCG lesion?

Immediately after the injection, a wheal is formed which disappears in about an hour. Two to three weeks later a small indurate, slightly tender nodule forms and grows slowly during the following week. In most cases the nodule becomes a small superficial pustule which ulcerates and then rapidly crusts.

This crust separates and leaves a small scar. This whole process is completed in 3 months. Leave the ulcer untreated. A porous dressing may be applied if there is a profuse discharge. In some children, instead of a scar, there is a nodule<sup>(6)</sup>.

Wheal----Papule----Pustule----Ulcer-----Crust-----Scar  
←----- 3 months -----→

### ● If a child has tuberculous infection and he received BCG vaccine, what will be the course of the BCG lesion?

In a child suffering from tuberculous infection (past exposure or disease) the course of BCG lesion is accelerated. Papule with induration takes place within 24 to 28 hours, pustule is formed by 5 to 7 days, and scab by 10 to 12 days. This acceleration of the whole BCG reaction occurs even in malnourished children<sup>(7)</sup>. This signifies pre-existing immunity and is known as Koch's phenomenon. If there is an accelerated response, then one should look for other signs and symptoms to exclude the possibility of active tuberculosis.

### ● If BCG Vaccine is given to a person with active tuberculosis, will he/she be harmed by the Vaccine?

Since the vaccine is attenuated and the dose is very small no harm will be done. It does not produce any adverse reaction. There may be an accelerated response at the site of BCG inoculation (Koch's phenomenon)<sup>(6)</sup>.

### ● If BCG vaccine is given to a person with healed tuberculous lesion, will the healed lesion flare up?

Several years ago there were concerns that in such cases the tuberculous lesion may flare up but this concern is not supported by data<sup>(7)</sup>.

### ● What will happen if a tuberculin positive person receives BCG Vaccine?

If a positive reactor is vaccinated, there is an accelerated response with an ulcer at the injection site after only 3 days, lasting about 3 weeks. There is no evidence that this is detrimental to health<sup>(7)</sup>.

### ● What is the ideal age for giving BCG?

At or as soon as possible after birth<sup>(4)</sup>.

## Efficacy of Vaccine and Immunity

### What is the efficacy of BCG vaccine?

BCG is one of the oldest vaccines in use. It was first used in humans in 1921<sup>(9)</sup>. Proper evaluation of its safety and efficacy began in 1930s. Several controlled population-based trials have been carried out. In 8 such trials carried out since then, the protective efficacy against pulmonary tuberculosis has ranged from 0 to 80% (see table). However it provides almost complete protection against miliary tuberculosis and tuberculous meningitis<sup>(8,9)</sup>.

### ● Does BCG vaccine provide any protection against leprosy?

Yes, BCG does protect against leprosy. In controlled trails in four population's efficacy ranged from 20% to 80%<sup>(10)</sup>.

### ● What is the correlation of tuberculin sensitivity and protective effect of BCG Vaccine?

The use of tuberculin testing is recommended for testing delayed type hypersensitivity (DTH) reaction to the vaccine, but this has also been questioned by several workers on the basis of data from population based studies. Fine on the basis on several studies conclude that "the data for human populations have shown no evidence of a relationship between (DTH) and protection"<sup>(10)</sup>. One the basis of MRC trail Hart conclude that "with highly effective tuberculous vaccines, the degree of protection conferred on the individual is independent of the degree of tuberculin skin test sensitivity induces in that individual by the vaccination" Comstock has also concluded that "the lack of correlation is obvious and underscores the futility of predicting potency from conversion rates"<sup>(11)</sup>. However, tuberculin testing is still recommended for determining the DTH reaction to vaccine till improved alternative is available.

### ● What is the period of protection with BCG?

Duration of protection conferred by the vaccine is a matter of dispute. Results from several studies suggest that the protective effect lasts for 7 to 12 years<sup>(12)</sup>.

### ● Should BCG booster be recommended?

It is still a matter of debate whether booster doses are indicated or advisable<sup>(12)</sup>. Currently WHO-EPI does not recommend BCG booster dose<sup>(4)</sup>.

## Indications

### ● What are the indications for BCG Vaccination?

The indications for BCG Vaccination are<sup>(7,8,9)</sup>:  
 Infants and children in countries with high prevalence of tuberculosis, b) tuberculin negative individuals at high risk of repeated exposures to infective cases of tuberculosis, e.g. medical students, nurses, paramedical staff, doctors, etc. c) close contacts of persons with tuberculosis, d) individuals exposed to multiple drug resistant cases of tuberculosis.

## Contraindications:

### ● What are the contraindications for BCG vaccination?

The contraindications of BCG vaccination are patients<sup>(7,8,13,14)</sup>

a) with congenital disorders of immune function, b) with cellular or combined immunodeficiency's e.g. or

suspected cases of agammaglobulinemia, thymic aplasia, c) with extensive skin infections or burns, d) who have symptomatic HIV infection, e) on immunosuppressive therapy) on high dose corticosteroids.

### ● Can BCG be given to pregnant women?

Pregnancy is not an absolute contraindication for BCG vaccination. No untoward effects of BCG have been observed on fetus. However it would be prudent to defer immunization until pregnancy is over, unless there is immediate excessive risk of exposure, and the mother is tuberculin negative<sup>(8)</sup>.

### ● Is malnutrition a contraindication for BCG Vaccination?

Malnutrition is not contraindication; In fact malnourished children are more susceptible to tuberculosis<sup>(8,15)</sup>.

### ● Is there any correlation between malnutrition and a positive tuberculin reaction in malnourished children?

There is no significant correlation between nutritional status at the time of BCG vaccination and the development of positive tuberculin reaction five weeks later<sup>(8,15)</sup>.

### ● Is tuberculin positivity a contraindication to BCG vaccine?

Tuberculin positivity is not, per se a contraindication<sup>(7)</sup> however; tuberculin positivity is due to delayed type of hypersensitivity - an indicator of exposure to tuberculosis. Therefore in tuberculin positive individuals BCG is not required.

## Adverse reaction:

### ● What are the complications of BCG vaccine?

Following complications are described<sup>(8)</sup>.

- Koch's Phenomenon
- Erythema nodosum: Occasionally occurs after 4 to 6 weeks of vaccination,
- Deep abscess at the vaccination site.
- Excessive ulceration at the injection site.
- Lymph node enlargement and lymphadenitis.
- Osteomyelitis
- Disseminated tuberculosis due to BCG strain.
- Anaphylactoid reaction.

Koch's incidence and erythema nodosum are of no significance. Other complications are discussed below.

The incidence of complications varies depending on the vaccine dosage, age of the vaccines, strain of vaccine and the route and method of administration. The development of subcutaneous abscesses and regional adenitis after BCG administration is a relatively common complication. Local ulceration and regional supportive lymphadenitis are reported with a frequency of 0.1 to 5 per 1000 infants in different countries<sup>(7)</sup>. WHO literature reports that 0.1 to 4% of children under age 2 years develop lymph node enlargement leading to ulceration<sup>(4,7,8)</sup>. During the 1970s osteomyelitis due to BCG was being reported with an incidence of 5 per 100,000 in Finland and Sweden<sup>(16)</sup>. In Finland the incidence of BCG osteitis declined from 1978 to 1981 when a different BCG product was introduced<sup>(17)</sup>.

Dissemination of injected organism is extremely rare. A total of 35 fatal and 31 non fatal cases of disseminated disease due to BCG strain have occurred <sup>(7)</sup>. Population reports citing various reference reports an incidence of 0.1 per 100,000 vaccinated individuals. It is now recognized that severe or partial defects of cell-mediated immunity account for such adverse reactions. However two cases of tuberculous meningitis due to BCG in two previously healthy children with no immune function defects have been reported <sup>(8)</sup>. However, in these cases there may have been undetected immune deficiencies. Anaphylactoid reaction to BCG is one of the rarest reported complications. Only 6 cases of anaphylactoid reaction to BCG have been so far reported in medical literature <sup>(8)</sup>. Such reaction is still a mystery and no explanation has been forwarded.

● **What does BCG Lymphadenitis usually become manifest, and which nodes are commonly involved?**

It is most commonly observed 2 to 8 weeks after BCG vaccination. Delay of the symptoms can occur for up to eight months. The axillary, supraclavicular and the cervical lymph nodes ipsilateral to the vaccination site are mainly involved in BCG lymphadenitis. Younger children are more frequently affected <sup>(8)</sup>.

● **Should BCG ulcers be treated?**

BCG ulcer generally does not require any treatment.

If there is secondary infection then treat with Neomycin ointment <sup>(8)</sup>.

● **If a woman with open pulmonary tuberculosis gives birth to a baby, what would you do?**

In the developing countries the recommendations are <sup>(8)</sup>.

- \* Do not separate the baby from the mother.
- \* Continue breast feeding the baby and observe good personal hygiene.
- \* Minimize contact of the baby with mother if there are other household members capable of taking care of the baby.
- \* Start treatment of the mother immediately.
- \* Give INH to the baby 10-15 mg per kg body weight for three months.
- \* Screen other household members for tuberculosis.
- \* Do a Mantoux test (MT) at 3 months age. If MT is negative give BCG vaccine to the baby.
- \* If the MT is positive:
  - \* 10 mm to 14 mm: suggestive of tuberculous infection correlate with clinical signs and symptoms and actively evaluate the case.
  - \* 15 mm and above: tuberculous infection has occurred, correlate with clinical sign and symptoms and actively evaluate the case, trail of antituberculous therapy may be initiated if clinical signs and symptoms are positive or equivocal and investigations do not reveal the disease or are equivocal.

Table: efficacy of BCG vaccine Summary of 8 large controlled trials

| Trail                                | Intake Period | Vaccine Lab       | Duration of observation in years | Prevalence of Environmental bacteria | %age protection from BCG |
|--------------------------------------|---------------|-------------------|----------------------------------|--------------------------------------|--------------------------|
| North American Indians               | 1935-38       | Phipps            | 9-11                             | Low                                  | 80                       |
| Chicago Infants                      | 1937-48       | Tice              | 12-23                            | Low                                  | 75                       |
| Britain School Children              | 1950-52       | Copenhagen        | 15                               | Low                                  | 78                       |
| Georgia School Children              | 1947          | Tice              | 20                               | High                                 | 0                        |
| Puerto Rico Children                 | 1949-51       | NY-State          | 5.5-7.5                          | High                                 | 31                       |
| Georgia Alabama population           | 1950          | Tice              | 14                               | High                                 | 14                       |
| Southern India rural population      | 1950-55       | Madras            | 2.5-7                            | High                                 | 60                       |
| Southern India Chingleput population | 1968-71       | Copenhagen Madras | 7.5                              | High                                 | 0                        |

Source: Bacille Calmette-Guerin (BCG) Vaccine. Eickhoff TC. Plotkin SA Mortimer EA Jr. eds. Vaccine. Philadelphia: W.B Saunders, 1988, Table 17-2 p 377

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