

North West Regional TB Group

Guidance on TB Pre-Employment Screening in new NHS Employees

Based on NICE TB Guidelines
In line with DOH Guidance on Health Clearance for new Healthcare Workers

August 2008

The Guideline Group

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Review date January 2011
(awaiting further national guidance before updating)

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1. Introduction

Across the region occupational health departments are developing their own pre-employment TB screening protocols. But the national guidance is complex and not always easy to implement.

This document aims to support occupational health in managing pre-employment TB screening. It aims to facilitate implementation of NICE recommendations [1] and DOH recommendations [2].

2. Pre - employment screening for new NHS employees

The protection of staff and patients begins with pre-employment screening. It includes the adoption of safe practices for patient care and methods of detecting infection in staff at an early stage.

All new employees who will have contact with patients or clinical specimens should have a pre-employment assessment that includes:

- Recording any history or symptoms of tuberculosis
- Family history of TB
- Risk factors for TB
- Documentary evidence of TB skin testing (or interferon-gamma testing) and previous BCG vaccination, noting the presence or absence of a BCG scar
- Mantoux skin test (or interferon-gamma testing), and chest radiography where indicated.

The information can be obtained by questionnaire.

A BCG scar check should be carried out by an occupational health professional, not relying on the employee's personal assessment.

All staff with suspicious symptoms should have a medical assessment and possible further tests/investigations to exclude active TB.

All new staff should be provided with information on TB symptoms and when to seek medical advice

2.1 NICE guidelines

The NICE TB guidelines [1] published in March 2006 recommend different screening procedures for employees recently arrived from areas where tuberculosis incidence rates are greater than 40 per 100,000 per year and employees from areas with incidence levels below this threshold. The former are classed as **new entrants** and have to undergo the same screening procedures as all other new entrants.

Up to date information on countries with TB incidence greater than 40 per 100,000 per year can be obtained from the HPA website
http://www.hpa.org.uk/infections/topics_az/tb/epidemiology/who_table1.htm

2.2 HCW from high incidence areas (new entrants)

New employees arriving from countries where the annual incidence of TB is greater than 40 in 100, 000 and who have not been screened on entry, in the district of residence, or by a previous employer in the United Kingdom (UK) within the last 12 months should be referred for chest radiography.

New entrants will require a Mantoux skin test (or interferon gamma test) irrespective of previous BCG vaccination.

The results of the Mantoux test should be interpreted in light of any previous BCG vaccination.

A Mantoux test result of 6mm or more in an employee with no previous BCG vaccination, or 15mm or more in an employee with previous BCG vaccination is a **positive** result.

A positive test should result in a referral for medical assessment to exclude active disease and possible presence of latent infection. An interferon gamma test (IGT) is advised before treatment for latent infection considered.

If initial screening is with IGT, a positive result should lead to a medical assessment for presence of latent or active disease.

2.3 HCW from UK and other low incidence areas

A Mantoux test will only be necessary in new employees who do not have:

- a definite BCG scar or
- documentary evidence of a previous BCG or
- documented positive Tuberculin (Mantoux or Heaf) test or IGT within the last five years

If an employee new to the NHS has no (or inconclusive) evidence of prior BCG vaccination, a Mantoux or IGT should be performed

An employee with a positive Mantoux result (6mm or more) should have a medical assessment and a chest X-ray. These individuals should be referred to the TB clinic for consideration of TB treatment if the chest X-ray is abnormal, or for consideration of treatment of latent TB infection if the chest X-ray is normal and interferon-gamma test is positive.

If initial screening is with IGT, a positive result should lead to a medical assessment for presence of latent or active disease.

2.4 Screening staff with Mantoux

The table below shows the recommended action based on the Mantoux reading.

	Mantoux result	Action
No previous BCG	< 6mm	Advise BCG
	>= 6mm	IGT Medical assessment
Previous BCG (New Entrants Only)	<6mm	no action
	6mm to 14mm	Consistent with previous BCG
	>= 15mm	IGT Medical assessment

2.5 Interferon Gamma Test

Current evidence suggests that Interferon Gamma Test is a superior test for screening purposes compared to the Mantoux test.

At the present time, there are two Interferon Gamma tests on the market; Quantiferon Gold and the T-Spot test. Both can result in false negative results particularly in the presence of immunosuppression although the T-spot test is claimed to be more sensitive in immunosuppressed individuals.

Although the Mantoux test has some drawbacks, it remains a useful screening test in the absence of facilities for routine IGT.

Some individuals believe that the IGT should, if resources and diagnostic services allow, be the first line screening test instead of the Mantoux.

As more evidence becomes available, the IGT may, in the future, become the advised first line screening test. However at this moment in time, it is difficult to make a firm recommendation on this.

3. Latent TB

Latent TB infection may reactivate in later life particularly if an individual's immune system has become weakened - for example by diseases such as HIV, certain medical treatments such as chemotherapy, corticosteroids, or in old age.

A positive Mantoux and/or IGT suggests the presence of latent TB or active disease. Staff with a positive test should be referred to the chest clinic for exclusion of active disease and consideration for treatment for latent TB.

It is recommended that the HCW is counselled and informed of the implications of the positive test, in particular the risk of developing active disease in the future especially in the presence of immunosuppression.

Although treatment for latent TB should ideally be considered after a positive IGT, in some cases the decision to treat may need to be based solely on a positive Mantoux test.

An asymptomatic employee with positive Mantoux test and/or gamma interferon test, who is not treated for latent infection or refuses treatment, should be advised that he/she has dormant infection with a small risk of possible reactivation to active disease in the future. Such individuals should be reminded of the importance of prompt reporting of symptoms suspicious of tuberculosis. With consent the employee's GP should be informed.

It may be prudent to provide an annual information sheet to the HCW to maintain vigilance and alertness to symptoms suggestive of active disease.

At this moment in time, no restriction in area of work or duties is advised in individuals who have a positive Mantoux/ IGT who have declined treatment for latent TB.

4. BCG vaccination

BCG should not be administered to previously vaccinated individuals as there is an increased risk of adverse reactions and no evidence of additional protection.

Evidence of a previous BCG vaccination includes:

- documentary evidence or
- a clear, reliable history of vaccination or
- evidence of a characteristic scar.

Determining a reliable history of BCG vaccination may be complicated by:

- absent or limited documentary evidence
- unreliable recall of vaccination
- absence of a characteristic scar in some individuals vaccinated intradermally

- absence of a scar in a high proportion of individuals vaccinated percutaneously
- use of non-standard vaccination sites.

Individuals with an uncertain history of prior BCG vaccination should be tuberculin tested before being given BCG.

The final decision whether to offer BCG, where there is a possible history of previous vaccination but no proof, must balance the risk of possible revaccination against the potential benefit of vaccination.

Employees should be offered BCG vaccination, whatever their age, if they will have contact with patients and/or clinical specimens, are Mantoux negative (less than 6 mm) and have not been previously vaccinated

BCG vaccination does not provide full protection against infection. Therefore the importance of reporting possible symptoms of tuberculosis promptly should be re-emphasised.

4.1 HIV and BCG vaccination

BCG is contraindicated in symptomatic HIV-positive individuals or other conditions that cause immunosuppression.

In countries such as the UK where the risk of TB is low, it is recommended that BCG is also withheld from all those known to be or suspected to be HIV positive, regardless of clinical status.

The following individuals are considered to be at an increased risk of being HIV positive and should be offered a HIV test prior to BCG:

- anyone who has ever had sex with someone from a high HIV prevalence country such as sub-Saharan Africa, parts of Asia and Eastern Europe
- IV drug use or blood transfusion in any of the above countries
- A gay/bisexual man regardless of where they have come from

It is considered reasonably safe to give BCG vaccine, without a prior HIV test, to employees from low HIV prevalence countries who do not have any of the risk factors mentioned above.

Mantoux negative individuals from countries/groups with a high prevalence of HIV infection should be encouraged to have a HIV test before BCG vaccination especially since Mantoux tests, in the presence of immunosuppression, may be falsely negative. The final decision on whether to give BCG in these individuals without HIV test rests with the occupational health professional.

4.2 Refusal of BCG vaccination

If BCG vaccination is refused, the risks should be explained and the refusal recorded.

NICE guidelines state (R121 p77) that '**he or she should not work where there is a risk of exposure to TB**'.

If restriction is proposed as per NICE guidelines, the high risk areas would be respiratory and infectious disease wards, Intensive Care Units and pathology laboratories. However, there is no clinical area where there is NO risk.

Taking into account the risk of acquiring infection, which is generally considered to be low, and the lack of firm evidence on the efficacy and protective value of BCG in adults, it is thought that the risk of a non-vaccinated employee acquiring infection is likely to be low, and the risk of acquiring active disease and subsequent transmission to patients is likely to be very low.

The employer will need to consider each case individually, taking account of employment and health and safety obligations and in some cases, restriction may not be warranted.

It is advised that an annual information sheet is sent to the employee to maintain awareness to symptoms suggestive of active disease.

5. HIV positive and other immunocompromised HCWs

It is known that immunosuppressed individuals with latent TB have an increased risk of reactivation to active disease.

The **life-time** risk of active disease in immunocompetent individuals with latent TB is considered to be 10%.

Studies [1] on HIV positive patients with latent TB suggest an **annual** risk of developing active TB of approximately 10%. These estimates were derived from studies conducted in HIV patients not on anti-retroviral treatment with low CD4 counts.

It is felt that HIV patients on anti-retroviral treatment with normal CD4 count may not be at such an increased risk of developing active disease. More information on the issue is expected to be become available in the future.

An interferon gamma test is likely to be more sensitive as a screening tool than a Mantoux test in these individuals.

It is advised that, if resources allow, new employees who are known to have HIV or other conditions causing immunosuppression should have a interferon gamma test; those with a positive test should be referred for further medical assessment and treatment.

It is advised that an annual information sheet is sent to the employee to maintain awareness to symptoms suggestive of active disease.

6. Increased awareness

Reminders of the symptoms of TB, and the need for prompt reporting of such symptoms, should be provided to staff who:

- are in regular contact with TB patients or clinical materials
- have worked in a high-risk clinical setting for 4 weeks or longer

One-off reminders should be given after a TB incident on a ward

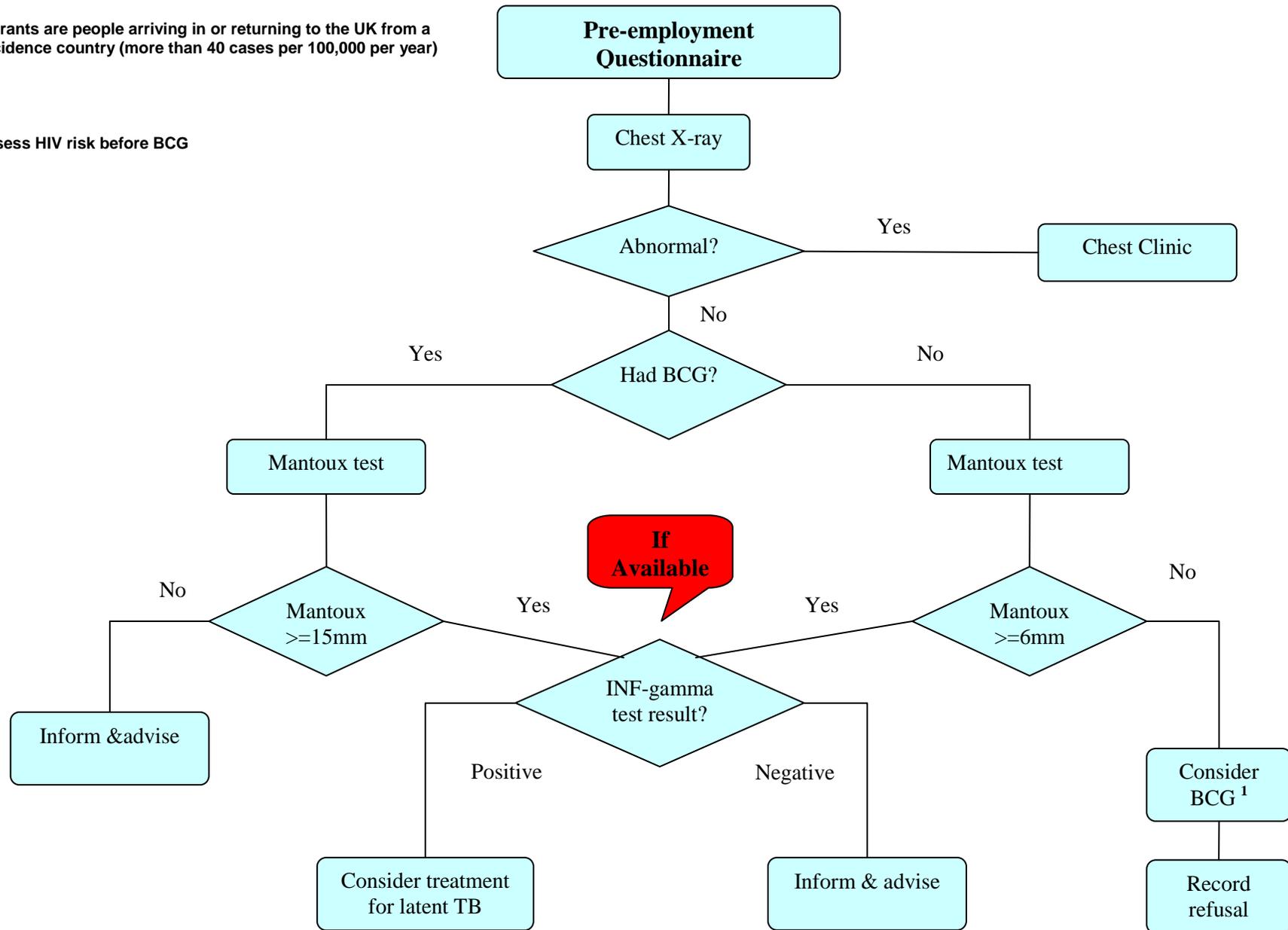
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Appendix A Screening new NHS employees from high incidence countries (new entrants)

New entrants are people arriving in or returning to the UK from a high-incidence country (more than 40 cases per 100,000 per year)

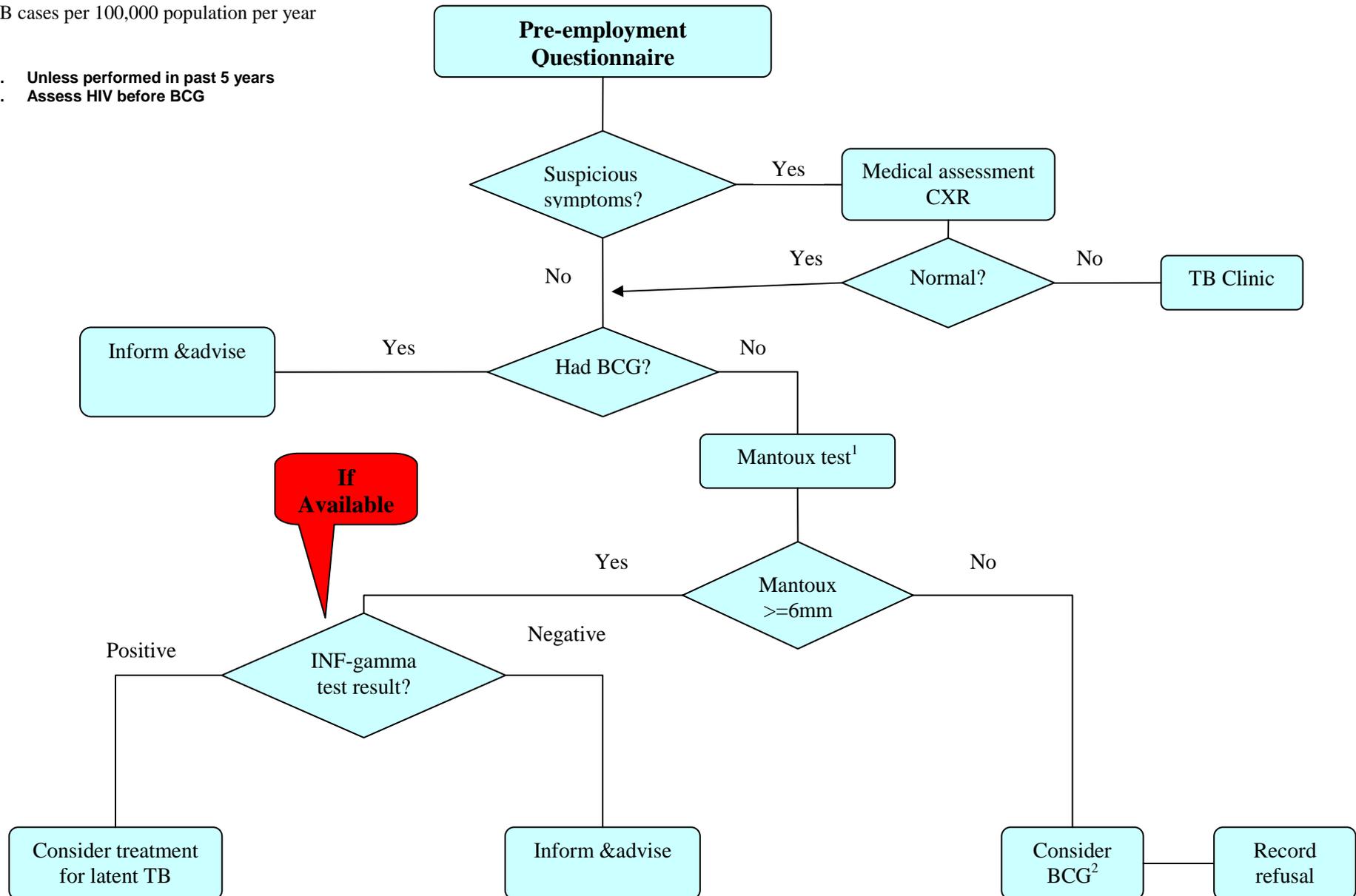
1. Assess HIV risk before BCG



Appendix B Screening new NHS employees from low incidence countries

Low incidence countries have less than 40 TB cases per 100,000 population per year

1. Unless performed in past 5 years
2. Assess HIV before BCG



Appendix C North West guidelines on interferon gamma testing

These tests measure Interferon gamma release from effector lymphocytes in response to stimulation by two tuberculosis antigens (ESAT 6 and CFP-10). They are more specific than the tuberculin skin test (TST) and will exclude most false positive TSTs due to prior environmental mycobacterial exposure or prior BCG vaccination.

Interferon gamma testing (IGT) is recommended in (NICE Guidelines R1):

- those with positive Mantoux results (≥ 6 mm non-BCG vaccinated, ≥ 15 mm if BCG vaccinated)
- or those in whom Mantoux testing may be less reliable (HIV positive, cytotoxic therapy, systemic corticosteroids, anti-TNF therapy)

Two commercially available assays are available. The Quantiferon-TB Gold assay measures interferon gamma release in whole blood whereas the T-SPOT TB test measures interferon gamma release from individual T-lymphocytes. Although both tests are measuring the same thing, their operating characteristics are different and their clinical utility remains incompletely understood. Their clinical utility may vary from laboratory to laboratory, so knowledge of local laboratory results may be important. Both tests are new and research and clinical experience with both tests is evolving.

The Quantiferon-Gold test includes internal positive (mitogen) and negative controls. Positive results will always be valid. The Quantiferon-Gold test works well in the immunocompetent and performs better when contacts are being tested, rather than individuals with symptomatic disease. Quantiferon is practical to run in the laboratory, capable of delivering rapid throughput during the investigation of an outbreak and is cheaper (£25 vs £75). For these reasons it has been introduced as a service tool by the Immunology Department at Central Manchester and Manchester Childrens NHS Trust. T-SPOT TB test is available at Medi-lab in Salford Quays (Medi-labs website www.medi-lab.co.uk) or contact Brian A. Owen on 01942 260414 or Paul Hayward on 0161 877 6336).

There are suggestions that the T-SPOT TB test may be more sensitive in the immunosuppressed (including children aged < 5 years), but current data is insufficient to quantify this difference (if real). A positive Quantiferon-Gold test in these groups will be valid, but the validity of negative test in this group is unclear at present.

Possible results and their interpretation from the Quantiferon-Gold test are as below:

Quantiferon result	Negative control	Mitogen	Test sample	Interpretation
Positive	-	+	+	Latent or active TB (see below)
Negative	-	+	-	No latent or active TB*
Indeterminate	-	-	-	Latent or active TB cannot be excluded**

* this is reliable in adults, but in children < 5 false negatives may occur, so only a positive test is clinically useful

** suggests insufficient T-cells or T-cells with impaired function so latent or active TB cannot be excluded

A positive IGT signifies an on-going immunological response to mycobacterial infection. This may be due to:

Active *M tuberculosis* infection

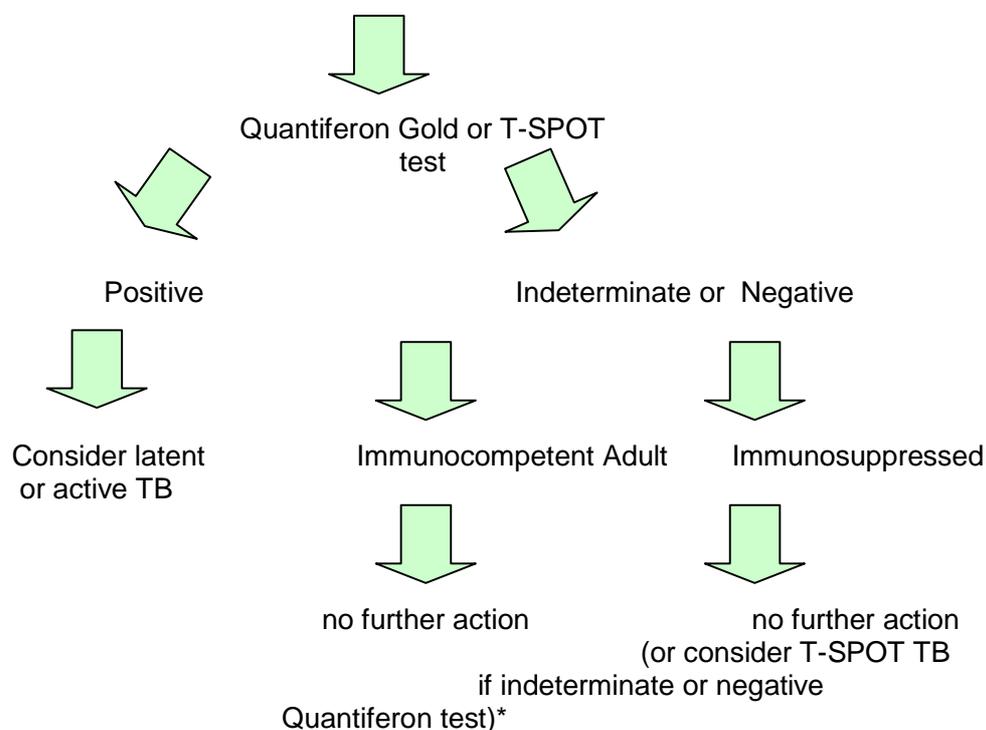
Latent *M tuberculosis* infection

Also *M kansasii*, *M szulgai* and *M marinum* infection.

It cannot separate active from latent infection.

Recommendation:

those with positive Mantoux results
(≥ 6 mm non-BCG vaccinated, ≥ 15 mm if BCG vaccinated)
or
those in whom Mantoux testing may be less reliable
(HIV positive, cytotoxic therapy, systemic corticosteroids, anti-TNF therapy)



* audit of results in 9 immunosuppressed adults found only 1 indeterminate result, with 7 -ve and 1 +ve . Only 3 under 5 yr olds have been tested and one was +ve. The decision to proceed to T-SPOT TB testing should be done on a case by case basis and depend on clinical risk.

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Appendix D FREQUENTLY ASKED QUESTIONS ABOUT BCG

Professor P D O Davies, Director, Tuberculosis Research Unit, Cardiothoracic Centre, Liverpool. UK

Does it work?

Trials of the vaccine have been undertaken since it was first developed in the 1920s. The results have been variable. About a third of the total trials have shown no protective effect. The remainders have shown protection of up to 80%* at best lasting a maximum of 15 years. No trials on second or subsequent vaccinations have shown any protective effect. (*Protective efficacy is a measure of the proportion of people who would have got the disease had they not had the vaccination. 80% protection means that 4 out of 5 individuals are protected. Efficacy for most vaccines exceeds 95%. BCG is therefore a relatively weak protective vaccine.)

In summary 50% randomised control trials show it to be effective.70% Case Control studies show it to be effective.

Why is the effectiveness variable?

The reasons for variability are not fully understood. There have been a number of theories put forward, none of which seem to provide a total explanation.

1. Methodological. All studies varied slightly in the way they were designed
2. Different vaccines. The development of BCG has meant that strains vary according to the time at which each has been developed. Different vaccine strains were used in the trials and are in use across the world today.
3. Tuberculin status of subjects. Within trials some individuals in both control or vaccinated groups may have been tuberculin positive and therefore had "natural " protection. This may not have been accounted for in some of the trials.
4. Different strains of M.tuberculosis. New molecular techniques have demonstrated that there are a large number of different strains of the bacterium. It is possible that different areas of the world have different strains, which may vary in virulence.
5. Genetic differences in population. There is variation in individual susceptibility to tuberculosis. This could have caused disparity in results.
6. Intensity of infecting dose. Infection and susceptibility to disease may be affected by the quantity of bacteria inhaled.
7. Nutritional differences. It is known that different nutritional states can vary susceptibility to disease. The poorly fed individual is more susceptible.
8. Protection of controls by environmental mycobacteria. These free living mycobacteria which resemble M.tuberculosis sometimes cause disease. They may be responsible for infecting individuals therefore providing partial immunity M.tuberculosis.

How is BCG used in the UK?

Studies carried out by the British Medical Research Council in the 1950s showed that BCG, when given to teenage school children gave about 75% protection for 15 years.(1). From 1953 until July 2005 it was national policy to vaccinate all children aged 12-13. Thus in theory the entire population received protection from early teenage years through to about the age of 30. The reason for choosing that age range was because in the 1950s cases rates were highest in young adults. The limited length of time for which BCG appeared to be protective would therefore be maximal at the age when most people suffered from the disease. Secondly the form of tuberculosis which preteenage children suffer from (primary) is not usually infectious, whereas the form suffered by adults is infectious.

However as rates of tuberculosis in teenagers and young adults have declined reasons for discontinuing the policy of teenage vaccination have emerged. (2,3) First it is no longer cost effective. The rates of disease in the group receiving protection are now so low that about 10,000 vaccinations are needed to prevent a single case (see below). This is to prevent disease which is usually relatively easy to treat in the age group 14 to 30.

Secondly the harm done in adverse effects from the vaccine, usually abscesses at the site of injection, outweigh the preventive effect.

BCG is still given at birth to babies born into high risk groups. These includes those who have a family history of tuberculosis, ethnic minorities at increased risk of TB and those born in areas with a high prevalence. BCG is also given to those who may be at risk of increased exposure to tuberculosis such as health care workers (2). Is the policy of BCG vaccination the same throughout the world? No, mainly because of variation in trial results. Most countries give BCG at birth to provide protection in the early years when infection can often lead to devastating widespread disease such as miliary tuberculosis or tuberculous meningitis. This is particularly important in high prevalence countries where the chance of being infected in very early life is high. Some countries such as the USA have chosen not to use it because most trials there have not shown any protective effect.

Why is there not international agreement on how to use BCG?

Again because of variation in trial results across the world. In 1994 a "metanalysis" of all the trials was published. (2) This looked at a total of 1264 articles, 70 in depth, 14 prospective trials and 12 casecontrol studies. The authors found that seven trials show a protective effect from death of 71%, five trials showed protection from meningitis of 64%, three, protection from disseminated disease of 78% and three, protection from laboratory confirmed disease of 83%.

The authors concluded that geographical site of study explained 66% of variability. They also found that on average BCG reduces risk of infection leading to disease by 50%.

This is probably an erroneous conclusion, as the efficacy of BCG cannot be averaged. Trials show it to be 80% protective in one place and 20% in another. Average efficacy should not be taken.

Is the efficacy of BCG waning?

Some workers believe that it is(5). This is because the BCG vaccine is continually being reproduced as part of the manufacturing process and in common with other live organisms, which undergo this process, may be becoming less virulent and therefore less able to provide immunity to those who are vaccinated. In contrast sequential studies from the UK show that the 75% efficacy has been maintained (6,7)

Does giving BCG prevent the use of the tuberculin test in determining the presence of infection with M. tuberculosis?

This is another area of controversy. BCG converts the tuberculin test from negative to positive. Workers are split as to whether it is possible to tell the difference between a positive test due to BCG alone and a positive test due to infection with M.tuberculosis whether the individual has had previous BCG or not. In the UK we believe it is possible to do this on the basis of the degree of positivity.(6) The USA do not use BCG partly for the reason that they do not believe it is possible to make the distinction.

The importance of this is the decision to give preventive therapy for Latent Tuberculosis Infection (LTBI). The USA has relied on prevention by determining whether infection (without disease) is present on the basis of regular tuberculin testing for those at risk of infection such as health workers. BCG is not given as it is believed to interfere with the interpretation of the tuberculin test. Other countries, such as the UK, do give BCG but in cases where infection has occurred in addition to BCG and where the risk of disease is appreciable, such as in cohouseholders of Sputum Smear positive patients, preventive therapy can be given if the tuberculin test is strongly positive.(7) Does BCG protect against drug resistant tuberculosis? The probable answer to this is yes though evidence for this is necessarily sketchy. It is probably more effective in preventing disease than providing preventive therapy to those infected; a procedure for which there is no evidence of any efficacy at all. For health care workers who may be exposed to drug resistant tuberculosis, even a low protective efficacy of BCG would make vaccination worthwhile.

In a recent study of a mathematical model, BCG was preferred by small margin over post-infection chemoprophylaxis. Threshold for protective efficacy was 26%. BCG should be considered for health care workers with risk of MDRTB exposure.(9)

Should BCG still be used in low prevalence countries? As rates of tuberculosis have declined the argument for continuing routine BCG to the whole population becomes weaker.(10) For example if rates of disease are 2/100,00 and even if it is assumed that BCG gives 80% protection for 15 years then vaccinating 100,000 people would prevent

$(0.8 \times 2) \times 15 = 24$ cases over 15 years. Conditions necessary to stop giving BCG include a good control programme, good reporting especially of TB meningitis and the prevalence of HIV. "Arguments against use of BCG vaccine in a mass programme are not about efficacy but cost effectiveness." (11)

Can BCG be harmful?

Abscesses at the site of BCG injection are frequently reported. It is often assumed that this is due to bad technique, as the injection should be given intracutaneously and an accidental intramuscular injection may result. Proximal lymph node swelling and abscess formation may rarely occur. If the injection is given at the correct site, over insertion of Deltoid in the upper arm, the swelling will develop in the axillary lymph nodes. Very rarely indeed, disseminated BCG disease may result in the immunocompromised infant. This is usually fatal. For this reason BCG should not be given to symptomatic HIV positive individuals.

Summary

Where tuberculosis is prevalent and the risk of infection is high such as in certain risk groups and developing countries, continuation of BCG is worthwhile. Where tuberculosis is uncommon a full programme BCG becomes no longer cost effective and resources are better directed at other methods of controlling the disease.

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Further reading.

Hans L Rieder BCG vaccination, in Clinical Tuberculosis 3rd Editn. Edit PDO Davies, Arnold, London 2003 pp337354. Also references 2 and 3 above for information from the National Institute of Health and Clinical Excellence and the Department of Health. All pages copyright ©Priory Lodge Education Ltd.