CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

April 26, 1996 / Vol. 45 / No. RR-4

MMWR™

Recommendations and Reports

MORBIDITY AND MORTALITY WEEKLY REPORT

The Role of BCG Vaccine in the Prevention and Control of Tuberculosis in the United States

A Joint Statement by the Advisory Council for the Elimination of Tuberculosis and the Advisory Committee on Immunization Practices

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control and Prevention (CDC)

The *MMWR* series of publications is published by the Epidemiology Program Office, Centers for Disease Control and Prevention (CDC), Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA 30333.

SUGGESTED CITATION

Centers for Disease Control and Prevention. The role of BCG vaccine in the prevention and control of tuberculosis in the United States: a joint statement by the Advisory Council for the Elimination of Tuberculosis and the Advisory Committee on Immunization Practices. MMWR 1996;45(No. RR-4):[inclusive page numbers].

Copies can be purchased from Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325. Telephone: (202) 783-3238.

Contents

Advisory Council for the Elimination of Tuberculosis (ACET)
September 1995

*These ACET members rotated off the council during 1995; however, they made substantive contributions to this report.

Advisory Committee on Immunization Practices (ACIP) 1995

*These ACIP members rotated off the committee; however, they made substantive contributions to this report.

LIAISON REPRESENTATIVES

American Academy of Family Physicians
Richard K. Zimmerman, M.D.
University of Pittsburgh
Pittsburgh, PA

American Academy of Pediatrics
Georges Peter, M.D.
Rhode Island Hospital
Providence, RI

American Academy of Pediatrics
Caroline B. Hall, M.D.
University of Rochester
Rochester, NY

American College of Obstetricians and Gynecologists
Marvin S. Amstey, M.D.
Highland Hospital
Rochester, NY

American College of Physicians
Pierce Gardner, M.D.
State University of New York at Stonybrook
Stonybrook, NY

American Hospital Association
William Schaffner, M.D.
Vanderbilt University
Nashville, TN

American Medical Association
Edward A. Mortimer, Jr., M.D.
Case Western Reserve University
Cleveland, OH

Canadian National Advisory Committee on Immunization
David W. Scheifele, M.D.
Vaccine Evaluation Center
Vancouver, British Columbia, Canada

Hospital Infections Control Practices Advisory Committee
David W. Fleming, M.D.
Oregon Health Division
Portland, OR

Infectious Diseases Society of America
William P. Glezen, M.D.
Baylor College of Medicine
Houston, TX

National Association of State Public Health Veterinarians
Keith A. Clark, D.V.M., Ph.D.
Texas Department of Health
Austin, TX

National Vaccine Program
Anthony Robbins, M.D.
Office of the Assistant Secretary for Health
Washington, DC

U.S. Department of Defense
Michael Peterson, D.V.M., Dr.P.H.
Office of the Surgeon General
Department of the Army
Falls Church, VA

U.S. Department of Veterans Affairs
Kristin L. Nichol, M.D., M.P.H.
Veterans Administration Medical Center
Minneapolis, MN

The following CDC staff members prepared this report:

Margarita E. Villarino, M.D., M.P.H.
Robin E. Huebner, Ph.D., M.P.H.
Ann H. Lanner
Lawrence J. Geiter, M.P.H.
Division of Tuberculosis Elimination
National Center for HIV, STD and TB Prevention (Proposed)

in collaboration with the

Advisory Council for the Elimination of Tuberculosis

and the

Advisory Committee on Immunization Practices

The Role of BCG Vaccine in the Prevention and Control of Tuberculosis in the United States

A Joint Statement by the Advisory Council for the Elimination of Tuberculosis and the Advisory Committee on Immunization Practices

Summary

*This report updates and replaces previous recommendations regarding the use of Bacillus of Calmette and Guérin (BCG) vaccine for controlling tuberculosis (TB) in the United States (*MMWR *1988;37:663–4, 669–75). Since the previous recommendations were published, the number of TB cases have increased among adults and children, and outbreaks of multidrug-resistant TB have occurred in institutions. In addition, new information about the protective efficacy of BCG has become available. For example, two meta-analyses of the published results of BCG vaccine clinical trials and case-control studies confirmed that the protective efficacy of BCG for preventing serious forms of TB in children is high (i.e., >80%). These analyses, however, did not clarify the protective efficacy of BCG for preventing pulmonary TB in adolescents and adults; this protective efficacy is variable and equivocal. The concern of the public health community about the resurgence and changing nature of TB in the United States prompted a re-evaluation of the role of BCG vaccination in the prevention and control of TB. This updated report is being issued by CDC, the Advisory Committee for the Elimination of Tuberculosis, and the Advisory Committee on Immunization Practices, in consultation with the Hospital Infection Control Practices Advisory Committee, to summarize current considerations and recommendations regarding the use of BCG vaccine in the United States.*

In the United States, the prevalence of M. tuberculosis *infection and active TB disease varies for different segments of the population; however, the risk for* M. tuberculosis *infection in the overall population is low. The primary strategy for preventing and controlling TB in the United States is to minimize the risk for transmission by the early identification and treatment of patients who have active infectious TB. The second most important strategy is the identification of persons who have latent* M. tuberculosis *infection and, if indicated, the use of preventive therapy with isoniazid to prevent the latent infection from progressing to active TB disease. Rifampin is used for preventive therapy for persons who are infected with isoniazid-resistant strains of* M. tuberculosis. *The use of BCG vaccine has been limited because a) its effectiveness in preventing infectious forms of TB is uncertain and b) the reactivity to tuberculin that occurs after vaccination interferes with the management of persons who are possibly infected with* M. tuberculosis.

In the United States, the use of BCG vaccination as a TB prevention strategy is reserved for selected persons who meet specific criteria. BCG vaccination should be considered for infants and children who reside in settings in which the likelihood of M. tuberculosis *transmission and subsequent infection is high,*

provided no other measures can be implemented (e.g., removing the child from the source of infection). In addition, BCG vaccination may be considered for health-care workers (HCWs) who are employed in settings in which the likelihood of transmission and subsequent infection with M. tuberculosis *strains resistant to isoniazid and rifampin is high, provided comprehensive TB infection-control precautions have been implemented in the workplace and have not been successful. BCG vaccination is not recommended for children and adults who are infected with human immunodeficiency virus because of the potential adverse reactions associated with the use of the vaccine in these persons.*

In the United States, the use of BCG vaccination is rarely indicated. BCG vaccination is not recommended for inclusion in immunization or TB control programs, and it is not recommended for most HCWs. Physicians considering the use of BCG vaccine for their patients are encouraged to consult the TB control programs in their area.

INTRODUCTION

Because the overall risk for acquiring *Mycobacterium tuberculosis* infection is low for the total U.S. population, a national policy is not indicated for vaccination with Bacillus of Calmette and Guérin (BCG) vaccine. Instead, tuberculosis (TB) prevention and control efforts in the United States are focused on a) interrupting transmission from patients who have active infectious TB and b) skin testing children and adults who are at high risk for TB and, if indicated, administering preventive therapy to those persons who have positive tuberculin skin-test results. The preferred method of skin testing is the Mantoux tuberculin skin test using 0.1 mL of 5 tuberculin units (TU) of purified protein derivative (PPD) (*1*).

BCG vaccination contributes to the prevention and control of TB in limited situations when other strategies are inadequate. The severity of active TB disease during childhood warrants special efforts to protect children, particularly those <5 years of age. In addition, TB is recognized as an occupational hazard for health-care workers (HCWs) in certain settings. In 1988, the Immunization Practices Advisory Committee and the Advisory Committee for Elimination of Tuberculosis published a joint statement on the use of BCG vaccine for the control of TB (*2*). Based on available information concerning the effectiveness of BCG vaccine for preventing serious forms of TB in children, this statement recommended BCG vaccination of children who are not infected with *M. tuberculosis* but are at high risk for infection and for whom other public health measures cannot be implemented. The statement recommended against BCG vaccination for HCWs at risk for occupationally acquired *M. tuberculosis* infection because a) BCG vaccination interferes with the identification of HCWs who have latent *M. tuberculosis* infection and the implementation of preventive-therapy programs in health-care facilities and b) the protective efficacy of BCG for pulmonary TB in adults is uncertain.

From 1985 through 1992, a resurgence in the incidence of TB occurred in the United States and included increases in the number of TB cases among adults and children and outbreaks of multidrug-resistant TB (MDR-TB) involving patients, HCWs, and correctional-facility employees. In addition, meta-analyses have been conducted recently using previously published data from clinical trials and case-control studies of BCG

vaccination. These developments have prompted a re-evaluation of the role of BCG vaccination in the prevention and control of TB in the United States. CDC, the Advisory Council for the Elimination of Tuberculosis (ACET), and the Advisory Committee on Immunization Practices (ACIP), in consultation with the Hospital Infection Control Practices Advisory Committee, are issuing the following report to summarize current considerations and recommendations regarding the use of BCG vaccine in the United States.

BACKGROUND

Transmission and Pathogenesis of *M. tuberculosis*

Most persons infected with *M. tuberculosis* have latent infection. Among immunocompetent adults who have latent *M. tuberculosis* infection, active TB disease will develop in 5%–15% during their lifetimes (*3–5*). The likelihood that latent infection will progress to active TB disease in infants and children is substantially greater than for most other age groups (*6*). Active TB disease can be severe in young children. Without appropriate therapy, infants <2 years of age are at particularly high risk for developing life-threatening tuberculous meningitis or miliary TB (*7*).

The greatest known risk factor that increases the likelihood that a person infected with *M. tuberculosis* will develop active TB disease is immunodeficiency, especially that caused by coinfection with human immunodeficiency virus (HIV) (*8–10*). Other immunocompromising conditions (e.g., diabetes mellitus, renal failure, and treatment with immunosuppressive medications) also increase the risk for progression to active TB disease, but the risk is not as high as the risk attributed to HIV infection (*8,11*). In addition, recency of infection with *M. tuberculosis* contributes to the risk for developing active TB disease. Among immunocompetent persons, the risk for active TB disease is greatest during the first 2 years after infection occurs; after this time period, the risk declines markedly (*8*). However, the risk for active TB disease among HIV-infected persons, who have a progressive decline in immunity, may remain high for an indefinite period of time or may even increase as the immunosuppression progresses. Furthermore, persons who have impaired immunity are more likely than immunocompetent persons to have a weakened response to the tuberculin skin test; this weakened response makes both the identification of persons who have latent *M. tuberculosis* infection and the decisions regarding whether to initiate TB preventive therapy more difficult.

Epidemiology of TB in the United States

From 1953, when national surveillance for TB began, through 1984, TB incidence rates in the United States declined approximately 6% per year. However, during 1985, the morbidity rate for TB decreased by only 1.1%, and during 1986, it increased by 1.1% over the 1985 rate (*12*). This upward trend continued through 1992, when the incidence was 10.5 cases per 100,000 population. For 1993, the reported incidence of TB was 9.8 cases per 100,000 population, representing a 5.2% decrease from 1992; however, this decline was still 14% greater than the 1985 rate (*13*). For 1994, the

number of cases decreased 3.7% from 1993, but this number still represented a 9.7% increase over the rate for 1985 (*14*).

In general, active TB disease is fatal for as many as 50% of persons who have not been treated (*15*). Anti-TB therapy has helped to reduce the number of deaths caused by TB; since 1953, the TB fatality rate has declined by 94%. According to 1993 provisional data for the United States, 1,670 deaths were attributed to TB, representing a mortality rate of 0.6 deaths per 100,000 population. The mortality rate for 1953 was 12.4 deaths per 100,000 population (*16*).

The prevalence of *M. tuberculosis* infection and active TB disease varies for different segments of the U.S. population. For example, during 1994, 57% of the total number of TB cases were reported by five states (i.e., California, Florida, Illinois, New York, and Texas), and overall incidence rates were twice as high for men as for women (*16*). For children, disease rates were highest among children ages ≤4 years, were low among children ages 5–12 years, and, beginning in the early teenage years, increased sharply with age for both sexes and all races. Cases of TB among children <15 years of age accounted for 7% of all TB cases reported for 1994.

During the 1950s, TB was identified as an occupational hazard for HCWs in certain settings (*17*). In the United States, the risk for acquiring *M. tuberculosis* infection diminished for most HCWs as the disease became less prevalent; however, the risk is still high for HCWs who work in settings in which the incidence of TB among patients is high. The precise risk for TB among HCWs in the United States cannot be determined because tuberculin skin-test conversions and active TB disease among HCWs are not systematically reported. However, recent outbreaks of TB in health-care settings indicate a substantial risk for TB among HCWs in some geographic areas.

Since 1990, CDC has provided epidemiologic assistance during investigations of several MDR-TB outbreaks that occurred in institutional settings. These outbreaks involved a total of approximately 300 cases of MDR-TB and included transmission of *M. tuberculosis* to patients, HCWs, and correctional-facility inmates and employees in Florida, New Jersey, and New York (*18–23*). These outbreaks were characterized by the transmission of *M. tuberculosis* strains resistant to isoniazid and, in most cases, rifampin; several strains also were resistant to other drugs (e.g., ethambutol, streptomycin, ethionamide, kanamycin, and rifabutin). In addition, most of the initial cases of MDR-TB identified in these outbreaks occurred among HIV-infected persons, for whom the diagnosis of TB was difficult or delayed. The fatality rate among persons who had active MDR-TB was >70% in most of the outbreaks.

TB Prevention and Control in the United States

The fundamental strategies for the prevention and control of TB include:

- **Early detection and treatment of patients who have active TB disease.** The most important strategy for minimizing the risk for *M. tuberculosis* transmission is the early detection and effective treatment of persons who have infectious TB (*24*).
- **Preventive therapy for infected persons.** Identifying and treating persons who are infected with *M. tuberculosis* can prevent the progression of latent infection to active infectious disease (*25*).

- **Prevention of institutional transmission.** The transmission of *M. tuberculosis* is a recognized risk in health-care settings and is a particular concern in settings where HIV-infected persons work, volunteer, visit, or receive care (*26*). Effective TB infection-control programs should be implemented in health-care facilities and other institutional settings (e.g., homeless shelters and correctional facilities) (*27,28*).

BCG vaccination is not recommended as a routine strategy for TB control in the United States (see Recommendations). The following sections discuss BCG vaccines, the protective efficacy and side effects associated with BCG vaccination, considerations and recommendations for the use of BCG vaccine in selected persons, and implementation and surveillance of BCG vaccination.

BCG VACCINES

BCG vaccines are live vaccines derived from a strain of *Mycobacterium bovis* that was attenuated by Calmette and Guérin at the Pasteur Institute in Lille, France (*29*). BCG was first administered to humans in 1921. Many different BCG vaccines are available worldwide. Although all currently used vaccines were derived from the original *M. bovis* strain, they differ in their characteristics when grown in culture and in their ability to induce an immune response to tuberculin. These variations may be caused by genetic changes that occurred in the bacterial strains during the passage of time and by differences in production techniques. The vaccine currently available for immunization in the United States, the Tice strain, was developed at the University of Illinois (Chicago, Illinois) from a strain originated at the Pasteur Institute. The Food and Drug Administration is considering another vaccine, which is produced by Connaught Laboratories, Inc., for licensure in the United States. This vaccine was transferred from a strain that was maintained at the University of Montreal (Montreal, Canada).

Vaccine Efficacy

Reported rates of the protective efficacy of BCG vaccines might have been affected by the methods and routes of vaccine administration and by the environments and characteristics of the populations in which BCG vaccines have been studied. Different preparations of liquid BCG were used in controlled prospective community trials conducted before 1955; the results of these trials indicated that estimated rates of protective efficacy ranged from 56% to 80% (*30*). In 1947 and 1950, two controlled trials that used the Tice vaccine demonstrated rates of protective efficacy ranging from zero to 75% (*31,32*). Since 1975, case-control studies using different BCG strains indicated that vaccine efficacies ranged from zero to 80% (*33*). In young children, the estimated protective efficacy rates of the vaccine have ranged from 52% to 100% for prevention of tuberculous meningitis and miliary TB and from 2% to 80% for prevention of pulmonary TB (*34–39*). Most vaccine studies have been restricted to newborns and young children; few studies have assessed vaccine efficacy in persons who received initial vaccination as adults. The largest community-based controlled trial of BCG vaccination was conducted from 1968 to 1971 in southern India. Although two different vaccine strains that were considered the most potent available were used in this study, no protective efficacy in either adults or children was demonstrated 5 years

after vaccination. These vaccine recipients were re-evaluated 15 years after BCG vaccination, at which time the protective efficacy in persons who had been vaccinated as children was 17%; no protective effect was demonstrated in persons who had been vaccinated as adolescents or adults (*39*).

The renewed interest in examining the indications for BCG vaccination in the United States included consideration of the wide range of vaccine efficacies determined by clinical trials and estimated in case-control studies. Two recent meta-analyses of the published literature concerning the efficacy of BCG vaccination for preventing TB attempted to calculate summary estimates of the vaccine's protective efficacy. The first of these meta-analyses included data from 10 randomized clinical trials and eight case-control studies published since 1950 (*40*). The results of this analysis indicated an 86% protective effect of BCG against meningeal and miliary TB in children in clinical trials (95% confidence interval [CI]=65%–95%) and a 75% protective effect in case-control studies (95% CI=61%–84%). The meta-analyst conducting this study determined that the variability in the rates of protective efficacy of BCG against pulmonary TB differed significantly enough between these 18 studies to preclude the estimation of a summary protective efficacy rate.

The second meta-analysis reviewed the results of 14 clinical trials and 12 case-control studies (*41*). The meta-analysts used a random-effects regression model to explore the sources of the heterogeneity in the efficacy of the BCG vaccine reported in the individual studies. Using a model that included the geographic latitude of the study site and the data validity score as covariates, they estimated the overall protective effect of BCG vaccine to be 51% in the clinical trials (95% CI=30%–66%) and 50% in the case-control studies (95% CI=36%–61%). The scarcity of available data concerning the protective efficacy afforded by both BCG vaccination of adults and the type of vaccine strain administered precluded the inclusion of these factors as covariates in the random-effects regression model. However, these researchers determined that vaccine efficacy rates were higher in studies conducted of populations in which persons were vaccinated during childhood compared with populations in which persons were vaccinated at older ages. Furthermore, they determined that higher BCG vaccine efficacy rates were not associated with the use of particular vaccine strains.

Eight studies of the efficacy of BCG vaccination in HCWs also were reviewed by the investigators conducting the second meta-analysis. In these eight studies, which were conducted during the 1940s and 1950s, the meta-analysts identified the following methodologic problems: small study population sizes; inadequate data defining the susceptibility status of study populations; uncertain comparability of control populations; incomplete assessment of ongoing exposure to contagious TB patients; inadequate follow-up of study populations; lack of rigorous case definitions; and differences in either BCG dose, vaccine strain, or method of vaccine administration. These methodologic weaknesses and the heterogeneity of the results were sufficiently substantial to preclude analysis of the data for the use of BCG vaccine in HCWs.

In summary, the recently conducted meta-analyses of BCG protective efficacy have confirmed that the vaccine efficacy for preventing serious forms of TB in children is high (i.e., >80%). These analyses, however, were not useful in clarifying the variable information concerning the vaccine's efficacy for preventing pulmonary TB in adolescents and adults. These studies also were not useful in determining a) the efficacy of BCG vaccine in HCWs or b) the effects on efficacy of the vaccine strain administered

and the vaccinee's age at the time of vaccination. The protective efficacy of BCG vaccine in children and adults who are infected with HIV also has not been determined.

Vaccine Safety

Although BCG vaccination often results in local adverse effects, serious or long-term complications are rare (Table 1) (*42*). BCG vaccinations are usually administered by the intradermal method, and reactions that can be expected after vaccination include moderate axillary or cervical lymphadenopathy and induration and subsequent pustule formation at the injection site; these reactions can persist for as long as 3 months after vaccination. BCG vaccination often results in permanent scarring at the injection site. More severe local reactions include ulceration at the vaccination site, regional suppurative lymphadenitis with draining sinuses, and caseous lesions or purulent drainage at the puncture site; these manifestations might occur within the 5 months after vaccination and could persist for several weeks (*43*). Higher rates of local reactions may result from using subcutaneous injection in comparison with reactions from intradermal injection. In the United States, a recent study of the effects of BCG in adults who volunteered to receive the vaccine indicated that local reactions after BCG vaccination (e.g., muscular soreness, erythema, and purulent drainage) often occurred at the site of subcutaneous injection (*44*).

Controlled studies have not been conducted to examine the treatment of regional lymphadenitis after BCG vaccination. The recommendations for management of BCG adenitis are variable (i.e., the recommended management ranges from no treatment to treatments such as surgical drainage, administration of anti-TB drugs, or a combination of drugs and surgery) (*43*). For adherent or fistulated lymph nodes, the World Health Organization (WHO) suggests drainage and direct instillation of an anti-TB drug into the lesion. Nonadherent lesions will heal spontaneously without treatment (*45*).

The most serious complication of BCG vaccination is disseminated BCG infection. BCG osteitis affecting the epiphyses of the long bones, particularly the epiphyses of the leg, can occur from 4 months to 2 years after vaccination. The risk for developing osteitis after BCG vaccination varies by country; in one review, this risk ranged from 0.01 cases per million vaccinees in Japan to 32.5 and 43.4 cases per million vaccinees in Sweden and Finland, respectively (*46*). Regional increases in the incidence of BCG osteitis have been noted following changes in either the vaccine strain or the method

TABLE 1. Age-specific estimated risks for complications after administration of Bacillus of Calmette and Guérin (BCG) vaccine

	Incidence per 1 million vaccinations	
Complication	**Age <1 year**	**Age 1–20 years**
Local subcutaneous abscess, regional lymphadenopathy	387	25
Musculoskeletal lesions	0.39–0.89	0.06
Multiple lymphadenitis, nonfatal disseminated lesions	0.31–0.39	0.36
Fatal disseminated lesions	0.19–1.56	0.06–0.72

Source: Lotte A, Wasz-Hockert O, Poisson N, et al. Second IUATLD study on complications induced by intradermal BCG-vaccination. Bull Int Union Tuberc 1988;63:47–59.

of production (*42*). The skeletal lesions can be treated effectively with anti-TB medications, although surgery also has been necessary in some cases. Case reports of other severe adverse reactions in adults have included erythema multiforme, pulmonary TB, and meningitis (*47–49*). Fatal disseminated BCG disease has occurred at a rate of 0.06–1.56 cases per million doses of vaccine administered (Table 1); these deaths occurred primarily among immunocompromised persons. Anti-TB therapy is recommended for treatment of disseminated BCG infection; however, because all BCG strains are resistant to pyrazinamide, this antibiotic should not be used (*50*).

The safety of BCG vaccination in HIV-infected adults has not been determined by controlled or large studies. This is a concern because of the association between disseminated BCG infection and underlying immunosuppression. Disseminated BCG disease after vaccination has occurred in at least one child and one adult who were infected with HIV (*51,52*). Persons who are infected with HIV are possibly at greater risk for lymphadenitis and other complications from BCG vaccine than are persons who are not infected with HIV (*53*). The administration of a larger-than-recommended dose of BCG vaccine was associated with increased rates of local reactions in infants born to HIV-seropositive women in Haiti; however, no adverse reactions occurred when the standard dose was administered (*54*). The results of similar studies in Zaire and the Congo did not demonstrate an association between HIV seropositivity and adverse responses to BCG vaccination (*55,56*). WHO currently recommends BCG vaccination for asymptomatic HIV-infected children who are at high risk for infection with *M. tuberculosis* (i.e., in countries in which the prevalence of TB is high). WHO does not recommend BCG vaccination for children who have symptomatic HIV infection or for persons known or suspected to be infected with HIV if they are at minimal risk for infection with *M. tuberculosis* (*57*).

In summary, millions of persons worldwide have been vaccinated with BCG vaccine, and serious or long-term complications after vaccination were infrequent. Possible factors affecting the rate of adverse reactions include the BCG dose, vaccine strain, and method of vaccine administration. Case reports have indicated that BCG-related lymphadenitis, local ulceration, and disseminated BCG disease—which can occur several years after BCG vaccination—may be more frequent among persons who have symptomatic HIV infection than among persons who are not infected with HIV or who have asymptomatic HIV infection (*52,58–64*).

Tuberculin Skin Testing and Interpretation of Results After BCG Vaccination

Postvaccination BCG-induced tuberculin reactivity ranges from no induration to an induration of 19 mm at the skin-test site (*65–74*). Tuberculin reactivity caused by BCG vaccination wanes with the passage of time and is unlikely to persist >10 years after vaccination in the absence of *M. tuberculosis* exposure and infection. BCG-induced reactivity that has weakened might be boosted by administering a tuberculin skin test 1 week to 1 year after the initial postvaccination skin test; ongoing periodic skin testing also might prolong reactivity to tuberculin in vaccinated persons (*70,72*).

The presence or size of a postvaccination tuberculin skin-test reaction does not predict whether BCG will provide any protection against TB disease (*75,76*). Furthermore, the size of a tuberculin skin-test reaction in a BCG-vaccinated person is

not a factor in determining whether the reaction is caused by *M. tuberculosis* infection or the prior BCG vaccination (*77*). The results of a community-based survey in Quebec, Canada, indicated that the prevalence of tuberculin reactions of ≥10 mm induration in adolescents and young adults was similar among those persons vaccinated during infancy and those never vaccinated. Although the prevalence of skin-test results of ≥10 mm induration was significantly higher among those persons vaccinated after infancy than among those never vaccinated, the size of the reaction did not distinguish between reactions possibly caused by BCG vaccination and those possibly caused by *M. tuberculosis* infection (*78*). The results of a different study indicated that if a BCG-vaccinated person has a tuberculin skin test after exposure to *M. tuberculosis* and this test produces a reaction >15 mm larger in induration than that of a skin test conducted before the exposure, the increase in size between the two tests is probably associated with newly acquired *M. tuberculosis* infection (*68*).

Tuberculin skin testing is not contraindicated for persons who have been vaccinated with BCG, and the skin-test results of such persons are used to support or exclude the diagnosis of *M. tuberculosis* infection. A diagnosis of *M. tuberculosis* infection and the use of preventive therapy should be considered for any BCG-vaccinated person who has a tuberculin skin-test reaction of ≥10 mm of induration, especially if any of the following circumstances are present: a) the vaccinated person is a contact of another person who has infectious TB, particularly if the infectious person has transmitted *M. tuberculosis* to others; b) the vaccinated person was born or has resided in a country in which the prevalence of TB is high; or c) the vaccinated person is exposed continually to populations in which the prevalence of TB is high (e.g., some HCWs, employees and volunteers at homeless shelters, and workers at drug-treatment centers).

TB preventive therapy should be considered for BCG-vaccinated persons who are infected with HIV and who are at risk for *M. tuberculosis* infection if they have a tuberculin skin-test reaction of ≥5 mm induration or if they are nonreactive to tuberculin. Responsiveness to tuberculin or other delayed-type hypersensitivity (DTH) antigens may be decreased in persons infected with HIV; this anergy (i.e., the inability to react to DTH antigens) could occur before the onset of signs and symptoms of HIV infection (*79*). The possibility of anergy in BCG-vaccinated persons who are infected with HIV is supported by the results of studies in Rwanda, where all children are vaccinated with BCG; these studies demonstrated decreased tuberculin skin-test responses after BCG vaccination of HIV-infected children in comparison with uninfected children (*80*). In addition, among BCG-vaccinated women in Uganda, those who were infected with HIV were more likely than women in an HIV-seronegative control group to be nonreactive to tuberculin (*81*). A diagnosis of active TB disease should be considered for BCG-vaccinated persons—regardless of their tuberculin skin-test results or HIV serostatus—if they have symptoms suggestive of TB, especially if they have been exposed recently to infectious TB.

RECOMMENDATIONS

The prevalence of *M. tuberculosis* infection and active TB disease varies for different segments of the U.S. population; however, the risk for *M. tuberculosis* infection in the overall U.S. population is low. The primary strategy for controlling TB in the United States is to minimize the risk for transmission by the early identification and treatment of patients who have active infectious TB. The second most important strategy is the identification of persons who have latent *M. tuberculosis* infection and, if indicated, the use of preventive therapy with isoniazid to prevent the latent infection from progressing to active TB disease. Rifampin is used for preventive therapy for persons who are infected with isoniazid-resistant strains of *M. tuberculosis*. The use of BCG vaccine has been limited because a) its effectiveness in preventing infectious forms of TB has been uncertain and b) the reactivity to tuberculin that occurs after vaccination interferes with the management of persons who are possibly infected with *M. tuberculosis*. The use of BCG vaccination as a TB prevention strategy is reserved for selected persons who meet specific criteria.

BCG Vaccination for Prevention and Control of TB Among Children

A diagnosis of TB in a child is a sentinel event, representing recent transmission of *M. tuberculosis* within the community. For example, in one study, almost all the children infected with *M. tuberculosis* had acquired infection from infected adults; many of these adults had resided in the same household as the child to whom they had transmitted infection (*82*). These findings underscore the importance of rapidly reporting TB cases to the public health department and of promptly initiating a thorough contact investigation to identify children at risk for TB infection and disease. The severity of active TB disease during childhood warrants special efforts to protect children, particularly those <5 years of age, from infection with *M. tuberculosis*. Children are protected primarily by the implementation of the first strategy of TB control, which is to interrupt transmission by promptly identifying and treating persons who have infectious TB. In adults, patient nonadherence to prescribed TB treatment can lead to prolonged infectiousness and increased transmission of *M. tuberculosis*. Directly observed therapy (DOT) is one method of ensuring adherence, and this practice should be considered for all adult TB patients. When an infectious adult fails to cooperate with anti-TB therapy, the health department should consider removing any child or children from contact with the adult until the patient is no longer infectious. Unless specifically contraindicated, preventive therapy should be administered to all tuberculin-positive children, even if the date of skin-test conversion or the source of *M. tuberculosis* infection cannot be exactly determined.

Recommendations for BCG Vaccination Among Children

BCG vaccination should be considered for an infant or child who has a negative tuberculin skin-test result if the following circumstances are present:

- the child is exposed continually to an untreated or ineffectively treated patient who has infectious pulmonary TB, and the child cannot be separated from the

presence of the infectious patient or given long-term primary preventive therapy; or

- the child is exposed continually to a patient who has infectious pulmonary TB caused by *M. tuberculosis* strains resistant to isoniazid and rifampin, and the child cannot be separated from the presence of the infectious patient.

BCG vaccination is not recommended for children infected with HIV (see BCG Vaccination for Prevention and Control of TB Among HIV-Infected Persons).

BCG Vaccination for Prevention and Control of TB Among HCWs in Settings Associated With High Risk for *M. tuberculosis* Transmission

In some geographic areas of the United States, the likelihood for transmission of *M. tuberculosis* in health-care facilities is high because of a high incidence of TB in the patient population. Even in these areas, >90% of TB patients are infected with *M. tuberculosis* strains that are susceptible to isoniazid or rifampin. In the absence of adequate infection-control practices, untreated or partially treated patients who have active TB disease can potentially transmit *M. tuberculosis* to HCWs, patients, volunteers, and visitors in the health-care facility.

The preferred strategies for the prevention and control of TB in health-care facilities are to use a) comprehensive infection-control measures to reduce the risk for *M. tuberculosis* transmission, including the prompt identification, isolation, and treatment of persons who have active TB disease; b) tuberculin skin testing to identify HCWs who become newly infected with *M. tuberculosis*; and c) if indicated, therapy with izoniazid or rifampin to prevent active TB disease in HCWs (*26*)

A few geographic areas of the United States are associated with both an increased risk for *M. tuberculosis* transmission in health-care facilities and a high percentage of TB patients who are infected with, and who can potentially transmit, *M. tuberculosis* strains resistant to both isoniazid and rifampin. In such health-care facilities, comprehensive application of TB infection-control practices should be the primary strategy used to protect HCWs and others in the health-care facility from infection with *M. tuberculosis*. BCG vaccination of HCWs should not be used as a primary strategy for two reasons. First, the protective efficacy of the vaccine in HCWs is uncertain. Second, even if BCG vaccination is effective in an individual HCW, other persons in the health-care facility (e.g., patients, visitors, and other HCWs) are not protected against possible exposure to and infection with drug-resistant strains of *M. tuberculosis*.

Recommendations for BCG Vaccination Among HCWs in High-Risk Settings

- BCG vaccination of HCWs should be considered on an individual basis in settings in which a) a high percentage of TB patients are infected with *M. tuberculosis* strains resistant to both isoniazid and rifampin, b) transmission of such drug-resistant *M. tuberculosis* strains to HCWs and subsequent infection are likely, and c) comprehensive TB infection-control precautions have been implemented

and have not been successful. Vaccination with BCG should not be required for employment or for assignment of HCWs in specific work areas.

- HCWs considered for BCG vaccination should be counseled regarding the risks and benefits associated with both BCG vaccination and TB preventive therapy. They should be informed about a) the variable data regarding the efficacy of BCG vaccination, b) the interference with diagnosing a newly acquired *M. tuberculosis* infection in a BCG-vaccinated person, and c) the possible serious complications of BCG vaccine in immunocompromised persons, especially those infected with HIV. They also should be informed concerning a) the lack of data regarding the efficacy of preventive therapy for *M. tuberculosis* infections caused by strains resistant to isoniazid and rifampin and b) the risks for drug toxicity associated with multidrug preventive-therapy regimens.

BCG vaccination is not recommended for HCWs who are infected with HIV or are otherwise immunocompromised. In settings in which the risk for transmission of *M. tuberculosis* strains resistant to both isoniazid and rifampin is high, employees and volunteers who are infected with HIV or are otherwise immunocompromised should be fully informed about this risk and about the even greater risk associated with immunosuppression and the development of active TB disease. At the request of an immunocompromised HCW, employers should offer, but not compel, a work assignment in which the HCW would have the lowest possible risk for infection with *M. tuberculosis* (*26*).

BCG Vaccination for Prevention and Control of TB Among HCWs in Settings Associated With Low Risk for *M. tuberculosis* Transmission

In most geographic areas of the United States, if adequate infection-control practices are maintained, the risk for *M. tuberculosis* transmission in health-care facilities is low. Furthermore, in such facilities, the incidence of disease caused by *M. tuberculosis* strains resistant to both isoniazid and rifampin is low.

Recommendation for BCG Vaccination Among HCWs in Low-Risk Settings

BCG vaccination is not recommended for HCWs in settings in which the risk for *M. tuberculosis* transmission is low.

BCG Vaccination for Prevention and Control of TB Among HIV-Infected Persons

Studies have been conducted outside the United States to determine the safety of BCG vaccination in HIV-infected children and adults (see Vaccine Safety); the results of these studies were inconsistent (*51–56,80*). Studies to examine the safety of BCG for HIV-infected persons in the United States have not been conducted. In addition, the protective efficacy of BCG vaccination in HIV-infected persons is unknown. Therefore, the use of BCG vaccine in HIV-infected persons is not recommended.

TB preventive therapy should be administered, unless contraindicated, to HIV-infected persons who might be coinfected with *M. tuberculosis*. In Uganda, the preliminary results of a study indicate that preventive therapy with isoniazid in HIV-infected persons was associated with few side effects and a 61% reduction in the risk for active TB disease (after a median length of follow-up of 351 days) (*83*). In Haiti, isoniazid prophylaxis reduced the risk for active TB disease by 83% among persons coinfected with *M. tuberculosis* and HIV; the results of this study also indicated possible additional benefits of reductions in other HIV-related conditions among those persons given preventive therapy with isoniazid (*84*).

Recommendation for BCG Vaccination Among HIV-Infected Persons

BCG vaccination is not recommended for HIV-infected children or adults in the United States.

CONTRAINDICATIONS

Until the risks and benefits of BCG vaccination in immunocompromised populations are clearly defined, BCG vaccination should not be administered to persons a) whose immunologic responses are impaired because of HIV infection, congenital immunodeficiency, leukemia, lymphoma, or generalized malignancy or b) whose immunologic responses have been suppressed by steroids, alkylating agents, antimetabolites, or radiation.

BCG VACCINATION DURING PREGNANCY

Although no harmful effects to the fetus have been associated with BCG vaccine, its use is not recommended during pregnancy.

IMPLEMENTATION OF BCG VACCINATION

In the United States, the use of BCG vaccination is rarely indicated. Before a decision to vaccinate a person is made, the following factors should be considered: a) the variable protective efficacy of BCG vaccine, especially in adults; b) the difficulty of interpreting tuberculin skin-test results after BCG vaccination; c) the possible risks for exposure of immunocompromised persons to the vaccine; and d) the possibility that other public health or infection-control measures known to be effective in the prevention and control of TB might not be implemented. Physicians who are considering BCG vaccination for their patients are encouraged to discuss this intervention with personnel in the TB control programs in their area. To obtain additional consultation and technical information, contact CDC's Division of Tuberculosis Elimination; telephone (404) 639-8120.

Vaccine Availability

The Tice strain, available from Organon, Inc., West Orange, New Jersey, is the only BCG vaccine licensed in the United States. The Food and Drug Administration is considering the licensure of a BCG vaccine produced by Connaught Laboratories, Inc.

Other BCG preparations are available for treatment of bladder cancer; these preparations are not intended for use as vaccines.

Vaccine Dose, Administration, and Follow-up

BCG vaccination is reserved for persons who have a reaction of <5 mm induration after skin testing with 5 TU of PPD tuberculin. The Tice strain of BCG is administered percutaneously; 0.3 mL of the reconstituted vaccine is usually placed on the skin in the lower deltoid area (i.e., the upper arm) (*85*) and delivered through a multiple-puncture disc. Infants <30 days of age should receive one half the usual dose, prepared by increasing the amount of diluent added to the lyophilized vaccine. If the indications for vaccination persist, these children should receive a full dose of the vaccine after they are 1 year of age if they have an induration of <5 mm when tested with 5 TU of PPD tuberculin. Freeze-dried vaccine should be reconstituted, protected from exposure to light, refrigerated when not in use, and used within 8 hours of reconstitution.

Normal reactions to the vaccine are characterized by the formation of a bluish-red pustule within 2–3 weeks after vaccination. After approximately 6 weeks, the pustule ulcerates, forming a lesion approximately 5 mm in diameter. Draining lesions resulting from vaccination should be kept clean and bandaged. Scabs form and heal usually within 3 months after vaccination. BCG vaccination generally results in a permanent scar at the puncture site. Accelerated responses to the vaccine might occur in persons infected previously with *M. tuberculosis*. Hypertrophic scars occur in an estimated 28%–33% of vaccinated persons, and keloid scars occur in approximately 2%–4% (*86,87*). Tuberculin reactivity develops 6–12 weeks after vaccination.

Tuberculin reactivity resulting from BCG vaccination should be documented. A vaccinated person should be tuberculin skin tested 3 months after BCG administration, and the test results, in millimeters of induration, should be recorded in the person's medical records. Vaccinated persons whose skin-test results are negative (i.e., <5 mm of induration) and who are enrolled in ongoing periodic skin-testing programs (e.g., HCWs) should continue to be included in ongoing testing programs if their skin-test results are <5 mm induration. Those vaccinees who have positive tuberculin skin-test reactions (≥5 mm of induration) after vaccination should not be retested except after exposure to a case of infectious TB; an increase in induration (i.e., ≥10 mm increase for persons <35 years of age and ≥15 mm increase for persons ≥35 years of age) from a previous to the current skin test may indicate a newly acquired *M. tuberculosis* infection (see Tuberculin Skin Testing and Interpretation of Results After BCG Vaccination).

SURVEILLANCE

All suspected adverse reactions to BCG vaccination (Table 1) should be reported to the manufacturer and to the Vaccine Adverse Event Reporting System (VAERS); telephone (800) 822-7967. These reactions occasionally could occur >1 year after vaccination.

References

1. CDC. The use of preventive therapy for tuberculous infection in the United States: recommendations of the Advisory Committee for Elimination of Tuberculosis. MMWR 1990;39(No. RR-8):9–12.

2. CDC. Use of BCG vaccines in the control of tuberculosis: a joint statement by the ACIP and the Advisory Committee for Elimination of Tuberculosis. MMWR 1988;37:663–4, 669–75.
3. Stead WW, To T, Harrison RW, Abraham JH III. Benefit-risk considerations in preventive treatment for tuberculosis in elderly persons. Ann Intern Med 1987;107:843–5.
4. Medical Research Council. BCG and vole bacillus vaccines in the prevention of tuberculosis in adolescence and early adult life. Bull World Health Organ 1972;46:371–85.
5. Zeidberg LD, Gass RS, Dillon A, Hutcheson RH. The Williamson County Tuberculosis Study: a twenty-four–year epidemiologic study. Am Rev Respir Dis 1963;87(no. 3[part 2]):1–88.
6. Miller FJW, Seal RME, Taylor MD. Tuberculosis in children. Boston: Little Brown, 1963.
7. Brailey M. Factors influencing the course of tuberculous infection in young children. Am Rev Tuberc 1937;36:347–54.
8. Rieder HL, Cauthen GM, Comstock GW, Snider DE Jr. Epidemiology of tuberculosis in the United States. Epidemiol Rev 1989;11:79–98.
9. Selwyn PA, Hartel D, Lewis VA, et al. A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. N Engl J Med 1989; 320:545–50.
10. Daley CL, Small PM, Schecter GF, et al. An outbreak of tuberculosis with accelerated progression among persons infected with the human immunodeficiency virus: an analysis using restriction-fragment-length polymorphisms. N Engl J Med 1992;326:231–5.
11. American Thoracic Society/CDC. Treatment of tuberculosis and tuberculosis infection in adults and children. Am J Respir Crit Care Med 1994;149:1359–74.
12. CDC. Tuberculosis, final data—United States, 1986. MMWR 1988;36:817–20.
13. CDC. Expanded tuberculosis surveillance and tuberculosis morbidity—United States, 1993. MMWR 1994;43:361–6.
14. CDC. Tuberculosis morbidity—United States, 1994. MMWR 1995;44:387–9, 395.
15. Lindhardt M. The statistics of pulmonary tuberculosis in Denmark, 1925–1934: a statistical investigation on the occurrence of pulmonary tuberculosis in the period 1925–1934, worked out on the basis of the Danish National Health Service file of notified cases and of deaths. Copenhagen: Ejnar Munksgaard, 1939.
16. CDC. Reported tuberculosis in the United States, 1994. Atlanta: US Department of Health and Human Services, Public Health Service, CDC, 1995.
17. Sepkowitz KA. Tuberculosis and the health care worker: a historical perspective. Ann Intern Med 1994;120:71–9.
18. CDC. Nosocomial transmission of multidrug-resistant tuberculosis among HIV-infected persons—Florida and New York, 1988–1991. MMWR 1991;40:585–91.
19. Edlin BR, Tokars JI, Grieco MH, et al. An outbreak of multidrug-resistant tuberculosis among hospitalized patients with the acquired immunodeficiency syndrome. N Engl J Med 1992; 326:1514–21.
20. Pearson ML, Jereb JA, Frieden TR, et al. Nosocomial transmission of multidrug-resistant *Mycobacterium tuberculosis*: a risk to patients and health care workers. Ann Intern Med 1992; 117:191–6.
21. CDC. Multidrug-resistant tuberculosis in a hospital—Jersey City, New Jersey, 1990–1992. MMWR 1994;43:417–9.
22. CDC. Outbreak of multidrug-resistant tuberculosis at a hospital—New York City, 1991. MMWR 1993;42:427, 433–4.
23. Valway SE, Greifinger RB, Papania M, et al. Multidrug-resistant tuberculosis in the New York State prison system, 1990–1991. J Infect Dis 1994;170:151–6.
24. American Thoracic Society/CDC. Control of tuberculosis in the United States. Am Rev Respir Dis 1992;146:1623–33.
25. Farer LS. Chemoprophylaxis. Am Rev Respir Dis 1982;125(no. 3[part 2]):102–7.
26. CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care facilities, 1994. MMWR 1994;43(No. RR-13).
27. CDC. Prevention and control of tuberculosis among homeless persons. MMWR 1992;41 (No. RR-5):13–23.
28. CDC. Prevention and control of tuberculosis in correctional institutions: recommendations of the Advisory Committee for the Elimination of Tuberculosis. MMWR 1989;38:313–20, 325.

29. Grange JM, Gibson J, Osborn TW, Collins CH, Yates MD. What is BCG? Tubercle 1983;64: 129–39.
30. Clemens JD, Chuong JJH, Feinstein AR. The BCG controversy: a methodological and statistical reappraisal. JAMA 1983;249:2362–9.
31. Rosenthal SR, Loewinsohn E, Graham ML, et al. BCG vaccination against tuberculosis in Chicago: a twenty-year study statistically analyzed. Pediatrics 1961;28:622–41.
32. Rosenthal SR, Loewinsohn E, Graham ML, et al. BCG vaccination in tuberculous households. Am Rev Respir Dis 1961;84:690–704.
33. Smith PG. Case-control studies of the efficacy of BCG against tuberculosis. In: International Union Against Tuberculosis, ed. Proceedings of the XXVIth IUAT World Conference on Tuberculosis and Respiratory Diseases. Singapore: Professional Postgraduate Services International, 1987:73–9.
34. Romanus V. Tuberculosis in *Bacillus Calmette-Guérin*–immunized and unimmunized children in Sweden: a ten-year evaluation following the cessation of general *Bacillus Calmette-Guérin* immunization of the newborn in 1975. Pediatr Infect Dis 1987;6:272–80.
35. Padungchan S, Konjanart S, Kasiratta S, Daramas S, ten Dam HG. The effectiveness of BCG vaccination of the newborn against childhood tuberculosis in Bangkok. Bull World Health Organ 1986;64:247–58.
36. Tidjani O, Amedome A, ten Dam HG. The protective effect of BCG vaccination of the newborn against childhood tuberculosis in an African community. Tubercle 1986;67:269–81.
37. Young TK, Hershfield ES. A case-control study to evaluate the effectiveness of mass neonatal BCG vaccination among Canadian Indians. Am J Public Health 1986;76:783–6.
38. Shapiro C, Cook N, Evans D, et al. A case-control study of BCG and childhood tuberculosis in Cali, Colombia. Int J Epidemiol 1985;14:441–6.
39. Tripathy SP. Fifteen-year follow-up of the Indian BCG prevention trial. In: International Union Against Tuberculosis, ed. Proceedings of the XXVIth IUAT World Conference on Tuberculosis and Respiratory Diseases. Singapore: Professional Postgraduate Services International, 1987:69–72.
40. Rodrigues LC, Diwan VK, Wheeler JG. Protective effect of BCG against tuberculous meningitis and miliary tuberculosis: a meta-analysis. Int J Epidemiol 1993;22:1154–8.
41. Colditz GA, Brewer TF, Berkey CS, et al. Efficacy of BCG vaccine in the prevention of tuberculosis: meta-analysis of the published literature. JAMA 1994;271:698–702.
42. Lotte A, Wasz-Hockert O, Poisson N, et al. Second IUATLD study on complications induced by intradermal BCG-vaccination. Bull Int Union Tuberc 1988;63:47–59.
43. Caglayan S, Yegin O, Kayran K, Timocin N, Kasirga E, Gun M. Is medical therapy effective for regional lymphadenitis following BCG vaccination? Am J Dis Child 1987;141:1213–4.
44. Brewer MA, Edwards KM, Palmer PS, Hinson HP. Bacille Calmette-Guérin immunization in normal healthy adults. J Infect Dis 1994;170:476–9.
45. World Health Organization. BCG vaccination of the newborn: rationale and guidelines for country programmes. Geneva, Switzerland: World Health Organization, 1986.
46. Lotte A, Wasz-Höckert O, Poisson N, Dumitrescu N, Verron M, Couvet E. BCG complications: estimates of the risks among vaccinated subjects and statistical analysis of their main characteristics. Adv Tuberc Res 1984;21:107–93.
47. Dogliotti M. Erythema multiforme—an unusual reaction to BCG vaccination. S Afr Med J 1980; 57:332–4.
48. Engbaek H, Vergmann B, Bunch-Christensen K. Pulmonary tuberculosis due to BCG in a technician employed in a BCG laboratory. Bull World Health Organ 1977;55:517–20.
49. Morrison WL, Webb WJS, Aldred J, Rubenstein D. Meningitis after BCG vaccination [Letter]. Lancet 1988;1:654–5.
50. Konno K, Feldmann FM, McDermott W. Pyrazinamide susceptibility and amidase activity of tubercle bacilli. Am Rev Respir Dis 1967;95:461–9.
51. Ninane J, Grymonprez A, Burtonboy G, Francois A, Cornu G. Disseminated BCG in HIV infection. Arch Dis Child 1988;63:1268–9.
52. CDC. Disseminated *Mycobacterium bovis* infection from BCG vaccination of a patient with acquired immunodeficiency syndrome. MMWR 1985;34:227–8.
53. von Reyn CF, Clements CJ, Mann JM. Human immunodeficiency virus infection and routine childhood immunisation. Lancet 1987;2:669–72.

54. O'Brien KL, Ruff AJ, Louis MA, et al. Bacillus Calmette-Guérin complications in children born to HIV-1-infected women with a review of the literature. Pediatrics 1995;95:414–8.
55. Colebunders RL, Lebughe I, Musampu M, Pauwels P, Francis H, Ryder R. BCG vaccine abscesses are unrelated to HIV infection [Letter]. JAMA 1988;259:352.
56. Lallemant-Le Coeur S, Lallemant M, Cheynier D, Nzingoula S, Drucker J, Larouze B. Bacillus Calmette-Guérin immunization in infants born to HIV-1-seropositive mothers. AIDS 1991; 5:195–9.
57. World Health Organization. Special programme on AIDS and expanded programme on immunization: joint statement—consultation on human immunodeficiency virus (HIV) and routine childhood immunization. Wkly Epidemiol Rec 1987;62:297–9.
58. Janier M, Moulonguet I, Casin I, et al. Abcès sous-cutané a *Mycobacterium bovis* variété BCG chez un patient séropositif VIH. Ann Dermatol Venereol 1989;116:35–7.
59. Lumb R, Shaw D. *Mycobacterium bovis* (BCG) vaccination: progressive disease in a patient asymptomatically infected with the human immunodeficiency virus. Med J Aust 1992;156: 286–7.
60. Boudes P, Sobel A, Deforges L, Leblic E. Disseminated *Mycobacterium bovis* infection from BCG vaccination and HIV infection [Letter]. JAMA 1989;262:2386.
61. Smith E, Thybo S, Bennedsen J. Infection with *Mycobacterium bovis* in a patient with AIDS: a late complication of BCG vaccination. Scand J Infect Dis 1992;24:109–10.
62. Blondon H, Guez T, Paul G, Truffot-Pernot Ch, Sicard D. Adénite à BCG 6 ans après la vaccination au cours d'un SIDA. Presse Med 1991;20:1091.
63. Reynes J, Perez C, Lamaury I, Janbon F, Bertrand A. Bacille Calmette-Guérin adenitis 30 years after immunization in a patient with AIDS [Letter]. J Infect Dis 1989;160:727.
64. Armbruster C, Junker W, Vetter N, Jaksch G. Disseminated Bacille Calmette-Guérin infection in an AIDS patient 30 years after BCG vaccination [Letter]. J Infect Dis 1990;162:1216.
65. Karalliedde S, Katugaha LP, Uragoda CG. Tuberculin response of Sri Lankan children after BCG vaccination at birth. Tubercle 1987;68:33–8.
66. Bahr GM, Stanford JL, Rook GAW, Rees RJW, Abdelnoor AM, Frayha GJ. Two potential improvements to BCG and their effect on skin test reactivity in the Lebanon. Tubercle 1986; 67:205–18.
67. Heyworth B. Delayed hypersensitivity to PPD-S following BCG vaccination in African children—an 18-month field study. Trans R Soc Trop Med Hyg 1977;71:251–3.
68. Baily GVJ, Narain R, Mayurnath S, Vallishayee RS, Guld J. Trial of BCG vaccines in South India for tuberculosis prevention: tuberculosis prevention trial, Madras. Indian J Med Res 1980;72(suppl):1–74.
69. Abrahams EW. Tuberculin hypersensitivity following BCG vaccination in Brisbane school children. Tubercle 1979;60:109–13.
70. Comstock GW, Edwards LB, Nabangxang H. Tuberculin sensitivity eight to fifteen years after BCG vaccination. Am Rev Respir Dis 1971;103:572–5.
71. Stewart CJ. Skin sensitivity to human, avian and BCG PPDs after BCG vaccination. Tubercle 1968;49:84–91.
72. Guld J, Waaler H, Sundaresan TK, Kaufmann PC, ten Dam HG. The duration of BCG-induced tuberculin sensitivity in children, and its irrelevance for revaccination: results of two 5-year prospective studies. Bull World Health Organ 1968;39:829–36.
73. Horwitz O, Bunch-Christensen K. Correlation between tuberculin sensitivity after 2 months and 5 years among BCG vaccinated subjects. Bull World Health Organ 1972;47:49–58.
74. Orefici G, Scopetti F, Grandolfo ME, Annesi I, Kissopoulos A. Study of a BCG vaccine: influence of dose and time. Boll Ist Sieroter Milan 1982;61:24–8.
75. Fine PEM, Pönnighaus JM, Maine NP. The relationship between delayed type hypersensitivity and protective immunity induced by mycobacterial vaccines in man. Lepr Rev 1986;57 (suppl 2):275–83.
76. Fine PEM, Sterne JAC, Pönnighaus JM, Rees RJW. Delayed-type hypersensitivity, mycobacterial vaccines and protective immunity. Lancet 1994;344:1245–9.
77. American Thoracic Society/CDC. The tuberculin skin test. Am Rev Respir Dis 1981;124:356–63.
78. Menzies R, Vissandjee B. Effect of Bacille Calmette-Guérin vaccination on tuberculin reactivity. Am Rev Respir Dis 1992;145:621–5.

79. CDC. Purified protein derivative (PPD)-tuberculin anergy and HIV infection: guidelines for anergy testing and management of anergic persons at risk of tuberculosis. MMWR 1991;40 (No. RR-5):27–33.
80. CDC. BCG vaccination and pediatric HIV infection—Rwanda, 1988–1990. MMWR 1991;40: 833–6.
81. CDC. Tuberculin reactions in apparently healthy HIV-seropositive and HIV-seronegative women—Uganda. MMWR 1990;39:638–9, 645–6.
82. Nolan RJ Jr. Childhood tuberculosis in North Carolina: a study of the opportunities for intervention in the transmission of tuberculosis to children. Am J Public Health 1986;76:26–30.
83. Whalen C, Nsubuga P, Johnson J, Mugerwa R, Ellner J. Preventive therapy for tuberculosis in HIV-infected Ugandans [Abstract 63]. In: Abstracts: plenary lectures and poster presentations of the challenge of tuberculosis. Washington, DC: The Lancet Conference 1995.
84. Pape JW, Jean SS, Ho JL, Hafner A, Johnson WD Jr. Effect of isoniazid prophylaxis on incidence of active tuberculosis and progression of HIV infection. Lancet 1993;342:268–72.
85. World Health Organization. Tuberculosis control: a manual on methods and procedures for integrated programs. Washington, DC: Pan American Health Organization, 1986; publication no. 498.
86. Gonzalez IO. Prevalencia de cicatrices hipertroficas y queloides segun el sitio de aplicacion de la vacuna BCG intradermica. Bol Oficina Sanit Panam 1980;88:481–8.
87. Chao CW. Post-vaccination keloid. Bull Int Union Tuberc 1972;47(suppl 2):178.

The *Morbidity and Mortality Weekly Report (MMWR)* Series is prepared by the Centers for Disease Control and Prevention (CDC) and is available free of charge in electronic format and on a paid subscription basis for paper copy. To receive an electronic copy on Friday of each week, send an e-mail message to *lists@list.cdc.gov*. The body content should read *subscribe mmwr-toc*. Electronic copy also is available from CDC's World-Wide Web server at *http://www.cdc.gov/* or from CDC's file transfer protocol server at *ftp.cdc.gov*. To subscribe for paper copy, contact Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402; telephone (202) 512-1800.

Data in the weekly *MMWR* are provisional, based on weekly reports to CDC by state health departments. The reporting week concludes at close of business on Friday; compiled data on a national basis are officially released to the public on the following Friday. Address inquiries about the *MMWR* Series, including material to be considered for publication, to: Editor, *MMWR* Series, Mailstop C-08, CDC, 1600 Clifton Rd., N.E., Atlanta, GA 30333; telephone (404) 332-4555.

☆U.S. Government Printing Office: 1996-733-175/27054 Region IV