25. Screening for Tuberculous Infection—*Including Bacille Calmette-Guérin Immunization*

RECOMMENDATION

Screening for tuberculous infection with tuberculin skin testing is recommended for asymptomatic high-risk persons. Bacille Calmette-Guérin (BCG) vaccination should be considered only for selected high-risk individuals (see ***Clinical Intervention***).

Burden of Suffering

About 10–15 million persons in the United States are infected with *Mycobacterium tuberculosis*.[1] More than 24,000 reported cases of tuberculosis (TB) occurred in the U.S. in 1994.[1a,2] This disease is associated with considerable morbidity from pulmonary and extrapulmonary pathology. Pulmonary symptoms are progressive and include cough, hemoptysis, dyspnea, and pleuritis. Extrapulmonary TB can involve the bones, joints, pericardium, and lymphatics, and it can cause spinal cord compression from Pott's disease. Death is more common in older patients and infants, with estimated case-fatality rates ranging from 0.3% in adolescents to 18.5% in the elderly.[3] Newborns and infants also experience significant morbidity from this disease.

The incidence of TB is greatest in Asians, Pacific Islanders, blacks, American Indians, Alaska Natives, and Hispanics. About one third of all reported cases in the U.S. occur in blacks, 20% occur in Hispanics, 14% occur in Asians and Pacific Islanders, and 1% occur in American Indians and Alaska Natives.[2] About 30% of new cases occur in foreign-born immigrants.[2] The prevalence in homeless persons is 1–7% for clinically active TB and 18–51% for asymptomatic *M. tuberculosis* infection.[4]

After experiencing a steady decline from 1963 to 1984, reported TB cases increased by 20% from 1985 to 1992.[2] A disproportionately large number of new cases are occurring among black and Hispanic persons, among whom there was a 41% increase in reported TB cases between 1985 and 1992.[2] Infection with human immunodeficiency virus (HIV) is a major contributor to the recent increase in TB cases. Persons infected with HIV

are more than 100 times more likely to develop active TB than are persons with competent immune systems, and the onset of the disease is often more rapid.[5] Reports of multidrug-resistant TB have also increased in recent years. Nationally, the proportion of new cases resistant to both isoniazid (INH) and rifampin increased from 0.5% in 1982 to 3.3% in the first quarter of 1991.[6] In New York City, as many as 33% of cases are resistant to INH or rifampin.[7] Reported case-fatality rates in patients with multidrug-resistant TB, most of whom are infected with HIV, have been as high as 72–89% (the rate is about 30–40% for immunocompetent individuals).[5] The latest data indicate a 9% decrease in annually reported TB cases from 1992 to 1994, in part reflecting intensified federal, state, and local TB control efforts.[1a]

Accuracy of Screening Tests

Tuberculin skin testing is the principal means of detecting *M. tuberculosis* infection in asymptomatic persons. Although some authors recommend chest radiography as a first-line test in high-risk populations,[8] roentgenography is generally considered to be inappropriate as the initial screening test for detecting tuberculous infection in asymptomatic persons. It is important, however, as a follow-up test to identify active pulmonary TB in infected persons identified through tuberculin testing. The most accurate tuberculin skin test is the Mantoux test, in which 5 units (5 TU) of tuberculin purified protein derivative (PPD) are injected intradermally to detect delayed hypersensitivity reactions within 48–72 hours.

The frequency of false-positive and false-negative tuberculin skin tests depends on a number of variables, including immunologic status, the size of the hypersensitivity reaction, and the prevalence of atypical mycobacteria. In certain geographic areas, cross-reacting atypical mycobacteria (as well as previous BCG vaccination) can produce intermediate size reactions, thereby limiting the specificity of the test.[9–11] False-positive results can also be produced by improper technique (e.g., measuring erythema rather than induration), hypersensitivity to PPD constituents, an Arthus reaction, and cellulitis. Prior BCG vaccination may produce false-positive indurations, but these are generally less than 10 mm in diameter. Moreover, because many BCG vaccinees either lose their immunity over time or do not convert, large indurations cannot be confidently attributed to prior BCG vaccination.[12,13] False-negative reactions, which are estimated to occur in about 5–10% of patients, can be observed early in infection before hypersensitivity develops, in anergic individuals and those with severe illnesses (including active TB), in newborns and infants less than 3 months of age, and as a result of improper technique in handling the PPD solution, administering the intradermal injection, and interpreting the results.[11] Other limitations of the Mantoux test include the time and skill

required for proper administration and variability among clinicians in interpreting results.[14]

Multiple puncture tests (e.g., tine, Mono-Vacc) are less expensive and easier to administer than the Mantoux test. Studies evaluating the accuracy of these devices, however, have produced inconsistent results. In general, the evidence suggests that multiple puncture tests have poor specificity and may have inadequate sensitivity when compared with the Mantoux test.[15–17] Some of this inaccuracy is due to inconsistencies in the dose of injected tuberculin delivered by multiple puncture tests. Patient compliance can also affect the effectiveness of tuberculin skin testing because patients must return to the clinician 48–72 hours after the injection to have the test interpreted. Studies in pediatric patients report noncompliance rates of 28–82%.[18–20]

Persons who are tuberculin test negative may need repeat testing, but there are inadequate data from which to determine the optimal frequency of PPD screening. In the absence of such data, clinical decisions regarding the need for repeat testing and its frequency should be based on the likelihood of further exposure to TB and the clinician's level of confidence in the accuracy of the test results. Some negative reactions to tuberculin skin tests require immediate retesting (two-step testing) to help determine whether future positive reactions are due to the booster phenomenon or to new conversion. A positive result on the second test, typically performed 1–3 weeks later, suggests that the patient has been previously infected (boosted reaction), whereas a negative result on the second test followed by a positive result on subsequent testing suggests recent conversion. Two-step testing has become more common in screening health care workers[21] and other population groups (e.g., elderly nursing home residents) for tuberculous infection.

Effectiveness of Early Detection

The early detection of tuberculin reactivity is of potential benefit because chemoprophylaxis with INH is an effective means of preventing the subsequent development of active TB.[22] A review of 14 controlled trials found that efficacy in preventing clinical disease ranges between 25% and 88% among persons assigned to a 1-year course of INH.[22] Among individuals who complete the course of chemoprophylaxis, efficacy is greater than 90%.[23,24] Some studies suggest that 6 months of INH therapy in adults are nearly as effective as 12 months of treatment.[23,26] Preventive INH therapy is also of potential public health value in preventing future disease activity and transmission of the organism to household members and other close contacts.

A number of factors, however, limit the effectiveness of INH chemo-prophylaxis. Some organisms are resistant to INH and other agents.[5] Patient compliance with a 6–12-month regimen is often difficult. The most important limitation of INH is its potential hepatotoxicity. INH-induced hepatitis occurs in about 0.3–2.3% of patients,[27] the frequency increasing with age and other factors (e.g., alcohol use). The condition can be fatal, but the exact frequency of fatal INH-induced hepatitis is uncertain. Mortality rates for persons with INH-related hepatitis were reported to be as high as 4–7% in one major study, with risk increasing directly with age (zero for persons less than 20 years of age, 0.3% for persons 20–34 years of age, 1.2% for persons 35–49 years of age, 2.3% for persons 50–64 years of age).[28] These data may overestimate the actual mortality from INH-induced hepatitis because the local incidence of cirrhosis-related deaths was increased in one of the communities participating in the study.[29] More recent analyses of published and unpublished data have estimated that the incidence of fatal INH-induced hepatitis is about 1–14/100,000 persons started on preventive therapy.[30,31] The risk may be lowered by performing periodic liver function tests while patients take INH. In persons who develop complications from INH, the resulting interruption of INH therapy before completion of the 1-year course may also lower the effectiveness of TB prevention.[24]

Although the benefits of INH probably outweigh its side effects in persons at high risk for developing active TB (see *Clinical Intervention* for description of high-risk groups), it is uncertain from available data whether low-risk, asymptomatic persons with a reactive tuberculin skin test are at sufficient risk of developing TB to justify the risks of INH-induced hepatitis. Epidemiologic calculations suggest that the annual incidence of TB in a low-risk population is less than 0.1%,[32,33] and that the lifetime probability of developing active TB ranges from 1.2% at age 20 to 0.37% at age 80.[34] Depending on the risk of INH-induced hepatitis, it is possible for complications from INH treatment to be more likely than the development of TB. In the absence of definitive clinical studies to clarify this issue, investigators have used decision analysis techniques to compare the benefits and risks of INH in tuberculin skin reactors of different ages. The results of these analyses have been inconsistent. One group concluded that benefits outweigh risks until the patient exceeds age 45;[35] another found that treatment was beneficial at all ages;[27] and another analysis concluded that INH should be withheld at all ages in the absence of other risk factors.[34] A decision analysis in young adults concluded that treatment was not beneficial in this age group.[32] An analysis for elderly tuberculin skin reactors concluded that INH would neither improve nor worsen 5-year survival but would decrease the risk of developing active disease.[33] An analysis for HIV-infected injection drug users concluded that, with the

exception of black women, such patients would benefit from INH therapy even in the absence of tuberculin skin testing.[36]

Bacille Calmette-Guérin (BCG) Vaccination

Primary prevention through vaccination represents an alternative approach to the prevention of TB. BCG, a live vaccine derived from attenuated *Mycobacterium bovis,* has been used worldwide for more than 50 years to prevent TB. Clinical trials of the efficacy of BCG have yielded inconsistent results since the early 1930s, however, with reported levels of protection ranging from –56% to 80%.[37,38] Observational studies have shown that the incidence of the disease is lower in vaccinated children than in unvaccinated controls.[39–43] Factors contributing to the wide variation in results in BCG vaccine efficacy include genetic changes in the bacterial strains as well as differences in production techniques, methods of administration, and the populations and environments in which the vaccine has been studied.[44] A meta-analysis of 14 trials and 12 case-control studies concluded that BCG offered 50% protection against TB overall and 64–71% protection against TB meningitis and TB-related death.[45]

The potential adverse effects of BCG vaccination include prolonged ulceration and local adenitis, which occur in about 1–10% of vaccinees. The risk varies with the type of vaccine used, the population, and the methods used to measure complications. Osteomyelitis and death from disseminated BCG infection are estimated to occur in one case per million doses administered.[44]

In the U.S., where the risk of becoming infected with *M. tuberculosis* is relatively low, the disease can currently be controlled most successfully by screening and early treatment of infected persons. However, BCG vaccination may have a role in the U.S. for persons with special exposures to individuals with active TB, such as uninfected children who are at high risk for continuous or repeated exposure to infectious persons who are undetected or untreated,[44] or a future role in light of escalating multidrug resistance.

Recommendations of Other Groups

The Centers for Disease Control and Prevention (CDC), American Thoracic Society (ATS), and other members of the Advisory Committee for Elimination of Tuberculosis recommend screening the following groups for tuberculous infection: persons infected with HIV; close contacts of persons with TB; persons with medical risk factors associated with TB; immigrants from countries with high TB prevalence; medically underserved low-income populations; injection drug users; and residents and employees of high risk facilities.[46] Similar recommendations have been issued by the American Academy of Family Physicians.[55] Although the Canadian

Task Force on the Periodic Health Examination recommends screening high-risk groups, it gave an "E" recommendation (good evidence against performing the maneuver in the periodic health examination) to screening low-risk persons.[46a] The American Academy of Pediatrics (AAP) recommends against routine annual skin testing of children who lack risk factors and live in low-prevalence communities. The AAP does recommend annual Mantoux testing of high-risk children, as well as consideration of less frequent periodic testing (e.g., at ages 1, 4–6, and 11–16 years) of low-risk children who live in high-prevalence communities or have unreliable histories.[47] The Bright Futures guidelines recommend annual testing for persons of low socioeconomic status, those in high prevalence areas, those exposed to TB, and immigrants.[48] The American Medical Association's Guidelines for Adolescent Preventive Services (GAPS) recommend annual testing for adolescents in high-risk settings including those in homeless shelters, correctional institutions, and health care facilities.[49]

Recommendations on how to perform tuberculin skin testing have been issued by the CDC and ATS.[11] The CDC has recently issued guidelines on preventing transmission in health care facilities, which include specific recommendations on the categories of health care workers to include in skin-testing programs and the frequency with which they should be tested.[50] Guidelines for the treatment of converters have been issued in a joint statement by the ATS, AAP, CDC, and Infectious Disease Society of America.[51,52] The CDC has also issued recommendations on multidrug preventive therapy for converters with suspected contact with drug-resistant TB.[5] Screening certain populations for tuberculous infection is required by law in 44 states.[7]

Recommendations on BCG vaccination have been issued in a joint statement by the Immunization Practices Advisory Committee and the Advisory Committee for Elimination of Tuberculosis.[44] They recommended limiting BCG vaccination in the U.S. to tuberculin-negative infants and children who cannot be placed on INH and who have continuous exposure to persons with active disease, those with continuous exposure to patients with organisms resistant to INH or rifampin, and those belonging to groups with a rate of new infections greater than 1% per year and for whom the usual surveillance and treatment programs may not be operationally feasible.

CLINICAL INTERVENTION

Screening for tuberculous infection by tuberculin skin testing is recommended for all persons at increased risk of developing tuberculosis (TB) ("A" recommendation). Asymptomatic persons at increased risk include persons infected with HIV, close contacts of persons with known or sus-

pected TB (including health care workers), persons with medical risk factors associated with TB, immigrants from countries with high TB prevalence (e.g., most countries in Africa, Asia, and Latin America), medically underserved low-income populations (including high-risk racial or ethnic minority populations), alcoholics, injection drug users, and residents of long-term care facilities (e.g., correctional institutions, mental institutions, nursing homes). The Mantoux test involves the intradermal injection of 5 units of tuberculin PPD and the subsequent examination of the injection site 48–72 hours later. Current minimum criteria for a positive skin test, based on observational data and expert opinion, are 15-mm diameter for low-risk individuals, 10-mm diameter for high-risk individuals (e.g., immigrants, medically underserved low-income populations, injection drug users, residents of long-term care facilities, persons with conditions that increase TB risk, infants, and children less than 4 years of age), and 5-mm diameter for persons at very high risk (e.g., persons infected with HIV, persons with abnormal chest radiographs, recent contacts of infected persons). Prior BCG vaccination is not currently considered a valid basis for dismissing positive results. Persons with negative reactions who are at increased risk of anergy (e.g., HIV-infected individuals) can be skin-tested for anergy,[53] but this procedure is now considered optional in current CDC guidelines.[46] Treatment decisions in HIV-infected anergic patients should be made on an individual basis.[54] The frequency of tuberculin skin testing is a matter of clinical discretion.

Persons with a positive PPD test should receive a chest x-ray and clinical evaluation for TB. Those lacking evidence of active infection should receive INH prophylaxis if they meet criteria defined in recent guidelines.[52] Briefly, these criteria recommend INH prophylaxis in persons under 35 years of age who are from high-prevalence countries; medically underserved, low-income, high-prevalence populations; or long-term care facilities. It is also recommended in persons of any age with HIV infection or increased risk of HIV infection, other medical conditions that increase the risk of TB, or close contact with patients with newly diagnosed TB or skin test conversion. Screening for HIV infection may be indicated in recent converters (see Chapter 28). Patients with possible exposure to drug-resistant TB should be treated according to current recommendations for multidrug preventive therapy.[5] Directly observed therapy—observation of the patient by a health care worker as the medication is taken—may be indicated in patients who are unlikely to be compliant.

BCG vaccination against TB should be considered only for tuberculin-negative infants and children who cannot be placed on INH and who have continuous exposure to persons with active disease, those with continuous exposure to patients with organisms resistant to INH or rifampin, and those belonging to groups with a rate of new infections greater than 1%

per year and for whom the usual surveillance and treatment programs may not be operationally feasible ("B" recommendation). These groups may also include persons with limited access to or willingness to use health care services.

The draft update of this chapter was prepared for the U.S. Preventive Services Task Force by Steven H. Woolf, MD, MPH.

REFERENCES

1. Centers for Disease Control. National action plan to combat multidrug-resistant tuberculosis. MMWR 1992;41(RR-11):5–48.
1a. Centers for Disease Control and Prevention. Tuberculosis morbidity—United States, 1994. MMWR 1995;44:387–389, 395.
2. Centers for Disease Control and Prevention. Tuberculosis morbidity—United States, 1993. MMWR 1994;43:361–366.
3. Centers for Disease Control and Prevention. Tuberculosis statistics in the United States, 1990. Atlanta: Centers for Disease Control and Prevention, 1992.
4. Centers for Disease Control. Prevention and control of tuberculosis among homeless persons: recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR 1992;41(RR-5): 13–23.
5. Centers for Disease Control. Management of persons exposed to multidrug-resistant tuberculosis. MMWR 1992;41(RR-11):61–71.
6. Bloch AB, Cauthen GM, Onorato IM, et al. Nationwide survey of drug-resistant tuberculosis in the United States. JAMA 1994;271:665–671.
7. Centers for Disease Control and Prevention. Tuberculosis control laws—United States, 1993. MMWR 1993;42(RR-15):1–28.
8. Davidson PT. Routine screening for tuberculosis on hospital admission. Chest 1988;94:228–230.
9. Tuberculin, PPD: generic statement. Fed Reg 1977;42:52709–52712.
10. Mellor J. False-positive results of Mantoux tests. Can Med Assoc J 1985;132:1403.
11. American Thoracic Society. Diagnostic standards and classification of tuberculosis. Am Rev Respir Dis 1990;142:725–735.
12. Snider DE Jr. Bacille Calmette-Guerin vaccinations and tuberculin skin tests. JAMA 1985;253: 3438–3439.
13. Skotniski EM. Post-BCG tuberculin testing: interpreting results and establishing essential baseline data. Can J Public Health 1993;84:307–308.
14. Bearman JE, Kleinman H, Glyer VV, et al. A study of variability in tuberculin test reading. Am Rev Respir Dis 1964;90:913–919.
15. Rudd RM, Gellert AR, Venning M. Comparison of Mantoux, tine, and "Imotest'' tuberculin tests. Lancet 1982;2:515–518.
16. Catanzaro A. Multiple puncture skin test and Mantoux test in Southeast Asian refugees. Chest 1985; 87:346–350.
17. Hansen JP, Falconer JA, Gallis HA, et al. Inadequate sensitivity of tuberculin tine test for screening employee populations. J Occup Med 1982;24:602–604.
18. Maqbool S, Asnes RS, Grebin B. Tine test compliance in a clinic setting. Pediatrics 1975;55:388–391.
19. Weinberger HL, Terry C. Tuberculin testing in a pediatric outpatient clinic. J Pediatr 1969;75:111–115.
20. Asnes RS, Maqbool S. Parent reading and reporting of children's tuberculin skin test results. Chest 1975;68 (Suppl 3):459–462.
21. Snider DE Jr, Cauthen GM. Tuberculin skin testing of hospital employees: infection, "boosting," and two-step testing. Am J Infect Control 1984;12:305–311.
22. Comstock GW, Woolpert SF. Preventive therapy. In: Kubica GP, Wayne LG, eds. The mycobacteria: a source book. New York: Marcel Dekker, 1984:1071–1081.
23. International Union Against Tuberculosis, Committee on Prophylaxis. Efficacy of various durations of isoniazid preventive therapy for tuberculosis: five years of follow-up in the IUAT trial. Bull WHO 1982; 60:555–564.

24. Stead WW, Teresa T, Harrison RW, et al. Benefit-risk considerations in preventive treatment for tuberculosis in elderly persons. Ann Intern Med 1987;107:843–845.
25. Deleted in proof.
26. Snider DE Jr, Caras GJ, Koplan JP. Preventive therapy with isoniazid: cost-effectiveness of different durations of therapy. JAMA 1986;255:1579–1583.
27. Rose DN, Schechter CB, Silver AL. The age threshold for isoniazid chemoprophylaxis: a decision analysis for low-risk tuberculin reactors. JAMA 1986;256:2709–2713.
28. Kopanoff DE, Snider DE Jr, Caras GJ. Isoniazid-related hepatitis: a U.S. Public Health Service cooperative surveillance study. Am Rev Respir Dis 1978;117:991–1001.
29. Comstock GW. Prevention of tuberculosis among tuberculin reactors: maximizing benefits, minimizing risks. JAMA 1986;256:2729–2730.
30. Snider DE Jr, Caras GJ. Isoniazid-associated hepatitis deaths: a review of available information. Am Rev Respir Dis 1992;145:494–497.
31. Salpeter SR. Fatal isoniazid-induced hepatitis: its risk during chemoprophylaxis. West J Med 1993;159:560–564.
32. Taylor WC, Aronson MD, Delbanco TL. Should young adults with a positive tuberculin test take isoniazid? Ann Intern Med 1981;94:808–813.
33. Cooper JK. Decision analysis for tuberculosis preventive treatment in nursing homes. J Am Geriatr Soc 1986;34:814–817.
34. Tsevat J, Taylor WC, Wong JB, et al. Isoniazid for the tuberculin reactor: take it or leave it. Am Rev Respir Dis 1988;137:215–220.
35. Comstock GW, Edwards PQ. The competing risks of tuberculosis and hepatitis for adult tuberculin reactors. Am Rev Respir Dis 1975;111:573–577.
36. Jordan TJ, Lewit EM, Montgomery RL, Reichman LB. Isoniazid as preventive therapy in HIV-infected intravenous drug abusers: a decision analysis. JAMA 1991;265:2987–2991.
37. Clemens JD, Chuong JJH, Feinstein AR. The BCG controversy: a methodological and statistical reappraisal. JAMA 1983;249:2362–2369.
38. Tripathy SP. Fifteen-year follow-up of the Indian BCG prevention trial. In: International Union Against Tuberculosis. Proceedings of the XXVIth IUAT World Conference on Tuberculosis and Respiratory Diseases. Singapore: Professional Postgraduate Services International, 1987:69–72.
39. Romanus V. Tuberculosis in Bacillus Calmette-Guerin-immunized children in Sweden: a ten-year evaluation following the cessation of general Bacillus Calmette-Guerin immunization of the newborn in 1975. Pediatr Infect Dis 1987;6:272–280.
40. Smith PG. Case-control studies of the efficacy of BCG against tuberculosis. In: International Union Against Tuberculosis. Proceedings of the XXVIth IUAT World Conference on Tuberculosis and Respiratory Diseases. Singapore: Professional Postgraduate Services International, 1987:73–79.
41. Padungchan S, Konjanart S, Kasiratta S, et al. The effectiveness of BCG vaccination of the newborn against childhood tuberculosis in Bangkok. Bull WHO 1986;64:247–258.
42. 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;67:269–281.
43. Slutkin G. Management of tuberculosis in urban homeless indigents. Public Health Rep 1986;101:481–485.
44. Immunization Practices Advisory Committee. 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;37:663–664, 669–675.
45. 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.
46. Centers for Disease Control and Prevention. Screening for tuberculosis and tuberculosis infection in high-risk populations: recommendations of the Advisory Committee for Elimination of Tuberculosis. MMWR 1995;44(RR–11):19–34.
46a. Canadian Task Force on the Periodic Health Examination. Canadian guide to clinical preventive health care. Ottawa: Canada Communication Group, 1994:754–765.
47. American Academy of Pediatrics, Committee on Infectious Diseases. Screening for tuberculosis in infants and children. Pediatrics 1994;93:131–134.
48. Green M, ed. Bright Futures: guidelines for health supervision of infants, children and adolescents. Arlington, VA: National Center for Education in Maternal and Child Health, 1994.

49. American Medical Association. AMA guidelines for adolescent preventive services (GAPS): recommendations and rationale. Chicago: American Medical Association, 1994.

50. Centers for Disease Control and Prevention. Guidelines for preventing the transmission of Mycobacterium tuberculosis in health-care facilities, 1994. MMWR 1994;43(RR-13):1–132.

51. American Thoracic Society. Control of tuberculosis in the United States. Am Rev Respir Dis 1992;146:1623–1633.

52. American Thoracic Society. Treatment of tuberculosis and tuberculosis infection in adults and children. Am J Respir Crit Care Med 1994;149:1359–1374.

53. Centers for Disease Control. 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(RR-5):1–5.

54. Centers for Disease Control and Prevention. USPHS/IDSA guidelines for the prevention of opportunistic infections in persons with human immunodeficiency virus: a summary. MMWR 1995;44(RR-8):1–34.

55. American Academy of Family Physicians. Age charts for periodic health examination. Kansas City, MO: American Academy of Family Physicians, 1994. (Reprint no. 510.)