CDPH/CTCA Joint Guidelines

Guidelines for the Assessment of Tuberculosis Patient Infectiousness and Placement into High and Lower Risk Settings

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Preface

The following Guidelines have been developed by the California Department of Public Health (CDPH), Center for Infectious Diseases, Tuberculosis Control Branch (TBCB), and the California TB Controllers Association (CTCA). These Guidelines provide statewide recommendations for tuberculosis (TB) control in California. If these Guidelines are altered for local use, then the logo should be removed and adaptation from this source document acknowledged.

No set of guidelines can cover all individual situations that can and will arise. When questions arise on individual situations not covered by these guidelines, consult with your local TB Controller or the CDPH, TBCB. As mandated by state law (Health and Safety Code, Section 121361), all decisions regarding the discharge or transfer of TB patients from health care facilities (HCFs) must be made by the local health officer (LHO) or designee of the jurisdiction in which the facility is located.

I. Background

Tuberculosis (TB) transmission has been documented in a variety of high risk settings, including health care facilities (HCFs), skilled nursing facilities (SNFs), correctional institutions, congregate living sites for HIV-infected persons, residential drug treatment facilities, and homeless shelters. TB transmission and the development of secondary TB cases can occur when infectious TB patients are housed or work in such settings. Since our publication of *Guidelines for the Placement or Return of TB Patients into High Risk Housing, Work, Correctional or In-Patient Settings*[1] in 1997, much work has been done to better define the patient characteristics associated with ongoing infectiousness after the initiation of appropriate anti-TB therapy[2,3,4,5,6,7,8,9]. In its *Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings*[10], and other publications[11], the Centers for Disease Control and Prevention (CDC) has recommended, for the purposes of assessing patient infectiousness, a change in the frequency and conditions of sputum specimen collection. Although the risk of transmission and secondary cases is likely to be lower in lower risk settings, including most residential and occupational settings, criteria for the release of TB patients into such settings have not previously been developed.

No research has been published comparing the yield for AFB smear using an 8 hour collection interval versus a 24 hour collection interval as previous guidelines required. However, there is available literature on the yield of induced versus spontaneous sputum specimens and on "spot" versus first morning sputum. In the 2005 CDC *Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings,* the recommendation was made that the interval between sputum sampling could be shortened to a minimum of eight hours, with at least one specimen an early AM one. Sensitivities of induced sputum have been reported to be as high as 74% in smear negative but culture confirmed pulmonary TB cases.[12] Early morning specimens are marginally better than spot specimens.[13]

Because of the robust data on the value of an induced specimen, we are recommending that at least one of the three specimens should be induced, if available. To conform to the CDC recommendations in *Controlling Tuberculosis in the United States,* the number of days on anti-TB therapy for smear negative patients to be considered non-infectious has been changed to five days from four days. Because the transmission of multidrug-resistant TB (MDR-TB) infection has more serious potential consequences for contacts, and because there is strong evidence for prolonged infectiousness even on treatment for MDR-TB patients, a more stringent set of criteria for release from isolation of these patients is warranted, and reflected in these guidelines.

II. Purpose

These guidelines have been developed to reduce the risk of TB transmission by:

1. Defining uniform criteria for patient non-infectiousness which should be assessed before placing patients in settings in which the risk of transmission and/or secondary TB cases is high.
2. Defining uniform criteria for patient non-infectiousness for placement of patients in settings in which the risk of both transmission and secondary TB cases is lower.

III. Risk Definitions: Settings, Disease Progression, and Drug Resistance

1. High Risk Setting*

a. A housing or work setting in which others will share air with the TB patient and which is characterized by one or more of the following factors:

   i. A large number or high density of persons.
   ii. The presence of persons at high risk of progression to active TB disease (see III.3., below)
   iii. The presence of persons who have not been previously exposed to the TB patient.

2. Lower Risk Setting*

All settings should be considered high risk until an assessment has been done by the local TB control program.

a. A **residential** setting not characterized as high risk, and:

   i. No other persons will share the air with the TB patient; OR
   ii. Other persons who will share the air with the TB patient are not at increased risk for progression to TB disease if infected (see III.3., below); OR
   iii. All persons at increased risk of progression to TB disease if infected, including all children under the age of five years, who will share the air with the TB patient, have been previously exposed to the TB patient, have had a complete medical evaluation and have been started on therapy, including window period treatment for presumed LTBI (TB1),[35] as appropriate.

b. A **work** setting not characterized as high risk, and in which no contacts are known or reasonably expected to be at increased risk of progression to TB disease if infected.

3. Persons at Increased Risk of Progression to TB Disease if Infected[14]

a. Children < 5 years of age.

b. Persons with medical conditions associated with an increased risk of progression to active TB disease, including:

   i. HIV infection (including persons at increased risk for HIV infection who have not been tested).
   ii. Diabetes mellitus, especially if insulin dependent or poorly controlled.
   iii. End-stage renal disease.

* Determination of risk should be done by the local TB control program

iv. Injection drug use, even if HIV negative.
v. Cancer of the head and neck.
vi. Immunosuppressive treatment, including chronic corticosteroids, anti TNF-α agents, post-transplant therapy and cancer chemotherapy.
vii. Other diseases characterized by immunosuppression, such as lymphoma or leukemia.
viii. Intestinal bypass or gastrectomy.
ix. Low body weight (> 10% below ideal body weight).
x. Chronic malabsorption.
xi. Malnutrition and clinical situations associated with rapid weight loss.
xii. Silicosis.

4. Persons at increased risk of MDR-TB[15]

a. Contact to an MDR TB case.

b. Current TB treatment (Rx) with evidence of treatment failure.

c. Prior TB treatment since 1970 (Exception: relapse of disease following completion of adequate therapy by Directly Observed Therapy (DOT) for an episode of pan-susceptible disease).

d. Immigration from or recent extended travel to, a country with a high incidence (≥ 4%) of MDR-TB among cases from that country diagnosed in the US.[†] At the present time these countries are:

i. Russia and other former Soviet states.
ii. Peru.

e. Other state or locally identified risk groups[‡], including:

i. Hmong refugees.
ii. Persons of Tibetan origin.

Persons at increased risk of MDR-TB:

- Contact to an MDR TB case.
- Current TB Rx with evidence of treatment failure.
- Prior TB treatment, unless DOT.
- Immigration from, or recent extended travel to, a country with a high incidence of MDR-TB.
- Other state or locally identified risk groups.

[†] Current data on the risk of MDR TB in US TB Cases, by Country of Origin, are available from the CDC, Division of TB Elimination (DTBE) (www.cdc.gov/tb)

[‡] Current data on epidemiologic groups at increased risk for MDR-TB are available from the CDPH, TBCB (510-620-3000) (www.cdph.ca.gov/programs/tb)

IV. Definition of Terms

1. Acid Fast Bacilli (AFB) smear negative: any respiratory specimen which is negative for AFB.[§16]
2. Acid Fast Bacilli (AFB) smear positive: any respiratory specimen positive for AFB by microscopy. Because fluorescent (auramine-rhodamine [A-R]) staining is potentially prone to artifact, if an AFB smear is positive on A-R, it is strongly recommended to confirm with Ziehl-Neelson (Z-N) staining. Because infectiousness has been associated with degree of smear positivity, and persons who are A-R positive but Z-N negative have low numbers of AFB on smear, these persons can be considered smear negative for the purpose of determining infectiousness.
3. Direct genetic test for drug resistance: direct test for mutations associated with isoniazid (INH) and rifamycin (RIF) resistance, for example, the molecular beacon test, gene sequencing, or line probe assay.
4. Drug susceptibility test (DST): phenotypic drug susceptibility test in liquid or solid media.
5. MDR-TB: confirmed TB disease resistant to INH and RIF based on the results of drug susceptibility testing (DST), or a direct genetic test (unless discordant with subsequent phenotypic DST).
6. Nucleic acid amplification test (NAAT): a test that detects, via the amplification of specific nucleic acid sequences, the presence of *M. tuberculosis* complex in clinical specimens. Examples include Amplicor® (approved on smear positive specimens only) or MTD® (approved for smear positive and smear negative specimens). Some labs use a homebrew PCR for *M. tuberculosis* complex identification.
7. Positive culture for *M. tb*: liquid or solid media with growth of AFB identified as *M. tb or M. tb complex,* with the exception of *the BCG strain of Mycobacterium bovis.*
8. Preliminary positive AFB culture: liquid or solid media with growth of AFB, identification pending.
9. Respiratory specimen: sputum, induced sputum, bronchoalveolar lavage, biopsy of tissue from the respiratory tract (not including pleura).
10. Sputum specimen[**] [17] [18] [19] [20] [21] [22] [23] [24]: spontaneous or induced sputum specimen of at least 2 ml (not saliva). Some labs will not accept a specimen less than 5 ml. In some situations, even a scant specimen if it is true sputum should be processed.[25]

[§] A concentrated specimen with fluorescent microscopy is the preferred diagnostic method.

[**] For patients unable to produce a spontaneous specimen, sputum induction using hypertonic saline should be performed. Because AFB smear positivity is increased significantly by induction compared with simple expectoration, when available an induced specimen is preferred. If sputum induction is unsuccessful, an alternative method of sampling such as bronchoscopy should be considered if clinically warranted. Gastric aspirates can be useful for obtaining cultures, especially in children, but are prone to false positive smears due to acid fast stomach organisms. An induction attempt that does not yield an adequate specimen ("dry" induction) may be considered equivalent to an adequate specimen that is smear and culture negative at the discretion of the TB Controller.

V. General Considerations for Determining the Risk of TB Transmission and Secondary TB Cases

The following factors should be considered in determining the risk of, and consequences of, transmission.

1. The patient's infectiousness:[9 10 11 14 26] **Infectiousness is positively correlated with the following factors:**

a. Disease in the lungs, airways or larynx.
b. Presence of cough.
c. Presence of a positive AFB smear in the sputum.[††]
d. Extent of infiltration on chest radiograph.
e. Cavitation on chest radiograph.
f. Failure of the patient to cover the mouth and nose when coughing.
g. Inappropriate or short duration of chemotherapy.
h. Non-adherence to chemotherapy.
i. Poor clinical or bacteriologic response to therapy.

For assessing patient infectiousness (except for MDR-TB), sputum specimens may be collected ≥ 8 hours apart. At least one should be early AM, induced, a broncho-alveolar lavage, or collected post-bronchoscopy.

2. The probability that exposed persons, if infected, will develop active disease (See III.3)

3. The potential for transmission of *M. tb* in the environment[11]

a. Environmental factors which increase the risk of transmission include:

i. Potential that others will share air with the case (either in the same room or via the building ventilation system). Use of HEPA filtration or ultraviolet germicidal irradiation (UVGI) may reduce the risk.[27 28 29]
ii. Poor supply of fresh air.[10]
iii. Larger number and higher density of persons in setting.[11]
iv. Longer duration of time spent in the setting.

b. Transmission of *M. tb* has been documented in a variety of settings. At a minimum, the following types of settings, should be considered high risk:

v. HCFs.[10]
vi. Correctional facilities (CFs).[30]

[††] Transmission of TB by AFB smear-negative cases prior to treatment can occur and is well-documented. Consequently, in certain circumstances, the determination of infectiousness may require the application of more stringent criteria, specifically; consistently negative sputum cultures (at least two consecutive respiratory specimens).

vii. Drug treatment residential facilities.[31]
viii. Other congregate living sites, especially those housing persons at increased risk of progression to TB disease if infected (see III.3), including shelters for homeless person[32], board and care facilities, and residential treatment facilities.[33]
ix. Public living accommodations, including single room occupancy hotels[34], if air is shared in common areas or through the building ventilation system.

4. Drug resistance of the patient's TB isolate

VI. Criteria for Infectiousness and Placement in High And Lower Risk Settings

CATEGORY	SETTING‡‡	CRITERIA§§
TB suspect **-Low suspicion of active TB** **-Not on treatment for suspected active TB**	High risk	3 consecutive respiratory specimens, including at least one early AM or induced sputum***, or BAL†††, collected at least 8 hours apart, are AFB smear negative.
	Lower risk	No restriction
TB case or suspect on treatment for active TB **-AFB smear positive** **-No risk factor for MDR-TB**	High risk	1. 3 consecutive respiratory specimens, including at least one early AM or induced sputum***, or BAL†††, collected at least 8 hours apart, are AFB smear negative; 2. At least 14 daily doses of treatment for TB , preferably by directly observed therapy (DOT), taken and tolerated; and 3. Clinical improvement.
	Lower risk‡‡‡	1. At least 14 daily doses of treatment for TB , preferably by DOT, taken and tolerated; 2. Bacteriologic response to therapy (progressively decreasing degree of smear positivity); and 3. Clinical improvement.
TB case or suspect on treatment for TB **-AFB smear negative X 3 §§§** **-No risk factor for MDR-TB**	High risk	1. At least 5 daily doses of treatment for TB taken and tolerated.
	Lower risk	1. Treatment for TB started (at least one dose taken and tolerated).
TB case (or suspect on treatment for TB) **-At increased risk for MDR-TB (see III.4)**	High or Lower risk	1. Obtain direct genetic test, if available, for Rifampin resistance 2. If direct genetic test not available, while phenotypic DST for Rifampin is pending, either criteria for patients with known MDR-TB or criteria for patients not at increased risk of MDR-TB may be applied, at the discretion of the local TB controller.
Known MDR-TB case (see IV.5)	High risk	1. 3 consecutive respiratory specimens collected on separate days, including at least one early AM or induced sputum***, or BAL†††, are AFB smear negative, and no subsequent sputum specimen is smear positive; 2. At least 14 daily doses of treatment for MDR-TB taken and tolerated by DOT; 3. Clinical improvement; and 4. At least 2 consecutive negative sputum cultures without a subsequent positive culture.
	Lower risk	1. 3 consecutive sputum specimens collected on separate days are AFB smear negative; 2. At least 14 daily doses of treatment for MDR-TB taken and tolerated by DOT; and 3. Clinical improvement.

‡‡ See Risk Definitions, above
§§ See Definition of Terms, above
*** If available, induced sputum is preferred.
††† If bronchoscopy is done, a post-bronchoscopic sputum specimen obtained at least 8 hours post bronchoscopy should be included as one of the 3 specimens.
‡‡‡ Note: A patient may be considered for placement in a lower risk setting without meeting these criteria if no previously unexposed persons will be present. (see Home Isolation, below)
§§§ The quality of sputum smear must be verified before smear negative status is confirmed, especially if cavitary disease is present

VII. Discharge or Transfer of TB Cases and Suspects from HCFs

H&S Code, Section 121361, requires that "HCFs shall discharge or transfer a person known or suspected to have active TB disease *only after notification and a written treatment plan is received and approved* by the local health officer (LHO) of the jurisdiction in which the facility is located." (italics added) This authority is often delegated by the LHO to the local TB Controller.

1. The written treatment plan shall include the following elements (H&S Code, Section 121362):
    a. Verified patient address (or address of the receiving facility);
    b. Name and contact information of the medical provider who has specifically agreed to provide medical care;
    c. Clinical information used to assess the patient's infectiousness; and
    d. Any other information required" by the LHO.
2. When reviewing the written treatment plan, the LHO or designee should take into consideration risk factors for MDR-TB, infectiousness of the case, and the type of setting the patient is entering or returning to using the criteria in VII to guide decision-making. In addition, before a discharge or transfer can be approved:
    a. Arrangements should be in place for continuation without interruption of an appropriate, prescribed course of TB medication, preferably by DOT;
    b. For patients returning home, a home evaluation, including an in person home visit, should be completed by the local TB program and documented. All contacts at increased risk of progression to TB disease if infected (see III.3) should be medically evaluated for TB and started on appropriate therapy, including window period treatment for presumed LTBI (TB1)[35]. The patient or guardian must agree to abide by home isolation instructions (see VIII);
    c. The patient's ability to ambulate and perform all activities of daily living should be appropriate for the discharge setting;
    d. Special medical needs (e.g., hemodialysis, cancer treatment) transportation to source of medical care, cooking, shopping, laundry and other issues that might present barriers to adherence with home isolation, or risk of transmission of TB to previously unexposed persons, especially new contacts at increased risk for progression to TB disease if infected (see III.3), should be addressed.

VIII. Home Isolation

Prior to meeting the criteria for non-infectiousness, TB patients may be placed in *home isolation*. To be placed in home isolation, the patient should have been started on a standard multidrug anti-TB treatment regimen; no infants and children <5 years or persons with HIV or other severely immunocompromising conditions are present in the

household or if present, are on appropriate LTBI treatment or window period treatment for presumed LTBI; all immunocompetent household members have been previously exposed to the patient; and the patient is willing to follow the restrictions imposed by the local TB control program. Parameters for home isolation need to be clarified to the patient and other residents. This should include conditions for entry of persons into the environment, circumstances where the patient may leave the residence, and precautions within the residence (separate room, etc). Special precautions for attendance at medical appointments should be clarified with the provider seeing the patient and the patient. Patients in home isolation may not work until they meet the criteria appropriate for their work setting. Patients who are nonadherent with the conditions of home isolation may be served a legal order to remain in home isolation (H&S Code, Section 121365[g]), and may be prosecuted if they violate such an order (H&S Code, Section 120280).

IX. References

[1] CDHS/CTCA Joint Guidelines. Guidelines for the Placement or Return of TB Patients into High Risk Housing, Work, Correctional or In-Patient Settings, 1997.

[2] Escombe AR et al. The Detection of Airborne Transmission of Tuberculosis from HIV-Infected Patients, Using an In Vivo Air Sampling Model. CID, 2007; 44:1349.

[3] Fennelly KP et al. Cough Generating Aerosols of M. tb. AJRCCM, 2004; 169:604.

[4] Jindani A et al. Bactericidal and Sterilizing Activities of Antituberculosis Drugs During the First 14 Days. AJRCCM, 2003; 167:1348.

[5] Reichler MR et al. Evaluation of Investigations Conducted to Prevent Transmission of TB. JAMA, 2002; 287:991.

[6] Baily WC et al. Predictive Model to identify Positive TST results During Contact Investigations. JAMA, 2002; 287:996.

[7] Borgdorff MW et al. Transmission of *Mycobacterium tuberculosis* Depending on the Age and Sex of Source Cases. Am J Epidemiology, 2001; 154:934.

[8] Marks SM et al. Outcomes of Contact Investigations of Infectious TB Patients. AJRCCM, 2000; 162:2033.

[9] Behr MA et al. Transmission of M. tb. from Patients Smear Negative for AFB. Lancet, 1999; 353:444.

[10] CDC. Guidelines for Preventing the Transmission of M. tb. in Health Care Settings. MMWR, 2005; 54 (RR-17).

[11] CDC/ATS/IDSA. Controlling TB in the US. MMWR, 2005; 54 (RR-12).

[12] Ganguly KC, Hiron MM, Mridha ZU, et.al. Comparison of sputum induction with broncho-alveolar lavage in the diagnosis of smear-negative pulmonary tuberculsosis. Mymensingh Med J. 2008 Jul;17(2):115-23

[13] Mase SR et al. Yield of Serial Sputum Specimen Examinations in the Diagnosis of Pulmonary TB: a Systematic Review. Int J Tuberc Lung Dis, 2007; 11:485

[14] CDC. Guidelines for the Investigation of contacts of persons with infectious tuberculosis. Recommendations from the National Tuberculosis Controller's Association and CDC, MMWR 2005;54 (No. RR-15):1-47.

[15] Francis J. Curry National TB Center. Drug Resistant TB - A Survival Guide for Clinicians, 2nd Ed. 2008; pp. 7-9, 18-21.

[16] Steingart, KR, Henry, M, Ing, V, Hopewell, PC et al. Fluorescence versus conventional sputum smear microscopy for tuberculosis: a systematic review. Lancet. September 2006; (6):570-581.

[17] Chang KC, Leung CC, Yew WW, Tam CM. Supervised and induced sputum among patients with smear-negative pulmonary tuberculosis. Eur Respir J. 2008 May; 31(5):1085-90.

[18] Brown M et al. Prospective Study of Sputum Induction, Gastric Washing and BAL for the Diagnosis of Pulmonary TB in Patients Who are Unable to Expectorate. Clin Infect Dis. 2007; 44:1415.

[19] Bell D et al. The Role of Induced Sputum in the Dx of PTB. J Infection, 2003; 47:317.

[20] Al-Zahrani K et al. Yield of Smear, Culture and Amplification Tests from Repeated Sputum Induction for the Diagnosis of Pulmonary TB. Int J Tuberc Lung Dis, 2001; 5:855.

[21] Li LM et al. Sputum Induction to Improve the Diagnostic Yield In Patients with Suspected Pulmonary TB. Int J Tuberc Lung Dis, 1999; 3:1137.

[22] Conde MB et al. Comparison of Sputum Induction with Fiberoptic Bronch in the Dx of TB, AJRCCM, 2000; 162:2238.

[23] Chawla, R, Pant, K, JAggi, OP, Chandrashekhar, S, Thukral, SS. Fibreoptic Bronchoscopy in smear-negative pulmonary tuberculosis. Eur Respir J. 1988 Oct: 1(9): 804-6.

[24] Morse, M, Kessler, J, Albrecht, S, et al. Induced sputum improves the diagnosis of pulmonary tuberculosis in hospitalized patients in Gaborone, Botswana. Int J Tuberc Lung Disease. 2008 Nov; 12 (11): 1279-85.

[25] Warren JR et al. A Minimum of 5 ml of Sputum Improves the Sensitivity of AFB Smear for M. tb. AJRCCM, 2000; 166:1559.

[26] Louden RG et al. Cough Frequency and Infectivity in Patients with Pulmonary TB. Am Rev Respir Dis. 1969; 99:109-111.

[27] Riley RL, Knight M, Middlebrook G. Ultraviolet susceptiblility of BCG and virulent tubercle bacilli. Am Rev Respi Dis 1976;113:413-8.

[28] Riley RL, Nardell EA. Clearing the air. The theory and application of Ultra Violet air disinfection. Am Rev Respir Dis 1989;139:1286-94.

[29] ECRI. TB engineering controls: mobile high efficiency filter air cleaners. Health Devices 1995;24:370-418.

[30] CDC. Prevention and Control of Tuberculosis in correctional facilities: Recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR 1996:45 (No. RR-8):1-27.

[31] Leonhardt KK, Gentile F, Gilbert BP, Aiken M. A cluster of tuberculosis among crack house contacts in San Mateo County, California. Am J Public Health 1994;84:1834-6.

[32] Moss AR, Hahn JA, Tulsky JP, Daley CL Small PM, Hopewell PC. Tuberculosis in the homeless. A prospective study Am J Respir Crit Care Med 2000;162:460-4.

[33] CDC. Transmission of multidrug-resistant tuberculosis from an HIV-positive client in a residential substance-abuse treatment facility--Michigan. MMWR Morb Mortal Wkly Rep. 1991 Mar 1;40(8):129-31.

[34] Zolopa AR, Hahn JA, Gorter R, Miranda J, Wlodarczyk D, Peterson J, Pilote L, Moss AR. HIV and tuberculosis infection in San Francisco's homeless adults. Prevalence and risk factors in a representative sample. JAMA. 1994 Aug 10;272(6):455-61.

[35] ATS/CDC Diagnostic Standards and Classification of Tuberculosis in Adults and Children. Am J Respir Crit Care Med Vol 161. pp 1376-1395, 2000

X. Additional Reading

Bifani PJ et al. Identification of a W Variant Outbreak of M. tb. via Population Based Molecular Epidemiology. JAMA, 1999; 282:2321

Brindle R et al. Serial Counts of M. tb. in Sputum as Surrogate Markers of the Sterilizing Activity of RIF and PZA in Treating Pulmonary TB. BMC Pulm Med, 2001; 1:2

Burgos M et al. Effect of Drug Resistance on the Generation of Secondary Cases of TB. J Infect Dis, 2003; 188:1878

Cambanis A et al. A One Day Method for the Diagnosis of Pulmonary TB in Rural Ethiopia. Int J Tuberc Lung Dis, 2006: 10:230

Cohen RA, Muzaffar S, Schwartz D, Bashir, S, et al. Diagnosis of Pulmonary TB Using PCR Assays on Sputum collected within 24 hours of hospital admission. Amer. J of Resp. & Critical Care Med. 1998. 157: 156-16.

Cruciani M et al. The Impact of Human Immunodeficiency Virus Type 1 on Infectiousness of Tuberculosis: A Meta-Analysis. CID, 2001; 33:1922

Earnest MA et al. Defining the Issues: Returning Patients with TB to Institutional Settings. Clin Infect Dis, 1995; 20:497

Fennelly KP. Variability of Airborne Transmission of Mycobacterium tuberculosis: Implications for Control of Tuberculosis in the HIV Era (Editorial). CID, 2007; 44:1358

Fennelly KP.The Role of Masks in Preventing Nosocomial Transmission of TB. Int J Tuberc Lung Dis, 1998; 2 (Suppl 1):103

Gopi PG et al. Smear Examination of Two Specimens for the Diagnosis of Pulmonary TB in Tiruvallur District, South India. Int J Tuberc Lung Dis, 2004; 8:824

Grybowski S et al. Contacts of Cases of Active Pulmonary TB. Bull IUT, 1975; 50:90

Gunnels JJ et al. Infectivity of Sputum Positive TB Patients on Chemotherapy. Am Rev Resp Dis, 1974; 109:323

Kamar SR et al. A Controlled Study of the Influence of Segregation of TB Patients for One Year on the Attack Rate of TB in a 5 Year Period in Close Family Contacts. Bull WHO, 1966; 34:517

Katamba A et al. Efficacy of a Third Serial Sputum Smear Examination in the Diagnosis of TB in Moldova and Uganda. Int J Tuberc Lung Dis, 2007; 11:659

Kato-Maeda M et al. The Nature and Consequence of Genetic Variability within M.tb. J Clin Invest, 2001; 107:533

Kenyon TA et al. Transmission of MDR M. tb. During a Long Airplane Flight. NEJM, 1996; 334:933

Leonard MD et al. How Many Sputum Specimens are Necessary to Diagnose Pulmonary TB? Am J Infect Control, 2005; 33:58

Lienhardt C et al. Risk Factors for Tuberculosis Infection in Sub-Saharan Africa. AJRCCM, 2003; 168:448

Lutong L et al. Association Of Prevalence Of Tuberculin Reactions With Closeness Of Contact Among Household Contacts Of New Smear-Positive Pulmonary TB Patients. AJRCCM, 2000; 4:275

Matthew P et al. Are Three Sputum AFB Smears Necessary for Discontinuing TB Isolation? J Clin Microbiol, 2002; 40:3482

Merrick ST et al. Comparison of Induced by Expectorated Sputum for the Dx of Pulmonary TB. Am J Infect Control, 1997; 25:463

Parry CM et al. The use of Sputum Induction for Establishing a Diagnosis in Patients with Suspected Pulmonary TB in Malawi. Tubercle and Lung Dis, 1995; 76:72

Riley RL, Moodie AS. Infectivity of Patients with Pulmonary TB in Inner City Homes. ARRD, 1974: 110:810

Riley RL, et.al. Infectiousness of air from a tuberculosis ward. Ultraviolet irradiation of infected air: comparative infectiousness of different patients. Am Rev Respir Dis, 1962; 85:511

Riley RL et al. Aerial Dissemination of Pulmonary TB. Am J Epi, 1959; 70:185

Sarin R et al. Diagnosis of TB Under RNTCP: Examination of Two or Three Sputum Specimens. Ind J Tub,
2001; 48:13

Shaw JB et al. Infectivity of Pulmonary TB in Relation to Smear Status. Am Rev TB, 1954; 69:724

Snider DE et al. Infection and Disease Among Contacts of TB Cases with Drug Resistant and Drug Susceptible Bacilli, Am Rev Resp Dis, 1985; 132:125

Telzak EE et al. Factors Influencing Time to Sputum Conversion Among Patients with Smear-Positive Pulmonary TB. Clin Infect Dis, 1997; 25:666

Tourbes ME et al. Comparison of Two Techniques of Sputum Induction in the Diagnosis of Pulmonary TB. Int J Tuberc Lung Dis, 2005; 9:56

Urbanczik R. Present Position of Microscopy and of Culture in Dx Mycobacteriology. Medical Microbiology, Infect Diseases, Virology, Parasitology, 1985; 261:87

Van der Elk EA et al. Heredity vs Environment in TB in Twins. AJRCCM, 2007; 176:1281

Van Deun A et al. Optimal TB Case Detection by Direct Sputum Smear Microscopy: How Much Better is More? Int J Tuberc Lung Dis, 2002; 6:222

Van Geuns el al. Results of contact examination in Rotterdam, 1967-1969. Bull Int Union Tuberc, 1975; 50:107

Walker D et al. An Incremental Cost-Effectiveness Analysis of the First, Second and Third Sputum Examination in the Diagnosis of Pulmonary TB. Int J Tuberc Lung Dis, 2000; 4:246

Warren JR et al. A Minimum of 5 ml of Sputum Improves the Sensitivity of AFB Smear for M. tb. AJRCCM, 2000; 166:1559