應用核酸增幅診斷結核病

Diagnosis of Tuberculosis with Nucleic Acid Amplification Test

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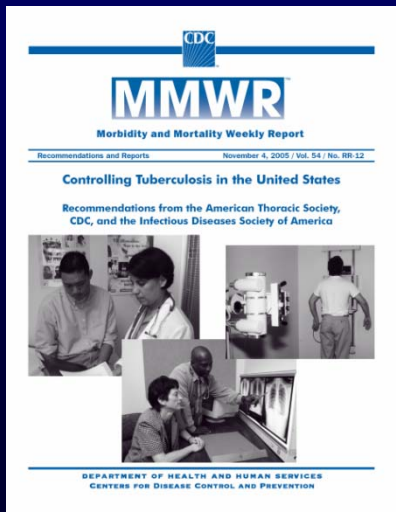
Basic Principles of TB Control

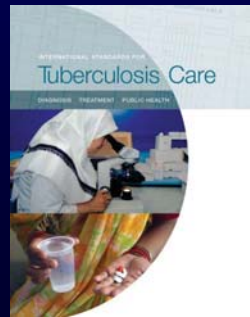
- Early and accurate detection, diagnosis, and reporting of TB cases leading to initiation and completion of treatment
- Identification of contacts of patients with infectious TB and treatment of those at risk with an effective drug regimen
- Identification of other persons with LTBI at risk for progression to TB disease and treatment of those persons with an effective drug regimen
- Identification of settings in which a high risk exists for transmission of *M. tuberculosis* and application of effective infection-control measures



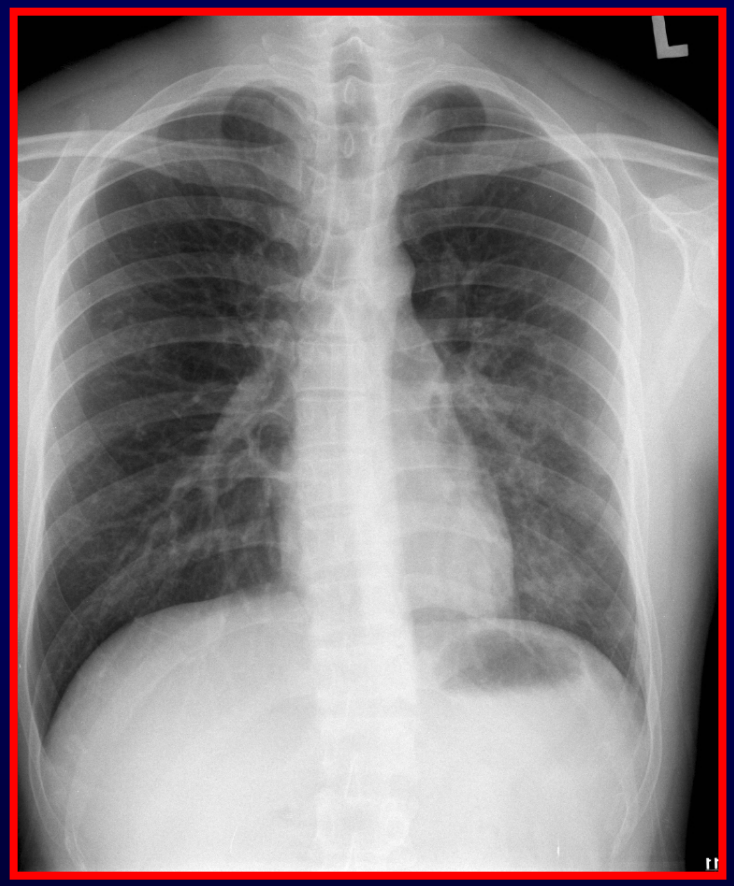
早期藉日光輔助判讀胸部X光片

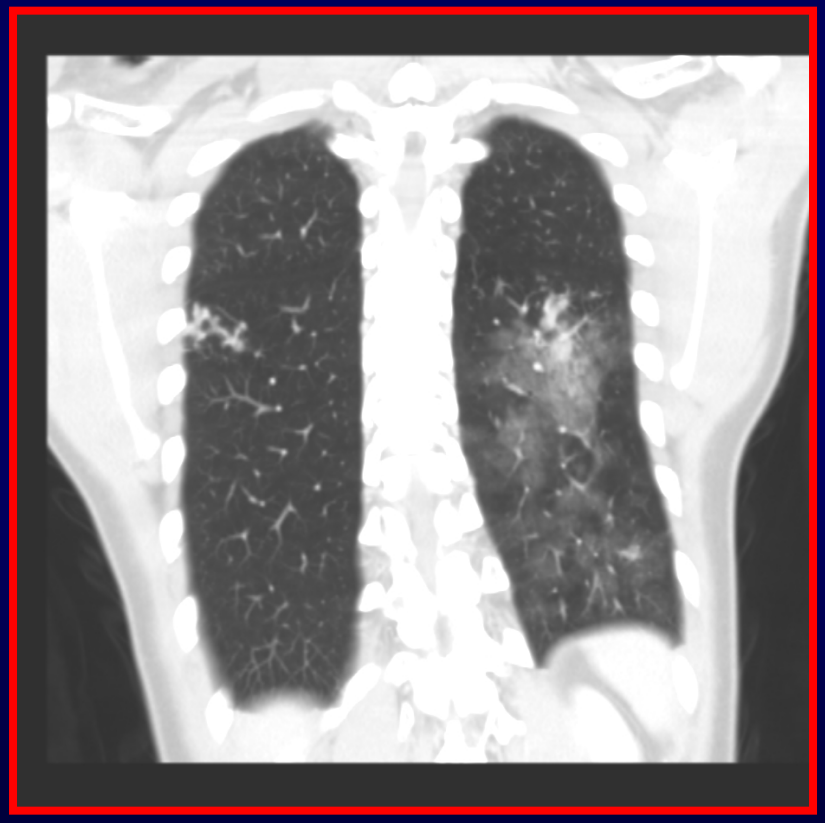
Standard 4

All persons with chest radiographic findings suggestive of tuberculosis should have sputum specimens submitted for microbiological examination



Pulmonary TB, 22 y/o, Male

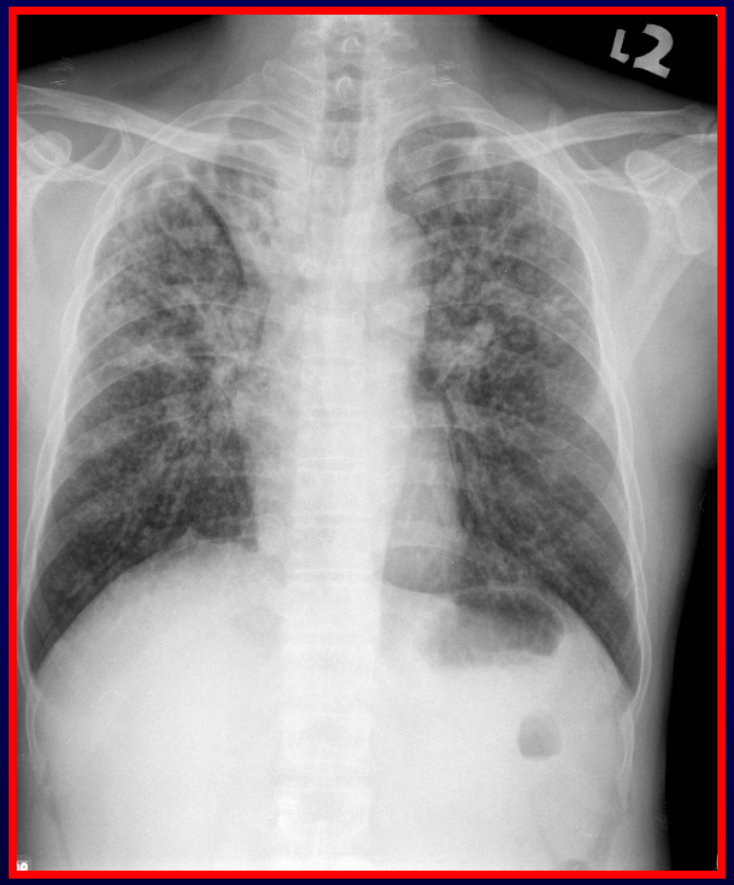


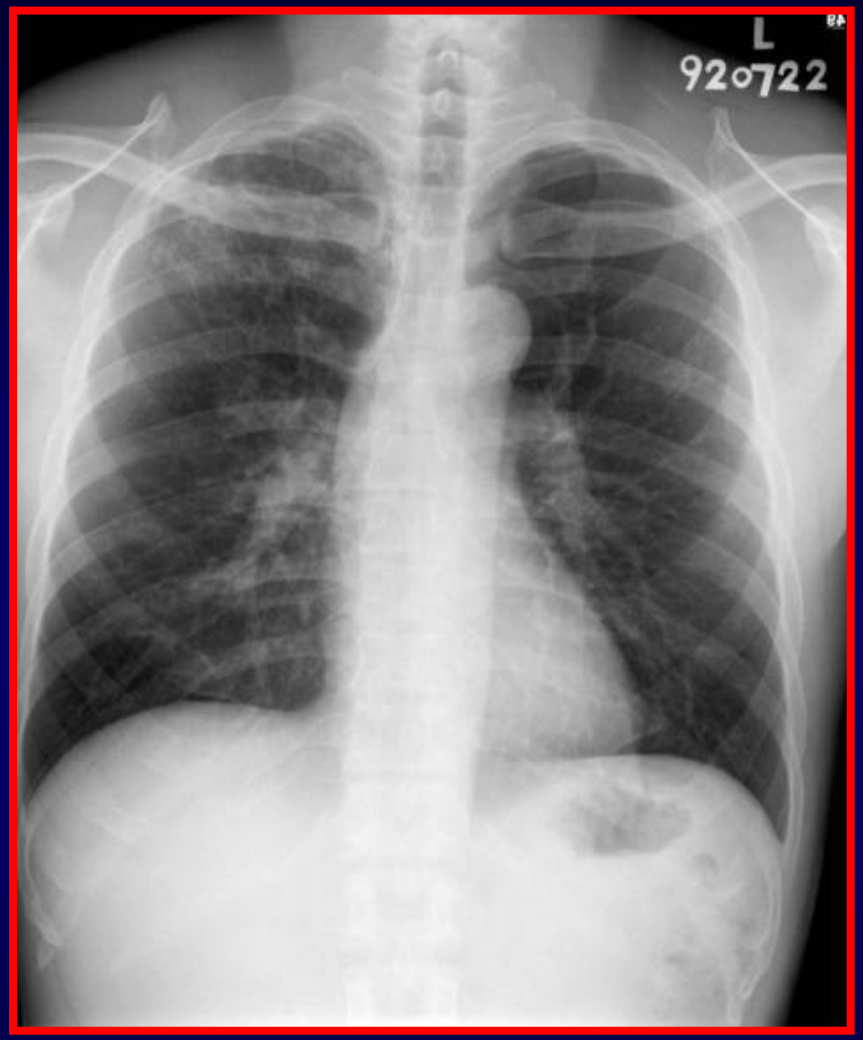


- Until recently, a laboratory-based diagnosis of pulmonary tuberculosis (TB) has relied on the use of specimens obtained from the respiratory tract of patients
  - By use of both smear microscopy and mycobacterial culture

Clin Infect Dis 2009;49:55–7

Acid-Fast Stain

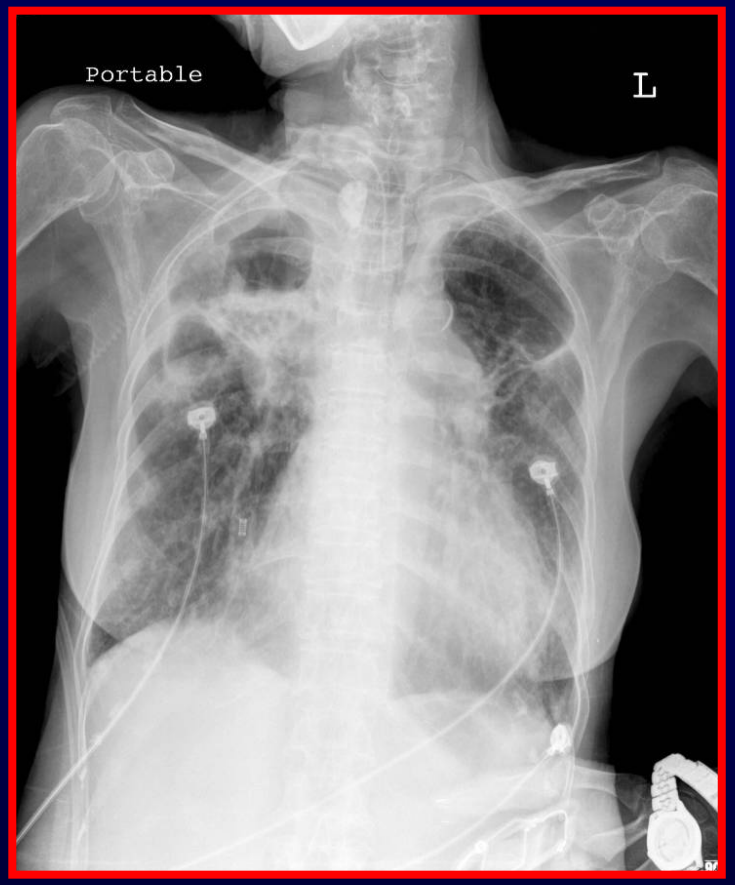




- Low sensitivity
  - 5,000 to 10,000 bacilli per milliliter ATS/CDC 2000

Acid-fast Bacteria Seen on Smear

- *M. tuberculosis*
- Nontuberculous mycobacteria (NTM)



Cause of Sputum Acid-Fast Smear-Positive

Mycobacterium tuberculosis or nontuberculous mycobacterium

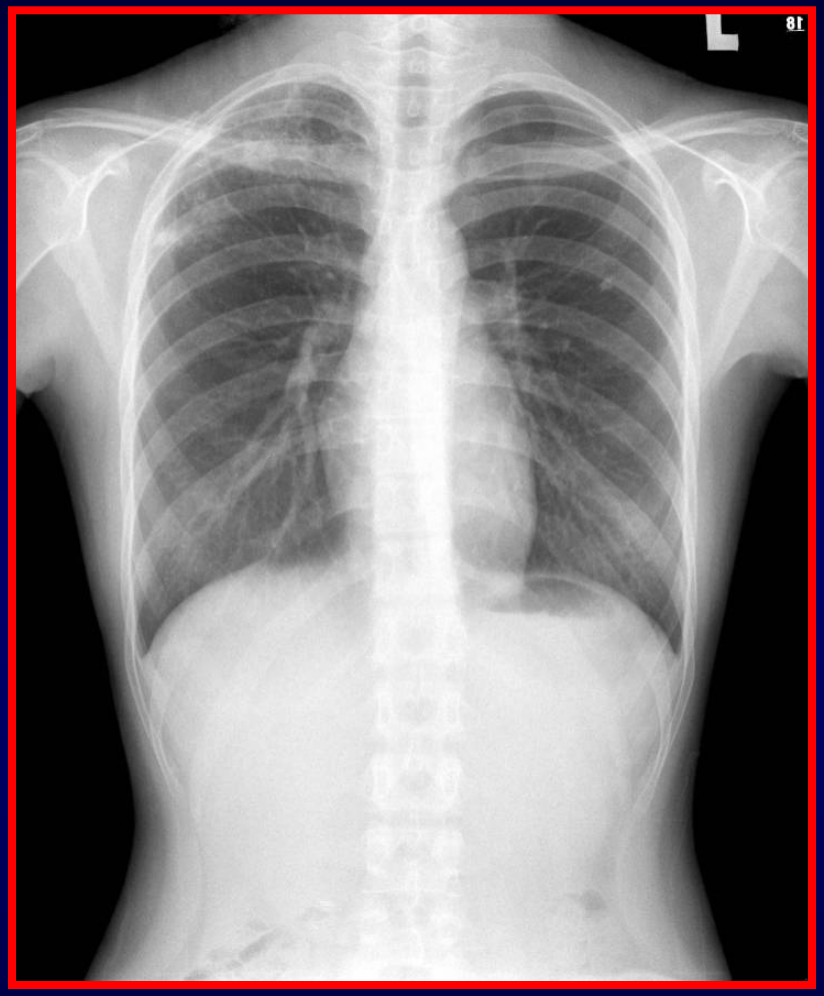
- From September 2005 to June 2006
  - 100 new patients with smear- positive sputum
- MTB group
  - 65 culture-positive for MTB
- NTM group
  - 30 (85.7%) culture-positive for NTM
  - 5(14.3%) culture- negative for mycobacteria
  - The increasing proportion of NTM patients in all with smear-positive sputum points out the necessity of applying a rapid and specific test for identification of *M. tuberculosis* in smear-positive sputum

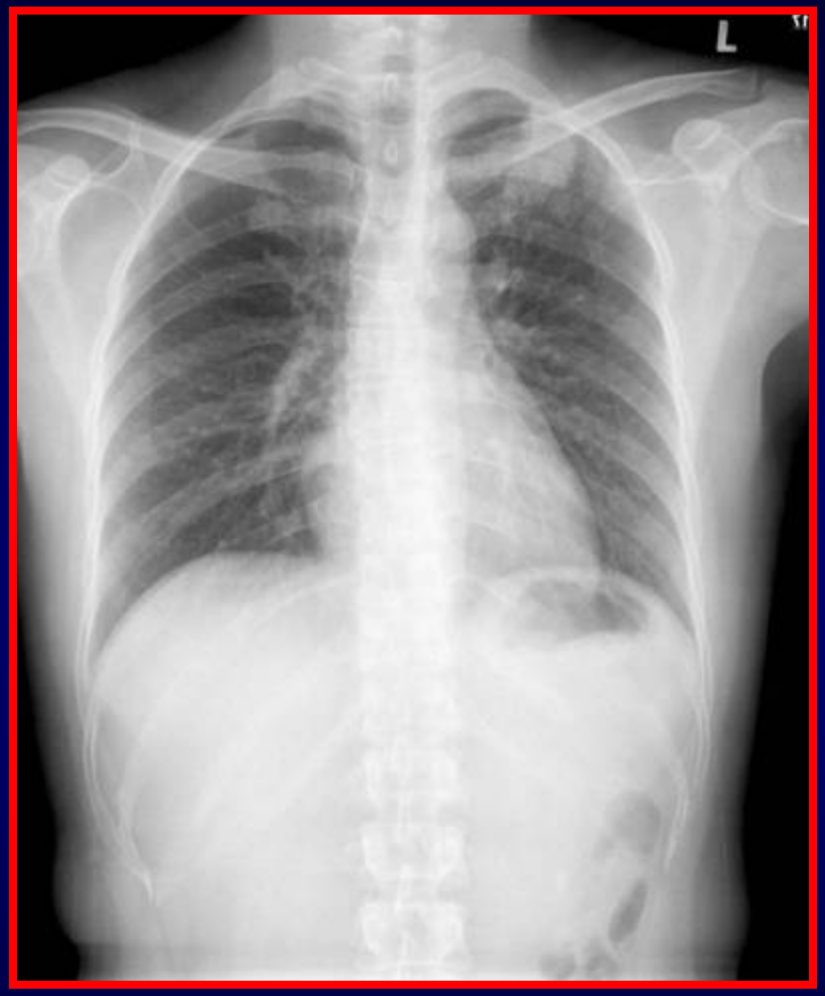
    Chest 2007

Mycobacterial Culture

- All clinical specimens suspected of containing mycobacteria should be inoculated onto culture media
  - Culture is much more sensitive than microscopy
  - Growth of the organisms is necessary for precise species identification
  - Drug susceptibility testing requires culture of the organisms
  - Genotyping of cultured organisms may be useful to identify epidemiological links between patients or to detect laboratory cross-contamination

ATS/CDC 2000

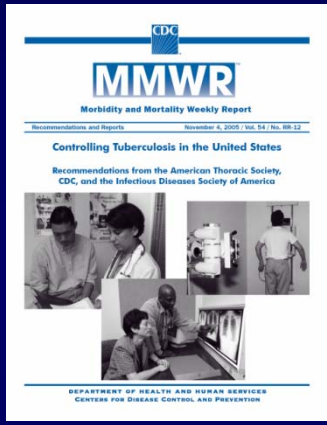


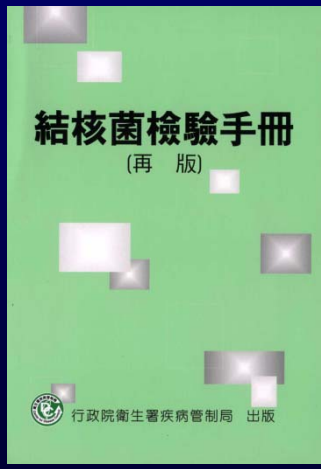


- Culture: 10 to 100 organisms per milliliter ATS/CDC 2000

Liquid Media Systems

- The use of liquid media systems
  - Can provide information in less time than solid media
  - should be available in all laboratories that perform culture for mycobacteria





- 培養分枝桿菌時
  - 最好是選擇液體培養基再加上LJ 斜面

Comparative Evaluation of the BACTEC MGIT 960 System with Solid Medium for Isolation of Mycobacteria

Int J Tuberc Lung Dis 2003; 7:569–574

Table 2 Time to detection (TTD) of all mycobacteria and *M. tuberculosis* complex in different systems

	TTD of all mycobacteria (days)			TTD of *M. tuberculosis* (days)		
Medium	Total	Smear (+)	Smear (−)	Total	Smear (+)	Smear (−)
MGIT 960	11.6	9.0	15.5	11.6	9.1	16.2
LJ	20.3	17.6	25.1	20.1	17.6	25.2
7H11	18.9	16.1	23.8	18.7	16.1	23.5

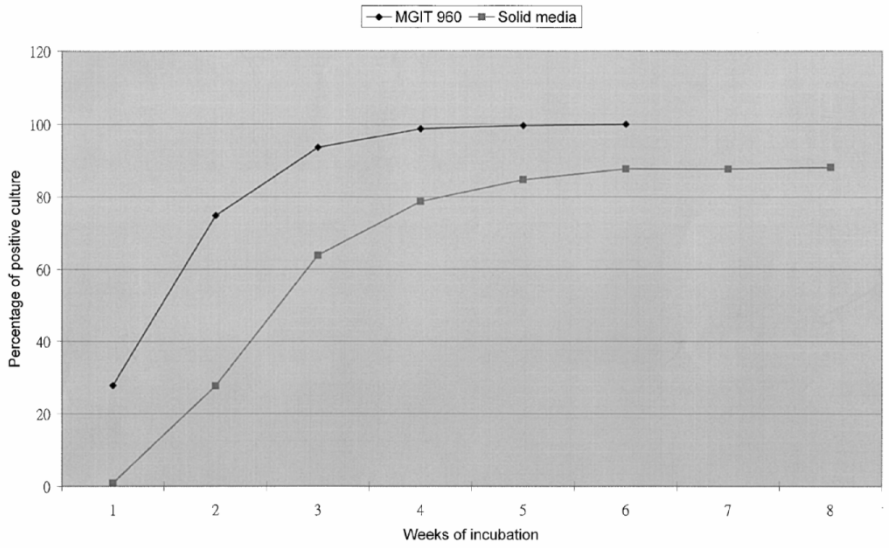
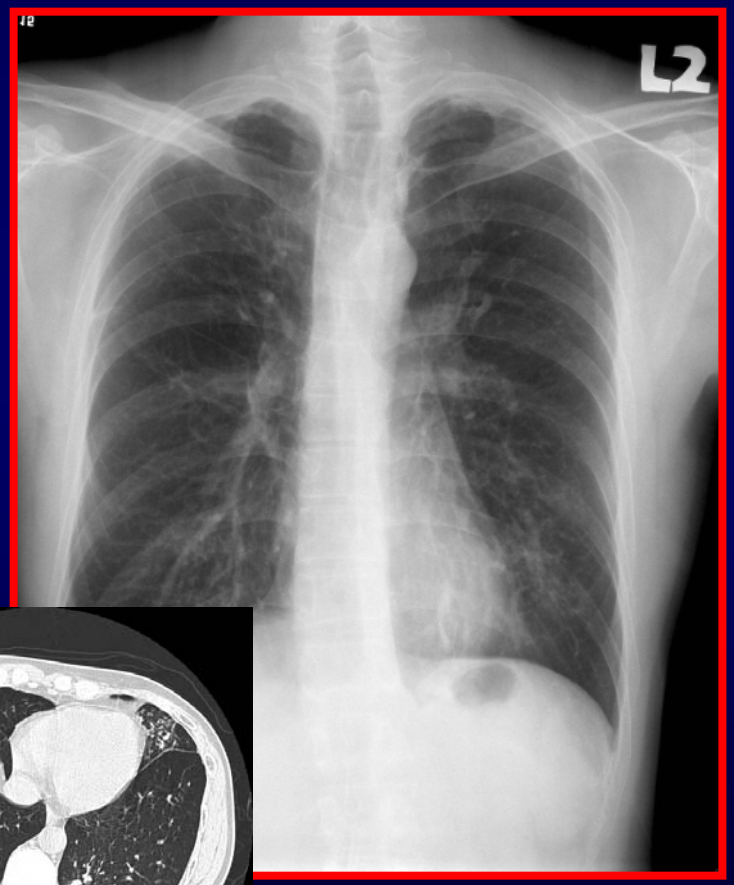
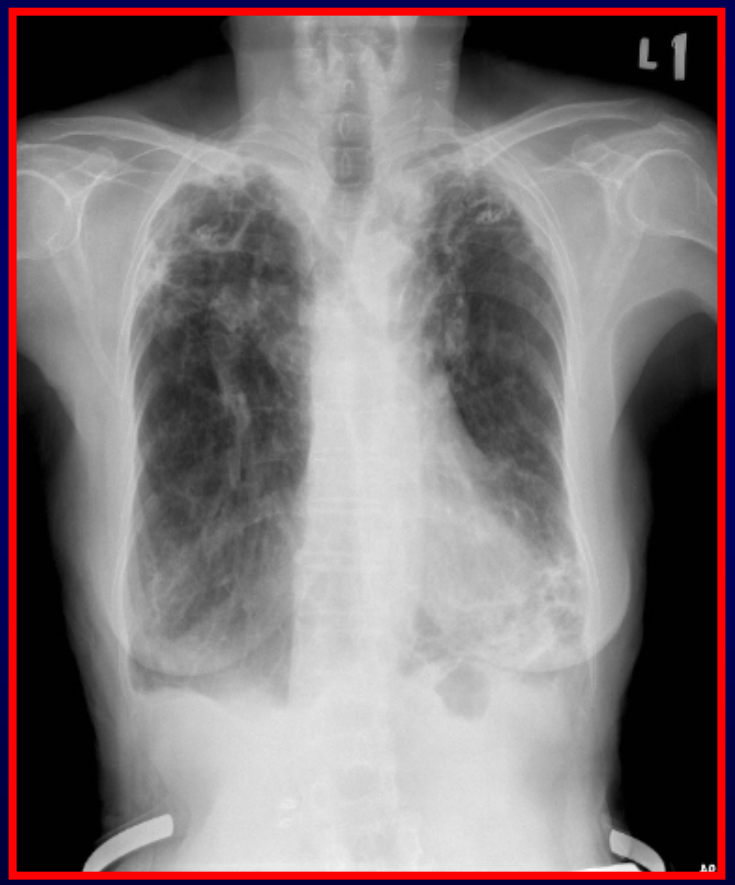
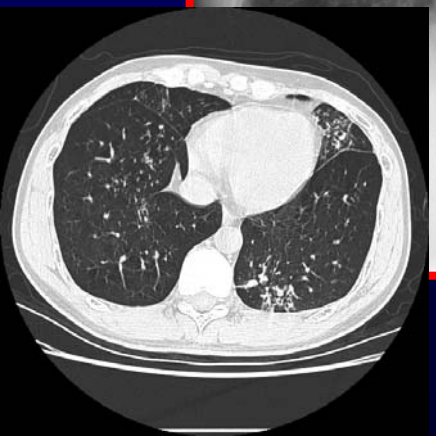


Figure Cumulative percentages of mycobacteria detected weekly by individual methods. BACTEC MGIT 960 system and solid media (Löwenstein-Jensen plus 7H11).

Positive MGIT=*Mycobacterium tuberculosis* ?



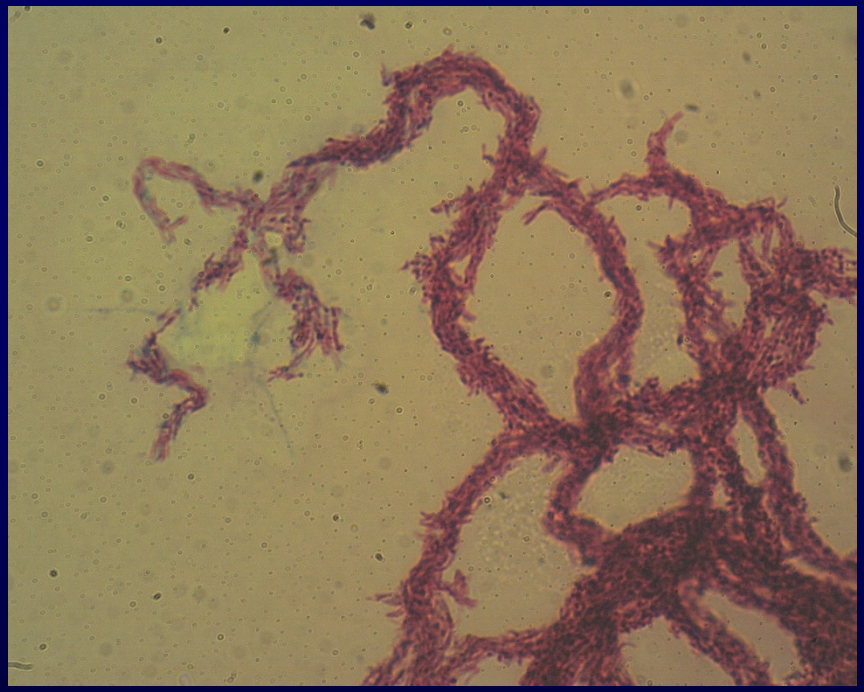




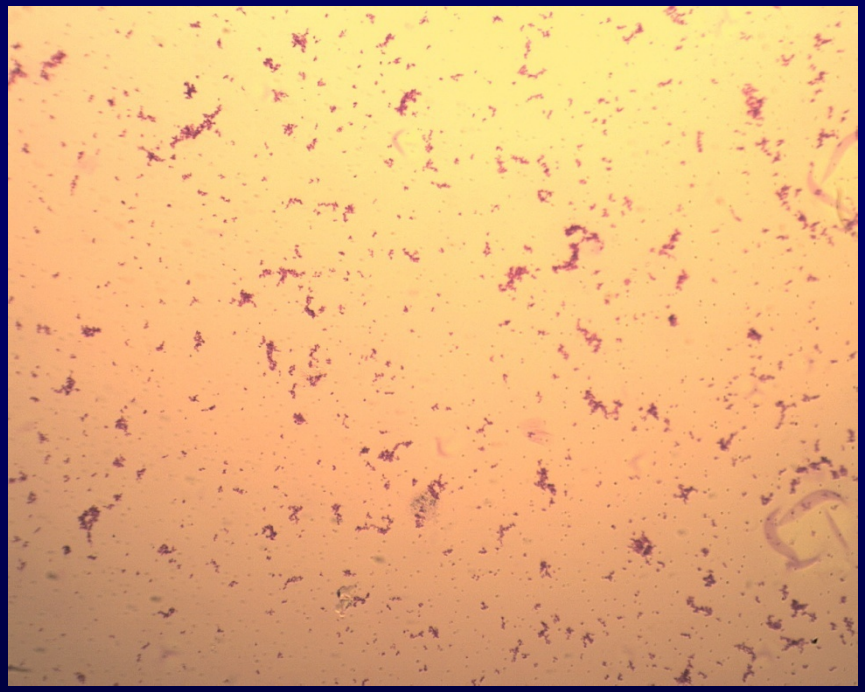
TMU-WFH (2005~2007): NTM: 25.7%

MGIT(+): Cord Formation

Cord(+)



Cord(-)

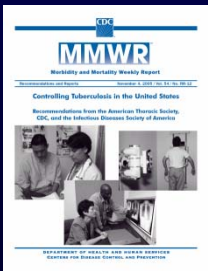


TMU-WFH :1658 MGIT(+) : Conclusive 1604(96.7%), Inconclusive 54 (3.3%)
Sensitivity: 96.5%, Specificity: 90.0%, PPV: 95.8%, NPV: 91.8%

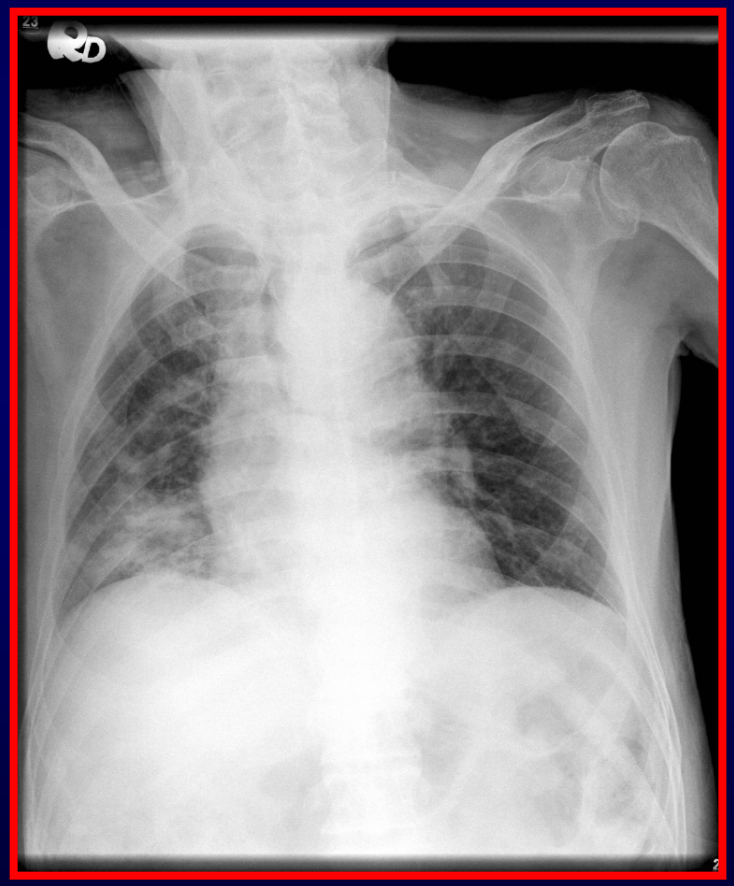
Laboratory Services for Optimal TB Control

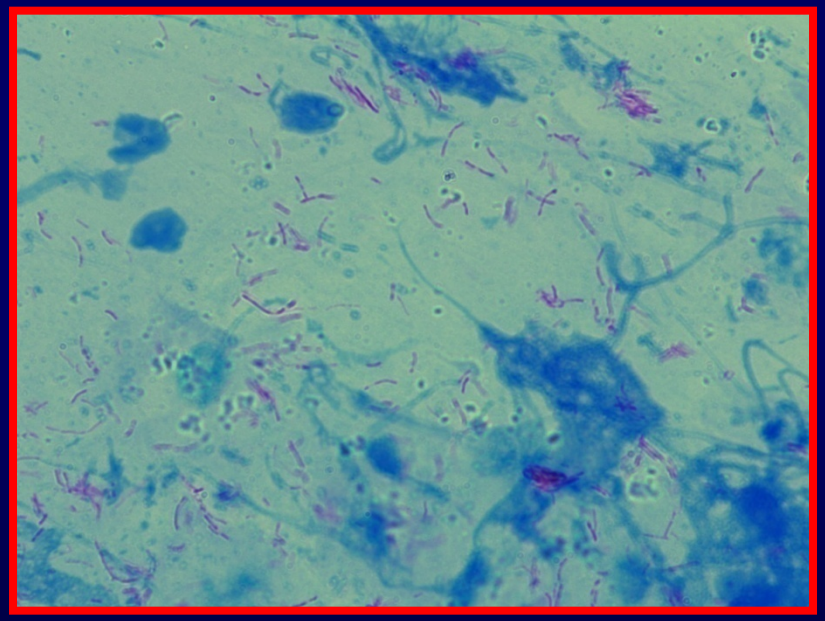
Essential Laboratory Tests

Test	Maximum turnaround time
Microscopy for acid-fast bacilli	≤24 hours from specimen collection or, if test is performed offsite, ≤24 hours from receipt in laboratory; if latter, time from specimen collection to laboratory receipt should be ≤24 hours
Nucleic acid amplification assay	≤48 hours from date of specimen collection
Mycobacterial growth detection by culture	≤14 days from date of specimen collection
Identification of cultured mycobacteria	≤21 days from date of specimen collection
Drug susceptibility testing	≤30 days from date of specimen collection
Drug susceptibility testing of second-line drugs	≤4 weeks from date of request



80 y/o, male (ICU)





Rapid and Reliable Detection and Identification of *M. tuberculosis* ?

Nucleic Acid Amplification Test

(Amplifying RNA or DNA from *M. tuberculosis*)

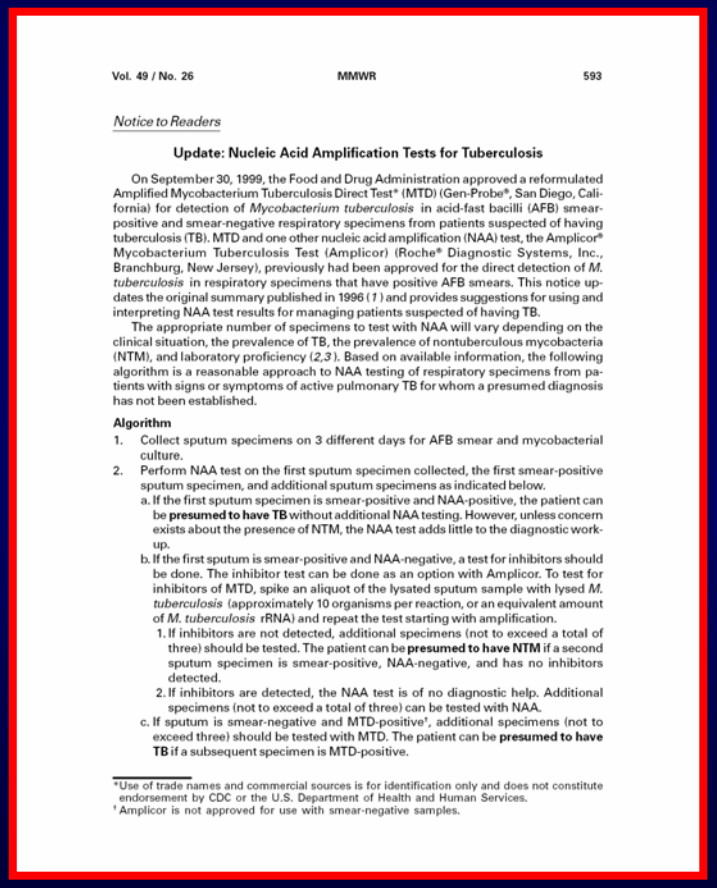
Nucleic Acid Amplification Assay

- The Amplified Mycobacterium tuberculosis Direct Test (MTD, Gen-Probe, San Diego, California)
  - FDA (1995): AFB smear-positive respiratory specimens
  - FDA (1999): AFB smear-negative respiratory specimens
- The Amplicor Mycobacterium tuberculosis Test (Amplicor, Roche Diagnostics, Basel, Switzerland)
  - FDA (1996): AFB smear-positive respiratory specimens

MMWR 2000

Update: Nucleic Acid Amplification Tests for Tuberculosis

MMWR 2000



Vol. 49 / No. 26 MMWR 593

Notice to Readers

Update: Nucleic Acid Amplification Tests for Tuberculosis

On September 30, 1999, the Food and Drug Administration approved a reformulated Amplified Mycobacterium Tuberculosis Direct Test* (MTD) (Gen-Probe®, San Diego, California) for detection of *Mycobacterium tuberculosis* in acid-fast bacilli (AFB) smear-positive and smear-negative respiratory specimens from patients suspected of having tuberculosis (TB). MTD and one other nucleic acid amplification (NAA) test, the Amplicor® Mycobacterium Tuberculosis Test (Amplicor) (Roche® Diagnostic Systems, Inc., Branchburg, New Jersey), previously had been approved for the direct detection of *M. tuberculosis* in respiratory specimens that have positive AFB smears. This notice updates the original summary published in 1996 (*1*) and provides suggestions for using and interpreting NAA test results for managing patients suspected of having TB.

The appropriate number of specimens to test with NAA will vary depending on the clinical situation, the prevalence of TB, the prevalence of nontuberculous mycobacteria (NTM), and laboratory proficiency (*2,3*). Based on available information, the following algorithm is a reasonable approach to NAA testing of respiratory specimens from patients with signs or symptoms of active pulmonary TB for whom a presumed diagnosis has not been established.

Algorithm

1. Collect sputum specimens on 3 different days for AFB smear and mycobacterial culture.
2. Perform NAA test on the first sputum specimen collected, the first smear-positive sputum specimen, and additional sputum specimens as indicated below.
   a. If the first sputum specimen is smear-positive and NAA-positive, the patient can be **presumed to have TB** without additional NAA testing. However, unless concern exists about the presence of NTM, the NAA test adds little to the diagnostic workup.
   b. If the first sputum is smear-positive and NAA-negative, a test for inhibitors should be done. The inhibitor test can be done as an option with Amplicor. To test for inhibitors of MTD, spike an aliquot of the lysated sputum sample with lysed *M. tuberculosis* (approximately 10 organisms per reaction, or an equivalent amount of *M. tuberculosis* rRNA) and repeat the test starting with amplification.
      1. If inhibitors are not detected, additional specimens (not to exceed a total of three) should be tested. The patient can be **presumed to have NTM** if a second sputum specimen is smear-positive, NAA-negative, and has no inhibitors detected.
      2. If inhibitors are detected, the NAA test is of no diagnostic help. Additional specimens (not to exceed a total of three) can be tested with NAA.
   c. If sputum is smear-negative and MTD-positive†, additional specimens (not to exceed three) should be tested with MTD. The patient can be **presumed to have TB** if a subsequent specimen is MTD-positive.

*Use of trade names and commercial sources is for identification only and does not constitute endorsement by CDC or the U.S. Department of Health and Human Services.
† Amplicor is not approved for use with smear-negative samples.

- A reasonable approach to NAA testing of respiratory specimens from patients with signs or symptoms of active pulmonary TB for whom a presumed diagnosis has not been established

結核病診治指引

Taiwan Guidelines for TB Diagnosis & Treatment

第三版

- 利用分生技術作為結核菌之快速偵測、分型、抗藥性菌株偵測及測定突變，是不可阻擋之趨勢，但現階段仍無法取代傳統之塗片耐酸性染色及培養，特別是藥物感受性試驗。

Updated Guidelines for the Use of Nucleic Acid Amplification Tests in the Diagnosis of Tuberculosis

CDC

MMWR

Morbidity and Mortality Weekly Report

www.cdc.gov/mmwr

Weekly January 16, 2009 / Vol. 58 / No. 1

Pneumonia Hospitalizations Among Young Children Before and After Introduction of Pneumococcal Conjugate Vaccine — United States, 1997–2006

Streptococcus pneumoniae is the leading bacterial cause of community-acquired pneumonia hospitalizations and an important cause of bacteremia and meningitis, especially among young children and older adults (*1*,*2*). A 7-valent pneumococcal conjugate vaccine (PCV7) was licensed and the Advisory Committee on Immunization Practices formulated recommendations for its use in infants and children in February 2000 (*2*). Vaccination coverage rapidly increased during the second half of 2000, in part through funding by CDC's Vaccines for Children program. Subsequently, active population- and laboratory-based surveillance demonstrated substantial reductions in invasive pneumococcal disease (IPD) among children and adults (*3*). In addition, decreases in hospitalizations and ambulatory-care visits for all-cause pneumonia also were reported (*4*,*5*). To gauge whether the effects of PCV7 on reducing pneumonia continue, CDC is monitoring pneumonia hospitalizations by using data from the Nationwide Inpatient Sample. This report provides an update for 2005 and 2006, the most recent years for which information is available. In 2005 and 2006, the incidence rates for all-cause pneumonia hospitalizations among children aged <2 years were 9.1 per 1,000 and 8.1 per 1,000, respectively. In 2006, the rate for all-cause pneumonia among children aged <2 years was approximately 35% lower than during 1997–1999. Most of this decrease occurred soon after the vaccine was licensed in 2000, and the rates have remained relatively stable since then. The rate for all-cause pneumonia among children aged 2–4 years did not change after PCV7 licensure and has remained stable. Continued monitoring of pneumonia-related hospitalizations among children is needed to track the effects of pneumococcal immunization programs.

The Nationwide Inpatient Sample contains data on inpatient stays from states that participate in the Healthcare Cost and Utilization Project, sponsored by the Agency for Healthcare Research and Quality. The project is a stratified probability sample of U.S. acute-care hospitals and the largest all-payer inpatient-care database available in the United States. In 2006, this database recorded information from approximately 8 million hospitalizations (approximately 20% of all U.S. hospitalizations) from 1,045 hospitals in 38 states. Data are weighted to generate national estimates while accounting for complex sampling design (*6*). For this analysis, all-cause pneumonia hospitalization was defined as a record in which *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes 480–486 (pneumonia) or 487.0 (influenza with pneumonia) were assigned as the primary diagnosis.

Trends in hospitalizations for nonpneumonia acute respiratory illness (ARI) also were evaluated to assess the possibility that, after PCV7 introduction, practitioners were less likely to assign a pneumonia code for respiratory conditions in a vaccinated child and more likely to make other respiratory diagnoses. A nonpneumonia ARI hospitalization was defined as a record with any of the following ICD-9-CM codes assigned as the primary diagnosis: 381–383 (otitis media and mastoiditis), 460–466 (acute respiratory infections, including acute bronchitis, bronchiolitis, acute nasopharyngitis, sinusitis, pharyngitis, tonsillitis, laryngitis, tracheitis, and other acute upper respiratory infections), 487 (influenza, excluding 487.0), 490 (bronchitis), 491 (chronic bronchitis), or 493 (asthma).

INSIDE

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

4. CDC. Interim guidelines for the evaluation of infants born to mothers infected with West Nile virus during pregnancy. MMWR 2004; 53:154–7.
5. Pinon JM, Dumon H, Chemla C, et al. Strategy for diagnosis of congenital toxoplasmosis: evaluation of methods comparing mothers and newborns and standard methods for postnatal detection of immunoglobulin G, M, and A antibodies. J Clin Microbiol 2001;39:2267–71.
6. Jamieson DJ, Theiler RN, Rasmussen SA. Emerging infections and pregnancy. Emerg Infect Dis 2006;12:1638–43.
7. Cono J, Cragan JD, Jamieson DJ, Rasmussen SA. Prophylaxis and treatment of pregnant women for emerging infections and bioterrorism emergencies. Emerg Infect Dis 2006;12:1631–7.
8. Tsai TF. Congenital arboviral infections: something new, something old. Pediatrics 2006;117:936–9.
9. Osorio JE, Schoepp RJ, Yuill TM. Effects of La Crosse infection on pregnant domestic rabbits and Mongolian gerbils. Am J Trop Med Hyg 1996;55:384–90.
10. Edwards JF, Karabatsos N, Collisson EW, de la Concha Bermejillo A. Ovine fetal malformations induced by in utero inoculation with Main Drain, San Angelo, and LaCrosse viruses. Am J Trop Med Hyg 1997;56:171–6.

Updated Guidelines for the Use of Nucleic Acid Amplification Tests in the Diagnosis of Tuberculosis

Guidelines for the use of nucleic acid amplification (NAA) tests for the diagnosis of tuberculosis (TB) were published in 1996 (*1*) and updated in 2000 (*2*). Since then, NAA testing has become a routine procedure in many settings because NAA tests can reliably detect *Mycobacterium tuberculosis* bacteria in specimens 1 or more weeks earlier than culture (*3*). Earlier laboratory confirmation of TB can lead to earlier treatment initiation, improved patient outcomes, increased opportunities to interrupt transmission, and more effective public health interventions (*4*,*5*). Because of the increasing use of NAA tests and the potential impact on patient care and public health, in June 2008, CDC and the Association of Public Health Laboratories (APHL) convened a panel of clinicians, laboratorians, and TB control officials to assess existing guidelines (*1*,*2*) and make recommendations for using NAA tests for laboratory confirmation of TB. On the basis of the panel's report and consultations with the Advisory Council for the Elimination of TB (ACET),* CDC recommends that NAA testing be performed on at least one respiratory specimen from each patient with signs and symptoms of pulmonary TB for whom a diagnosis of TB is being considered but has not yet been established, and for whom the test result would alter case management or TB control activities, such as contact investigations. These guidelines update the previously published guidelines (*1*,*2*).

Background

Conventional tests for laboratory confirmation of TB include acid-fast bacilli (AFB) smear microscopy, which can produce results in 24 hours, and culture, which requires 2–6 weeks to produce results (*5*,*6*). Although rapid and inexpensive, AFB smear microscopy is limited by its poor sensitivity (45%–80% with culture-confirmed pulmonary TB cases) and its poor positive predictive value (50%–80%) for TB in settings in which nontuberculous mycobacteria are commonly isolated (*3*,*6*,*7*).

NAA tests can provide results within 24–48 hours. The Amplified *Mycobacterium tuberculosis* Direct Test (MTD, Gen-Probe, San Diego, California) was approved by the Food and Drug Administration (FDA) in 1995 for use with AFB smear-positive respiratory specimens, and in a supplement application, an enhanced MTD test was approved in 1999 for use with AFB smear-negative respiratory specimens from patients suspected to have TB. In addition, the Amplicor *Mycobacterium tuberculosis* Test (Amplicor, Roche Diagnostics, Basel, Switzerland) was approved by FDA in 1996 for use with AFB smear-positive respiratory specimens from patients suspected to have TB. NAA tests for TB that have not been FDA-approved also have been used clinically (e.g., NAA tests based on analyte specific reagents, often called "home-brew" or "in-house" tests) (*8*,*9*).

Compared with AFB smear microscopy, the added value of NAA testing lies in its 1) greater positive predictive value (>95%) with AFB smear-positive specimens in settings in which nontuberculous mycobacteria are common and 2) ability to confirm rapidly the presence of *M. tuberculosis* in 50%–80% of AFB smear-negative, culture-positive specimens (*3*,*7*–*9*). Compared with culture, NAA tests can detect the presence of *M. tuberculosis* bacteria in a specimen weeks earlier than culture for 80%–90% of patients suspected to have pulmonary TB whose TB is ultimately confirmed by culture (*3*,*8*,*9*). These advantages can impact patient care and TB control efforts, such as by avoiding unnecessary contact investigations or respiratory isolation for patients whose AFB smear-positive specimens do not contain *M. tuberculosis*.

Despite being commercially available for more than a decade (*1*), NAA tests for TB have not been widely used in the United States largely because of 1) an uncertainty as to whether NAA test results influence case-management decisions or TB control activities; 2) a lack of information on the overall cost-effectiveness of NAA testing for TB; and 3) a lack of demand from clinicians and public health authorities. However, recent

* Additional information regarding ACET is available at http://www.cdc.gov/maso/facm/facmacet.htm.

Nucleic Acid Amplification Assay

Background

- AFB smear microscopy is limited by
  - Poor sensitivity
    - 45%–80% with culture-confirmed pulmonary TB cases
  - Poor positive predictive value
    - 50%–80% for TB in settings in which nontuberculous mycobacteria are commonly isolated

Sensitivities and Specificity of Nucleic Acid Amplification Methods

- Amplicor
  - Smear-positive: sensitivity 97%, Specificity >95%
  - Smear-negative: sensitivity 40-73%, Specificity >95%
- AMTD
  - Smear-positive: sensitivity 92-100%, Specificity >95%
  - Smear-negative: sensitivity 40-93%, Specificity >95%

Eur Respir J 2005; 26:339-350

Nucleic Acid Amplification Assay

Background

- Compared with AFB smear microscopy, the added value of NAA testing
  - Greater positive predictive value (>95%) with AFB smear-positive specimens in settings in which nontuberculous mycobacteria are common
  - Ability to confirm rapidly the presence of *M. tuberculosis* in 50%–80% of AFB smear-negative, culture-positive specimens

Reduction in Turnaround Time for Laboratory Diagnosis of Pulmonary Tuberculosis by Routine Use of a Nucleic Acid Amplification Test

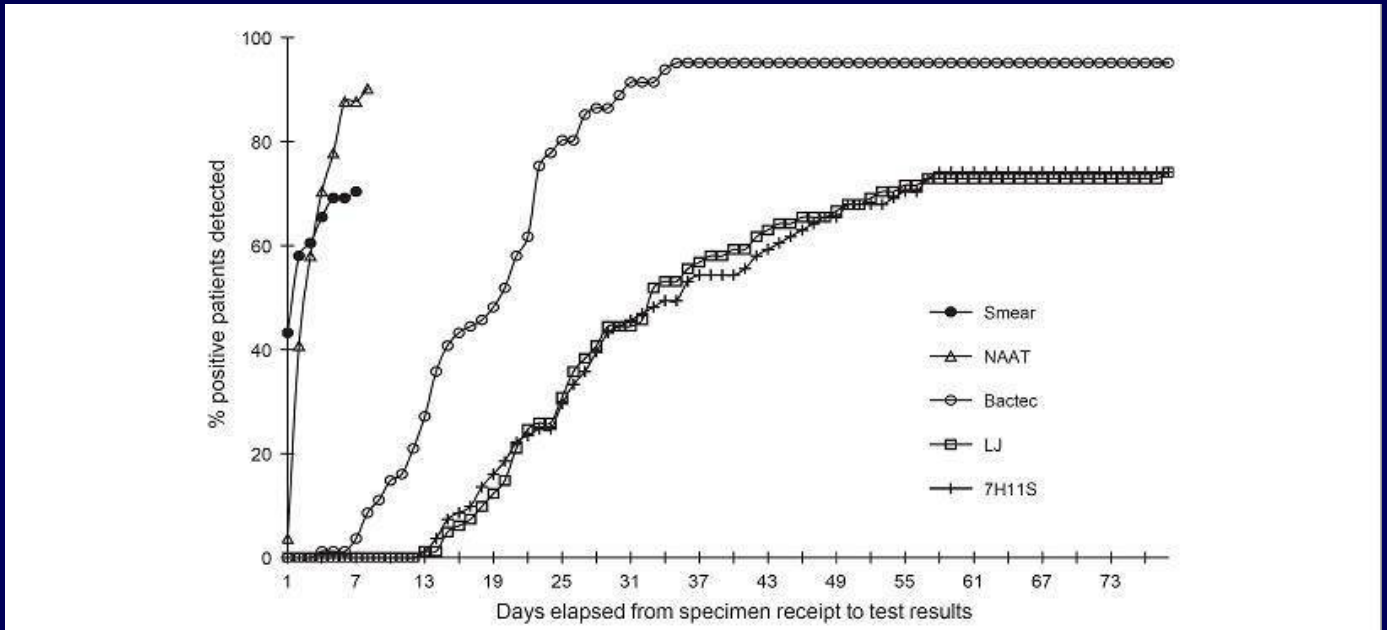


Fig. 2. TAT to report TB-positive patients. The elapsed time from specimen receipt to assay results was evaluated under normal working conditions in the laboratory. The results are expressed as the percentage of TB-positive patients that were reported as positive by the day indicated. The results include all 3 specimens for AFB smear and culture techniques and the first specimen for NAAT.

- Identification and testing every first diagnostic specimen by NAAT has the potential to reduce the overall TAT for laboratory TB diagnosis by approximately 2 weeks

Diagn Microbiol Infect Dis 2005; 52: 247–254

Nucleic Acid Amplification Assay

Background

- Compared with culture
  - NAA tests can detect the presence of *M. tuberculosis* bacteria in a specimen weeks earlier than culture for 80%–90% of patients suspected to have pulmonary TB whose TB is ultimately confirmed by culture

Updated Recommendation

- NAA testing become a standard practice in the United States to aid in the initial diagnosis of patients suspected to have TB, rather than just being a reasonable approach

- NAA testing should be performed on at least one respiratory specimen from each patient with signs and symptoms of pulmonary TB for whom
  - A diagnosis of TB is being considered but has not yet been established
  - The test result would alter case management or TB control activities

Interpret NAA Test Results
in Correlation with the AFB Smear Results (1)

- AFB smear (+) and NAA (+)
  - Presume the patient has TB and begin anti-TB treatment
- AFB smear (-) and NAA (+)
  - Use clinical judgment whether to begin anti-TB treatment while awaiting culture results and determine if additional diagnostic testing is needed

Interpret NAA Test Results
in Correlation with the AFB Smear Results (2)

- AFB smear (+) and NAA (-)
  - Use clinical judgment to determine whether to begin anti-TB treatment while awaiting culture results and determine if additional diagnostic testing is needed
  - A patient can be presumed to have an infection with nontuberculous mycobacteria if a second specimen is smear positive and NAA negative and has no inhibitors detected

- AFB smear (-) and NAA (-)
  - Use clinical judgment to determine whether to begin anti-TB treatment while awaiting results of culture and additional diagnostic tests

Cautions (1)

- NAA testing should become standard practice for patients suspected to have TB
  - All clinicians and public health TB programs should have access to NAA testing for TB to shorten the time needed to diagnose TB from 1–2 weeks to 1–2 days
  - The currently available NAA tests should not be ordered routinely when the clinical suspicion of TB is low
    - The positive predictive value of the NAA test is <50% for such cases

Cautions (2)

- To maximize benefits of NAA testing, the interval from specimen collection to communication of the laboratory report to the treating clinician should be as brief as possible (within 48 hours of specimen collection)
- For procedural and economic reasons, NAA testing might be impractical in laboratories with a small volume of testing
  - Referral of samples for NAA testing to high-volume laboratories might be preferable to improve cost-efficiency, proficiency, and turnaround times

Cautions (3)

- Clinicians should interpret all laboratory results on the basis of the clinical situation
  - A single negative NAA test result should not be used as a definitive result to exclude TB
    - Especially when the clinical suspicion of TB is moderate to high

Cautions (4)

- NAA testing has the potential to provide overall cost savings to the treatment center and TB control program through reduced costs for isolation, reduced costs of contact investigations of persons who do not have TB, and increased opportunities to prevent transmission

Feasibility of Shortening Respiratory Isolation with a Single Sputum Nucleic Acid Amplification Test

TABLE 2. DISTRIBUTION OF SUBJECTS ACCORDING TO NUCLEIC ACID AMPLIFICATION AND SPUTUM SMEAR RESULTS

	Tuberculosis* (*n* = 46)		No Tuberculosis (*n* = 447)
	Smear Positive (*n* = 35)	Smear Negative (*n* = 11)	
First-sputum NAA test result			
Positive	35	5	0
Negative	0	6	447
Sputum smear results			
Any of three smears positive	35	NA	17
First smear positive	32	NA	8

Definition of abbreviation: NAA = nucleic acid amplification.
* Confirmed by culture.

- The first-sputum NAA had a higher sensitivity (0.87) and specificity (1.0)
- The smear sensitivity (0.76) and specificity (0.96)

Am J Respir Crit Care Med 2008; 178: 300–305

Performance of Nucleic Acid Amplification Tests for Diagnosis of Tuberculosis in a Large Urban Setting

Background. A diagnosis of tuberculosis (TB) relies on acid-fast bacilli (AFB) smear and culture results. Two rapid tests that use nucleic acid amplification (NAA) have been approved by the US Food and Drug Administration for the diagnosis of TB based on detection of *Mycobacterium tuberculosis* from specimens obtained from the respiratory tract. We evaluated the performance of NAA testing under field conditions in a large urban setting with moderate TB prevalence.

Methods. The medical records of patients with suspected TB during 2000–2004 were reviewed. Analysis was restricted to the performance of NAA on specimens collected within 7 days after the initiation of treatment for TB. The assay's sensitivity, specificity, and positive and negative predictive values (PPV and NPV, respectively) were evaluated.

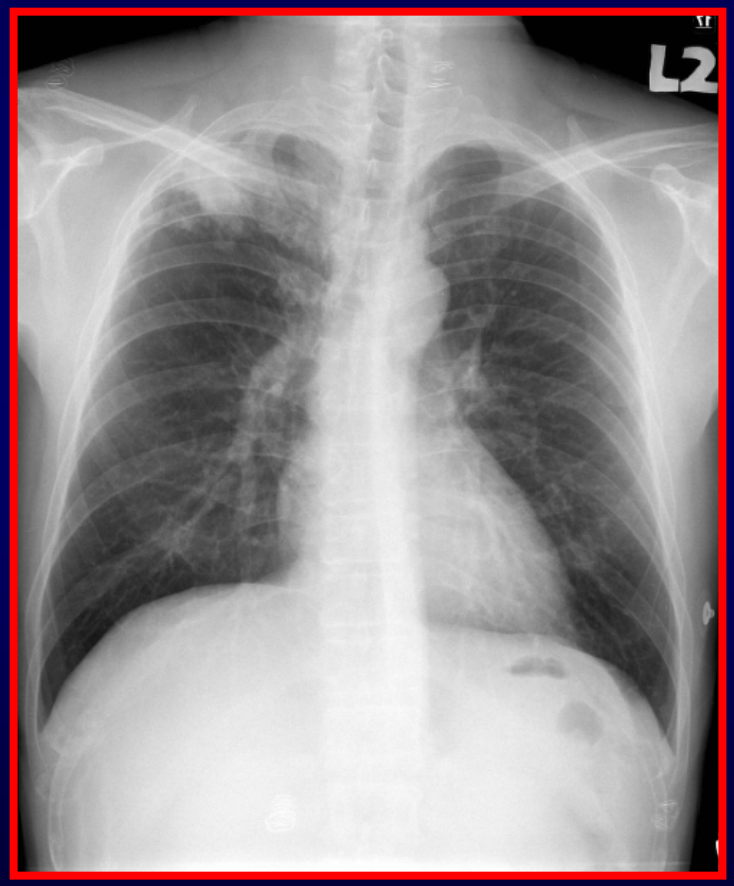
Results. The proportion of patients with confirmed or suspected TB whose respiratory tract specimens were tested by use of NAA increased from 429 (12.9%) of 3334 patients in 2000 to 527 (15.6%) of 3386 patients in 2004; NAA testing among patients whose respiratory tract specimens tested positive for AFB increased from 415 (43.6%) of 952 patients in 2000 to 487 (55.5%) of 877 patients in 2004 ($P < .001$ for both trends). Of the 16,511 patients being evaluated for pulmonary TB, 4642 (28.1%) had specimens that tested positive for AFB on smear. Of those 4642 patients, 2241 (48.3%) had NAA performed on their specimens. Of those 2241 patients, 1279 (57.1%) had positive test results. Of those 1279 patients, 1262 (98.7%) were confirmed to have TB. For 1861 (40.1%) of the 4642 patients whose specimens tested positive for AFB on smear, the NAA test had a sensitivity of 96.0%, a specificity of 95.3%, a PPV of 98.0%, and an NPV of 90.9%. For 158 patients whose specimens tested negative for AFB on smear, the NAA test had a sensitivity of 79.3%, a specificity of 80.3%, a PPV of 83.1%, and an NPV of 76.0%, respectively. For the 215 specimens that tested positive for AFB by smear, we found a sensitivity, specificity, PPV, and NPV of 97.5%, 93.6%, 95.1%, and 96.8%, respectively. A high-grade smear was associated with a better test performance.

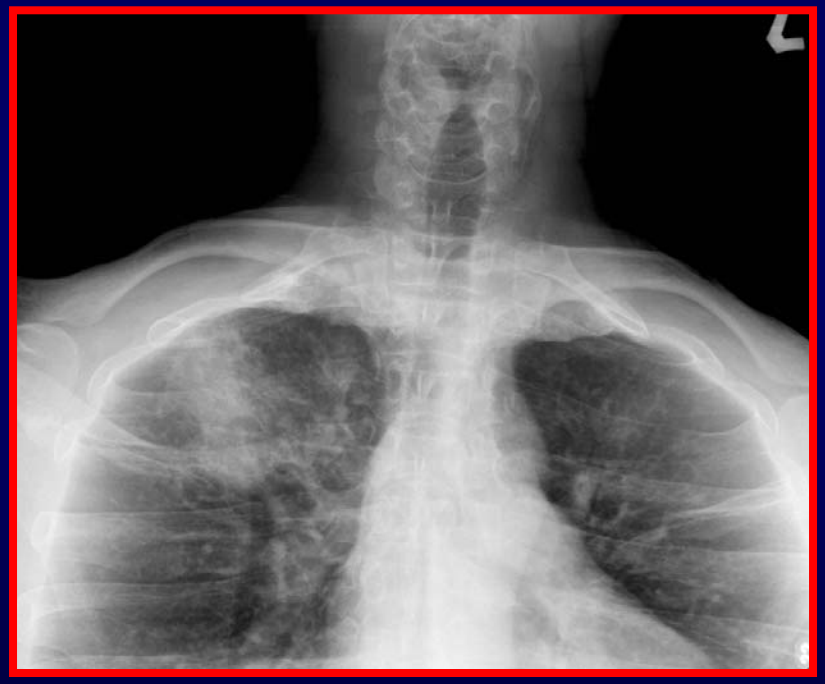
Conclusion. NAA testing was helpful for determining whether patients whose specimens tested positive for AFB on smear had TB or not. This conclusion supports the use of this test for early diagnosis of pulmonary and extrapulmonary TB.

Clin Infect Dis 2009; 49:46–54

Pulmonary TB, 46 y/o, Male

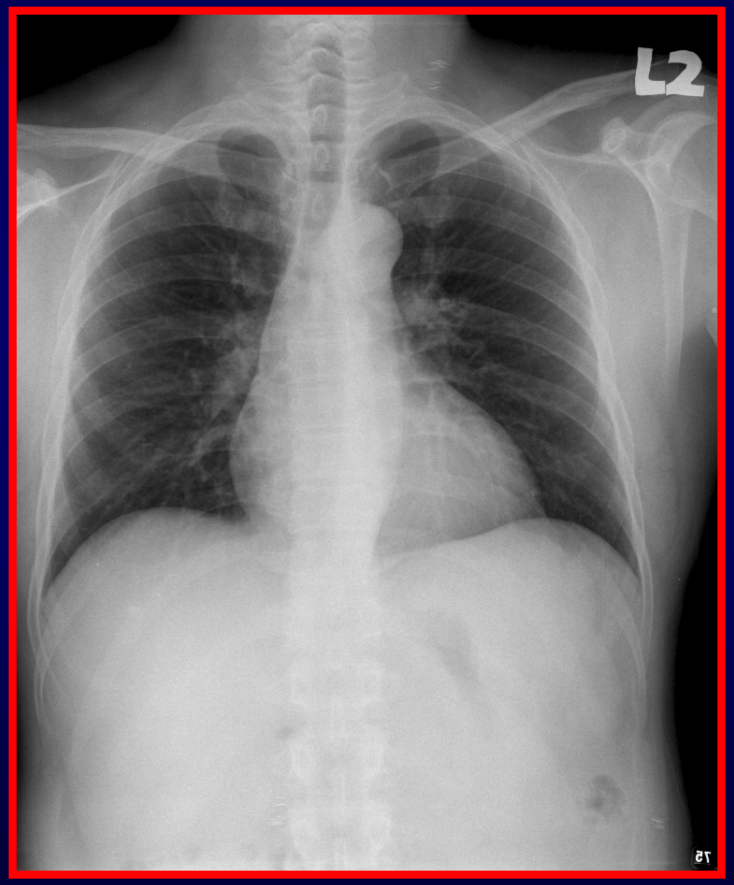
Sputum AFS(+), NAA(+)





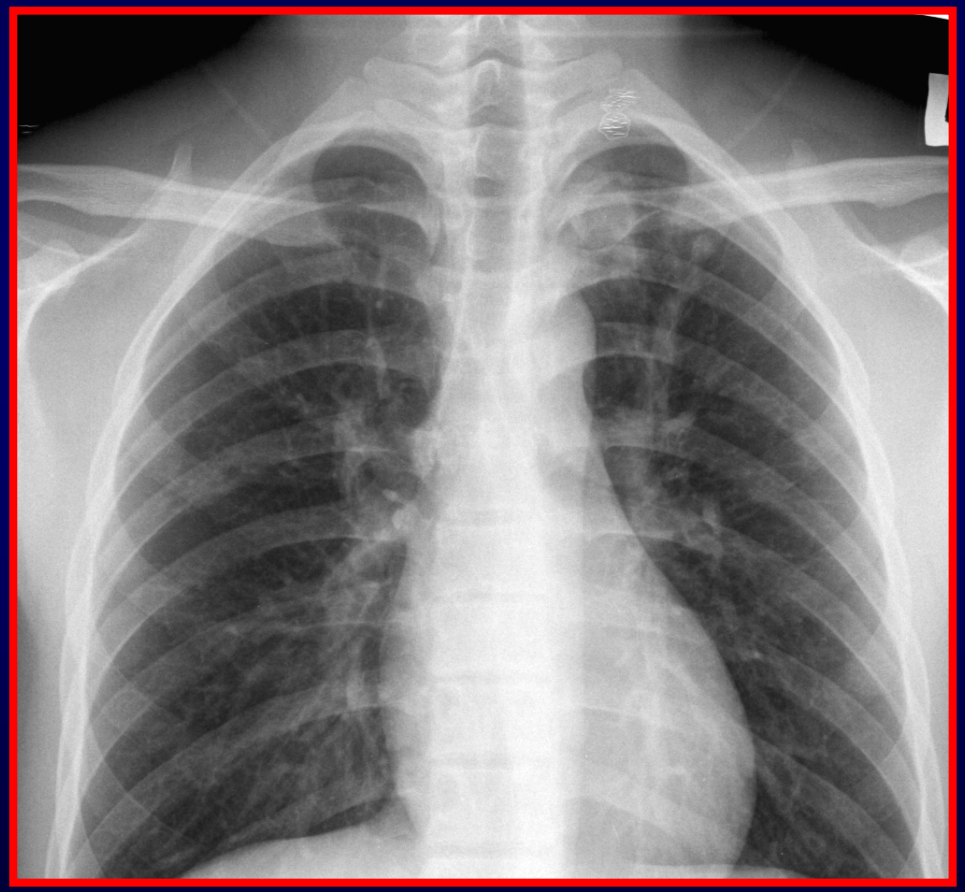
TB Contact, 40 y/o, Male

Sputum AFS(+), NAA(-)



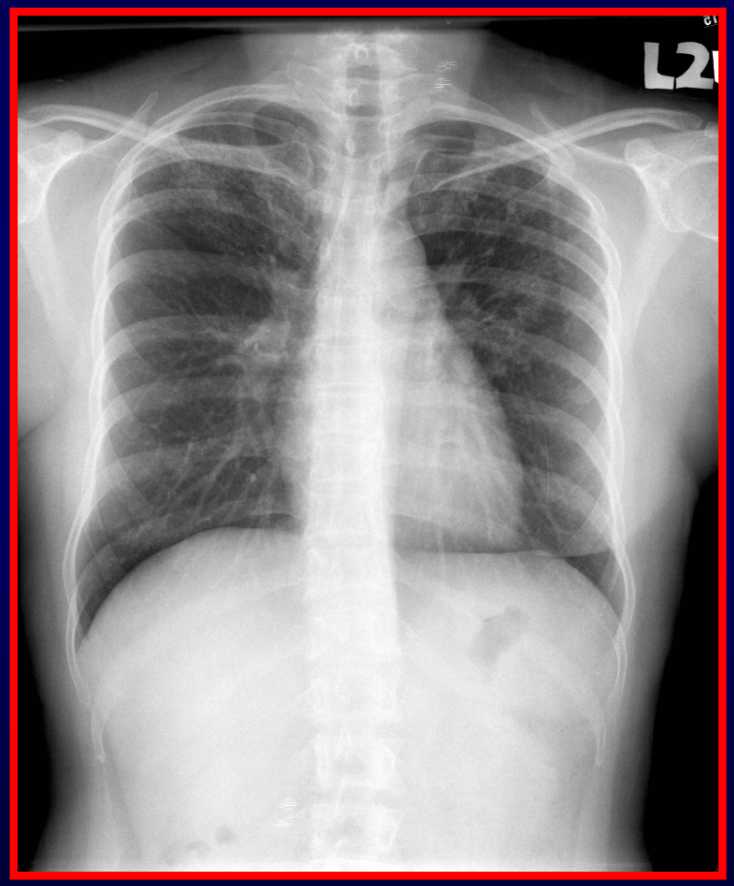
Pulmonary TB, 16 y/o, Male

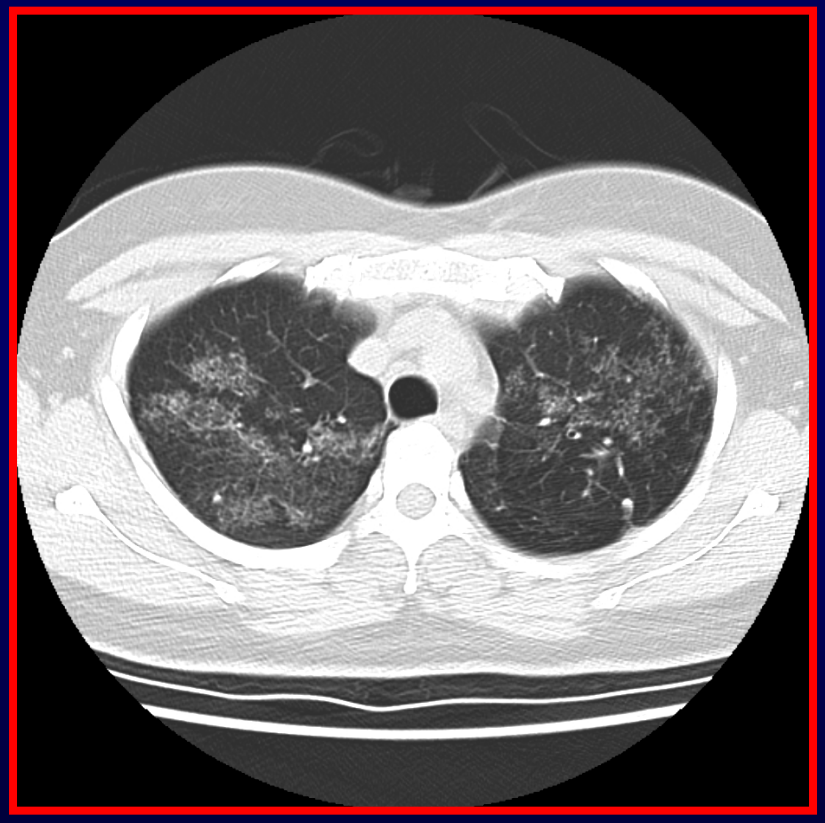
Sputum AFS(-), NAA(+)



MDR-TB, 42 y/o, Female

Sputum AFS(+), NAA(-)





EDITORIAL COMMENTARY

Coming-of-Age of Nucleic Acid Amplification Tests for the Diagnosis of Tuberculosis

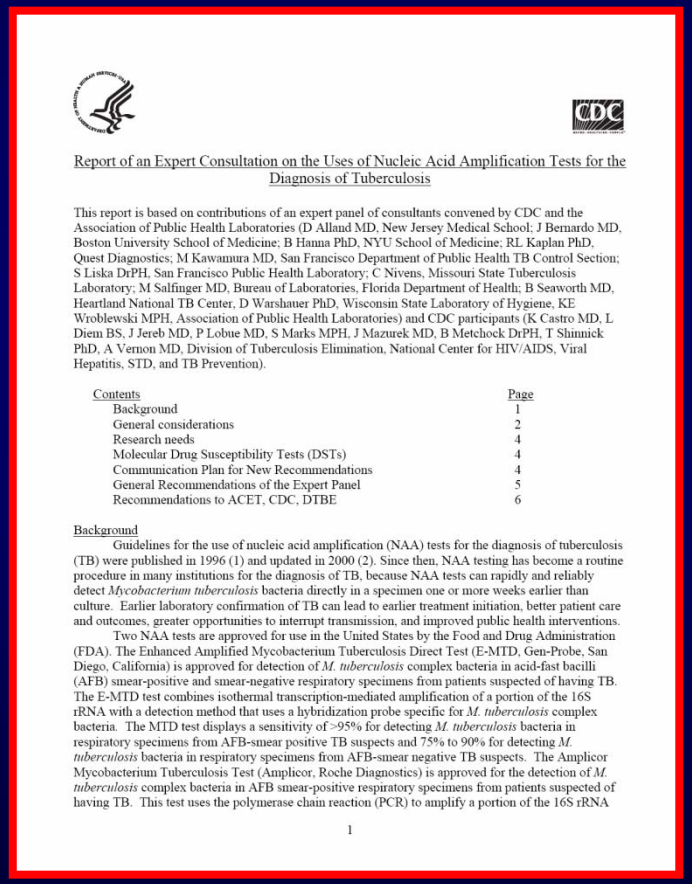
Susan E. Dorman

Johns Hopkins University School of Medicine, Center for Tuberculosis Research, Baltimore, Maryland

Clin Infect Dis 2009;49:55–7

Report of an Expert Consultation on the Uses of Nucleic Acid Amplification Tests for the Diagnosis of Tuberculosis

- Laboratories performing NAA testing should participate in a NAA proficiency testing program



Report of an Expert Consultation on the Uses of Nucleic Acid Amplification Tests for the Diagnosis of Tuberculosis

This report is based on contributions of an expert panel of consultants convened by CDC and the Association of Public Health Laboratories (D Alland MD, New Jersey Medical School; J Bernardo MD, Boston University School of Medicine; B Hanna PhD, NYU School of Medicine; RL Kaplan PhD, Quest Diagnostics; M Kawamura MD, San Francisco Department of Public Health TB Control Section; S Liska DrPH, San Francisco Public Health Laboratory; C Nivens, Missouri State Tuberculosis Laboratory; M Salfinger MD, Bureau of Laboratories, Florida Department of Health; B Seaworth MD, Heartland National TB Center, D Warshauer PhD, Wisconsin State Laboratory of Hygiene, KE Wroblewski MPH, Association of Public Health Laboratories) and CDC participants (K Castro MD, L Diem BS, J Jereb MD, P Lobue MD, S Marks MPH, J Mazurek MD, B Metchock DrPH, T Shinnick PhD, A Vernon MD, Division of Tuberculosis Elimination, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention).

Background

Guidelines for the use of nucleic acid amplification (NAA) tests for the diagnosis of tuberculosis (TB) were published in 1996 (1) and updated in 2000 (2). Since then, NAA testing has become a routine procedure in many institutions for the diagnosis of TB, because NAA tests can rapidly and reliably detect *Mycobacterium tuberculosis* bacteria directly in a specimen one or more weeks earlier than culture. Earlier laboratory confirmation of TB can lead to earlier treatment initiation, better patient care and outcomes, greater opportunities to interrupt transmission, and improved public health interventions.

Two NAA tests are approved for use in the United States by the Food and Drug Administration (FDA). The Enhanced Amplified Mycobacterium Tuberculosis Direct Test (E-MTD, Gen-Probe, San Diego, California) is approved for detection of *M. tuberculosis* complex bacteria in acid-fast bacilli (AFB) smear-positive and smear-negative respiratory specimens from patients suspected of having TB. The E-MTD test combines isothermal transcription-mediated amplification of a portion of the 16S rRNA with a detection method that uses a hybridization probe specific for *M. tuberculosis* complex bacteria. The MTD test displays a sensitivity of >95% for detecting *M. tuberculosis* bacteria in respiratory specimens from AFB-smear positive TB suspects and 75% to 90% for detecting *M. tuberculosis* bacteria in respiratory specimens from AFB-smear negative TB suspects. The Amplicor Mycobacterium Tuberculosis Test (Amplicor, Roche Diagnostics) is approved for the detection of *M. tuberculosis* complex bacteria in AFB smear-positive respiratory specimens from patients suspected of having TB. This test uses the polymerase chain reaction (PCR) to amplify a portion of the 16S rRNA

1

CDC 2008

響應 世界衛生組織 Global Stop TB Partnership 十年減半計畫(2006~2015)

支持行政院衛生署同步成立 Taiwan Stop TB Partnership，共同對抗結核病

達成 **接軌國際、擴大聯盟、落實都治、十年減半**

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(以上依各單位代表人姓氏筆劃順序排列)

歡迎各界響應，請洽衛生署疾病管制局

http://www.cdc.gov.tw