Imaging of Possible Tuberculosis
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. LoBue PA, Enarson DA, Thoen TC. Tuberculosis in humans and its epidemiology, diagnosis and treatment in the United States. *Int J Tuberc Lung Dis.* 2010;14(10):1226-1232.	Review/Other-Dx	N/A	To assess TB in humans and its epidemiology, diagnosis and treatment in the United States	TB is a pulmonary and systemic disease caused by Mycobacterium TB complex species. TB is spread from person to person by airborne transmission. Several factors determine the probability of transmission, including the infectiousness of the sources patient and the nature of the environment where exposure occurs. This initial infection (primary TB) rapidly progresses to disease in some persons (especially children and immunocompromised persons), but resolves spontaneously in most individuals. This condition in which the organism lies dormant is known as LTBI. In the United States, the diagnosis of LTBI is made with either the tuberculin skin test or an interferon-gamma release assay. LTBI is treated with isoniazid (usually for 9 months) to prevent progression to TB disease. Up to 5% of immunocompetent persons will progress to TB disease at some time in the future, even decades after infection, if they are not treated for LTBI. PTB disease is diagnosed using a combination of CXR and microscopic examination, culture and nucleic acid amplification testing of sputum. Treatment of drug-susceptible TB consists of at least 6 months of an isoniazid and rifampin-containing regimen (with ethambutol and pyrazinamide for the first 2 months). In the United States, drug-resistant TB is relatively rare (approximately 1% of all patients), and is treated with an 18–24 months individualized regimen based on drug susceptibility test results.	4

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2. Rozenshtein A, Hao F, Starc MT, Pearson GD. Radiographic appearance of pulmonary tuberculosis: dogma disproved. *AJR Am J Roentgenol.* 2015;204(5):974-978.	Review/Other-Dx	N/A	To review the origins of the classic teaching on PTB, its evolution in the modern literature, and the evidence that led to its demise.	Use of molecular epidemiologic techniques that entail DNA fingerprinting has led to the discovery that the radiographic appearance of PTB does not depend on the time since infection. It has been confirmed that the upper lobe cavitary disease typical in adults is the disease of the immunocompetent host, whereas lower lung zone disease, adenopathy, and effusions, which are uncommon in adults, are the hallmarks of TB in an immunocompromised host.	4
3. Eisenberg RL, Romero J, Litmanovich D, Boiselle PM, Bankier AA. Tuberculosis: value of lateral chest radiography in pre-employment screening of patients with positive purified protein derivative skin test results. *Radiology.* 2009;252(3):882-887.	Observational-Dx	875 adults	To test the hypothesis that lateral radiography adds no clinically relevant information to that acquired with posteroanterior radiography in individuals with positive purified protein derivative skin test results.	The posteroanterior radiograph revealed abnormalities in all 91 (10.4%) subjects with positive findings at radiography. The lateral radiograph revealed no abnormality in 75 subjects (83.4%). All abnormalities seen on lateral radiographs were also seen on posteroanterior radiographs. When abnormalities were seen on both images, the information on the lateral image never caused the radiologist to change the decision he or she made on the basis of the posteroanterior image alone.	2
4. Piccazzo R, Paparo F, Garlaschi G. Diagnostic accuracy of chest radiography for the diagnosis of tuberculosis (TB) and its role in the detection of latent TB infection: a systematic review. *J Rheumatol Suppl.* 2014;91:32-40.	Review/Other-Dx	67 paper articles	To evaluate the role of CXR in the diagnostic flow chart for TB infection, focusing on LTBI in patients requiring medical treatment with biological drugs.	In recent findings, patients scheduled for immunomodulatory therapy with biologic drugs are a group at risk of TB reactivation and, in such patients, detection of LTBI is of great importance. CXR for diagnosis of PTB has good sensitivity, but poor specificity. Radiographic diagnosis of active disease can only be reliably made on the basis of temporal evolution of pulmonary lesions. In vivo tuberculin skin test and ex vivo interferon-g release assays are designed to identify development of an adaptive immune response, but not necessarily LTBI. CT is able to distinguish active from inactive disease. CT is considered a complementary imaging modality to CXR in the screening procedure to detect past and LTBI infection in specific subgroups of patients who have increased risk for TB reactivation, including those scheduled for medical treatment with biological drugs.	4

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5. Wisnivesky JP, Henschke C, Balentine J, Willner C, Deloire AM, McGinn TG. Prospective validation of a prediction model for isolating inpatients with suspected pulmonary tuberculosis. *Arch Intern Med.* 2005;165(4):453-457.	Observational-Dx	516 individuals	To prospectively validate a clinical decision rule to predict the need for respiratory isolation in inpatients with suspected TB.	Of the 516 patients, 19 were found to have TB (prevalence, 3.7%; 95% CI, 2.2%–5.7%). The prediction rule had a sensitivity of 95% (95% CI, 74%–100%) and a specificity of 35% (95% CI, 31%–40%). Using a prevalence of TB of 3.7%, the positive predictive value was 9.6% and the negative predictive value was 99.7%.	2
6. Yeh JJ, Yu JK, Teng WB, et al. High-resolution CT for identify patients with smear-positive, active pulmonary tuberculosis. *Eur J Radiol.* 2012;81(1):195-201.	Observational-Dx	183 patients	To investigate a proposed triage protocol using HRCT to initiate respiratory isolation for patients with AFB smear positive PTB in the emergency room before the sputum smear results are known, with the ultimate intention of reducing the spatial and financial burden to hospitals, while minimizing any additional risk to patients and healthcare workers. No intravenous contrast was administered.	Utilizing multivariate analysis, 5 variables were found to be independent risk factors predictive of G1: (1) consolidation involving the apex segment of right upper lobe, posterior segment of the right upper lobe, or apico-posterior segment of the left upper lobe; (2) consolidation involving the superior segment of the right or left lower lobe; (3) presence of a cavitary lesion; (4) presence of clusters of nodules; (5) absence of centrilobular nodules. A G1 prediction score was generated based on these 5 criteria to help differentiate G1 from G2. The area under the receiver operating characteristic curve was 0.96 +/- 0.012 in our prediction model. With an ideal cut-off point score of 3, the specificity, sensitivity, positive predictive value, and negative predictive value are 90.9%, 96.4%, 90.0% and 96.8%, respectively.	2
7. Matsuoka S, Uchiyama K, Shima H, et al. Relationship between CT findings of pulmonary tuberculosis and the number of acid-fast bacilli on sputum smears. *Clin Imaging.* 2004;28(2):119-123.	Observational-Dx	173 patients	To investigate the relationship between CT findings in patients with active PTB and the number of AFB on sputum smears. No intravenous contrast was administered.	The frequency of micronodules and nodules did not significantly differ among the 4 groups. In contrast, the frequency of consolidation and cavitation increased with the number of AFB ($P<.0001$). Differences in the number of lobes involving micronodules, nodules, consolidation and cavitation were significant between Group D and the other groups ($P<.0001$), but not between Groups A or B and C. The number and maximum size of cavities significantly differed between Group D and the other groups ($P<.0001$).	2

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8. Ors F, Deniz O, Bozlar U, et al. High-resolution CT findings in patients with pulmonary tuberculosis: correlation with the degree of smear positivity. *J Thorac Imaging.* 2007;22(2):154-159.	Observational-Dx	61 male patients	To investigate a relationship between the degree of smear positivity and radiologic extent of disease based on HRCT findings and, the degree of smear positivity and different parenchymal changes on HRCTs of the PTB patients.	A significance correlation between radiologic extent of the disease based on HRCT and the degree of smear positivity was found (r = 0.63, *P*=0.0001). There were also significant correlations between the degree of smear positivity and the scores of different HRCT findings. Nodule, cavity, and bronchial lesions are the most important contributors of the predictive properties of the total score. There were significant differences for the scores of HRCT findings between smear-positive and smear-negative patients.	3
9. Yeh JJ, Neoh CA, Chen CR, Chou CY, Wu MT. A high resolution computer tomography scoring system to predict culture-positive pulmonary tuberculosis in the emergency department. *PLoS One.* 2014;9(4):e93847.	Observational-Dx	4140 patients	The goal of this study is to investigate the efficacy of a HRCT screening protocol for detecting the presence or absence of culture-positive PTB, and to examine the post-test probability in areas with different prevalence of TB.	The post-test probability ratios between both phases in 3 prevalence areas were analyzed. In the derivation phase, a multivariate analysis model identified cavitation, consolidation, and clusters/nodules in right or left upper lobe (except anterior segment) and consolidation of the superior segment of the right or left lower lobe as independent positive factors for culture-positive PTB, while consolidation of the right or left lower lobe (except superior segment) were independent negative factors. An ideal cutoff point based on the receiver operating characteristic curve analysis was obtained at a score of 1. The sensitivity, specificity, positive predictive value, and negative predictive value from derivation phase were 98.5% (130/132), 99.7% (3997/4008), 92.2% (130/141), and 99.9% (3997/3999). Based on the predicted positive likelihood ratio value of 328.33 in derivation phase, the post-test probability was observed to be 91.5% in the derivation phase, 92.5% in the validation phase, 94.5% in a high TB prevalence area, 91.0% in a moderate prevalence area, and 76.8% in moderate-to-low prevalence area.	2

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10. Nakanishi M, Demura Y, Ameshima S, et al. Utility of high-resolution computed tomography for predicting risk of sputum smear-negative pulmonary tuberculosis. *Eur J Radiol.* 2010;73(3):545-550.	Observational-Dx	116 patients	To investigate whether or not HRCT can predict risk for sputum smear-negative PTB.	A positive tuberculin skin test alone among clinical laboratory findings was significantly associated with an increase of risk of PTB. Multivariate regression analysis showed that large nodules, tree-in-bud appearance, lobular consolidation and the main lesion being located in S1, S2, and S6 were significantly associated with an increased risk of PTB. Stepwise regression analysis showed that coexistence of the above 4 factors was most significantly associated with an increase in the risk for PTB. Ranking of the results using our HRCT diagnostic criteria by blinded observers revealed good utility and agreement for predicting PTB risk.	2
11. Lyu J, Lee SG, Hwang S, et al. Chest computed tomography is more likely to show latent tuberculosis foci than simple chest radiography in liver transplant candidates. *Liver Transpl.* 2011;17(8):963-968.	Observational-Dx	2564 liver transplant recipients	To analyze the ability of pre-liver transplant chest CT scans to predict the development of post-liver transplant TB.	36 of 2549 liver transplant recipients (1.4%) were diagnosed with TB after liver transplant (median = 10 months, range = 1–80 months). 28 patients (77.8%) successfully completed the treatment. There were no significant differences in the clinical characteristics of the 2 groups. Abnormal CT findings (40.0% vs 17.3%, *P*=0.018) and CXR findings (25.0% vs 11.8%, *P*=0.044) suggestive of healed TB were significantly more frequent in the TB group vs the control group. Of the 10 patients who underwent chest CT and developed TB, 5 (50%) showed abnormal findings only on chest CT scans, whereas their CXR results were normal.	2
12. Rizzi EB, Schinina V, Cristofaro M, et al. Detection of Pulmonary tuberculosis: comparing MR imaging with HRCT. *BMC Infect Dis.* 2011;11:243.	Observational-Dx	50 patients	To compare MRI with HRCT for assessing PTB. No intravenous contrast was administered.	Artifacts did not interfere with the diagnostic value of MRI. Both HRCT and MRI correctly diagnosed PTB and identified pulmonary abnormalities in all patients. There were no significant differences between the 2 techniques in terms of identifying the location and distribution of the lung lesions, though the higher resolution of MRI did allow for better identification of parenchymal dishomogeneity, caseosis, and pleural or nodal involvement.	1

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13. Barreto MM, Rafful PP, Rodrigues RS, et al. Correlation between computed tomographic and magnetic resonance imaging findings of parenchymal lung diseases. *Eur J Radiol.* 2013;82(9):e492-501.	Review/Other-Dx	N/A	To describe and correlate the MRI and CT features of several common patterns of parenchymal lung disease (air trapping, atelectasis, bronchiectasis, cavitation, consolidation, emphysema, ground-glass opacities, halo sign, interlobular septal thickening, masses, mycetoma, nodules, progressive massive fibrosis, reverse halo sign and tree-in-bud pattern).	No results stated in abstract.	4
14. Ahmadihosseini H, Sadeghi R, Zakavi R, Kakhki VR, Kakhki AH. Application of technetium-99m-sestamibi in differentiation of active from inactive pulmonary tuberculosis using a single photon emission computed tomography method. *Nucl Med Commun.* 2008;29(8):690-694.	Observational-Dx	36 patients	To study the usefulness of 99mTc-methoxyisobutylisonitrile scintigraphy for differentiation between active and inactive PTB.	All of the 12 patients in the control group had negative scintigraphy on both planar and SPECT images. 20 patients with active PTB had positive 99mTc-methoxyisobutylisonitrile scintigraphy on planar images (sensitivity of 87.5%). SPECT images were positive in 23 patients with active PTB (sensitivity of 95.8%). Both semiquantitative and visual assessment of planar and SPECT images showed statistically significant differences between active and inactive PTB patients (P<0.001). Comparison of 15 and 60 min image sets did not show any statistically significant difference (P=0.956 and 0.457 for planar and SPECT images, respectively).	2
15. Raziei G, Masjedi MR, Fotouhi F, et al. The role of 99mTc-MIBI scintigraphy in the management of patients with pulmonary tuberculosis. *Eur Rev Med Pharmacol Sci.* 2012;16(5):622-629.	Observational-Dx	34 patients	To determine whether 99mTc-methoxyisobutylisonitrile scanning could improve diagnostic accuracy of PTB and help clinical decision making for an accurate management.	34 patients with active PTB (15 males and 19 females; mean age of 47.85 +/- 1.91 years) and 28 cases with inactive PTB (9 male and 19 females; mean age of 53.96 +/- 2.33 years) were included in this study. The sensitivity, specificity, accuracy, positive and negative predictive values of 99mTc-methoxyisobutylisonitrile were 88.2%, 75%, 82.2%, 81.1% and 84% respectively. The mean value of lesion/non-lesion in the active PTB for 99mTc-methoxyisobutylisonitrile was 1.45 +/- 0.18 and lesion/neck soft tissue was 1.57 +/- 0.26 which was significant statistically (P<0.00).	2

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16. Kaneko K, Sadashima E, Irie K, et al. Assessment of FDG retention differences between the FDG-avid benign pulmonary lesion and primary lung cancer using dual-time-point FDG-PET imaging. *Ann Nucl Med.* 2013;27(4):392-399.	Observational-Dx	77 patients	To clarify FDG retention differences between FDG-avid benign pulmonary lesions and primary lung cancers, and between tuberculous and non-tuberculous benign pulmonary lesions using dual-time-point FDG-PET imaging.	Benign pulmonary lesions and primary lung cancers showed similar high retention indexes (mean +/- SD 33.6 +/- 22.6 and 32.5 +/- 23.7, respectively; *P*=0.95). In benign pulmonary lesions, both tuberculous and non-tuberculous lesions showed high retention indexes (39.1 +/- 25.8 and 30.3 +/- 20.3, respectively; *P*=0.43). However, benign pulmonary lesions and primary lung cancers exhibited a different relationship between retention index and standardized uptake value-1hr. Benign pulmonary lesions tended to show lower retention indexes with higher standardized uptake value-1hr, and a mild negative correlation, whereas primary lung cancers showed persistent high retention indexes and no significant correlation. Glut-1 and HK-2 expression was found in 75% and 12.5% of nontuberculous benign pulmonary lesions, respectively.	4
17. Liu SF, Liu JW, Lin MC, Lee CH, Huang HH, Lai YF. Monitoring treatment responses in patients with pulmonary TB using serial lung gallium-67 scintigraphy. *AJR Am J Roentgenol.* 2007;188(5):W403-408.	Observational-Dx	30 patients	To monitor treatment responses in patients with PTB using serial lung gallium-67 scintigraphy.	30 patients (24 men and 6 women) with PTB were enrolled. 86 paired semiquantitations of sputum AFB-67Ga-scintigraphic studies were collected. 26 patients were cured of their PTB. The pulmonary 67Ga uptake increased in proportion to the higher score of semiquantitation of sputum AFB (*P*=0.009, for trend).	2

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18. Liu Y, Weinberg MS, Ortega LS, Painter JA, Maloney SA. Overseas screening for tuberculosis in U.S.-bound immigrants and refugees. *N Engl J Med.* 2009;360(23):2406-2415.	Review/Other-Dx	2,714,223 US bound immigrants	To analyze the prevalence of smear-negative and inactive TB among immigrants and refugees, examine time trends for the prevalence of these conditions, and analyze the results of the post-arrival follow-up evaluation.	From 1999 through 2005, a total of 26,075 smear-negative cases of TB (i.e., cases in which a CXR was suggestive of active TB but sputum smears were negative for AFB on 3 consecutive days) and 22,716 cases of inactive TB (i.e., cases in which a CXR was suggestive of TB that was no longer clinically active) were diagnosed by overseas medical screening of 2,714,223 U.S.-bound immigrants, representing prevalences of 961 cases per 100,000 persons (95% CI, 949 to 973) and 837 cases per 100,000 persons (95% CI, 826 to 848), respectively. Among 378,506 U.S.-bound refugees, smear-negative TB was diagnosed in 3923 and inactive TB in 10,743, representing prevalences of 1036 cases per 100,000 persons (95% CI, 1004 to 1068) and 2838 cases per 100,000 persons (95% CI, 2785 to 2891), respectively. Active PTB was diagnosed in the United States in 7.0% of immigrants and refugees with an overseas diagnosis of smear-negative TB and in 1.6% of those with an overseas diagnosis of inactive TB.	4
19. Paquette K, Cheng MP, Kadatz MJ, Cook VJ, Chen W, Johnston JC. Chest radiography for active tuberculosis case finding in the homeless: a systematic review and meta-analysis. *Int J Tuberc Lung Dis.* 2014;18(10):1231-1236.	Meta-analysis	16 studies	To evaluate the use of CXR screening in active case finding for TB in homeless populations through a systematic review and meta-analysis.	16 studies addressing CXR screening of homeless populations for active TB in low-incidence regions were analyzed. The pooled prevalence of active TB in the 16 study cohorts was 931 per 100,000 population screened (95% CI, 565–1534) and 782/100,000 CXR performed (95% CI, 566–1079). 6 of 7 longitudinal screening programs reported a reduction in regional TB incidence after implementation of the CXR-based active case finding program.	M

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20. Jeong YJ, Lee KS. Pulmonary tuberculosis: up-to-date imaging and management. *AJR Am J Roentgenol.* 2008;191(3):834-844.	Review/Other-Dx	N/A	To elaborate the new concept of the diagnosis and treatment of PTB, to review the characteristic imaging findings of various forms of PTB, and to assess the role of CT in the diagnosis and management of PTB.	Fast and more accurate TB testing such as bacterial DNA fingerprinting and whole-blood interferon-γ assay has been developed. Miliary or disseminated primary pattern or atypical manifestations of PTB are common in patients with impaired immunity. CT plays an important role in the detection of TB in patients in whom the CXR is normal or inconclusive, in the determination of disease activity, in the detection of complication, and in the management of TB by providing a roadmap for surgical treatment planning. PET scans using FDG or 11C-choline can sometimes help differentiate tuberculous granuloma from lung malignancy.	4
21. Eisenberg RL, Pollock NR. Low yield of chest radiography in a large tuberculosis screening program. *Radiology.* 2010;256(3):998-1004.	Observational-Dx	2586 adults	To assess the frequency and spectrum of abnormalities on routine screening CXRs in the pre-employment evaluation of health care workers with positive tuberculin skin test results.	Of the 159 (6.1%) CXR examinations that yielded abnormal results, there were no findings that were consistent with active TB. There were 92 cases of calcified granulomas, calcified lymph nodes, or both; 25 cases of apical pleural thickening; 16 cases of fibrous scarring; and 31 cases of noncalcified nodules. All cases of fibrous scarring involved an area smaller than 2 cm(2). All noncalcified nodules were 4 mm in diameter or smaller, with the exception of 1 primary lung malignancy and 1 necrotizing granuloma (negative for AFB) that grew Mycobacterium kansasii on culture.	3

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22. Vinkeles Melchers NV, van Elsland SL, Lange JM, Borgdorff MW, van den Hombergh J. State of affairs of tuberculosis in prison facilities: a systematic review of screening practices and recommendations for best TB control. *PLoS One.* 2013;8(1):e53644.	Review/Other-Dx	52 articles	To explore screening practices for detection of TB and describes limitations of TB control in prison facilities worldwide.	The most common screening tool was symptom questionnaires (63.5%), mostly reporting presence of cough. Microscopy of sputum with Ziehl-Neelsen staining and solid culture were the most frequently combined diagnostic methods (21.2%). CXR and tuberculin skin tests were used by 73.1% and 50%, respectively, as either a screening and/or diagnostic tool. Median TB prevalence among prisoners of all included studies was 1,913 cases of TB per 100,000 prisoners (interquartile range: 332–3,517). The overall annual median TB incidence was 7.0 cases per 1000 person-years (interquartile range: 2.7–30.0). Major limitations for successful TB control were inaccuracy of diagnostic algorithms and the lack of adequate laboratory facilities reported by 61.5% of studies. The most frequent recommendation for improving TB control and case detection was to increase screening frequency (73.1%).	4

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  c) the study is an expert opinion or consensus document.
- M = Meta-analysis

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

AFB = Acid-fast bacilli

CI = Confidence interval

CT = Computed tomography

CXR = Chest radiograph

FDG-PET = Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography

HRCT - High-resolution computed tomography

LTBI = Latent tuberculosis infection

MRI = Magnetic resonance imaging

PTB = Pulmonary tuberculosis

SPECT = Single photon emission computed tomography

TB = Tuberculosis