



PREVENTION OPPORTUNITIES UNDER THE BIG SKY

TUBERCULOSIS IN MONTANA: State of the art diagnostic testing available

From 2000 to 2009, 7 to 21 (median 13) cases of tuberculosis (TB) were reported each year in Montana. In order to confirm the diagnosis of TB it is necessary to isolate *Mycobacterium tuberculosis* from a patient specimen. This TB organism grows slowly in laboratory culture. If a specimen has a large number of organisms, culture evidence for TB may develop within one to two weeks. However, for a specimen containing only a few organisms it may take up to six weeks for evidence to develop. While awaiting confirmatory evidence clinicians and public health officials have either initiated treatment empirically or delayed treatment decisions.

Recent advances in TB diagnostic testing have markedly reduced the time necessary to detect TB, and to detect certain drug resistant strains. This issue of *Montana Public Health* describes TB cases reported in Montana during the last ten years and TB diagnostic testing available at or through the Montana Public Health Laboratory (MTPHL).

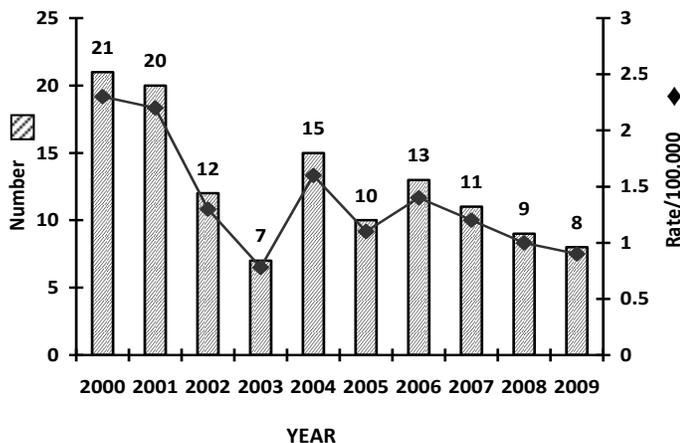
TB in Montana. The annual number of TB cases reported in Montana has decreased (Figure) from an average of 15 cases per year in 2000-2004 to an average 10 cases per year in 2005-2009. During this period the number of cases that were foreign born increased from an average 1 case per year in the first half of the decade to 3 cases per year in the second half of the decade, while the number of American Indian cases decreased from an average 8 to an average 3 cases per year. Of the 126 cases reported during the decade, 5 were less than 18 years of age, none had HIV infection, and 2 had multidrug-resistant TB (in 2003 and 2006). The rate of TB cases reported per 100,000 persons in Montana decreased from 2.3 to 0.9 (Figure) and was below the US rate during this entire time (the U.S. rate decreased from 5.8 per 100,000 in 2000 to 4.2 in 2008).

TB diagnostic testing available at MTPHL. The MTPHL performs TB culture tests which remain the gold standard for laboratory confirmation of TB. Culture isolation of the TB organism is also essential to allow drug susceptibility testing and genotyping. In addition, the MTPHL performs nucleic acid amplification tests (NAAT) which can markedly reduce the time necessary to detect the presence of TB.

The NAAT uses transcription mediated amplification to identify ribosomal RNA of *M. tuberculosis*.¹ It is FDA approved for testing concentrated sediments from sputum, bronchial or tracheal specimens whether or not the specimens are smear positive. This allows testing to detect a high likelihood of TB within 24-48 hours after receipt of a specimen at the laboratory. Although NAAT is quite sensitive and very specific, it is not perfect. It is very important to interpret the test results in light of the level of clinical suspicion for TB (see Recommendation box on page 2). The NAAT should not be used to screen for TB when clinical suspicion is low; the positive predictive value of the test can be less than 50% in low risk clinical situations. In contrast, when the patient's signs, symptoms and exposure history lead to a high level of clinical suspicion NAAT can facilitate initiation of treatment and efforts to interrupt spread of disease.

The Montana TB Control Program is always available to assist clinicians with testing and treatment decisions, and to assist local public health authorities with contact investigation and efforts to interrupt transmission of infection. Through the Montana TB Control Program, expert physician consultation is also available from the Francis J. Curry Regional TB Training and Medical Consultation Center.

FIGURE. Number and rate of TB cases, Montana, 2000-2009



Rapid molecular testing to detect certain drug-resistant TB organisms. The prevalence of resistance to medications used to treat TB has decreased in the U.S. but increased elsewhere in the world in recent years.^{2,3} While definitive drug-resistance testing requires isolation of the TB organism by laboratory culture tests and subsequent, time-consuming resistance testing, resistance to isoniazid, rifampin and other 1st and 2nd line drugs used to treat TB can be reliably predicted more quickly with molecular testing methods. This testing, where DNA is sequenced for the identification of drug resistance associated mutations, is available through the MTPHL and is performed at either CDC or designated regional laboratories.

At the current time this molecular testing for isoniazid and rifampin is available in specific circumstances, e.g., for patients at high risk to have multidrug-resistant TB.

The testing is automatically ordered by the Montana TB Control Program under the following circumstances:

1. person at high risk for drug-resistant TB (e.g., person lived in area of the world in which resistance rate is high, or person has previously been treated for TB)
2. very ill patient for whom results of testing may alter treatment
3. person for whom results might influence public health control decision (e.g., should use of public transportation be restricted?)
4. initial isolate contains a mixture of *M. tuberculosis* and other mycobacteria, or only nonviable *M. tuberculosis*
5. persons who work with populations in high profile settings (e.g., physicians, nurses, school or daycare employees)

Recommendation for specimen collection and interpretation of NAAT⁴

1. Collect sputum to test for acid fast bacillus (AFB) by microscopy and to submit for culture
2. At least one specimen, preferably the first collected, from each high suspect patient should be tested by NAAT
3. The NAAT result should be interpreted in light of the AFB smear results and clinical presentation
 - a. If the NAAT result is positive and the AFB smear result is positive, presume the patient has TB and begin treatment while awaiting culture results.
 - b. If the NAAT result is positive and the AFB smear result is negative, use clinical judgment whether to begin treatment while awaiting culture results. Consider testing an additional specimen using NAAT. A patient can be presumed to have TB, pending culture results, if two or more specimens are NAAT positive.
 - c. If the NAAT result is negative and the AFB smear result is positive, an additional specimen should be tested with NAAT. Use clinical judgment to determine whether to begin treatment while awaiting culture results. A patient can be presumed to have an infection with nontuberculous mycobacteria if a second specimen is also smear positive and NAAT negative.
 - d. If the NAAT result is negative and the AFB smear result is negative, use clinical judgment to determine whether to begin treatment while awaiting results of culture. Currently available NAAT are not sufficiently sensitive (75%-90%) to exclude the diagnosis of TB in AFB smear-negative patients who are clinically suspected to have TB.

For more information, contact the MT TB Control Program, Denise Ingman, 406-444-0275, dingman@mt.gov or the MTPHL, Susie Zanto, 1-800-821-7284, szanto@mt.gov.

References:

1. Gen-Probe Amplified Mycobacterium tuberculosis direct test product insert. <http://www.gen-probe.com/pdfs/pi/IN0014.pdf>
2. CDC. Reported tuberculosis in the U.S., 2008. Atlanta, GA: U.S. Department of Health & Human Services, CDC, October 2008.
3. WHO. The WHO/IUATLD Global Project on Anti-Tuberculosis Drug Resistance Surveillance. *Antituberculosis Drug Resistance in the World Report No.* 4 Vol. WHO/HTM/TB2008.394. Geneva, Switzerland, 2008.
4. CDC. Updated guidelines for the use of nucleic acid amplification tests in the diagnosis of TB. MMWR 2009; 58: 7-10.

2,300 copies of this public document were published at an estimated cost of \$0.419 per copy, for a total of \$1,328.70, which includes \$365.00 for printing and \$963.70 for distribution.
January 2010 Vol 5 Issue 1



1400 Broadway
Helena, MT 59620-2951

Anna Whiting Sorrell, Director, DPHHS
Steven Helgerson, MD, MPH, State Med. Officer
Jane Smilie, MPH, Administrator, PHSD