

Draft Interim
USAPI Standards for the Management of
Tuberculosis and Diabetes
(PITCA Ratified 12-01-2010)

Diabetes mellitus (DM)-related tuberculosis is a synergistic problem driven by concurrent epidemics of both diseases in the U.S. Associated Pacific Islands (USAPI). Among USAPI's, diabetes rates are some of the highest in the world. In 2007, the estimated prevalence of diabetes in the US was 10.7% (adults \geq 20 years, CDC, BRFSS). In 2002, the diabetes prevalence estimates for Pohnpei, Federated States of Micronesia was 32.1% (adults aged 25-64 years, fasting blood glucose [FBG] \geq 126 mg/dL). At the same time, latent tuberculosis infection (LTBI) and active tuberculosis (TB) among USAPI's are nearly 10 times the current US rate. In contrast to a US TB rate 4.2 (per 100,000 in 2008), TB rates are as high as 198 in the Marshall Islands and 169 in Micronesia (2008).

Recent evidence (see references) as well as local Pacific Island experience has reemphasized the dynamic of these two epidemics, specifically the impact of DM on the epidemiology and severity of TB disease, and the complex interactions of treating both diseases. Diabetes impacts tuberculosis by: 1) tripling the rate of developing active TB from latent TB infection, 2) increasing mortality and severity of disease, and 3) slowing the response to effective TB treatment. In 2008, a Harvard meta-analysis reviewed 13 observational studies that included over 1.7 million participants and found that the relative risk of active TB was 3.11 among those with DM versus those without DM.

Additional studies have shown that TB differs in patients with diabetes. Atypical presentations of exclusively lower lobe lung lesions are more common among persons with diabetes and although not demonstrated consistently in every study, most show evidence of increased severity of disease, namely more symptoms, a higher frequency of cavitation and smear positivity. A Texas study in 2008 found that persons with diabetes on average achieved sputum

culture conversion five days later than persons without diabetes. An Indonesian study in 2007 with similar findings showed both slower smear and culture conversion in persons with diabetes. In 2008 and 2009, two separate studies in Taiwan showed significantly higher mortality among persons with diabetes. One possible reason for this poorer response to treatment might be that blood levels of rifampin, both peak and AUC (area under the curve), are significantly lower in persons with diabetes, averaging about half that in persons without diabetes. (A lower mg/kg dose in overweight persons with diabetes may play a role.)

Conversely, tuberculosis and its treatment can worsen control of diabetes and diabetes-related neuropathy. Rifampin, a drug that stimulates the liver's cytochrome P₄₅₀ enzyme system, interacts negatively with commonly used hypoglycemic drugs, including sulfonylureas (such as glipizide) and thiozolidinediones (such as Avandia or Actos). Blood levels of these drugs are lower when rifampin is being used and can negatively impact diabetes control. Monitoring blood sugars and adjusting anti-diabetic medications while on rifampin are thereby crucial to establishing and maintaining adequate glucose control. Persons with diabetes also have a higher incidence of peripheral neuropathy while taking isoniazid (INH) for active TB or LTBI.

Recent reports from the USAPI TB Programs indicate 30-75% of TB cases in adult Pacific Islanders are complicated by coexistent diabetes. In response to growing awareness of these converging epidemics, TB programs of the USAPI have expressed the urgent need for guidance for improved patient management and treatment outcomes.

These standards and clinical guidelines are intended to help address the immediate needs of TB programs and clinicians to prevent, identify, evaluate, and manage both conditions. Routine TB screening of persons with diabetes is recommended for early case detection as well as identifying persons with diabetes with LTBI who would benefit from preventive treatment. Logical strategies for glucose control, education, and support of patients throughout treatment for active TB disease and LTBI are presented in the table below.

Screening for DM in persons with active TB

Standard 1.0 Every person with tuberculosis (TB) over the age of 18 should be screened for diabetes mellitus (DM)

Guideline 1.1 The diagnosis of DM may be made using one of the following criteria:

A fasting plasma glucose \geq 126 mg/dl

A random plasma glucose \geq 200 mg/dl

A hemoglobin A1c \geq 6.5 %

Guideline 1.2 Abnormal glucose values should be verified with a repeat test in patients who have no symptoms of DM

Guideline 1.3 Rifampin can elevate blood glucose in TB patients. Glucose testing should be repeated after 2-4 weeks of TB treatment, or if symptoms of hyperglycemia develop while on TB treatment

Screening for TB in persons with DM

Standard 2.0 Persons from the USAPI with DM who are at increased risk of TB should be screened for active TB disease and latent TB infection (LTBI)

Guideline 2.1 A tuberculin skin test (TST) or interferon gamma releasing assay (IGRA) for TB should be done at the time of DM diagnosis

Guideline 2.2 Screening should be repeated as often as the local TB epidemiology may warrant

Standard 3.0 Patients identified with suspected or confirmed active TB should be referred to the local TB Program for TB management

Standard 4.0 Persons with DM who are identified with LTBI should be encouraged to take isoniazid (INH) preventive therapy for 9 months*

Guideline 4.1 Because persons with DM are at increased risk of peripheral neuropathy, they should receive vitamin B6 to help prevent INH induced neuropathy (10 – 25 mg/day)

Guideline 4.2 Patients with LTBI should be educated for the potential side effects of INH therapy. Monthly monitoring for adherence and side effects is recommended*

* Targeted tuberculin testing and treatment of latent tuberculosis infection, MMWR 2000;49.

Treating TB in persons with DM

Standard 5.0 Ensure that TB treatment is appropriately adjusted in persons with DM

Guideline 5.1 Ensure that TB medications are properly dosed

5.1.1 Check creatinine for diabetic nephropathy, and if present, adjust the frequency of pyrazinamide (PZA) and ethambutol (EMB) according to ATS-CDC guidelines*

5.1.2 Administer B₆ to prevent INH induced peripheral neuropathy (10 – 25 mg/day)

Guideline 5.2 Observe closely for TB treatment failure* in persons with DM

5.2.1 Be aware of poor absorption of some TB meds in DM

5.2.2 Manage the many interactions between TB and DM meds

5.2.3 Be aware of a possible slight increase in TB drug resistance in persons with DM and active TB

Guideline 5.3 “Assure the Cure”

5.3.1 Consider extending treatment to 9 months for persons with DM, especially those patients with cavitary disease **or** delayed sputum clearance.* Patients with DM have relative immune suppression and often a higher burden of TB disease

5.3.2 Upon completion of therapy, obtain sputum for AFB smear and culture

5.3.3 Evaluate patients at 6 months and one year after treatment for evidence of relapse

*Treatment of Tuberculosis, American Thoracic Society, CDC, and Infectious Diseases Society, MMWR 2003;52

Managing DM in persons with active TB

Standard 6.0 Glucose testing should be repeated in TB Clinic during TB therapy

Guideline 6.1 TB patients with a diagnosis of DM should have their blood glucose checked at least weekly for the first 4 weeks, and less frequently thereafter if the diabetes is well controlled. (Monthly blood glucose measurement during TB treatment is recommended)

Standard 7.0 Use the frequent contact in clinic with TB patients to help manage DM

Guideline 7.1 There should be a glucometer in every TB clinic for monitoring blood glucose

Guideline 7.2 All clinic staff should reinforce lifestyle changes at TB clinic visits

Guideline 7.3 If available, refer persons with DM to the Diabetes Clinic for long-term diabetes care. Ensure the DM clinician is aware of TB diagnosis and TB medications

Standard 8.0 Use the frequent DOT contact with TB patients to help manage DM

Guideline 8.1 DOT workers should encourage lifestyle changes at every patient encounter

8.1.1 Dietary changes and physical activity are the most important in this effort

8.1.2 DOT workers should use structured culturally-appropriate diabetes educational materials*

Guideline 8.2 Consider delivering DM meds with TB meds via DOT for selected poorly-controlled persons with DM who have suspected non-adherence to diabetic medications

* National Diabetes Education Program, US Dept of Health and Human Services: <http://www.yourdiabetesinfo.org/>

* Pacific Diabetes Education Program, a program of CDC and Papa Ola Lokahi: <http://www.pdep.org/>

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