

**Embargo:**

4 PM, Thurs., Aug. 30, 2001

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## **Severe and Fatal Liver Injury Connected to Latent TB Treatment**

### *Guidelines for the Treatment Of Latent TB Infection Revised*

The Centers for Disease Control and Prevention has investigated reports of 21 patients who were hospitalized because of severe liver injury associated with a two-month treatment regimen of rifampin and pyrazinamide (RIF-PZA) for latent TB infection (LTBI). Sixteen of the patients recovered and five died. Findings from the investigations into these cases are included in the August 31 edition of CDC's *Morbidity and Mortality Weekly Report (MMWR)*.

CDC previously published findings from an investigation into two cases of severe liver damage associated with RIF-PZA. Only one of the patients recovered. These cases were outlined in the April 20 edition of the *MMWR*, at which time CDC requested reports of additional cases.

### **CDC and ATS Revise Guidelines for Latent TB Treatment**

As a result of these investigations, CDC and the American Thoracic Society are issuing revised treatment guidelines for LTBI to limit the circumstances in which the combination of RIF-PZA is prescribed and to strengthen the level of patient counseling and monitoring recommended for LTBI treatment regimens.

For most individuals with LTBI, the new guidelines recommend the nine-month regimen of daily INH as the preferred treatment. CDC recommends providers use RIF-PZA with caution, especially in those currently taking other medications that have been associated with liver injury, and those with alcoholism even if alcohol usage is discontinued during treatment.

However, with careful clinical and laboratory monitoring as outlined in the recommendations, RIF-PZA remains an option for patients at high risk of developing active TB disease and who are unlikely to complete a nine-month regimen of isoniazid (INH). For HIV-negative individuals with LTBI, the new guidelines recommend the nine-month regimen of daily INH as the standard treatment.

While available data do not suggest excessive risk of severe side effects associated with RIF-PZA among HIV-positive individuals, providers should consider the use of INH when completion of this longer regimen can be assured. Patients co-infected with HIV and LTBI are at increased risk for developing active TB disease.

## **Guidelines Emphasize TB Testing and Treatment for People at High Risk**

The goal of testing people for TB is to find and treat those who have LTBI and are at high risk of developing active TB disease. Those at high risk include individuals with LTBI who are HIV-infected, were recent contacts of someone with active TB, injection drug users, and residents or employees of high-risk congregate settings, which include correctional facilities, nursing homes, homeless shelters, hospitals, and other health care facilities. Furthermore, providers are reminded that treatment is recommended for foreign-born people with LTBI who have lived in the United States for less than five years and who were born in countries with high rates of TB. After five years, treatment decisions should be made on the same basis as other patients.

Because all regimens for treating LTBI have been associated with liver injury, careful monitoring during treatment is important to avoid severe damage. Any additional cases of severe liver damage associated with treatment of LTBI should be reported to the CDC's Division of TB Elimination. These recommendations should not affect patients receiving treatment for active TB.

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## **Related MMWRs**

*For information about the previous MMWR on severe liver damage associated with RIF-PZA:*

### **Fatal and Severe Hepatitis Associated With Rifampin and Pyrazinamide for the Treatment of Latent Tuberculosis Infection – New York and Georgia, 2000**

The findings from the April 20 MMWR article – *Fatal and Severe Hepatitis Associated With Rifampin and Pyrazinamide for the Treatment of Latent Tuberculosis Infection --- New York and Georgia, 2000* – underscored the need for clinical monitoring for adverse effects in all patients receiving treatment for LTBI to help prevent severe liver damage as a result of LTBI treatment.

*For a copy of the April 20 MMWR:* <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5015a3.htm>

*For information about the original recommendations:*

### **Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection**

The recommendation on the treatment on LTBI was included in the *Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection* statement developed by a panel of 47 experts from three continents. American Thoracic Society (ATS) and CDC convened the panel. The Infectious Diseases Society of America also endorsed the panel's statement. The American Academy of Pediatrics endorsed sections of the statement relating to infants and children. It was published as a supplement to the April 2000 issue of the ATS's *American Journal of Respiratory and Critical Care Medicine*, and was reprinted in CDC's *Morbidity and Mortality Weekly Report* on June 9, 2000.

*For a copy of the June 20, 2000 MMWR:*  
<http://www.cdc.gov/epo/mmwr/preview/mmwrhtml/rr4906a1.htm>