

Abstracts of current literature on epidemiology, diagnosis, and treatment

Series Editor: Jihad Slim, MD

## EFFECT OF INITIAL DRUG RESISTANCE ON OUTCOMES IN TUBERCULOSIS PATIENTS RECEIVING SHORT-TERM CHEMOTHERAPY

The authors performed a retrospective analysis to determine the effect of initial drug resistance on treatment outcome and acquired drug resistance in new patients receiving standardized short-course chemotherapy for tuberculosis. During 1996 to 2000, 2194 patients in Tomsk Oblast, Russian Federation, received a category 1 treatment regardless of drug susceptibility testing results, which were available for 1681 patients. Treatment failure occurred in 99 patients, of whom 73 were identified as having consistently positive culture results during treatment. Drug resistance patterns before and during treatment for these patients were then compared, revealing that pretreatment drug resistance was strongly associated with treatment failure. In patients with pretreatment resistance to either isoniazid or rifampin but not both, 17 (70.8%) of 24 cases of treatment failure now had acquired multidrug resistance. In patients with pretreatment pan-susceptible or streptomycin-resistant strains, 13 (41.9%) of 31 cases acquired multidrug resistance. The remaining 18 patients had newly acquired multidrug resistance. Determining whether patients are infected with drug-resistant tuberculosis and prescribing the appropriate second-line agents is necessary to decrease transmission of resistant strains and prevent the creation of multidrug-resistant strains. When patients' drug resistance status is unknown, physicians should be aware that patients who do not respond to directly observed short-course chemotherapy are at high risk for developing multidrug-resistant tuberculosis and need to be treated accordingly.

*Seung KJ, Gelmanova IE, Peremitin GG, et al. The effect of initial drug resistance on treatment response and acquired drug resistance during standardized short-course chemotherapy for tuberculosis. Clin Infect Dis 2004;39:1321-8.*

## DEXAMETHASONE FOR THE TREATMENT OF TUBERCULOUS MENINGITIS

Investigators conducted a randomized, double-blind, placebo-controlled trial in patients aged 14 years and older who had tuberculous meningitis, with or without HIV coinfection, to determine whether adjunctive treatment with dexamethasone reduced the risk of death or severe disability after 9 months of follow-up. Patients were recruited from 2 centers in Ho Chi Minh City, Vietnam, and were randomly assigned to receive dexamethasone (n = 274) or placebo (n = 271). Ten patients were lost to follow-up. Treatment with dexamethasone was associated with reduced risk of death (relative risk [RR], 0.69 [95% confidence interval [CI], 0.52-0.92]; P = 0.01). However, dexamethasone neither significantly reduced the proportion of severely dis-

abled patients (34/187 [18.2%] of dexamethasone versus 22/159 [13.8%] of placebo patients; P = 0.27) nor the proportion of patients who had died or were severely disabled after 9 months (odds ratio, 0.81 [95% CI, 0.58-1.13]; P = 0.22). Treatment effect was consistent across subgroups defined by disease-severity grade (stratified RR of death, 0.68 [95% CI, 0.52-0.91]; P = 0.007) and by HIV status (stratified RR of death, 0.78 [95% CI, 0.59-1.04]; P = 0.08). Significantly fewer adverse events occurred in the dexamethasone group than in the placebo group (26/274 [9.5%] versus 45/271 [16.6%]; P = 0.02). Adjunctive therapy with dexamethasone improves survival rates in patients aged 14 years and older with tuberculous meningitis but does not confer protection against severe disability.

*Thwaites GE, Nguyen DB, Nguyen HD, et al. Dexamethasone for the treatment of tuberculous meningitis in adolescents and adults. N Engl J Med 2004;351:1741-51.*

## OUTCOME OF HIV-ASSOCIATED TUBERCULOSIS IN THE ERA OF HAART

Researchers compared the characteristics and outcomes of patients coinfecting with tuberculosis (TB) and HIV who were treated and followed-up for TB at a London HIV clinic before (pre-1996: n = 36) or during the highly active antiretroviral therapy (HAART) era (during or after 1996: n = 60) as well as investigated the effect of HAART and other factors on new AIDS-defining illnesses and occurrence of death. During 3.6 years of follow-up, 49 patients died or had an AIDS event. Compared with patients in the pre-HAART group, those in the HAART group had a lower risk of death (cumulative at 4 years, 43% versus 22%; P = 0.012) and of death or having an AIDS event (69% versus 43%; P = 0.023). Event risk within the first 2 months of TB treatment was exceptionally high in patients with CD4+ cell counts below 100 cells/mm<sup>3</sup> and declined thereafter. HAART use during follow-up was associated with a notable reduction in event risk (adjusted hazard ratio, 0.38 [95% CI, 0.16-0.91]). HAART substantially reduces new AIDS events and death in patients coinfecting with TB. Patients whose CD4+ count is below 100 cells/mm<sup>3</sup> are at high risk for events during the intensive phase of anti-TB treatment. These data should be considered when deliberating on whether to delay HAART in coinfecting patients with CD4+ count below 100 cells/mm<sup>3</sup>.

*Dheda K, Lampe FC, Johnson MA, Lipman MC. Outcome of HIV-associated tuberculosis in the era of highly active antiretroviral therapy. J Infect Dis 2004;190:1670-6.*

*Dr. Slim is an assistant professor of medicine, Seton Hall University, South Orange, NJ. Abstracts written by Rita E. Gould, Hospital Physician.*

Copyright 2005 by Turner White Communications Inc., Wayne, PA. All rights reserved.