

## ID Journal Club 5-30-06

1. Ferrara G, Losi M, D'Amico R *et al.* Use in routine clinical practice of **two commercial blood tests for diagnosis of infection with Mycobacterium tuberculosis**: a prospective study. *Lancet* 2006; 367(9519):1328-34.

Abstract: BACKGROUND: Two commercial blood assays for the diagnosis of latent tuberculosis infection--T-SPOT.TB and QuantiFERON-TB Gold--have been separately compared with the tuberculin skin test. Our aim was to compare the efficacy of all three tests in the same population sample. METHODS: We did a prospective study in 393 consecutively enrolled patients who were tested simultaneously with T-SPOT.TB and QuantiFERON-TB Gold because of suspected latent or active tuberculosis. 318 patients also had results available for a tuberculin skin test. FINDINGS: Overall agreement with the skin test was similar (T-SPOT.TB kappa=0.508, QuantiFERON-TB Gold kappa=0.460), but fewer BCG-vaccinated individuals were identified as positive by the two blood assays than by the tuberculin skin test ( $p=0.003$  for T-SPOT.TB and  $p<0.0001$  for QuantiFERON-TB Gold). Indeterminate results were significantly more frequent with QuantiFERON-TB Gold (11%, 43 of 383) than with T-SPOT.TB (3%, 12 of 383;  $p<0.0001$ ) and were associated with immunosuppressive treatments for both tests. Age younger than 5 years was significantly associated with indeterminate results with QuantiFERON-TB Gold ( $p=0.003$ ), but not with T-SPOT.TB. Overall, T-SPOT.TB produced significantly more positive results (38%,  $n=144$ , vs 26%,  $n=100$ , with QuantiFERON-TB Gold;  $p<0.0001$ ), and close contacts of patients with active tuberculosis were more likely to be positive with T-SPOT.TB than with QuantiFERON-TB Gold ( $p=0.0010$ ). INTERPRETATION: T-SPOT.TB and QuantiFERON-TB Gold have higher specificity than the tuberculin skin test. Rates of indeterminate and positive results, however, differ between the blood tests, suggesting that they might provide different results in routine clinical practice.

2. Geng E, Kreiswirth B, Burzynski J, Schluger NW. **Clinical and radiographic correlates of primary and reactivation tuberculosis**: a molecular epidemiology study. *JAMA* 2005; 293(22):2740-5.

Abstract: CONTEXT: The traditional teaching that pulmonary tuberculosis characterized by lymphadenopathy, effusions, and lower or mid lung zone infiltrates on chest radiography represents "primary" disease from recently acquired infection, whereas upper lobe infiltrates and cavities represent secondary or reactivation disease acquired in the more distant past, is not based on well-established clinical evidence. Furthermore, it is not known whether the atypical radiograph common in human immunodeficiency virus (HIV)-associated tuberculosis is due to a preponderance of primary progressive disease or altered immunity. OBJECTIVE: To analyze the relationship between recently acquired and remotely acquired pulmonary tuberculosis, clinical and demographic variables, and radiographic features by using molecular fingerprinting and conventional epidemiology. DESIGN, SETTING, AND POPULATION: A retrospective, hospital-based series of 456 patients treated at a New York City medical center between 1990 and 1999. Eligible patients had to have had at least 1 positive respiratory culture for Mycobacterium tuberculosis and available radiographic data. MAIN OUTCOME MEASURES: Radiographic appearance as measured by the presence or absence of 6 features: upper lobe infiltrate, cavitory lesion, adenopathy, effusions, lower or mid lung zone infiltrate, and miliary pattern. Radiographs were considered typical if they had an upper lobe infiltrate or cavity whether or not other features were present. Atypical

radiographs were those that had adenopathy, effusion, or mid lower lung zone infiltrates or had none of the above features. RESULTS: Human immunodeficiency virus infection was most commonly associated with an atypical radiographic appearance on chest radiograph with an odds ratio of 0.20 (95% confidence interval, 0.13-0.31). Although a clustered fingerprint, representing recently acquired disease, was associated with typical radiograph in univariate analysis (odds ratio, 0.68; 95% confidence interval, 0.47-0.99), the association was lost when adjusted for HIV status. CONCLUSIONS: Time from acquisition of infection to development of clinical disease does not reliably predict the radiographic appearance of tuberculosis. Human immunodeficiency virus status, a probable surrogate for the integrity of the host immune response, is the only independent predictor of radiographic appearance. The altered radiographic appearance of pulmonary tuberculosis in HIV is due to altered immunity rather than recent acquisition of infection and progression to active disease.

3. Ruiz-Palacios GM, Perez-Schael I, Velazquez FR *et al.* Safety and efficacy of **an attenuated vaccine against severe rotavirus gastroenteritis**. N Engl J Med 2006; 354(1):11-22. Notes: CORPORATE NAME: Human Rotavirus Vaccine Study Group. Abstract: BACKGROUND: The safety and efficacy of an attenuated G1P[8] human rotavirus (HRV) vaccine were tested in a randomized, double-blind, phase 3 trial. METHODS: We studied 63,225 healthy infants from 11 Latin American countries and Finland who received two oral doses of either the HRV vaccine (31,673 infants) or placebo (31,552 infants) at approximately two months and four months of age. Severe gastroenteritis episodes were identified by active surveillance. The severity of disease was graded with the use of the 20-point Vesikari scale. Vaccine efficacy was evaluated in a subgroup of 20,169 infants (10,159 vaccinees and 10,010 placebo recipients). RESULTS: The efficacy of the vaccine against severe rotavirus gastroenteritis and against rotavirus-associated hospitalization was 85 percent ( $P < 0.001$  for the comparison with placebo) and reached 100 percent against more severe rotavirus gastroenteritis. Hospitalization for diarrhea of any cause was reduced by 42 percent (95 percent confidence interval, 29 to 53 percent;  $P < 0.001$ ). During the 31-day window after each dose, six vaccine recipients and seven placebo recipients had definite intussusception (difference in risk, -0.32 per 10,000 infants; 95 percent confidence interval, -2.91 to 2.18;  $P = 0.78$ ). CONCLUSIONS: Two oral doses of the live attenuated G1P[8] HRV vaccine were highly efficacious in protecting infants against severe rotavirus gastroenteritis, significantly reduced the rate of severe gastroenteritis from any cause, and were not associated with an increased risk of intussusception. (ClinicalTrials.gov numbers, NCT00139347 and NCT00263666.)
4. Schildgen O, Sirma H, Funk A *et al.* Variant of **hepatitis B virus with primary resistance to adefovir**. N Engl J Med 2006; 354(17):1807-12. Abstract: The reverse-transcriptase inhibitor lamivudine (Zeffix, GlaxoSmithKline) is often used to treat chronic infection with hepatitis B virus (HBV) until resistance develops. Treatment may then be switched to the reverse-transcriptase inhibitor adefovir (Hepsera, Gilead), which has a lower frequency of resistance. Here, we describe three cases of primary adefovir resistance that were sensitive to tenofovir (Viread, Gilead). All three cases involved a rare HBV variant with a valine at position 233 of the reverse-transcriptase domain instead of isoleucine (rtI233V), as in the wild-type virus. This HBV variant also displayed resistance to adefovir and sensitivity to tenofovir in vitro.