

ID Journal Club Additions 5-16-06

1. Centanni M, Gargano L, Canettieri G *et al.* **Thyroxine in goiter, Helicobacter pylori infection, and chronic gastritis.** N Engl J Med 2006; 354(17):1787-95.
Abstract: BACKGROUND: Malabsorption of thyroxine has been described in patients treated with drugs that modify an acidic environment. We determined whether there is an increased need for thyroxine in patients with euthyroid multinodular goiter and impaired secretion of gastric acid. METHODS: We assessed the dose of thyroxine required to obtain a low level of thyrotropin (0.05 to 0.20 mU per liter) in 248 patients with multinodular goiter. Of these 248 patients, 53 also had Helicobacter pylori-related gastritis and 60 had atrophic gastritis of the body of the stomach (31 with evidence of H. pylori infection and 29 without such evidence). The reference group comprised 135 patients with multinodular goiter and no gastric disorders. In addition, variation in the level of serum thyrotropin was prospectively studied in 11 patients treated with thyroxine before and after H. pylori infection and both before and during treatment with omeprazole in 10 patients treated with thyroxine who had gastroesophageal reflux. RESULTS: The daily requirement of thyroxine was higher (by 22 to 34 percent) in patients with H. pylori-related gastritis, atrophic gastritis, or both conditions than in the reference group. In prospective studies, the occurrence of H. pylori infection in the 11 patients treated with thyroxine led to an increase in the level of serum thyrotropin (P=0.002), an effect that was nearly reversed on eradication of H. pylori infection. In a similar way, omeprazole treatment was associated with an increase in the level of serum thyrotropin in all 10 patients treated with thyroxine, an effect that was reversed by an increase in the thyroxine dose by 37 percent. CONCLUSIONS: Patients with impaired acid secretion require an increased dose of thyroxine, suggesting that normal gastric acid secretion is necessary for effective absorption of oral thyroxine.
2. Grandiere-Perez L, Jacqueline C, Lemabecque V, Patey O, Potel G, Caillon J. **Eagle effect in Corynebacterium diphtheriae.** J Infect Dis 2005; 191(12):2118-20.
Abstract: The in vivo relevance of the paradoxical bactericidal effect (the Eagle effect) is not evident. We found in vitro a paradoxical bactericidal effect of amoxicillin on 2 strains of nontoxicogenic Corynebacterium diphtheriae. Then, using an experimental rabbit model of endocarditis, we evaluated the in vivo relevance of this phenomenon. Rabbits were assigned to the following groups: no treatment (control group), continuous amoxicillin infusion simulating a dosage of 200 mg/kg/day in humans, and continuous amoxicillin infusion simulating a dosage of 20 mg/kg/day in humans. The low dosage (20 mg/kg/day) was significantly more effective than the high dosage (200 mg/kg/day) against both strains (P<.025), confirming the paradoxical bactericidal effect observed in vitro.
3. Humair JP, Revaz SA, Bovier P, Stalder H. **Management of acute pharyngitis in adults: reliability of rapid streptococcal tests and clinical findings.** Arch Intern Med 2006; 166(6):640-4.
Abstract: BACKGROUND: How to use clinical score, the rapid streptococcal antigen test (RSAT), and culture results is uncertain for efficient management of acute pharyngitis in adults. METHODS: This prospective cohort study included 372 adult patients with pharyngitis treated at a Swiss university-based primary care clinic. In eligible patients with 2 to 4 clinical symptoms and signs (temperature >or=38 degrees C, tonsillar exudate, tender cervical adenopathy, and no cough or rhinitis), we performed an RSAT and obtained a throat culture. We measured sensitivity and specificity of RSAT with culture as a gold standard and compared appropriate antibiotic use with cost per patient appropriately treated for the following 5 strategies: symptomatic treatment, systematic RSAT, selective RSAT, empirical antibiotic treatment, and systematic culture. RESULTS: RSAT had high sensitivity (91%) and specificity (95%) for the diagnosis of streptococcal pharyngitis. Systematic throat culture resulted in the highest antibiotic use, in 38% of patients with streptococcal pharyngitis. Systematic RSAT led to nearly optimal treatment (94%) and antibiotic prescription (37%), with minimal antibiotic overuse (3%) and underuse (3%). Empirical antibiotic treatment in patients with 3 or 4 clinical symptoms or signs resulted in a lower rate of appropriate therapy (59%) but higher rates of antibiotic use (60%), overuse (32%), and underuse (9%). Systematic RSAT was more cost-effective than strategies based on empirical treatment or culture: 15.00 dollars, 26.00 dollars, and 32.00 dollars, respectively, per patient appropriately treated. CONCLUSIONS: The RSAT we used is a valid test for diagnosis of pharyngitis in adults. A clinical approach combining this RSAT and clinical findings

efficiently reduces inappropriate antibiotic prescription in adult patients with acute pharyngitis. Empirical therapy in patients with 3 or 4 clinical symptoms or signs results in antibiotic overuse.

4. Kapetanovic MC, Saxne T, Sjöholm A, Truedsson L, Jonsson G, Geborek P. **Influence of methotrexate, TNF blockers and prednisolone on antibody responses to pneumococcal polysaccharide vaccine in patients with rheumatoid arthritis.** *Rheumatology (Oxford)* 2006; 45(1):106-11.
Abstract: OBJECTIVE: To compare antibody responses to 23-valent pneumococcal vaccine (Pneumovax) in controls and patients with established rheumatoid arthritis (RA) treated with TNF blockers, methotrexate (MTX) or a combination of both. METHODS: Patients with RA (n = 149) and healthy controls (n = 47) were vaccinated. Treatment with TNF blockers (etanercept or infliximab) and MTX was given to 50 patients, and 62 patients were treated with TNF blockers alone or with other DMARDs. MTX alone was given to 37 patients. Concentrations of immunoglobulin G (IgG) antibodies against pneumococcal capsular polysaccharides 23F and 6B were measured by enzyme-linked immunoassay before and 4-6 weeks after vaccination. An immune response was defined as a twofold or higher increase in antibody concentration following vaccination. RESULTS: Prevacination antibody levels for both 23F and 6B were similar in the patient groups. Antibody concentrations after vaccination increased significantly in all groups. Patients treated with TNF blockers without MTX showed better immune responses than those treated with TNF blockers in combination with MTX (P = 0.037 for 23F and P = 0.004 for 6B) or MTX alone (P<0.001 for both 23F and 6B). RA patients given MTX alone had the lowest immune responses. Prednisolone treatment did not influence the responses. CONCLUSIONS: Patients treated with TNF blockers and controls showed similar responses to vaccination. In contrast, patients treated with MTX had reduced responses regardless of anti-TNF treatment. The findings do not argue against the use of pneumococcal vaccination in RA patients undergoing treatment with TNF blockers.

5. Petersen RC, Thomas RG, Grundman M *et al.* **Vitamin E and donepezil for the treatment of mild cognitive impairment.** *N Engl J Med* 2005; 352(23):2379-88.
Notes: CORPORATE NAME: Alzheimer's Disease Cooperative Study Group.
Abstract: BACKGROUND: Mild cognitive impairment is a transitional state between the cognitive changes of normal aging and early Alzheimer's disease. METHODS: In a double-blind study, we evaluated subjects with the amnesic subtype of mild cognitive impairment. Subjects were randomly assigned to receive 2000 IU of vitamin E daily, 10 mg of donepezil daily, or placebo for three years. The primary outcome was clinically possible or probable Alzheimer's disease; secondary outcomes were cognition and function. RESULTS: A total of 769 subjects were enrolled, and possible or probable Alzheimer's disease developed in 212. The overall rate of progression from mild cognitive impairment to Alzheimer's disease was 16 percent per year. As compared with the placebo group, there were no significant differences in the probability of progression to Alzheimer's disease in the vitamin E group (hazard ratio, 1.02; 95 percent confidence interval, 0.74 to 1.41; P=0.91) or the donepezil group (hazard ratio, 0.80; 95 percent confidence interval, 0.57 to 1.13; P=0.42) during the three years of treatment. Prespecified analyses of the treatment effects at 6-month intervals showed that as compared with the placebo group, the donepezil group had a reduced likelihood of progression to Alzheimer's disease during the first 12 months of the study (P=0.04), a finding supported by the secondary outcome measures. Among carriers of one or more apolipoprotein E epsilon4 alleles, the benefit of donepezil was evident throughout the three-year follow-up. There were no significant differences in the rate of progression to Alzheimer's disease between the vitamin E and placebo groups at any point, either among all patients or among apolipoprotein E epsilon4 carriers. CONCLUSIONS: Vitamin E had no benefit in patients with mild cognitive impairment. Although donepezil therapy was associated with a lower rate of progression to Alzheimer's disease during the first 12 months of treatment, the rate of progression to Alzheimer's disease after three years was not lower among patients treated with donepezil than among those given placebo.