

# UPDATE

Abstracts and news from the medical literature of interest to the primary-care physician

## New Vaccine Against HPV Could Prevent Cervical Cancer

A large industry-funded study showed convincing evidence that a new vaccine protected nearly perfectly against persistent HPV-16 infection and preneoplastic conditions caused by the infection. Almost all cases of cervical cancer are associated with human papillomavirus (HPV) infection. Cervical cancer is the second leading cause of cancer death in women. HPV-16 is present in 50% of all cervical cancer cases.

A multicentre team randomised 2,392 young women to receive three doses of an intramuscular vaccine that contained HPV-16 virus-like particles (not live virus) or placebo. Of the women chosen, 64% did not have evidence of HPV-16 infection at the beginning of the study. After a median followup of 17.4 months, significantly more cases of persistent HPV-16 infection were found in the placebo group than in the vaccine group (3.8 cases per 100 woman-years versus zero cases). All nine cases of HPV-16-related cervical intraepithelial neoplasia occurred in the placebo group. Among women who were infected with HPV-16 at the beginning of the study, rates of persistent HPV-16 infection were 6.3 and 0.6 cases per 100 woman-years in the placebo and vaccine groups, respectively.

Koutsky LA, Ault KA, Wheeler CM, et al: A controlled trial of a human papillomavirus type 16 vaccine. *N Engl J Med* 2002; 347:1645-51.

Crum CP: The beginning of the end for cervical cancer? *N Engl J Med* 2002; 347: 1703-5.

## Diagnosing Bacterial Vaginosis

In two recent studies, researchers addressed bacterial vaginosis (BV). BV is associated with increased rates of adverse pregnancy outcomes and increased risks of human immunodeficiency virus infection, urinary tract infections and postoperative infections of the upper genital tract. Diagnosis is established by grey-white discharge, clue cells on microscopic examination, possible whiff test, and vaginal pH greater than 4.5. Diagnosis can also be established by the Gram stain-based classification which in a study in Japan showed a 78% sensitivity, 96% specificity, 83% positive predictive value, and a 94% negative predictive value. In a U.S. study, 40% of women who were at a high risk for BV also reported douching once a month. Douching within the past seven days increased the risk of BV by twofold.

Obata-Yasuoka M, Ba-Thein W, Hamada H, et al: A multiplex polymerase chain reaction-based diagnostic method for bacterial vaginosis. *Obstet Gynecol* 2002; 100:759-64.

Ness RB, Hillier SL, Richter HE, et al: Douching in relation to bacterial vaginosis, lactobacilli, and facultative bacteria in the vagina. *Obstet Gynecol* 2002; 100: 765-72.

## Rhythm Control vs. Rate Control for Patients with AF

The two methods physicians use for treating patients with atrial fibrillation (AF) are rhythm control, which restores sinus rhythm, or rate control, which allows persistent AF while controlling ventricular rate.

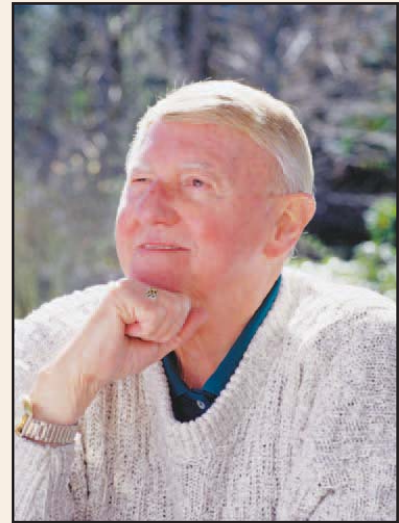
Though cardiologists favour rhythm control to treat patients with atrial fibrillation, landmark trials show that older patients fare no better with the procedure than with rate control.

North American researchers enrolled 4,060 patients with recent AF who were 65 years or older and had a risk factor for stroke. Patients were randomised to rhythm control (anti-arrhythmic drugs and cardioversion, as necessary) or to rate control (beta blockers, calcium channel blockers, digoxin, or a combination of these therapies).

These patients were followed for three and a half years. Both groups received warfarin.

The estimated five-year mortality in the rhythm control group was 23.8%, and in the rate control group 21.3%. The rhythm control group had significantly higher rates of hospitalisation and adverse events causing drug discontinuation as well.

Dutch researchers also did a randomised study with 522 patients for 2.3 years which showed that cardiovascular death, heart failure, thromboembolism, bleeding, a need for a pacemaker or severe drug side effects occurred in 22.6% of patients in the rhythm control group than in the rate control group (17.6%). The research showed women and hypertensive patients had particularly poor outcomes with the rhythm control strategy.



The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators: A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med* 2002; 347:1825-33.

Van Gelder IC, Hagens VE, Bosker HA, et al: A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. *N Engl J Med* 2002; 347:1834-4.

Falk RH: Management of atrial fibrillation: Radical reform or modest modification? *N Engl J Med* 2002; 347:1883-4.

## $\beta_1$ -Blockers May Help Patients with Peripheral Arterial Disease or Asthma

Clinicians don't often prescribe  $\beta$ -blockers for patients with peripheral arterial disease or asthma, to avoid blockade  $\beta_2$ -receptors and potential vasoconstriction or bronchoconstriction. But in new randomised, blinded, placebo-controlled trials evidence showed that because  $\beta_1$ -blockers more selectively antagonise the chronotropic and inotropic cardiac  $\beta_1$ - receptors than the widely distributed  $\beta_2$ -receptors, the benefits of  $\beta_1$ -blockers might outweigh their risks in these patients.


In 19 single-dose trials (240 participants), compared to placebo,  $\beta_1$ -blockade showed a significant reduction of 7% in forced expiratory volume in one second (FEV<sub>1</sub>), but with a significant increase of 5% in FEV<sub>1</sub> after a  $\beta$ -agonist was given. No differences between placebo and  $\beta_1$ -blockers were noted in respiratory symptoms. In 10 studies of treatment lasting three days to four weeks with 141 participants, compared with placebo,  $\beta_1$ -blockade showed no significant differences in FEV<sub>1</sub> response and with a significant 9% increase in FEV<sub>1</sub> after a  $\beta$ -agonist was given. There were no significant differences in symptoms or inhaler use.

Salpeter SR, Ormiston TM, Salpeter EE: Cardioselective  $\beta$ -blockers in patients with reactive airway disease. *Ann Intern Med* 2002; 137:715-25.

Epstein PE: Fresh air and  $\beta$ -blockade. *Ann Intern Med* 2002; 135:766-7.

## Predicting Cardiovascular Risk

There is evidence that C-reactive protein (CRP) is associated with cardiovascular disease. CRP is usually a marker of inflammation. A study comparing the value of CRP levels and LDL cholesterol levels for predicting cardiovascular risk showed the CRP level predicted a first cardiovascular event somewhat better than the LDL level did.

LDL cholesterol and CRP levels were measured at baseline in about 28,000 apparently healthy women with the mean age of 55. The relative risk for a first event was 2.3 in the highest quintile of CRP compared with the lowest quintile, after adjustment for other factors. With LDL, the corresponding relative risk was 1.5. The probability of event-free survival was about 99% in women whose CRP and LDL levels were both below the population medians, but was only about 96.5% in women whose CRP and LDL levels were both above the population medians. Subgroups with high CRP/low LDL levels and low CRP/high LDL levels had intermediate probabilities. 

Ridker PM, Rifai N, Rose L, et al: Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events *N Engl J Med* 2002; 347:1557-65.

Mosca L: C-reactive protein-To screen or not to screen? *N Engl J Med* 2002; 347:1615-7.