

## RESEARCH DIGEST

Aikpokpo N, Department of Medicine, University College Hospital, Ibadan  
Sigbeku O. F., Department of Oral Pathology, University College Hospital, Ibadan

### Statins' Preventive Effects Evident Years After Stopping

Treatment with pravastatin for 5 years may lower the risk for coronary events for up to 10 additional years, according to a *New England Journal of Medicine* report.

Some 5800 men with hypercholesterolemia who had been randomized to either daily pravastatin or placebo in a 5-year trial were followed for an additional 10 years. (After the trial, roughly a third of both groups took statins, but their long-term outcomes were assigned to their original groups).

The pravastatin group, which had a 40% risk reduction in cardiovascular deaths or nonfatal infarction during the trial, had an 18% reduction in the post-trial period. Similar reductions occurred in other composite cardiovascular endpoints.

"There should no longer be any doubt" about the beneficial effects of lowering LDL cholesterol in preventing and treating CHD, an editorialist writes. The remaining questions, he says, are when treatment should start and what the target LDL levels should be.

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### Cochlear Implants Linked to Bacterial Meningitis Cases

The FDA reminded physicians on Wednesday that patients with cochlear implants for inner-ear malformations, especially implants with a positioner, are at risk for bacterial meningitis from *Streptococcus pneumoniae*. This warning follows the deaths of two children within the past years, ages 9 and 11 years, who had implants with a positioner and were not fully vaccinated. (Only one implant model has a positioner, and it was withdrawn from the market 5 years ago).

To decrease the risk for meningitis in this population, the FDA recommends:

- following the CDC's vaccination guidelines;
- educating implant recipients and their caregivers about the early signs of meningitis;
- treating middle ear infections early;
- considering prophylactic antibiotics perioperatively.

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### Hormonal Therapy After Prostatectomy May Increase Cardiovascular Death

Men who receive androgen-deprivation therapy (ADT) after undergoing prostatectomy for prostate cancer

may be at increased risk for cardiovascular death, reports an industry-funded study in the *Journal of the National Cancer Institute*.

Researchers examined outcomes among nearly 5000 patients who had been treated for localized prostate cancer; two-thirds had undergone radical prostatectomy, while the rest received nonsurgical therapy. Overall, 20% also received ADT (median duration, 4 months).

During a median follow-up of 4 years, ADT use was associated with increased risk for cardiovascular death among prostatectomy patients (adjusted hazard ratio, 2.6). For patients treated non-surgically, a higher 5-year estimate of cardiovascular death with ADT use, observed only in patients 65 or older, did not achieve statistical significance.

The authors say their findings "underscore the importance of careful cardiovascular evaluation and intervention before initiating ADT in patients with localized prostate cancer."

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### Negative Interpersonal Relationships May Increase Heart Disease Risk

People who have frequent negative interactions with the person to whom they feel closest may be at increased risk for heart disease, reports the *Archives of Internal Medicine*.

Some 9000 British civil servants without histories of coronary disease completed questionnaires on their interactions with their closest personal relation (most often a spouse) during the previous year. The incidence of myocardial infarction or angina was evaluated during about 12 years of follow-up.

In analyses controlling for demographic and biological confounders (e.g., age, sex, marital status, obesity, hypertension, diabetes, and cholesterol level), patients in the highest tertile of negative interactions were 34% more likely to experience coronary events than those in the lowest tertile.

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### Limited Weight Gain Improves Pregnancy Outcomes for Obese Women

Pregnancy outcomes may improve for obese women if they gain little or no weight while pregnant, according to a study in *Obstetrics and Gynecology*.

The population-based cohort study followed more than 120,000 obese pregnant women. It found that those who gained less than the recommended 15 pounds had a significantly reduced risk for preeclampsia, cesarean delivery, or large-for-gestational-age birth. However, these women were at increased risk for small-for-gestational-age birth.

The authors say their findings indicate that guidelines for gestational weight gain should be developed for obese women.

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### **No Evidence That Individualized Herbal Medicine Effective**

A review in *Postgraduate Medical Journal* finds no convincing evidence to support the use of individualized herbal medicine for any ailment.

Individualized herbal medicine, as practiced by traditional herbalists, involves prescribing mixtures of several herbs rather than single substances or standardized combinations. A systematic review found three relatively small randomized clinical trials of this approach.

Two showed no statistically significant benefit of individualized herbal medicine over placebo for treating osteoarthritis of the knee (20 patients enrolled, 14 analyzed) or preventing chemotherapy-related toxicity (120 enrolled, 111 analyzed). The third found it better than placebo for irritable bowel syndrome but inferior to standardized herbal treatment (116 enrolled, 99 analyzed).

The authors conclude: "Because of the high potential for adverse events and negative herb-herb and herb-drug interactions, this lack of evidence for effectiveness means that its use cannot be recommended."

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### **CT Colonography as Effective as Colonoscopy in Detecting Advanced Neoplasia**

Detection of advanced colonic neoplasms is as effective with computed tomographic colonography as with traditional optical colonoscopy, reports an industry-supported study in the *New England Journal of Medicine*.

Two cohorts, comprising some 3100 patients each, underwent either colonography or colonoscopy. Researchers then compared the procedures' detection rates for advanced adenomas and adenocarcinomas. (Patients undergoing colonography were offered same-day colonoscopic removal of polyps measuring 6 mm

or more, but could also select colonographic surveillance).

The number of advanced neoplasms was similar in the two groups, although the colonoscopic cohort had a fourfold higher rate of polyp removal. Invasive carcinomas were detected more often in the colonographic cohort.

The authors acknowledge that the absence of randomized assignment was a "major limitation." Writing in *Journal Watch General Medicine*, Allan S. Brett also cautions that "the accuracy of [colonography] will vary from center to center, depending on technique and experience."

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### **New Guideline for Low Back Pain Management**

The American College of Physicians and the American Pain Society have published an updated practice guideline for the management of low back pain in primary care.

The guideline, which appears in the current *Annals of Internal Medicine*, includes recommendations on both evaluation and treatment. Among the recommendations:

- Imaging should not be part of the routine work-up of patients with nonspecific pain.
- Clinicians should provide patients with information on the expected course of their condition.
- When considering medication use, clinicians should usually start with acetaminophen or NSAIDs.
- For patients who do not improve, nondrug therapies such as spinal manipulation, acupuncture, and yoga may be considered.

The ACP and APS also provide an algorithm for the initial evaluation and subsequent management of patients.

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### **Panic Attacks a Risk Factor for Cardiovascular Events and Death in Postmenopausal Women**

Full-blown panic attacks are an independent risk factor for cardiovascular events, a study of postmenopausal women published in the *Archives of General Psychiatry* finds.

Some 3400 women between ages 51 and 83, participants in the Women's Health Initiative, completed a questionnaire on whether they had experienced a panic attack over the previous 6 months. Researchers then followed the group for about 5 years,

looking for cardiovascular events such as myocardial infarction and stroke, as well as all-cause mortality.

Among the women reporting a full-blown panic attack, the risk for adverse outcomes was significantly increased relative to those with no panic (hazard ratio for MI or coronary heart disease death, 4.20; HR for all-cause mortality, 1.75), even after controlling for other risk factors and depression. Women reporting less severe panic attacks also showed higher risks, but theirs did not achieve statistical significance. The authors speculate that the association may be mediated by coronary vasospasm.

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### **Lamisil Oral Granules Approved for Scalp Ringworm in Children**

The FDA has approved Lamisil oral granules for the treatment of tinea capitis (scalp ringworm) in children ages 4 years and older.

The granules, which can be sprinkled on food, were developed after the FDA requested that the manufacturer creates a child-friendly formulation. The medication is to be given once daily for 6 weeks; the actual dosage depends on the child's weight.

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### **Case Series Details MIs in Otherwise Healthy Adolescents**

A series of nine myocardial infarctions in adolescents shows that the condition, though uncommon, can be readily diagnosed, according to a study in *Pediatrics*.

The cases were seen in an emergency room over an 11-year span. All patients presented with typical radiating chest pain, and all had elevations in CK and CK-MB enzymes. There was no evidence of drug abuse, and all had normal coronary angiograms. Not all patients had typical ST-segment elevation on electrocardiogram (just six had typical features).

All patients responded to nitroglycerin and were placed on calcium-channel blockers.

The authors say that since angiography excluded atherosclerotic and thrombotic causes, vasospasm may have caused the infarctions. They write that "acute typical chest pain in the adolescent presenting to the emergency department cannot be presumed noncardiac."

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### **ACC/AHA Update Guidelines for Cardiac Patients Undergoing Noncardiac Surgery**

The American College of Cardiology and the American Heart Association published updated

guidelines on *Circulation's* website Thursday to help evaluate people with heart disease who are undergoing noncardiac surgery.

Among the additions or modifications to the 2002 version of the recommendations:

- Patients should not stop taking statins before their noncardiac surgery.
- Physicians should not perform prophylactic revascularization in patients with stable coronary artery disease before noncardiac surgery.
- Patients undergoing intermediate- or low-risk noncardiac surgery are not required to undergo noninvasive stress testing.

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### **FDA Warns on Hydrocodone in Pediatric Cough Suppressants, May Enforce Ban**

The FDA says it will act against the improper use of hydrocodone in pharmaceutical products, especially in over-the-counter cough suppressants marketed for pediatric use.

The narcotic is widely used to treat both pain and coughs. Several products containing hydrocodone are marketed for children, and some contain dosing information for children as young as 2 years old, despite the fact that the drug has not been shown to be safe and effective in children under 6. The agency is particularly concerned over similarities in the names of approved and unapproved products.

Companies have until the end of October to cease manufacturing and marketing the unapproved pediatric products containing hydrocodone and until the end of the year to cease manufacturing and marketing other unapproved products containing the drug.

In addition, the *New York Times* reports that the FDA is considering an outright ban on OTC cold and cough medications for children younger than 6 years.

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### **Report Finds Serious Problems with FDA's Oversight of Clinical Trials**

The FDA lacks the tools to adequately monitor clinical trials, concludes a report from the Inspector General for the Department of Health and Human Services.

The report estimates that the agency inspected only 1% of clinical trial sites between 2000 and 2005. Many of the problems involve limitations in the agency's data collection: It has no registry of clinical trials or institutional review boards (IRBs), and it tracks inspection information inconsistently.

The report recommends that the FDA:

- create a database of all clinical trials;
- create a registry of all IRBs;
- create a complete database of all inspections;
- seek increased regulatory authority over clinical trials.

Commenting on the report, Arthur Caplan, chairman of the department of medical ethics at the University of Pennsylvania, tells the *New York Times* that “in many ways, rats and mice get greater protection as research subjects in the United States than do humans.”

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### **Thiazolidinediones Associated with Heart Failure, but Not Increased Mortality**

As a class, thiazolidinediones (rosiglitazone and pioglitazone) are associated with congestive heart failure when used to treat type 2 diabetes and prediabetes, a *Lancet* meta-analysis finds. However, the heart failure may have a different character than heart failure due to left-ventricular dysfunction, the authors write.

In an analysis of seven randomized controlled trials comprising 20,000 subjects, researchers found a higher CHF risk from thiazolidinediones, but it was not associated with an increased risk for cardiovascular mortality. Whether the fluid retention associated with the drug is more benign than ventricular-related failure “cannot be confirmed without a comparison of outcomes” of CHF in the control and treatment groups, the authors note.

“It seems that the jury is still out for thiazolidinediones as a class,” an editorial says. It concludes by pointing out the need for industry and regulatory reform, lest the thiazolidinediones “simply become the latest in a series of preventable drug disasters.”

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### **Meta-Analysis Reaffirms Benefits of Occupational Therapy After Stroke**

Occupational therapy after stroke improves performance and reduces deterioration in personal activities of daily living, according to a meta-analysis in the *British Medical Journal*.

The study, based on nine trials involving nearly 1300 patients, found that poststroke occupational therapy focusing specifically on daily living activities in an outpatient or nursing home setting improved performance scores by the equivalent of 5%. Occupational therapy also reduced the risk for death, deterioration, dependency, or institutionalization by one-third.

The NNT to prevent deterioration in ADL is roughly 11. “Focused occupational therapy should be available to everyone who has had a stroke,” the authors write.

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### **HDL Levels Remain Predictive of Heart Risk Even in the Face of Very Low LDL**

HDL levels retain their prognostic value in patients treated with statins — even among those who achieve very low LDL levels — researchers report in the *New England Journal of Medicine*.

A post hoc analysis from the industry-funded Treating to New Targets study examined the predictive value of HDL levels on nearly 10,000 adults with coronary heart disease after 3 months of atorvastatin treatment.

After multivariate adjustment, the 5-year risk for major cardiovascular events was reduced by 25% among patients in the highest quintile of HDL cholesterol compared with those in the lowest quintile. Even among patients who had achieved LDL levels below 70 mg/dL, risk remained significantly reduced (by 39%) in the highest HDL quintile.

Writing in *Journal Watch General Medicine*, Allan S. Brett concludes: “Whether patients with both low LDL and low HDL would benefit from additional drug therapies to raise HDL cholesterol is unclear.”

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### **Real and Sham Acupuncture Similarly Beneficial for Low Back Pain**

Acupuncture may be better than conventional therapy for the treatment of chronic low back pain, but it seems to offer no benefit over sham acupuncture, according to a study in *Archives of Internal Medicine*.

Nearly 1200 adults with chronic back pain for at least 6 months were randomized to undergo acupuncture, sham acupuncture, or conventional therapy that included physiotherapy, exercise, and medication. All interventions involved ten 30-minute treatment sessions, with five additional sessions for patients who experienced pain reduction after the first ten. At 6 months, the response rate was significantly higher with real acupuncture (48%) and sham acupuncture (44%) than with conventional therapy (27%). The difference between the two acupuncture groups was not significant.

The authors say the lack of difference between acupuncture groups “forces us to question the underlying action mechanism of acupuncture and to ask whether the emphasis placed on ... traditional Chinese acupuncture points may be superfluous.”

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### **HIV Vaccine Proves Ineffective**

A vaccine designed to elicit a strong T-cell reaction against HIV in uninfected individuals has failed in a clinical trial, the *New York Times* reports.

Merck stopped the trial (called STEP) early, after an interim analysis of 1500 subjects showed that vaccine recipients had the same rate of acquiring HIV as placebo recipients. In addition, the viral load in infected subjects in both groups was similar, according to the *Times*.

In a press release, Merck said that the STEP investigators have been told to stop vaccinating volunteers. Merck also said that “enrollment and vaccination in a second Phase II trial of this vaccine being conducted by the [HIV Vaccine Trials Network] in South Africa called Phambili, and two additional Phase I trials, have been discontinued.”

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### **More Hypoglycemia with Biphasic or Prandial Insulin vs. Basal Insulin**

When added to oral diabetes agents, biphasic or prandial insulin lowers glycated hemoglobin levels more than basal insulin — but at the expense of more hypoglycemic episodes — reports a study released early online in the *New England Journal of Medicine*.

Some 700 patients with type 2 diabetes who had suboptimal glycated hemoglobin (7%–10%) while taking metformin and sulfonylurea were randomized to one of three insulin regimens: biphasic insulin aspart twice daily (70/30), prandial insulin aspart three times daily, or basal insulin detemir once daily.

At 1 year, mean glycated hemoglobin was significantly lower in the biphasic group (7.3%) and prandial group (7.2%) than in the basal group (7.6%). However, hypoglycemia occurred more often with prandial than biphasic insulin, and with biphasic than basal insulin.

Editorialists conclude that biphasic and prandial formulations are “suboptimal choices for insulin initiation and probably expose patients to an unnecessarily high risk of hypoglycemia without clinically important benefit.”

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### **HPV Vaccine May Protect Against Additional Strains**

The human papilloma virus vaccine (Gardasil) may provide cross-protection against 10 strains of the virus, in addition to the 4 strains it targets, according to an Associated Press story. The vaccine's manufacturer, Merck, presented the data yesterday at the Interscience Conference on Antimicrobial Agents and Chemotherapy.

The vaccine may now protect against 90% of the strains that cause cervical cancer.

Women should still get regular Pap smears because the vaccine does not cover all HPV strains, Michael Segarra, of North Brunswick (New Jersey) Pediatrics, told the AP.

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### **Frequent Nocturnal Hemodialysis Reduces LV Mass**

Patients undergoing hemodialysis 6 nights a week show a greater reduction in left ventricular mass than those on a conventional treatment schedule.

Writing in *JAMA*, Canadian researchers report randomizing some 50 patients to a schedule of either 6 nights a week of home hemodialysis or conventional 3-days-a-week treatment. After 6 months, those on frequent nocturnal dialysis showed a nearly 18-g decrease in left ventricular mass, while those on conventional treatment showed a 1.8-g increase.

An editorialist comments that proving a survival benefit will be elusive, given the difficulty in recruiting patients, but he says the study succeeded in “clearly demonstrating reduced [left ventricular hypertrophy] with nocturnal hemodialysis.”

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### **ACCP Issues New Lung Cancer Guidelines**

New guidelines from the American College of Chest Physicians recommend against low-dose helical CT, serial chest radiographs, or sputum cytologic evaluation to screen for lung cancer.

The guidelines, published as a supplement in *Chest*, advise against screening even in high-risk patients, including smokers. “Currently available research data do not show that lung cancer screening alters mortality outcomes,” W. Michael Alberts, who chaired the project, says in a press release.

The guidelines also recommend against potential chemopreventive agents — including vitamin E, retinoids, N-acetylcysteine, and aspirin — for people at risk for lung cancer.

The other recommendations include guidelines for the management of patients with solitary pulmonary nodules.

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