Diagnosis of DVT with D-dimer testing and the Wells score

Venous thromboembolism refers to a spectrum of disease that includes both pulmonary embolus and deep-venous thrombosis (DVT). More than 250,000 people in the United States are diagnosed annually with venous thromboembolic disease; an estimated equal number of cases goes undiagnosed.¹

Clinicians and official guidelines take a variety of diagnostic approaches toward patients with a suspected DVT. Historically, clinicians have used compression ultrasound and impedance plethysmography in the outpatient setting to diagnose clinically suspected DVT. More recently, the D-dimer assay has expanded diagnostic options. Nevertheless, D-dimer interpretation can be limited by the test’s low specificity and the necessity of knowing the pretest probability of disease to properly use the results.

Utility of D-dimer testing

The sensitivity of the D-dimer test also varies with the assay used. One meta-analysis of 12 studies compared a highly sensitive ELISA D-dimer assay with a less sensitive (and less expensive) SimpliRED D-dimer assay. In studies using the highly sensitive ELISA assay, for patients with negative D-dimer results and low or intermediate pretest probability of disease, the 3-month incidence of DVT was 0.5%. However, using the SimpliRED assay, the 3-month incidence of DVT with a negative D-dimer results and low pretest probability was 0.5% but the incidence was 3.5% with a negative D-dimer and an intermediate pretest probability. This meta-analysis suggests that the SimpliRED assay misses some DVTs in patients with intermediate pretest probabilities of the disease.²

New evidence concerning the utility of D-dimer testing for DVT comes from a meta-analysis funded by the United Kingdom National Health Service Health Technology Assessment R&D Program.³ The authors compared the accuracy and cost effectiveness of various algorithms for diagnosing DVT, with the goal of identifying a practical, cost-effective strategy. They included 14 studies of algorithms for the diagnosis of suspected DVT that combined Wells scoring (a risking system that formalizes assessment of the pretest probability,
TABLE 1

The Wells score

1 point each for:

- Active cancer
- Paralysis, paresis, recent plaster immobilization of lower limb
- Recently bedridden for >3 days or major surgery during past 4 weeks
- Localized tenderness along distribution of deep venous system
- Entire leg swollen
- Calf swelling >3 cm compared to asymptomatic leg
- Pitting edema
- Collateral superficial veins

−2 points for:

- Alternative diagnosis as likely or more likely than that of DVT

Interpretation: ≥3 points=High probability of DVT
1–2 points=Intermediate probability of DVT
0–1 points=Low probability of DVT
DVT=deep-venous thrombosis.

TABLE 2

Two protocols for DVT diagnosis

I. Obtain Wells score first

A. Wells score is low or intermediate—check D-dimer
   1. D-dimer is normal—send home
   2. D-dimer is elevated—obtain ultrasound

B. Wells score is high—obtain ultrasound
   1. Ultrasound is positive—treat
   2. Ultrasound is negative—obtain D-dimer
      a. D-dimer is low—send home
      b. D-dimer is elevated—repeat ultrasound 1 week

II. Obtain D-dimer first

A. D-dimer is elevated—obtain ultrasound
   1. Ultrasound is positive—treat
   2. Ultrasound is negative—repeat ultrasound 1 week

B. D-dimer is normal—do Wells Score
   1. Wells score is low or indeterminate—send home
   2. Wells score is high—obtain ultrasound
      a. Ultrasound is positive—treat
      b. Ultrasound is negative—repeat ultrasound 1 week

DVT=deep-venous thrombosis.

Two effective algorithms

Two algorithms maximized cost effectiveness (TABLE 2). For both protocols, patients could have been safely sent home when there was a low to intermediate risk Wells score and a normal D-dimer. Both protocols also call for an ultrasound if either the D-dimer or the Wells score is elevated. Protocol I was the least expensive (£10,000 per QALY), whereas protocol II had the maximum net benefit to the entire healthcare system (while costing £20,000–£30,000 per QALY). Importantly, protocols that relied on ultrasound for all patients were not cost effective (costing >£40,000 per QALY).

A key weakness of this study was that the authors did not include algorithms that involved plethysmography. The authors also stressed that their results are most applicable to outpatients with a suspected first DVT, and not to inpatients, patients with suspected recurrent DVT, pregnant patients, or intravenous drug abusers.

Summary

In summary, the data suggest that when patients present in a clinic setting with a suspected first DVT, high-sensitivity D-dimer testing should be combined with Wells scoring to determine which patients need ultrasound imaging and which may be reassured with no further intervention.

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Dear EBP Readers,

Diversity is not only politically correct, it is vital to a healthy academic community. Diversity challenges dogma, creates new kinds of questions, and enriches the goals and objectives of research beyond narrow self-interests. One of our goals at EBP is to foster healthy intellectual diversity by recruiting and training new contributors.

This year has been a remarkably productive in that regard. The Family Physicians Inquiries Network (FPIN) has signed up 14 new academic programs, and several have indicated an interest in helping produce HelpDesk Answers (HDAs), in particular. This is in addition to the 11 programs recruited by FPIN in 2006 that are already providing fresh material for HDAs and other feature articles.

FPIN has 4 tools to provide information to practicing physicians. PEPID PCP is an electronic clinical reference tool (online and PDA) that includes links to other FPIN publications. HDAs are short reviews answering a clinical question, published here in EBP. Clinical Inquiries are longer reviews published by a team (author, clinical librarian, and clinical commentator) in The Journal of Family Practice and American Family Physician. FPIN has also recently launched a new endeavor, PURIs (Priority Update of the Research Literature), which will be published in The Journal of Family Practice.

FPIN members have so many ways to contribute that deciding who to recruit as HDA authors has been a bit of a challenge. Who stands to benefit from authorship? Who has the skills or wants to develop them? Who will have the most fun doing it?

The answers have become clearer over the last year as we have worked with so many new programs. I now believe that HDAs, when written in conjunction with an experienced mentor-coauthor, are well-suited to being written by high-achieving medical students, PharmD candidates, and family medicine residents (who need to fulfill their RRC-mandated academic project requirement). They are also great for newer faculty developing their academic skills.

We hope you’ve had a productive year, and hope to hear your feedback!

Regards,

Jon O. Neher, MD

PS:
We are now taking orders for the 2007 EBP Compendium. Go to: www.ebponline.net, and click on the “Subscribe Now” link.
Evidence-Based Answer

Sinus surgery does not confer additional benefit to that obtained by medical treatment in chronic rhinosinusitis. (SOR B, based on a single RCT.) It should be reserved for patients who failed medical management. (SOR C, expert opinion.)

A 2006 Cochrane review surveyed 2,159 abstracts and found a single, unblinded RCT including 90 patients (average age 43 years) that compared functional endoscopic sinus surgery (FESS) with medical therapy for chronic sinusitis. Inclusion criteria were chronic rhinosinusitis diagnosed by a health professional, symptoms for more than 12 weeks, and endoscopic or radiologic evidence of sinusitis. Medical therapy included 2 weeks of high-dose erythromycin (500 mg BID) followed by 10 weeks of low-dose erythromycin (250 mg BID) concomitant with nasal steroids. The primary outcome was a global improvement in symptoms; patients were followed for 1 year. The study found that FESS was “not superior” to medical treatment. FESS did appear to be safe, as there were no major complications noted.

This result contrasts with an earlier systematic review that identified 45 papers addressing the focused clinical question: “In adults with chronic sinusitis who have failed medical therapy, does FESS improve symptoms and/or quality of life?” This report did not include the RCT used in the Cochrane review. The review did include 2 articles that were bench research or expert opinion, 42 articles that were retrospective case studies, and 1 article that was a prospective cohort study. The authors concluded, based primarily on studies with a Level of Evidence of 4, that there was “substantial” evidence that FESS improves symptoms.

Current guidelines recommend that surgical intervention be reserved for cases of chronic sinusitis that are refractory to medical treatment and for patients with anatomic obstruction. FESS is the most widely used strategy. Patients who are considered candidates for this procedure have typically required more than 3 courses of antibiotics for sinusitis within a 12-month period.

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A Society for Healthcare Epidemiology of America–commissioned guideline recommends considering MRSA decolonization for selected patients and healthcare workers as an adjunctive measure to control the spread of MRSA in healthcare settings.1 To be considered for decolonization therapy, healthcare workers should be implicated in an outbreak, but the criteria for selecting patients for decolonization are not clearly delineated. The guideline does discourage widespread and prolonged use of decolonization therapy to limit resistance. These recommendations are “strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies and a strong theoretical rationale.” The literature search for the guideline was accomplished using Medline and the authors’ personal files. Other than limiting studies to the English language, the criteria for selecting and combining the evidence were not described further.

The Healthcare Infection Control Practices Advisory Committee of the Centers for Disease Control and Prevention recommends considering decolonization therapy as part of intensified control efforts if routine control measures such as standard precautions, contact precautions, and environmental disinfection fail.2 Experts in infectious diseases or healthcare epidemiology should be consulted for each case to decide the appropriate use of decolonization therapy. This recommendation is “suggested for implementation and supported by suggestive clinical or epidemiologic studies or a theoretical rationale.” The literature search strategy and the process to select and combine the evidence were not described.

An expert panel convened by the Centers for Disease Control and Prevention to describe strategies to manage MRSA in the community states, “it may be reasonable to administer decolonization regimens when (1) an individual patient has multiple documented recurrences of MRSA infection or (2) ongoing MRSA transmission is occurring in a well-defined, closely associated cohort (such as a household).”3 This suggestion should be considered only after standard prevention measures are unsuccessful. The guideline does not include a description of the literature search strategy or study selection criteria and there was no grading of the evidence or strength of recommendations.

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Are topical counter-irritants (salicylate-containing products) effective for acute musculoskeletal injury?

Evidence-Based Answer
Topical counter-irritants are effective in relieving pain from acute musculoskeletal injury without causing an increase in adverse events. (SOR B, based on a meta-analysis of lower quality studies.)

Products containing menthol, salicylate, and nicotinic ester are believed to act by topical counter-irritation, thus altering perceived pain. A meta-analysis reviewed randomized controlled trials (RCTs) evaluating the effect of topical treatments whose primary active ingredient was classified as a counter-irritant. Studies of topical non-steroidal anti-inflammatory drugs (NSAIDs) or capsaicin products were excluded. Although 14 studies were identified, 5 were excluded because of the lack of placebo control or efficacy results and another 6 evaluated medication use only in chronic conditions.

Ultimately, with respect to acute musculoskeletal pain, a total of 3 randomized placebo-controlled trials with 182 patients were included, all of which used a salicylate-containing compound.4 The acute injuries included low back strains, ankle sprains, and other unspecified minor traumatic athletic injuries. Defining effectiveness as at least 50% improvement in perceived pain, pooled data showed a mean response rate of 67% (25%–90%) for the topical counter-irritant group versus only 18% (0%–59%) for the placebo group (P<.001). The number needed to treat was 2 (95% CI, 2–3) for 50% pain relief for at least 3 days after the acute injury. A lack of efficacy in the placebo group contradicted the

idea that rubbing alone is a major contributor to the therapeutic effect of topical counter-irritants. In addition, the meta-analysis identified 5 RCTs, once again including only salicylate compounds as the active ingredient, involving 418 patients that reported on adverse effects. Four patients of 208 (1.92%) in the treatment group and 4 of 210 (1.90%) in the placebo group reported adverse effects from the topical treatments (most commonly local skin irritation), a difference that was not statistically significant.

No studies were identified that examined the therapeutic effect of these medications in combination with or compared to other conventional treatment for acute musculoskeletal injury (ice, NSAIDs, etc).

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What are the potential long-term risks of proton pump inhibitors?

Evidence-Based Answer
The chronic use of proton pump inhibitors (PPIs) is associated with an increased risk of hip fracture in older adults, pneumonia in adults and children, gastroenteritis in children, and Clostridium difficile infection in hospitalized patients. (SOR B, based on cohort and case-control studies.)

PPIs have previously been deemed safe for long-term use with respect to risk of gastric carcinoid, atrophic gastritis, and gastric cancer. However, with their wide adoption for multiple indications, other issues have come to light.

Two studies have suggested that the hypochlorhydria induced by PPIs may affect calcium absorption, thereby leading to decreased bone mineralization and increased risk of fracture. A British nested case-control study used the General Practice Research Database to examine the medical records of 1.8 million patients older than 50 years and compared fracture rates between users and nonusers of PPIs. A total of 13,556 patients...
sustained hip fractures during the time period examined. After adjusting for other confounding risk factors for hip fractures such as age, sex, medication use, and comorbid medical conditions, the authors found a significantly increased risk of hip fracture among individuals using PPIs for longer than 1 year (adjusted odds ratio [AOR] 1.62; 95% CI, 1.41–1.89). The risk increased with the duration of therapy, and among individuals taking higher doses of PPIs (AOR 2.65; 95% CI, 1.80–3.90). Use of histamine 2 receptor antagonists (H2RAs) was analyzed separately and was not found to significantly increase risk of hip fracture.

A Danish case-control study also showed an increased risk of hip fracture with long-term PPI use (OR 1.45; 95% CI, 1.28–1.65). However, this study did not find increased risk with higher doses and longer duration of therapy, possibly due to differences in study design and a shorter time interval of the study.

A multicenter, prospective cohort study in Italy examined the incidence of gastroenteritis and community-acquired pneumonia in 95 children using acid-suppressing medications (47 on ranitidine and 44 on omeprazole) compared with 95 controls during a 4-month period. The study found a significant increase in gastroenteritis (OR 3.58; 95% CI, 1.36–2.62) and community-acquired pneumonia (OR 6.39; 95% CI, 1.38–29.70) in otherwise healthy children age 4 to 36 months who received acid-suppressing medications versus the control group. This finding was thought to be due to reduction in the efficacy of the nonspecific defense mechanism provided by gastric acidity. A case-control study in the Netherlands showed a similar increased risk of pneumonia in adults using acid-suppressing medications, both PPIs and H2RAs (OR 1.89; 95% CI, 1.36–2.62).

Two studies conducted by a group in Montreal examined the incidence of *Clostridium difficile* diarrhea in hospitalized patients using acid-suppressing medications. A cohort study of 1,187 hospitalized patients, after adjusting for antibiotic exposure, showed a significantly increased risk of *C difficile* diarrhea among patients who had received PPIs (AOR 2.1; 95% CI, 1.2–3.5), but not among patients who had received H2RAs. A case-control study at a different hospital of 94 patients with *C difficile* diarrhea found a similar increased risk associated with PPI use (AOR 2.6; 95% CI, 1.3–5.0).

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Evidence-Based Medicine Ratings

Evidence-Based Practice utilizes a simplified rating system known as the “Strength of Recommendation Taxonomy” (SORT).

1. **Strength of Recommendation (SOR) ratings** are given as key recommendations for readers. SORs should be based upon the highest quality evidence available.
   - A. Recommendation based on consistent and good-quality patient-oriented evidence
   - B. Recommendation based on inconsistent or limited-quality, patient-oriented evidence
   - C. Recommendation based on consensus, usual practice, opinion, disease-oriented evidence, or case series for studies of diagnosis, treatment, prevention, or screening

2. **Levels of Evidence** determine whether a study measuring patient-oriented outcomes is of good or limited quality, and whether the results are consistent or inconsistent between studies.
   - **Study quality**
     1. Good-quality, patient-oriented evidence (eg, validated clinical decision rules, systematic reviews, and meta-
        analyses of randomized controlled trials [RCTs] with consistent results, high-quality RCTs, or diagnostic cohort studies)
     2. Lower-quality, patient-oriented evidence (eg, unvalidated clinical decision rules, lower-quality clinical trials, retrospective cohort studies, case control studies, case series)
     3. Other evidence (eg, consensus guidelines, usual practice, opinion, case series for studies of diagnosis, treatment, prevention, or screening)
Trial of labor after multiple cesareans

Bottom Line
The American College of Obstetricians and Gynecologists (ACOG) currently recommends that only women with a history of prior vaginal delivery be offered a trial of labor after multiple cesareans. However, a recent large, prospective cohort study found that although the risk of major morbidity is slightly increased, the risk of uterine rupture does not rise with multiple cesarean sections (when compared with a single cesarean). Given the relatively low absolute risk of major morbidity seen in the study, offering a trial of labor to women with multiple prior cesareans may be appropriate after proper counseling.

Evidence Summary
The mantra “once a cesarean always a cesarean” is now true 9 times out of 10: the United States vaginal birth after cesarean (VBAC) rate has dropped steadily since 1996.1 One area of controversy has been the safety of offering a trial of labor after cesarean (TOLAC) to women with more than 1 prior cesarean.

Historically, a TOLAC was offered to women who had more than 1 previous cesarean with lower transverse uterine incisions.2 The practice was challenged by a 1999 retrospective study of deliveries at Brigham and Women’s Hospital in Boston in which the uterine rupture rate among 3,757 women with 1 prior cesarean was 0.8% compared with 3.7% for the 134 women with 2 prior cesareans (odds ratio [OR] 4.8; 95% CI, 1.8–13.2; P=.001).3 Of the 3,757 women undergoing a TOLAC, women with a prior vaginal delivery were less likely to have a uterine rupture than women without a prior vaginal delivery (OR 0.26; 95% CI, 0.08–0.88). This study was unique in that it used a regression analysis to control for other factors that might affect the uterine rupture rate.

Based on this result, a 2004 ACOG Practice Bulletin recommended that “for women with 2 prior cesarean deliveries, only those with a prior vaginal delivery should be considered candidates for a spontaneous trial of labor.”2

In 2006, a prospective observational study of 45,988 women with a singleton pregnancy and a history of cesarean found that uterine rupture was not increased, but major maternal morbidity was slightly increased for TOLAC in women with a history of multiple cesareans compared with a single cesarean (OR for major morbidity 1.35; 95% CI, 1.03–1.75).4 The uterine rupture rate among 16,915 women with 1 prior cesarean was 0.7% compared with 0.9% for the 975 women with multiple prior cesareans (P=.37). Major maternal morbidity was defined as uterine rupture, endometritis, hysterectomy, transfusion, thromboembolic disease, and operative injury. Multivariate analysis was used to control for confounding factors. The authors pointed out that the absolute risk of major morbidity was low (0.6% for hysterectomy and 3.2% for transfusion) and recommended that “vaginal birth after multiple cesarean deliveries should remain an option for eligible women.”4

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The practice of evidence-based medicine can be divided into the following components:

- Identifying a problem or area of uncertainty
- Asking a relevant, focused, clinically important question that is answerable
- Selecting the most likely resources to search
- Searching and appraising the evidence found
- Assessing the clinical importance of the evidence
- Assessing the clinical applicability of the evidence
- Acting on and appropriately applying the evidence
- Assessing the outcomes of your actions
- Authoring—summarizing and storing records for future reference
Is heart rate variability biofeedback an effective adjunct treatment for asthma?

Summary
Heart rate variability (HRV) biofeedback training decreases steroid medication use for adults with asthma (SOR B, based on a randomized controlled trial) and produces slight improvements in spirometry results for children (SOR C, based on a case series study). To achieve these gains, patients needed 10 to 15 training sessions with continued home practice. Although these effects are promising, the exact clinical utility of HRV biofeedback for asthma remains to be determined.

The Evidence
HRV is a measure of beat-to-beat fluctuations in heart rate and is considered to be a reflection of autonomic function and balance. HRV has been found to be low in patients with asthma and other cardiovascular and central nervous system disorders.1 HRV biofeedback increases HRV by training in slow-paced breathing (about 5–6 breaths per minute) using biofeedback equipment and ECG and/or blood volume pulse, with visual or auditory feedback.

In a clinical trial, 94 volunteers with a history of asthma were randomized to 1 of 4 treatment groups: HRV biofeedback with training in pursed lips abdominal breathing, HRV biofeedback alone, a placebo biofeedback procedure, and a wait list control. The groups’ inhaled steroid medication was individually titrated by asthma specialists blinded to the experimental condition until the patients were stabilized on the lowest possible dose. The treatment groups each received 10 weekly biofeedback sessions and were instructed to practice for 20 minutes twice daily. Patients also completed questionnaires about asthma symptoms and monitored home peak flow readings. Respiratory resistance was measured and steroid medication use evaluated at sessions 1, 4, 7, and 10. Medication use was scored according to the 13-step score described in National Heart, Lung, and Blood Institute guidelines (eg, score 5=fluticasone 44 µg, 2p BID [176 µg]; score 6=fluticasone 110 µg, 1p BID [220 µg]; score 7=salmeterol or montelukast sodium; and score 8=fluticasone 110 µg 2p BID [440 µg]).1

The mean medication score for the HRV biofeedback groups fell significantly—from 8.14 to 5.49 for the full protocol group and 7.42 to 5.12 for the HRV biofeedback alone group (P<.0001 for each). The mean medication level also decreased for the placebo group, from 6.95 to 6.05 (P<.02), but not the wait list group. In terms of severity class, the 2 HRV biofeedback groups moved from “moderate persistent” to “mild persistent” and the 2 groups without HRV biofeedback remained in the “moderate persistent” range. The HRV groups also showed significant pre versus post decreases in airway resistance, whereas the wait and placebo groups did not. No changes were noted in spirometry for any of the groups.1

In a case series, 20 children (9–16 years old) with mild to moderate untreated asthma were given 13 to 15 half-hour HRV biofeedback training sessions on consecutive days. Spirometry was measured at the end of the first and last training sessions. The mean FEV1 prior to training was 1.94, and increased slightly to 2.05 (P<.003) after training, while FEV50% increased from 2.38 to 3.62 (P<.0002). However, the authors pointed out that although these changes were statistically significant they were less than the threshold accepted for clinical significance.2

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“Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research.”
A recent meta-analysis suggested that taking rosiglitazone may result in an increased incidence of MI. An observed increased rate of death from cardiovascular causes was considered “borderline significant” ($P = .06$). In response to this article, an unscheduled interim analysis of the ongoing RECORD trial was published that investigated rosiglitazone’s effect on cardiovascular outcomes. The results from this interim analysis conflict with the data reported in the meta-analysis (TABLE). Subsequently, another meta-analysis demonstrated an increased risk of heart failure with both rosiglitazone and pioglitazone, but no increase in cardiovascular death.

Recent media coverage of this debate has left the general public and many professionals questioning the clinical significance of the information, as well as the appropriateness of rosiglitazone for treatment of patients with type 2 diabetes.

In September 2007, a meta-analysis was released that evaluated pioglitazone’s effects on ischemic cardiovascular events. This report included 19 trials and more than 16,000 patients. Pioglitazone showed a statistically significant decrease in the combined endpoints of death/MI/stroke (hazard ratio [HR] 0.82; 95% CI, 0.72–0.94) and death/MI (HR 0.85, 95% CI, 0.73–0.99).

Context
Rosiglitazone and pioglitazone each increase insulin sensitivity by acting as a peroxisome proliferator-activated receptor-gamma (PPAR-γ) agonist. PPAR-γ genes are also important in fatty acid metabolism. These effects on fatty acid metabolism with rosiglitazone result in an average increase in triglycerides of 13.1±7.8mg/dL and in low-density lipoprotein of 21.3±1.6mg/dL. Curiously, pioglitazone has an opposite, potentially beneficial effect on lipids. PPAR-γ agonists are also associated with edema. On August 15, 2007, the US Food and Drug Administration issued a black box warning for both rosiglitazone and pioglitazone counseling against their use for patients with NYHA class III and IV heart failure.

The Data
In the June 2007 issue of the New England Journal of Medicine, Nissen and Wolski published a meta-analysis evaluating risk of MI and death from cardiovascular causes in patients receiving rosiglitazone. Forty-two articles were reviewed, including unpublished data and the results from 2 large trials, the DREAM and ADOPT trials. The results indicated a statistically significant risk of MI as well as an increased risk of death described as “borderline significant” (TABLE). Most of the
studies included in the meta-analysis were small short-term studies that did not look at cardiovascular outcomes as a primary endpoint. Studies with no cardiac outcomes were excluded from the meta-analysis.

In response to this article, an interim analysis was published the following month from the investigators of the RECORD trial. The RECORD trial is an ongoing prospective trial that is studying rosiglitazone for cardiac outcomes and regulation of glycemia in diabetes. The interim analysis showed a nonsignificant hazard ratio for its primary endpoint of hospitalization and death, but in order to assess the cardiovascular outcomes it is necessary to look at secondary endpoints (TABLE). Finally, another meta-analysis was published focusing on the risk of the development of heart failure and cardiovascular death in patients given rosiglitazone or pioglitazone. This analysis showed cardiovascular death was not increased with either medication. However, only 7 articles were included in this meta-analysis.

When evaluating the risks associated with rosiglitazone, it is important to consider the benefits of tight glycemic control. Although no data are available that conclusively confirm the macro-vascular benefit of tight glycemic control, current data suggest that patients who are not under control may be at higher risk of cardiovascular complications. This question may be better defined when the results from the large ACCORD trial become available.

The conflicting data raise questions about the true hazards associated with rosiglitazone. In general, meta-analyses are a good predictor of trends that are later confirmed by large-scale trials. Unfortunately, the RECORD trial does not address this as a primary endpoint. Long-term prospective studies are needed that address this issue directly. Until then, exercising caution would be appropriate and other options, which may include pioglitazone, should be considered before using rosiglitazone.

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<td>CHD 1.14 (1.07–1.21)</td>
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CHD=congestive heart disease; CHF=congestive heart failure; CI=confidence interval; CVD=cardiovascular disease; HbA1c=hemoglobin A1c; HR=hazard ratio; MI=myocardial infarction; OR=odds ratio; PAD=peripheral artery disease; RR=relative risk.


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Infants and Food Allergies

What is a food allergy? In a small number of people, specific foods trigger an allergic reaction involving the respiratory system (causing runny nose, cough, or asthma), digestive system (causing abdominal pain, diarrhea, or vomiting), or skin (causing rash or itching). The number and intensity of these symptoms differs from person to person. The amount of food needed to produce a reaction also varies, and symptoms can occur within minutes or not appear until a day later. Because symptoms of food allergy can mimic many other illnesses, tracking down the true cause is often difficult. Food allergies often show up during infancy and occasionally last a lifetime.

Is there anything parents can do to prevent food allergies?

So far, there is no guarantee that a parent can prevent food allergies. Your child’s risk of developing allergies is increased if either parent or any other sibling has allergies. There are, however, accepted guidelines that may help lessen this risk:

• Breast-feeding for at least 4 to 6 months is ideal to minimize allergies and strengthen the baby’s immune system. If the infant is not breast-feeding and the family already has a history of food allergies, the infant should receive hydrolyzed formulas (avoiding cow’s milk or soy-based formulas). If the mother has significant food allergies herself, she should avoid eating those foods while breast-feeding.
• It is a good idea to wait until your infant is 4 to 6 months of age before introducing solid food, so your baby’s digestive system is more fully developed. Begin with less allergy-prone foods, such as fruits, vegetables, and rice. The American Academy of Pediatrics recommends that dairy products be avoided until an infant is 1 year old, eggs until a child is 2 years old, and peanuts, tree nuts, and fish until a child is 3 years of age.
• Parents are the best detectors of food allergies. If you notice physical symptoms, pay attention to when they occur and if they disappear when the food is eliminated. For children with confirmed allergies, keeping careful records and reading food packaging will be important to prevent symptoms.

If your child has chronic symptoms of any type, talk to your doctor about whether the problem could be a food allergy or something else. Over-the-counter medications are not recommended for treating food allergies. Skin and blood tests are available for severe cases, but they can give false results. The description of symptoms by the parent will be most important in clarifying a diagnosis. Fortunately, once they are recognized, most food allergies can be managed with careful attention to diet.

For more information

Feeding Your 4- to 7-Month Old (Nemours Foundation)
http://kidshealth.org/parent/nutrition_fit/nutrition/feed47m.html

Food Allergies (American Academy of Family Physicians)
http://www.kidshealth.org/PageManager.jsp?dn=familydoctor&lic=44&cat_id=161&article_set=20850&ps=104

Introducing Solid Foods: What You Need to Know (Mayo Foundation for Medical Education and Research)
http://www.mayoclinic.com/health/healthy-baby/PR00029
1. Which of the following statements is true regarding the treatment of patients with chronic sinusitis?
   - a. An early systematic review, based on lower quality evidence, concluded that surgery relieved symptoms
   - b. A randomized controlled trial showed therapy with antibiotics and nasal steroids to be superior to surgery
   - c. Guidelines recommend surgery for patients with 2 episodes of sinusitis requiring antibiotics in any given year
   - d. All of the above

2. Which of the following screening tools has been shown to reduce healthcare costs when used as a first test for outpatients with suspected first deep-venous thrombosis (DVT)?
   - a. Formal DVT risk scoring
   - b. Calf plethysmography
   - c. Compression ultrasound
   - d. Venous angiography

3. Heart rate variability biofeedback training is related to which of the following outcomes in adults with asthma?
   - a. Improved spirometry
   - b. Decreased inhaled steroid use
   - c. Decreased oxygen need
   - d. Decreased mortality

4. How do rosiglitazone and pioglitazone affect cardiovascular health?
   - a. They increase the rate of heart failure by promoting fluid retention
   - b. They increase the rate of myocardial infarction by increasing thrombosis
   - c. They decrease the rate of myocardial infarction by improving glucose control
   - d. They raise low-density lipoprotein cholesterol

5. In which group of women does ACOG recommend allowing a trial of labor after multiple cesareans?
   - a. Women with favorable clinical pelvimetry
   - b. Women with favorable pelvimetry by computed tomography scan
   - c. Women with a history of successful vaginal delivery
   - d. Women whose fetus has an estimated weight of <4,000 g

6. Which of the following statements is true regarding eradication of methicillin-resistant Staphylococcus aureus (MRSA)?
   - a. In a hospital outbreak, all healthcare workers in the institution should be cultured and then treated if found to be colonized with MRSA
   - b. MRSA eradication can be attempted for individual patients with multiple documented MRSA infections
   - c. Hospitals should use decolonization therapy for prolonged periods of time until MRSA outbreaks are under control
   - d. Decolonization therapy should be considered a routine control measure for MRSA infections

7. Topical counter-irritants may be effective acutely for which of the following conditions?
   - a. Fracture of the tibia
   - b. Shoulder dislocation
   - c. Ankle sprain
   - d. Compartment syndrome

8. Long-term use of proton pump inhibitors is associated with an increased risk of
   - a. Gastric carcinoid
   - b. Atrophic gastritis
   - c. Hip fracture
   - d. Helicobacter pylori septicemia
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