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INSIDE

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Prophylactic Antibiotics and Cesarean Section

ABSTRACT & COMMENTARY

By Alison Edelman, MD, MPH

Assistant Professor, Assistant Director of the Family Planning Fellowship Department of Obstetrics & Gynecology, Oregon Health & Science University, Portland

Dr. Edelman reports no financial relationship to this field of study.

Synopsis: *Comparison of antibiotic dosing prior to skin incision vs after cord clamping for prevention of post-cesarean infectious morbidity.*

Source: Sullivan S, et al. Administration of cefazolin prior to skin incision is superior to cefazolin at cord clamping in preventing post cesarean infectious morbidity: a randomized, controlled trial. *Am J Obstet Gynecol.* 2007;196:455,e1-455.e5.

THE TITLE SAYS IT ALL IN THIS RANDOMIZED CONTROLLED TRIAL by Sullivan and colleagues —"Administration of cefazolin prior to skin incision is superior to cefazolin at cord clamping in preventing post-cesarean infectious morbidity."[1] This study compared the administration of prophylactic antibiotics (cefazolin) prior to skin incision (15-60 minutes) vs after cord clamping in women undergoing a non-emergent cesarean section with a gestational age greater than 24 weeks and no recent exposure to antibiotics. Women were monitored for evidence of infectious morbidity (endomyometritis, wound infection, and pyelonephritis) during their hospital stay and up to 6 weeks postpartum. Total infectious morbidity was decreased in the group that received antibiotics prior to skin incision [Relative Risk 0.4 (95% CI 0.18-0.87)]. The main reason for this decrease in infectious morbidity was due to fewer cases of endomyometritis [1% vs 5%; Relative Risk 0.2 (95% CI 0.2-0.94)] whereas the difference in wound infections was not statistically significant [3% vs 5%; Relative Risk 0.52 (95% CI 0.18-1.5)]. There were no differences in neonatal outcomes between the two groups (sepsis, septic workups, or NICU admissions).

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COMMENTARY

What evidence do we have for the use of prophylactic antibiotics for cesarean sections? A recent Cochrane Review[2] provides us with the highest level of evidence (Level 1) for which antibiotics to use and for which cesarean sections to use them, but falls short on recommendations for timing. Prophylactic antibiotics used for cesarean sections in both nonlaboring and laboring women have resulted in a significant decrease of post-cesarean fever, endomyometritis, urinary tract infection, and wound infection. A single dose of ampicillin or a first generation cephalosporin have similar efficacy at preventing post-cesarean infectious morbidity. No added benefit was found with broader spectrum antibiotics or multiple doses. Unfortunately due to lack of evidence, this review was unable to determine the optimal timing for administering prophylactic antibiotics.

Administration of antibiotics within one hour prior to skin incision is routine for surgeries requiring antibiotic prophylaxis, and, in fact is a JCAHO hospital quality improvement measure.[3] So why does the practice of delaying prophylactic antibiotics until cord clamping exist with cesarean sections? The rationale given in the literature is the concern regarding neonatal exposure to antibiotics and adversely impacting a neonatal sepsis workup. However, no evidence exists to support these claims. In fact, data from animal and human studies have shown that adequate serum levels need to be present prior to bacterial exposure to prevent infection, that a delay in administration increases postsurgical infectious morbidity, and that no untoward neonatal effects have been proven to occur from the exposure.[1,2,4-6]

Until recently there were no studies sufficiently powered to determine a difference in infectious morbidity between antibiotics administered prior to incision vs after cord clamping. Two recent studies attempt to answer this question but their results are conflicting. In 2005, Thigpen, et al[6] found no harm in giving prophylactic antibiotics but also found no difference in infectious morbidity with antibiotics administered prior to skin incision vs after cord clamping. This study had several key limitations, including the failure to achieve their desired sample size. In addition, a large number of women were already receiving antibiotics (penicillin) for GBS prophylaxis and the study population had overall higher rates of infectious morbidity. These limitations may have blunted the differences between groups.

In contrast, Sullivan, et al[1] had a sample size adequate to determine differences in infectious morbidity between the two groups. This study excluded women who had recently received antibiotics (1 week or less) which, although not explicitly stated, most likely means women with chorioamnionitis and/or positive GBS cultures. The study did include women with diabetes and obesity; both of which can also increase the baseline risk for infection.[7,8] In addition, cesarean sections were performed for a variety of indications (Stage 1 and 2 arrest, nonreassuring fetal status, scheduled). All in all, this study's findings appear to be valid and very generalizable to the general obstetrical population.

The most exciting studies to me are those that challenge our current standard of practice—the study by Sullivan et al is one such study. This study provides us with good but limited evidence to support dosing prophylactic antibiotics prior to skin incision in cesarean sections. More studies are needed to support these results, but at the very least women at high risk for post-cesarean infectious morbidity (ie, diabetes, obesity) should receive antibiotics prior to skin incision. Finally, the evidence is good, extensive, and consistent in regard to providing prophylactic antibiotics for all women undergoing cesarean section with either a single dose of ampicillin or first generation cephasporin. ■

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Results from the Cancelled WISDOM Trial

ABSTRACT & COMMENTARY

By Leon Speroff, Editor

Synopsis: *Cancelled WISDOM clinical trial agrees with WHI results: hormone therapy is associated with an increased risk of cardiovascular events in older postmenopausal women.*

Source: Vickers MR, et al. BMJ. 2007;335:239-250.

WISDOM WAS A MULTICENTER, RANDOMIZED, placebo-controlled clinical trial of postmenopausal hormone therapy that began recruitment in 1999 in the U.K. and in 2000 in Australia and New Zealand. The trial was prematurely cancelled in 2002 after the initial publication of results in the Women's Health Initiative (WHI). This report summarizes the outcomes in 5,692 women (26% of the target number of 22,300) who started treatment. Treatment arms were similar to those in the WHI: daily combined estrogen-progestin with 0.625 mg conjugated equine estrogens (CEE) and 2.5 or 5.0 mg medroxyprogesterone acetate or estrogen only with 0.625 mg CEE daily. The women taking combined estrogen-progestin had significantly increased rates of cardiac events and venous thrombosis. The numbers were much smaller in the estrogen-only arm, but there was a similar trend. Rates for stroke and breast cancer were no different comparing treatment and placebo groups. All but two of the 11 cardiovascular events in treated women were in participants over age 64 who had one or more recognized cardiovascular risk factors. The authors concluded that the results were similar to those in the WHI, reflecting the impact of starting or restarting hormone therapy in older women.[1]

COMMENTARY

The participants in the WISDOM trial were similar to those in WHI with an average age of 62.8 years and a distance from menopause of 15 years. The mean follow-up time was 11.9 months. Of course, the small number of events and the short follow-up time do not allow strong conclusions. However, the cardiovascular results come as no surprise, consistent with the current recognition that only the oldest women in the WHI experienced an increase in cardiovascular clinical events. Even venous thrombosis may be concentrated in women with risk factors for this condition, such as obesity or previous cardiovascular disease.

A trend toward a reduction in fractures in the WISDOM trial was also consistent with the finding in the WHI of a potent preventive effect in a general population of women. The cancer outcomes are not meaningful given the short follow-up; only a small number of women achieved a follow-up of 3 years before cancellation of the trial.

Now we are left with no on-going clinical trials of hormone therapy measuring clinical events. To my knowledge, there are 3 trials in progress measuring the effect of hormone therapy in relatively young postmenopausal women on surrogate cardiovascular markers, mainly ultrasonographic assessment of intima media thickness in carotid arteries. Results from

these trials are still several years away from being available. Given the difficulties of funding and compliance, it is unlikely that a long-term clinical trial of hormone therapy in the younger postmenopausal years will be performed in the near future. Nevertheless, the accurate and current appraisal of the WHI data that is finally public knowledge allows us to once again have reason to believe that hormone therapy offers primary prevention against coronary heart disease when treatment is started in the early postmenopausal years. A recent reassessment of the WHI results supports this conclusion, even finding no increase in stroke when women over the age of 60 or those with cardiovascular risk factors were excluded.[2] In my view, it is appropriate to return this possible benefit into the decision-making process for women considering hormone therapy for symptom control.

The publicity and responses that followed the first reports from the WHI led to about a 30% to 40% discontinuation rate of hormone therapy among women throughout the world. This raises two serious questions. First, in the coming years will data emerge documenting a rise in coronary heart disease and fractures in this population of women? Second, is restarting hormone therapy in these women associated with an increased risk of cardiovascular events? I believe the answer is "yes" to both of these questions. We now recognize that many of the women who discontinued treatment have returned asking for resumption of therapy. There are no relatively inexpensive markers or tests to assess their current state of atherosclerosis and risk of clinical events. This must be a subjective judgment on the part of the clinician. If a substantial length of time has passed since discontinuation and there is concern now for progression of atherosclerosis and an increase in risk, prior to resuming treatment with a low dose of estrogen, it is worth considering a 3-month period of treatment with statins to stabilize any plaques that have developed. ■

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Complications of Exteriorization Compared with *In Situ* Uterine Repair at Cesarean Delivery under Spinal Anesthesia

ABSTRACT & COMMENTARY

By John C. Hobbins, MD

Professor and Chief of Obstetrics, University of Colorado Health Sciences Center, Denver

Dr. Hobbins reports no financial relationship to this field of study.

Synopsis: *Exteriorization increases pain, nausea, and vomiting vs* in situ *repairs during Cesarean section.*

Source: Siddiqui M, et al. Complications of exteriorized compared with *in situ* uterine repair at cesarean delivery under spinal anesthesia. *Obstet and Gynecol.* 2007;110:570-575.

IT IS STILL COMMON PRACTICE TO EXTERIORIZE THE uterus during repair of the uterine incision during cesarean section. The rationale to support this maneuver is that it makes the job easier, faster, and it decreases blood loss.

Investigators from Toronto recently set out to test the concept and to see if there was a downside to uterine exteriorization. They invited 79 healthy patients about to have a scheduled Cesarean section to participate in a study in which half had their uteri exteriorized during uterine reconstruction and half did not. The authors attempted to standardize as many therapeutic variables as possible between groups. Spinal anesthesia was maintained at a level below T5; hypotension was scrupulously avoided by early administration of phenylephrine; oxytocin was given uniformly with delivery of the shoulder; and assisted delivery of the placenta was undertaken in all patients.

The authors' primary outcome was the incidence of intra- and post-operative nausea and vomiting. However, many other variables were evaluated.

The incidence of nausea and vomiting was 38% vs 18%; tachycardia was 18% vs 3%; hypotension was 28% vs 15%; and perceived and observed pain was 26%

vs 13%—all higher in the "exteriorized" patients. The odds ratio for tachycardia, in particular, was 8.3.

All this was happening while the median time of uterine repair was, although significant, only one minute shorter. The average total operation time (36 minutes vs 37 minutes) and estimated blood loss (625 cc vs 653 cc) were not a statistically significant different between groups. The authors' conclusion was that "uterine repair should be done in utero where possible."

COMMENTARY

It is very satisfying to have the uterus out and beautifully exposed while closing the incision with what now is back in vogue—two layers. However, if this convenience makes the patient more uncomfortable and more vulnerable to tachycardia and hypotension without any downside, why do it? The authors noted that the greatest effect on the maternal cardiovascular system seemed to occur when the uterus was reinserted into the abdominal cavity. This could be due to compression on the inferior vena cava. The visceral pain seemed to coincide with traction on the uterus, activating unmyelinated neural fibers as powerful stimulators of nausea and vomiting.

Obviously, the study should give us some pause for thought as we are about to lift the uterus out of the abdomen during cesarean section. It seems that it will only add, on average, one extra minute to the procedure if we leave it in. ■

Can Clinical Empathy be Taught?

ABSTRACT & COMMENTARY

By Frank W. Ling, MD

Clinical Professor, Dept. of Obstetrics and Gynecology, Vanderbilt University School of Medicine, Nashville
Dr. Ling reports no financial relationship to this field of study.

Synopsis: *collaborative efforts between faculties of medicine and theater can be effective in teaching clinical empathy.*

Source: Dow Alan W, et al. Using Theater to Teach Clinical Empathy: A Pilot Study. *Society of General Internal Medicine.* 2007;2007:1114-1118.

IT IS ONE THING TO BE EMPATHETIC, BUT IT IS SOMEthing quite different to be able to convey empathy to the patient. This skill of becoming connected to the patient is what the investigators termed "clinical empathy" At Virginia Commonwealth University, a preliminary investigation included 20 internal medicine residents with 14 undergoing 6 hours of classroom instruction and workshop sessions with professors of theater. The curriculum was focused on increasing measurable clinical empathy in office encounters.

The intervention group showed significant improvement after the instruction in all 6 subscores ($p < .011$); and, when compared to the control group, it had better post-test scores in 5 of 6 subscores ($p < .01$). The 6 subgroup categories were: Empathy, Relating, Nonverbal, Verbal, Respect, and Overall Impression.

COMMENTARY

What?! How could this study possibly have any relevance to my practice? I'll bet that's what some of the readers are silently screaming as they peruse this. Give me a few minutes, and I'll explain. Since it is highly unlikely that another paper like this will be published soon, I felt it important that the topic be addressed when there was at least an article with data available. Admittedly the numbers are small, it is nonrandomized and nonblinded. As a result, the level of evidence is not strong. The importance of empathy in clinical medicine is, however, unquestioned.

As one of the 6 core competencies identified in 1994 by the Accreditation Council for Graduate Medical Education, "Interpersonal and Communication Skills" is still not taught in a uniform or rigorous fashion. Certainly those of us trained long before the development of the Core Competencies did not have a formal curriculum in it, even though it was certainly discussed as part of the "art of medicine."

The authors hypothesized that clinical encounters are similar to interplay that goes on between actors who must pick up on the subtleties of relationships between themselves and their colleagues. Whereas clinical teachers are not trained to instruct on developing these interactive skills, theater faculty is so trained. Thus was born the concept of crossing over between the 2 fields.

Just listing the topics covered in the sessions will help the reader appreciate the potential issues that each of us faces whenever we work with our own patient population: insight into patient behavior, building patient trust, active listening, listening for subtext, listening for values and strengths, making links to one's

own experiences, strategies for acknowledging the patient's feelings, skills in physical expressiveness, body language, eye contact, breathing rhythms, and time management.

As I read and re-read this article in preparation for presenting it in this forum, it struck me that each of us has the potential to address our doctor-patient relationships without the formal training … at least as a starting point. Whenever you're in the patient room, do you sit? Do you make eye contact? Do you give the impression that you care? Are you watching how the patient is positioned? Are you hearing the message of what she is saying or are you listening to just the words?

As Yogi Berra, the Hall of Fame catcher once said, "You can observe a lot just by watching." How true… and he never went to medical school.

The authors provide the following quotation from Francis Weld Peabody: "The secret of the care of the patient is caring for the patient." I think that statement can help carry each of us forward in our daily practices with each individual patient encounter. ■

Do Different OCP's Cause Different Problems?

ABSTRACT & COMMENTARY

By Frank W. Ling, MD

Synopsis: *Except for progestin-only pills (more breakthrough bleeding and fewer periods), there is little variation in the frequency of symptoms related to various pill formulations.*

Source: Moreau C, et al. Oral Contraceptive Tolerance: Does the Type of Pill Matter? *Obstet Gynecol.* 2007;109:1277.

Between 2000 and 2004 these French investigators studied 2863 women to determine the frequency of reported symptoms (weight gain, nausea, breast tenderness, swollen legs, fewer periods, breakthrough bleeding, painful/heavy periods) relative to the type of OCP taken (estrogen dose, progestin component, sequence of administration). Because there was little difference in the frequency of these symptoms (except for the progestin-only pills), the authors recommend that future research focus on the effectiveness of counseling as it relates to tolerance of OCPs.

■ COMMENTARY

Does this resonate with your experience in the office? How good are you picking a pill off the sample shelf that has few, if any, side effects? In this study, each year more than half of the subjects had at least one of the symptoms — the most common being weight gain 25%, painful periods 21%, swollen legs 21%, and heavy menstrual bleeding 16%. Extended regimen pills with low estrogen were more likely to have less frequent symptoms. Lower frequency of symptoms was also more likely with a third generation pill compared with second generation pills.

The authors astutely state that reported symptoms do not necessarily tie that symptom to the pill itself so that assuming that the symptom is due to taking the specific OCP would be an overstatement. As has been reported previously, there are more irregularities when progestin-only pills were taken. There was no evidence that less estrogen resulted in fewer symptoms reported. Also, there was no significant improvement in reported symptoms with newer progestin components, which have been touted to have fewer side effects.

What this study does is further reinforce what most of us have found out in our daily practices, ie, pills are pills and the attempt to find the "best" pill is fraught with pitfalls. This is not to say that there are logical approaches to patients with various symptoms, but the clinician is faced with trying to determine if the symptom is related to the OCP or not as a first dilemma. Then how to address the symptom is next. These data remind us to counsel the patients as completely as possible about potential symptoms, but also to make sure that we do not ascribe symptoms to the pills unless appropriate. Until more specific guidelines are available, each of us need to continue to treat each pill taker as an individual, but also treat each type of OCP as an individual, ie, they don't all act the same ways in all patients.

Confused? No need to be. Just make sure that you continue to keep your ears and mind open to new information as it becomes available, but also trust your clini-

cal judgement and experience. It's potentially more valuable than any data you read. ■

CME Questions

29. The following statements regarding cesarean sections and prophylactic antibiotics are true except:

a. All women should receive prophylactic antibiotics when undergoing cesarean section.
b. Multiple doses of prophylactic antibiotics provide no benefit over a single dose.
c. Administration of prophylactic antibiotics prior to skin incision adversely impacts the neonate.
d. Adequate antibiotic serum levels need to be present prior to bacterial inoculation to prevent infection.

30. The following statements regarding postmenopausal hormone therapy and cardiovascular disease are true except:

a. Young, healthy postmenopausal women may have no increased risk of heart attacks or strokes.
b. Young, healthy postmenopausal women may have no increased risk of venous thrombosis.
c. Primary prevention of coronary heart disease in appropriate patients should not be considered a benefit of hormone therapy.
d. Not all postmenopausal women have an increased risk of cardiovascular disease with hormone therapy.

31. Exteriorization of the uterus can trigger hypotension, nausea, and vomiting because:

a. Neural fibers on the visceral surface are stimulated.
b. There is compression of the IVC when reinserted.
c. Visceral pain is a powerful stimulator of nausea and vomiting.
d. The anesthesia level was inconsistent in this study and, therefore, affected the incidence of the above outcomes.

32. Which of the following variables was significantly different between groups?

a. the uterine repair time
b. the blood loss
c. the operative time
d. operator satisfaction

Answers: 29 (c); 30 (c); 31 (d); 32 (a)

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- To present the latest data regarding diagnosis and treatment of various diseases affecting women, including cancer, sexually transmitted diseases, and osteoporosis;
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- To discuss the pros, cons, and cost-effectiveness of new testing procedures.

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Are Thiazolidinediones (TZDs) Safe?

In this issue: *Are thiazolidinediones safe? New study shows Zometa reduces risk of hip fractures and improves survival; Merck HIV vaccine proven ineffective in clinical trials; no causal association found between exposure to mercury from thimerosal; and FDA approvals.*

There's no hotter topic in medicine right now than the safety of the thiazolidinediones (TZDs) rosiglitazone (Avandia) and pioglitazone (Actos). Several meta-analysis have pooled data from multiple clinical trials and come to different conclusions regarding the safety of the drugs. The September 12 issue of *JAMA* contained two papers, both meta-analysis, the of first which suggests that pioglitazone is associated with a significantly lower risk of death, myocardial infarction, or stroke among a diverse population of patients with diabetes. An increase in heart failure was noted, although no increase in mortality (*JAMA* 2007; 298:1180-1188).

The second paper looked at rosiglitazone and noted that in patients with impaired glucose tolerance or type 2 diabetes, use of rosiglitazone for at least 12 months was associated with a significantly increased risk of myocardial infarction and heart failure, again without a significant increase risk of cardiovascular mortality (*JAMA* 2007; 298:1189-1195). This followed on conflicting meta-analysis regarding the risk of rosiglitazone published in the *New England Journal of Medicine* in June and July, the first of which suggested the rosiglitazone was associated with an increase risk of myocardial infarction and increased risk of death from cardiovascular causes (*NEJM* 2007; 356:2457-2471), while the second showed an increased risk of heart failure but no increased risk of myocardial infarction or death from cardiovascular causes (*NEJM* 2007;357:28-38). The studies led to congressional hearings, multiple editorials in medical journals and eventually led the FDA to recommend black box warnings regarding the risk of heart failure for both drugs in July. But despite cries from consumer groups suggesting that this was the Cox-2 debacle redux, the FDA stopped short of taking rosiglitazone off the market. The most recent entry into the fray is a new meta-analysis from the Lahey Clinic in Boston. This review analyzed over 3000 studies of which 7 were used for the analysis—all randomized double-blind clinical trials of drug-related congestive heart failure in prediabetic or diabetic patients given either rosiglitazone or pioglitazone. In over 20,000 patients, 360 had congestive heart failure, 214 on TZDs and 146 on comparators. As with other studies there was an increase risk of heart failure associated with both drugs (relative risk 1.72, 95% CI 1.21-2.24, P= 0.002), but again no increase in cardiovascular death was noted with either drug (RR 0.93). The authors suggest that TZDs cause worsening heart failure, but are not associated with progressive systolic or diastolic dysfunction of the left ventricle that leads to death. They also suggest that more studies are needed (*Lancet* 2007;370:1129-1136). The take home message from all the studies is to use caution in TZDs in patients with diabetes and heart failure (NYHA I and II), and to carefully monitor patients for worsening signs and symptoms including weight gain and edema. Initiation of these drugs in patients with established NYHA Class III or IV heart failure is contraindicated.

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Zometa and hip fractures

A single 5 mg infusion of zoledronic acid (Zometa) within 90 days of a hip fracture reduced the risk of new fractures and improved survival according to new study. Zoledronic acid is a long acting bisphosphonate that is approved for once yearly treatment of postmenopausal osteoporosis. The drug is effective at reducing vertebral, hip, and non-vertebral fractures in women with osteoporosis. In this current study, 1065 men and women with hip fractures were assigned to receive yearly intravenous zoledronic acid 5 mg IV or placebo, the infusions were administered within 90 days of surgical repair of a hip fracture. All patients received vitamin D and calcium. Mean age was 74.5 years, with approximately 75% women. The rate of new clinical fracture was 8.6% in the zoledronic acid group and 13.9% in the placebo group (35% risk reduction, $P = 0.001$). The respective rates of new clinical vertebral fractures were 1.7% vs 3.8% ($P = 0.02$) and for non-vertebral fractures 7.6% vs 10.7% ($P = 0.03$). The death rate was 28% less in the zoledronic acid group (101 of 1054 [9.6%] vs 141 of 1057 [13.3%], $P= 0.01$). No cases of osteonecrosis of the jaw were reported and no adverse effects of healing fractures were noted. The authors conclude that an annual infusion of zoledronic acid within 90 days of a low trauma hip fracture was associated with reduced rate of new fractures and improved survival (published early at www.NEJM.org September 17, 2007).

Merck HIV Vaccine Ineffective in Clinical Trial

After years of development and clinical trials Merck has announced that their HIV vaccine is ineffective in a large clinical trial, and the company has halted further test vaccinations. Other HIV vaccines have also failed but many had hoped that the Merck vaccine, which worked by stimulating T cells, might be more effective. The trial, which was begun in 2004 vaccinated 3000 uninfected volunteers in the US and Latin America. Among 741 patients who received a least one dose of the vaccine, 24 new HIV infections were identified, compared to 21 infections in 762 patients who received placebo. Work continues on other HIV vaccines, currently 30 worldwide are in clinical trials, but the failure of the Merck vaccine is seen is a major setback for HIV researchers.

Thimerosal and Mercury Exposure

Thimerosal has been the subject of intense scrutiny for years regarding its potential link to various neuropsychological deficits in children. Thimerosal has been used as a preservative in vaccines and gamma globulin for decades, although it is rarely used now because it is metabolized to mercury and thiosalicylate, potentially leading to high mercury levels in children. In a new study from the CDC and several large HMOs, 1047 children between ages of seven and 10 years were enrolled and tested for 42 neuropsychological outcomes, then the medical records were examined for history of exposure to mercury from thimerosal. Prenatal mercury exposure from thimerosal was associated with better performance on one measure of language and poor performance on one measure of attention and executive functioning. Exposure in infancy up to seven months old was associated with better performance in one measure, fine motor coordination, and on one measure of attention and executive functioning. Increasing mercury exposure from birth to 28 days was associated with poorer performance on one measure of speech articulation and better performance on one measure of fine motor coordination. The authors conclude that they could not find a causal association between early exposure to mercury from thimerosal and deficits in neuropsychological functioning at age 7 to 10 years (*NEJM* 2007; 357: 1281-1292).

FDA Actions

Eli Lilly has received approval from the FDA to market raloxifene (Evista) for the indication of reducing the risk of breast cancer in postmenopausal women with osteoporosis and postmenopausal women who are at high risk for invasive breast cancer. Raloxifene is a selective estrogen receptor modulator (SERM) that is already approved for prevention and treatment of osteoporosis in postmenopausal women. The drug was recently required to add labeling regarding an increased risk of fatal strokes in women taking the drug. It also carries a black box warning regarding risk of thromboembolism in women who are at high risk (those with an active or past history or thromboembolism).

Just in time for the winter flu season, the FDA has approved nasal influenza vaccine (FluMist) for use in children between the ages of 2 and 5. Previously the vaccine was only approved for children 5 years old and older and adults up to age 49. The CDC is recommending all children between the ages of 6 months to 59 months receive a flu vaccine. Children ages 2-8 who have never received a flu vaccine will initially require two doses of fluMist at least one month apart.

The FDA has approved a new oral granules form of terbinafine for the treatment of tinea capitis (ringworm) in children. The preparation may be sprinkled on food, allowing easier administration to children who may not otherwise take medicine over the two weeks required to treat tinea. Terbinafine granules are indicated for the treatment of tinea capitis in children age 4 years and older. It is marketed by Novartis AG as Lamisil Oral Granules. ■