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A monthly update of developments in female reproductive medicine

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Benefits of Group B Strep Prophylaxis

ABSTRACT & COMMENTARY

Source: Locksmith GJ, et al. *Am J Obstet Gynecol* 1999;180:416-422.

To determine the efficacy of group b streptococcal (GBS) prevention strategies to reduce the rates of maternal and neonatal infection, Locksmith and colleagues compared outcomes resulting from the use of three different protocols between August 1, 1991, and April 30, 1998. During the first two years of the study, GBS cultures were obtained only when patients were admitted with preterm premature rupture of the membranes (PPROM) or preterm labor, and intrapartum treatment was given when the patient had a recognized risk factor for early onset of GBS infection and a positive culture result. During the next three years, the American College of Obstetricians and Gynecologists (ACOG) protocol was adopted with intrapartum antibiotics offered to women whose colonization status was unknown but who had risk factors including delivery before 37 weeks gestation, PPRM, membrane rupture greater than 18 hours, maternal fever indicating chorioamnionitis, and a previous infant with GBS infection. In the last two years of the study, the Centers for Disease Control and Prevention (CDC) protocol was followed, with cultures performed on all patients between 35-37 weeks gestation and antibiotics administered to all of those with a positive culture. If the colonization status was not known, antibiotics were given on the basis of risk factors. In the past, patients with an infant affected by GBS disease or GBS bacteriuria were uniformly treated. During the first year of the study, patients with PPRM who were managed expectantly received intravenous ampicillin followed by oral amoxicillin until culture results were known. Thereafter, they were given intravenous ticarcillin and clavulanic acid followed by amoxicillin.

The universal screening protocol recommended by the CDC significantly reduced the rates of clinical chorioamnionitis and postpartum endometritis when compared to the selective screening and ACOG protocols. While there was a trend toward a reduced rate of neonatal infection with the ACOG and CDC protocols, this difference was not statistically significant. The ACOG protocol did signif-

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icantly lower the rate of neonatal GBS infection in infants delivered to mothers with risk factors (selective screening 7.20/1000, ACOG protocol 2.15/1000, CDC protocol 3.13/1000). Most of the neonatal GBS infections in patients managed with these protocols occurred as a result of protocol failures; that is, the patient was not a candidate for prophylaxis or was given antibiotics but an infection still developed.

Locksmith et al conclude that universal screening for GBS infection prevention significantly reduced the rates of clinical chorioamnionitis and endometritis and may decrease neonatal GBS infection as well. However, the size of the study population was not sufficient to demonstrate this difference.

■ **COMMENT BY STEVEN G. GABBE, MD**

GBS infection is an important cause of neonatal morbidity and mortality. The rate of neonatal GBS infection in the United States each year is nearly 2/1000 or approximately 10,000 cases of neonatal GBS septicemia. The mortality associated with GBS infection is 5% in term infants and rises to 25% in preterm infants. Intrapartum chemoprophylaxis with intravenous penicillin G (5 million U initially and then 2.5 million U every 4 hours until delivery) or intravenous ampicillin (2 g loading dose followed by 1 g every 4 hours until delivery) significantly reduces neonatal colonization and bacteremia. In this ret-

rospective study by Locksmith et al, the experience with three different protocols used over seven years is presented. It has been estimated that an investigation of 110,000 women would be required to demonstrate a significant difference in neonatal outcome. In the present investigation, a little more than 20,000 women were studied. While significant differences in the neonatal GBS attack rates were not seen, the ACOG and CDC protocols did demonstrate greater efficacy, particularly when patients with risk factors were managed with the ACOG protocol. GBS is also an important cause of chorioamnionitis and endometritis, and Locksmith et al have shown a significant reduction in the rates of these complications with universal screening.

While this study does have some problems—patient management is likely to change over seven years—different culture techniques were used during the study, and the overall rate of positive cultures was not reported. This investigation provides a “real life” overview of the application of the recommended protocols for the prevention of GBS infection. However, despite the best efforts of the clinicians, there were protocol failures. Which strategy should be adopted? It would appear reasonable for the clinician to choose either the CDC protocol based upon cultures at 35-37 weeks or the ACOG protocol based on clinical risk factors. ❖

OB/GYN Clinical Alert, ISSN 0743-8354, is published monthly by American Health Consultants, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

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Registration Number: R128870672.

Periodical postage paid at Atlanta, GA.

POSTMASTER: Send address changes to **OB/GYN Clinical Alert**, P.O. Box 740059, Atlanta, GA 30374.

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Back issues: \$17. One to nine additional copies, \$100 each; 10 or more additional copies, \$60 each. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

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The Interpregnancy Interval Revisited

ABSTRACT & COMMENTARY

Synopsis: *Interpregnancy intervals less than six months or greater than 120 months are associated with increased risks of low birth weight, preterm birth, and neonates who are small for gestational age.*

Source: Zhu BP, et al. *N Engl J Med* 1999;340: 589-594.

Relatively little is known about how the interpregnancy interval affects perinatal outcomes. Zhu and colleagues examined vital statistics data in Utah, where the average parity is high and confounding risk factors, such as substance abuse, are less prevalent. Zhu et al looked at 173,205 live births between 1989 and 1996 to evaluate three adverse outcomes: low birth weight, preterm birth, and small size for gestational age (SGA), comparing these with the interpregnancy level. They attempted to control for numerous potential

confounders: maternal age, height, weight, number of prenatal visits, race, education, substance abuse, and other factors.

As expected, risks of low birth weight, preterm birth, and SGA birth were high when the interpregnancy interval was less than three months. With intervals less than six months, there was a 40% increased risk of low birth weight (95% CI, 1.3-1.6), a 40% increased risk of preterm birth (95% CI, 1.3-1.5), and a 30% increased risk of SGA delivery (95% CI, 1.2-1.4). The risks dropped off rapidly with an increasing interpregnancy interval. The lowest risks correlated with an interval of 1.5-2 years.

When the interpregnancy interval exceeded two years, risks slowly began to rise again. After a 10-year interval, there was a doubled risk of low birth weight (95% CI, 1.7-2.4), a 50% increase in preterm birth (95% CI, 1.3-1.7), and an 80% increase in SGA births (95% CI, 1.6-2.0). Both short and long interpregnancy intervals persisted as independent perinatal risk factors after controlling for confounders.

■ COMMENT BY ELIZABETH MORRISON, MD, MSED

With periconception care prominently featured in the draft objectives of the Health People 2010 initiative,¹ researchers are paying more attention to birth spacing and related issues. Few recent studies have shed light on the relationship between the interpregnancy interval and pregnancy outcomes. This study provides intriguing information that can help us counsel parents as they plan to expand their families.

As we would expect, short interpregnancy intervals correlate with adverse perinatal outcomes, though not any more strongly than primiparity does. This relationship has been attributed to a postpartum “maternal depletion syndrome.” The more surprising finding was that longer interpregnancy intervals are associated with adverse outcomes, which, in some cases, may exceed the risks of short intervals. It is not clear what causes this relationship. Zhu et al hypothesize that beneficial maternal physiologic characteristics may gradually revert back to the primigravid state after a previous gestation, or that unmeasured confounders may lead both to long interpregnancy levels and to adverse birth outcomes. A limitation in the study is its fairly low representation of nonwhite mothers, whose interpregnancy intervals may affect outcomes differently.

In any case, the discovery by Zhu et al of a J-shaped association between interpregnancy interval and perinatal outcomes provides useful information for clinicians providing periconception care. The American College of Obstetricians and Gynecologists (ACOG) recommends

that we discuss birth spacing when we provide preconception counseling.² As we discuss parents’ desires for family planning, we can now offer families more conclusive information about the optimal interpregnancy interval. ❖

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Isoflavones from Red Clover Improve Systemic Arterial Compliance but not Plasma Lipids in Menopausal Women

ABSTRACT & COMMENTARY

Synopsis: Arterial compliance improved in menopausal women who ingested isoflavones derived from red clover. The effect size was comparable to that seen in hormone replacement therapy.

Source: Nestel PJ, et al. *J Clin Endocrinol Metab* 1999;84:895-898.

Isoflavones (phytoestrogens) are found in many legumes, including soy. They have been credited with conferring cardioprotection. For example, epidemiological studies suggested the reason Japanese women living in Japan had less cardiovascular disease than Japanese women living in the United States was due to consumption of a diet high in legumes and, therefore, isoflavones. Nestel and associates have performed several studies looking at modification of arterial compliance in postmenopausal women by weight loss, diet, hormone replacement therapy, and soy-derived isoflavones. The present study extended their previous work by examining isoflavones derived from red clover. Specifically, red clover contains genistein, diadzein, and their methylated precursors biochanin A and formononetin. (Soy contains genistein and diadzein.) Twenty-six women began the trial and 13 completed all aspects of the active intervention. Most of the drop-outs were menopausal women who quit their hormone replacement regimen to enroll and then could not tolerate the ensuing hot flashes. Subjects were postmenopausal women younger than 70

years of age who were not currently taking hormones or who had discontinued hormones at least four weeks before the study began. The study involved a three-week observation and dietary training interval followed serially by five weeks of placebo, five weeks of 80 mg of red clover-derived isoflavones, and five weeks of a 160 mg daily dose of isoflavones. Arterial compliance was measured by ultrasound at the end of each treatment window. Decreased arterial compliance is an important risk factor for cardiovascular disease because it leads to systolic hypertension and increased left ventricular work. Compliance was unchanged after placebo and increased after five weeks of either dose of isoflavones. Blood pressure and lipids did not change throughout the study.

■ COMMENT BY SARAH L. BERGA, MD

This study is a good example of what needs to be done to determine the effects of various food supplements now being “hawked” to the American public. In this study, isoflavones derived from red clover had a similar effect upon arterial compliance as did isoflavones derived from soy or flax. Notably, estrogen replacement therapy also had a similar effect upon arterial compliance as did isoflavones. Nestel et al interpret the relatively short response time as evidence for endothelial-related arterial relaxation.

A logical question that one might ask after reading this report is whether isoflavones might be recommended as a substitute for hormone replacement therapy. One needs to keep in mind that the present study only looked at a few cardiovascular end points, so it would not allow one to adequately determine if isoflavones were a substitute for hormones for cardioprotection. Further, based on this report, nothing can be said about the effects of isoflavones upon other tissues and age-related disorders. Thus, it is premature to recommend isoflavones as substitutes for hormones.

This brings me to the next point. Nestel et al should study the effects of isoflavones and estrogens together to see if there is synergism. The rationale for such a study includes the observation that many women were unable to complete the study because of vasomotor symptoms. Clearly, isoflavones will not be a panacea for the spectrum of symptoms linked temporally to menopause. Although isoflavones are referred to as phytoestrogens, they are primarily antioxidants and they do not have the same range of effects upon the brain as do estrogens, which are also antioxidants. The two together might be far better than either one alone. Synergism of this type is the rule rather than the exception. I raise this point because the choice facing patients regarding the use of dietary supplements is often framed as an either/or sce-

nario. The either/or approach is likely to be short-sighted and I recommend abandoning such a simplistic line of reasoning. It reminds me of the old question about whether calcium and exercise could substitute for estrogen use for protection against osteoporosis. We now know that there is synergism between exercise, calcium and vitamin D intake, and estrogen use in bone maintenance. Performing all of these interventions is far better than any one of them alone. I predict we will find similar synergism between estrogens and isoflavones in cardiovascular protection and possibly in protection from dementia. ❖

Concurrent Cisplatin-Based Radiotherapy and Chemotherapy for Locally Advanced Cervical Cancer

ABSTRACT & COMMENTARY

Synopsis: *Regimens of radiotherapy and chemotherapy that contain cisplatin improve the rates of survival and progression-free survival among women with locally advanced cervical cancer.*

Source: Rose PG, et al. *N Engl J Med* 1999;340:1144-1153.

Rose and associates performed a randomized trial of radiotherapy in combination with three concurrent chemotherapy regimens: cisplatin alone; cisplatin, fluorouracil, and hydroxyurea; and hydroxyurea alone in patients with locally advanced cervical cancer. Women with primary untreated invasive squamous cell carcinoma, adenosquamous carcinoma, or adenocarcinoma of the cervix of stage IIB, III, or IVA without involvement of the para-aortic lymph nodes, were enrolled. All patients received external beam radiotherapy according to a strict protocol. Patients were randomly assigned to receive one of three chemotherapy regimens: cisplatin alone on a weekly basis for six weeks; cisplatin on day 1 and 29, followed by fluorouracil for 96 hours starting on days 1 and 29, and oral hydroxyurea twice weekly for six weeks; or oral hydroxyurea twice weekly for six weeks. The study included 526 women. The median duration of follow-up was 35 months. Both groups that received cisplatin had a higher rate of progression-free survival

than the group that received hydroxyurea alone ($P < 0.001$ for both comparisons). The relative risks of progression of disease or death were 0.57 in group 1 and 0.55 in group 2, as compared with group 3. The overall survival rate was significantly higher in groups 1 and 2 than in group 3, with relative risks of death of 0.61 and 0.58, respectively. Rose et al conclude that regimens of radiotherapy and chemotherapy that contain cisplatin improve the rates of survival and progression-free survival among women with locally advanced cervical cancer.

■ COMMENT BY DAVID M. GERSHENSON, MD

Approximately 14,000 new cases of invasive cervical cancer are annually diagnosed in the United States. However, cervical cancer represents one of the most common cancers among females worldwide, particularly in developing countries. In 1996, the National Institutes of Health (NIH) Consensus Conference Statement on Cervical Cancer concluded that “there is no evidence that hydroxyurea or any other concomitant agent should be incorporated into standard practice.” Since 1996, information from five phase III randomized trials has become available. The totality of these data represents the most dramatic advance in the treatment of cervical cancer in the past 40 years. In fact, the emergence of this information prompted the National Cancer Institute to issue a Clinical Announcement in February 1999—two months prior to publication of three of these articles in the *New England Journal of Medicine*.

The RTOG study findings demonstrated that concurrent radiation and chemotherapy with cisplatin and 5FU leads to improved survival in women with stages IB or IIA (bulky or with positive pelvic lymph nodes), IIB, III, and IVA cervical cancer. This treatment was compared to extended field radiation, which covered the pelvis and para-aortic lymph nodes. In the combined therapy arm, there was a significant reduction in both distant and locoregional recurrences.

Based on early studies from Roswell Park Cancer Center showing promising results with hydroxyurea in the treatment of cervical cancer, over the past several years the Gynecologic Oncology Group (GOG) has invested a tremendous amount of resources and energy in studying the activity of this drug on cervical cancer. The GOG presented here demonstrated improved survival associated with concurrent radiation and chemotherapy with either weekly cisplatin or the combination of cisplatin and 5FU; both regimens were superior to radiation plus hydroxyurea. The results of this study have finally put hydroxyurea on the shelf.

A third article accompanied these two important

studies in the April 15, 1999 issue of the *New England Journal of Medicine*.¹ In this phase III trial, patients with bulky (greater than 4 cm) stage IB cervical cancer with negative lymph nodes were randomized to one of two arms: 1) pelvic radiation and intracavitary radiation with weekly cisplatin followed by extrafascial hysterectomy; or 2) pelvic radiation and intracavitary radiation followed by extrafascial hysterectomy. The survival rate for women who received weekly cisplatin as part of their treatment was superior—83% vs. 74%; this difference in survival was statistically significant.

Two other as yet unpublished studies were included in the National Cancer Institute (NCI) Clinical Announcement. In yet another GOG study in which patient accrual was completed in 1990, patients with locally advanced cervical cancer (stages IIB, III, and IVA without positive para-aortic nodes) were randomized to receive one of two treatments: 1) pelvic and intracavitary radiation plus chemotherapy with cisplatin and 5FU; or 2) pelvic and intracavitary radiation plus chemotherapy with hydroxyurea. Patients who received the chemotherapy combination of cisplatin and 5FU had a statistically significant improvement in survival—67% vs. 57%. In a study of the Southwest Oncology Group (SWOG), which was recently presented at the annual meeting of the Society of Gynecologic Oncologists, patients with stages IA2, IB, and IIA cervical cancer found to have metastatic disease in the pelvic lymph nodes, positive parametrial involvement, or positive surgical margins at time of radical hysterectomy and bilateral pelvic lymphadenectomy were randomized to one of two treatments: 1) pelvic radiation plus the combination of cisplatin and 5FU; or 2) radiation alone. The women who received the combination of radiation and chemotherapy had a statistically significant improvement in three-year survival—87% vs. 77%.

The findings of these studies indicate that platinum-based chemotherapy should be added to radiation for women with locally advanced cervical cancer or for women who are found to have specific unfavorable histopathological factors at the time of radical hysterectomy. Future studies will undoubtedly refine our knowledge and attempt to define the optimal chemotherapy regimen. Every obstetrician-gynecologist should be aware of this dramatic change in the standard treatment of a large proportion of women with invasive cervical cancer. ❖

Reference

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Fetal Solvent Syndrome

ABSTRACT & COMMENTARY

Synopsis: *A study concludes that occupational exposure to organic solvents during pregnancy is associated with an increased risk of major fetal malformations, especially in women who are symptomatic. Such exposure to organic solvents should be minimized during pregnancy.*

Source: Khattak S, et al. *JAMA* 1999;281:1106-1109.

To determine pregnancy and fetal outcome associated with maternal occupational exposure to organic solvents, Khattak and associates conducted a prospective, observational, controlled study of 125 women exposed to organic solvents and 125 control subjects matched for age, gravidity, and smoking and drinking status. The exposed women were factory workers, laboratory technicians, artists, and printing industry workers. The organic solvents to which they were exposed included aliphatic acid and aromatic hydrocarbons, phenols, trichloroethylene, xylene, vinyl chloride, acetone, and other related compounds. Thirteen major malformations were observed in the exposed women and only one in the control population. The malformations involved a wide range of organ systems including the heart and central nervous system. Women who were symptomatic from their exposure, including irritation of the eyes or respiratory system, breathing difficulties, and headache, delivered 12 of the 13 malformed infants. Those who were exposed for seven or more months were likely to have fetal distress in labor. While their infants had birth weights that were nearly 400 g lower, low birth weight was not increased. Review of past obstetric history revealed a higher rate of prior miscarriages in the exposed population.

Khattak et al conclude that occupational exposure to organic solvents during pregnancy is associated with an increased risk of major fetal malformations, especially in women who are symptomatic. Such exposure to organic solvents should be minimized during pregnancy.

■ COMMENT BY STEVEN G. GABBE, MD

This prospective investigation, the first to examine fetal malformations associated with organic solvents, supports earlier retrospective studies. Most of the women worked in factories or as laboratory technicians. They were exposed to a wide variety of organic solvents, perhaps explaining the wide range of malformations seen. The timing and extent of the exposure are also

important factors.

Women considering a pregnancy should be asked about occupational hazards including exposures to dangerous chemicals at home. Clearly, close and continuous exposure to organic solvents should be avoided. ❖

Special Feature

Imaging of the Sella Turcica

By Leon Speroff, MD

Over the years, the screening approach I have recommended for patients with galactorrhea and amenorrhea is the combination of a prolactin level and the lateral coned-down view of the sella turcica. With the availability of more sophisticated (and more expensive) imaging techniques, the coned-down view of the sella turcica fell out of favor with radiologists. In some areas, it is even difficult to find a radiologist who is experienced in reading the lateral coned-down view. Modern endocrinologists have supported this movement away from the coned-down view, citing the greater accuracy of the more modern techniques. Let me make an argument for the continued use of the coned-down view, and for some of you, a return to the coned-down view.

There has been growing conservatism in the management of small pituitary tumors because of an appreciation that the majority of these tumors never change.¹⁻³ I recommend a conservative approach of close surveillance, advocating dopamine agonist treatment for those prolactin-secreting tumors that display rapid growth or for those tumors that are already large, and reserving surgery only for those tumors that are unresponsive to medical therapy. This means that small tumors (microadenomas that are < 10 mm in diameter) need not be treated at all. Hence, the initial x-ray evaluation for amenorrheic patients with or without galactorrhea can be the coned-down lateral view of the sella turcica. This will detect the presence of a large tumor, although an incredibly rare suprasellar extension might escape this method. The coned-down lateral view of the sella is also a good screen for other lesions, such as a craniopharyngioma. Combining this screening technique with the prolactin assay, we are able to select those few patients who require more sensitive sellar imaging.

For the greatest accuracy, the diagnostic modality

of choice is either thin-section coronal computed tomography (CT scan) with intravenous contrast enhancement or magnetic resonance imaging (MRI) with gadolinium enhancement. CT scanning (capable of high-resolution 1.5 mm cuts) is able to evaluate the contents of the sella turcica as well as the suprasellar area; however, total accuracy is not achieved.⁴ MRI is even more sensitive than the CT scan, but it is also more expensive and it requires a lengthy period of time to obtain the images. MRI provides highly accurate assessments without biologic hazard, and it is better for evaluation of extrasellar extensions and the empty sella turcica.⁵ Most neuroradiologists and neurosurgeons prefer MRI, as do I. My intention, however, is to be conscious of cost and to isolate those few patients who require sophisticated but expensive imaging.

If the prolactin level is greater than 100 ng/mL or if the coned-down view of the sella turcica is abnormal, I recommend CT scan evaluation or MRI. A double floor of the sella is often seen on the coned-down view and, in the absence of enlargement and/or demineralization, is interpreted as a normal variation rather than asymmetrical depression of the sellar floor by a tumor. The presence of visual problems and/or headaches should also encourage CT scan or MRI evaluation. Headaches are definitely correlated with the presence of a pituitary adenoma.⁶ Although they are usually bifrontal, retro-orbital, or bitemporal, no locations or features are specific for pituitary tumors.

The prolactin level of 100 ng/mL for determining a more aggressive approach has been empirically chosen. Both in my own experience and that of others, large tumors are most frequently associated with prolactin levels greater than 100 ng/mL. Large masses associated with prolactin levels less than 100 ng/mL are more likely to be tumors other than prolactin-secreting adenomas, causing stalk compression and interruption of the normal dopamine regulation of pro-

lactin secretion. These tumors will be associated with abnormal changes present in the coned-down view of the sella turcica.

If imaging rules out an empty sella syndrome or a suprasellar problem, treatment is dictated by the patient's desires, the size of the tumor, and the rapidity of growth of the tumor. The above approach to the problem of pituitary tumors implies that patients with prolactin levels less than 100 ng/mL and with normal coned-down views of the sella turcica can be offered a choice between treatment and surveillance. An annual prolactin level and a periodic coned-down view (at first annually and then at increasing intervals) are indicated for continued observation to detect an emerging and slow-growing tumor. Dopamine agonist therapy is recommended for patients wishing to achieve pregnancy and for those patients who have galactorrhea to the point of discomfort. Thus far, long-term therapy with a dopamine agonist has not been proven to be successful in producing a complete reversal of the problem (with either permanent suppression of elevated prolactin levels or elimination of small tumors). Thus, a strong argument can be made for a "need not to know" the presence of a pituitary microadenoma. If treatment and management are not changed, it is not necessary to document the presence of a microadenoma.

Reasons why the diagnosis of microadenoma is not necessary include:

- Microadenomas are common.
- Microadenomas rarely grow during pregnancy.
- Microadenomas rarely progress to a macroadenoma (≥ 10 mm in diameter)
- There is a significant recurrence rate after surgery.
- The natural course is unaffected by dopamine agonist treatment.
- There is no contraindication to hormone therapy or oral contraception.
- It is better to avoid the problem of the pituitary incidentaloma.

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Contemporary reviews point out the shortcomings of the coned-down view of the sella turcica, citing the limitation of excluding only macroadenomas.⁷ Indeed, reviews of my textbook have faulted the chapter on amenorrhea for being less than state-of-the-art, emphasizing that where I use the coned-down view, MRI should be uniformly obtained. I would argue that the state-of-the-art approach is to use the MRI when necessary (to avoid the compulsion to document the presence of a microadenoma for the reasons stated above) to be cost-effective. This takes strength of conviction when your radiologist reports that a coned-down view of the sella turcica is not sufficient. ❖

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CME Questions

25. In the study by Locksmith et al universal screening and intrapartum chemoprophylaxis to prevent neonatal GBS infection was associated with a reduction in which of the following?
- Neonatal pneumonia
 - Wound infection
 - Chorioamnionitis
 - Neonatal meningitis
 - Neonatal bacteremia
26. When the interpregnancy interval is less than six months, risks of low birth weight and preterm birth increases by:
- 5%.
 - 20%.
 - 40%.
 - 70%.
27. Which of the following statements is false?
- Phytoestrogens derived from soy, flax, and red clover have comparable effects upon arterial compliance when administered to menopausal women.
 - The degree to which phytoestrogen use benefits a given menopausal woman can be monitored by longitudinally following lipoprotein profiles.
 - Phytoestrogen use has not been shown to be a substitute for

- hormone replacement therapy in menopausal women.
- Two common phytoestrogens are genistein and diadzein.
- The phytoestrogens that are isoflavones are best thought of as antioxidants.

28. In the investigation by Khattak et al, women exposed to organic solvents were at an increased risk for which of the following?

- Birth weight of less than 2500 g
- Major fetal malformations
- Preterm birth
- Placental abruption
- Pre-eclampsia

29. The following are true regarding imaging of the sella turcica except:

- Pituitary microadenomas are usually not apparent on lateral coned-down views of the sella turcica.
- The purpose of the lateral coned-down view of the sella turcica is to detect the presence of a macroadenoma.
- CT scanning of the sella turcica is more accurate than MRI.
- Large prolactin-secreting pituitary tumors usually are associated with blood prolactin levels of more than 100 ng/mL.

Correction

An error appeared in the April 1999 issue of *OB/GYN Clinical Alert*. On page 92 in Dr. Berga's abstract and commentary, the headline should have read: "Estrogen Supplementation Attenuates Glucocorticoid and Catecholamine Responses to Mental Stress in Perimenopausal Women." We regret any confusion this may have caused. ❖

Readers are Invited . . .

Readers are invited to submit questions or comments on material seen in or relevant to *OB/GYN Clinical Alert*. Send your questions to: Holland Johnson—Reader Questions, *OB/GYN Clinical Alert*, c/o American Health Consultants, P.O. Box 740059, Atlanta, GA 30374. Or, you can reach the editors and customer service personnel for *OB/GYN Clinical Alert* via the Internet by sending e-mail to holland.johnson@medec.com. You can also visit our home page at <http://www.ahcpub.com>. We look forward to hearing from you. ❖

In Future Issues:

Dietary Intake of Fat and Fatty Acids and the Risk of Breast Cancer