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Early Feeding and the Incidence of Gastrointestinal Symptoms After Major Gynecologic Surgery

ABSTRACT & COMMENTARY

Macmillan and associates have reported the findings of a study in which they compared early feeding with traditional postoperative dietary management for development of postoperative gastrointestinal symptoms after major gynecologic surgery for benign conditions. Women were randomly allocated to early feeding of low residue diets six hours postoperatively or traditional dietary management of clear liquids with normal bowel sounds, and regular diet with passage of flatus. Demographic data were collected, and women answered questionnaires on their perception of bowel function and pain. Complete data were available for 139 women—67 allocated to the early feeding group and 72 to the late feeding group. The incidence of postoperative ileus for the study population was 4.4% and did not differ between groups (early 3% vs late 5.8%; $P = 0.68$). There were no differences in patient demographics, surgical procedures, anesthesia used, and intraoperative complications between groups. With the exception of more complaints of nausea in the late feeding group (23% vs 13%; $P = 0.04$), there were no differences in other postoperative complications, pain medicine, requirements, fluid and caloric intake, median pain scores, and gastrointestinal function. The low incidence of perioperative complications made the power to detect differences between groups low. MacMillan et al concluded that low residue diet six hours after major gynecologic surgery for benign indications was not associated with increased postoperative gastrointestinal complaints, including ileus. (MacMillan SLM, et al. *Obstet Gynecol* 2000;96:604-608).

COMMENT BY DAVID M. GERSHENSON, MD

This study confirms other recent studies of patients who undergo major abdominal surgeries: early feeding is consistently not associated with an increased incidence of gastrointestinal problems, including ileus. The findings of these studies shatter

Volume 17 • Number 8 • December 2000 • Pages 57-64

INSIDE

Ovarian cancer risk in relation to oral contraceptives **page 58**

Pregnancy outcome after genetic amniocentesis complicated by ruptured membranes **page 59**

Oral contraceptives and the risk of breast cancer **page 60**

Treatment of GDM with oral hypoglycemic drugs **page 61**

time-honored practices of withholding feeding until the patient has active bowel sounds or passes flatus. We must overlook the fact that the impetus for several of these studies was the pressure for early discharge exerted by HMOs (and based on no prospective data). In fact, for many major abdominal procedures, including oncologic surgeries, shorter hospital stays have been proven to be safe and cost-effective. It should be pointed out that, for purposes of this study, patients with histories of malignancy, inflammatory bowel disease or obstruction, or those with current or past surgeries that involved extensive lysis of adhesions of the bowel were excluded. The incidence of ileus was 4.4% in this study, with an incidence of severe ileus of 0.7%. That fits with my experience in gynecologic oncology patients. For patients who do develop postoperative ileus, management should initially include supportive care consisting of no oral intake, intravenous hydration, and antiemetics. Radiologic studies should be used as needed. If the patient has vomiting despite these measures, a nasogastric tube should be placed. ❖

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Ovarian Cancer Risk in Relation to Estrogen/Progestin Dose and Use Characteristics of Oral Contraceptives

ABSTRACT & COMMENTARY

Synopsis: *Use of lower dose oral contraceptives formulations afforded the same protection against ovarian cancer as did higher dose preparations.*

Source: Ness RB, et al. *Am J Epidemiol* 2000;152: 233-241.

Oral contraceptive (oc) use has many benefits and some risks. In an effort to maximally minimize risks, the standard doses of ethinyl estradiol have been gradually decreased over the intervening decades. The customary dose now ranges from 20-35 µg daily rather than the 50-80 µg daily dose range used in the past. While this strategy has been associated with a decrement in some risks and nuisance side effects,[1] concern has been raised that the newer formulations may not afford the same protection against ovarian and endometrial cancers. The present study was undertaken to determine if the risk reduction for ovarian cancer was comparable with the use of lower dose OC preparations.

Ness and colleagues conducted a population-based, case-control investigation designed to determine the degree of risk reduction of ovarian cancer across generations of women. Cases were women 20-69 years of age who had been diagnosed with epithelial ovarian cancer within the six months prior to interview. There were a total of 767 cases in the final cohort. Controls aged 65 years or younger were ascertained by random digit dialing. Controls aged 65-69 years of age were ascertained through Health Care Financing Administration lists. There were 1367 controls. Standard 1.5-hour interviews were conducted by trained interviewers in the homes of participating women. Detailed demographic and reproductive information was obtained.

The risk of ovarian cancer was reduced approximately 40% for OC users overall, after adjusting for age, gravidity, family history of ovarian cancer, and race. There was no correlation between estrogen and progestin dose and risk reduction. Thus, the lower dose OC preparations yielded comparable odds ratios. Not unexpectedly, pregnancies and live births were associated with a reduced risk of ovarian cancer; most of the effect occurred with the first reproductive event. Com-

pared with white women, those in other racial groups were less likely to have ovarian cancer. Women who breastfed, particularly those who did so longer than 12 months, were somewhat less likely to develop ovarian cancer. Neither age at menarche nor age at menopause was associated with ovarian cancer risk, nor was body mass index. Women who initiated use at or about age 35 years were afforded the same protection. Very long-term use (≥ 10 years) was associated with an even greater risk reduction.

COMMENT BY SARAH L. BERGA, MD

The main mechanism by which OC use is thought to guard against the development of ovarian cancer is suppression of ovulation. Since lower dose preparations are generally as efficacious as higher dose preparations in this regard (when used as directed), it has been predicted that lower dose preparations would afford comparable protection against ovarian cancer. This study has provided the best evidence to date in support of this hypothesis. This is certainly good news. Not only do lower dose preparations have fewer of the nuisance side effects that lead women to discontinue oral contraceptives,[2] but they also reduce the risk of serious complications such as venous thromboembolic events.

This study raises again the question as to how low can we go with the steroid doses in oral contraceptives? To my mind, the ideal OC is one that suppresses ovulation reliably, produces amenorrhea, and provides sufficient estrogen for bone accretion, optimal brain function, maintenance of the urogenital tract, and promotion of cardiovascular health. At a recent meeting, it was suggested that the ideal OC should also not suppress or even enhance libido. While safety and contraceptive efficacy remain paramount, we must recognize that quality-of-life parameters gate satisfaction and, therefore, continued use. This study suggests that we should be able to redesign oral contraceptives to yield excellent safety profiles. Now we need to also focus our attention on the design of better instruments that capture the quality-of-life side of this equation, so that we can focus on those aspects and bleeding patterns.

The issue of lowering the estrogen dose may prove even more critical for that subset of women with BRCA mutations. It has been shown that oral contraceptives reduce the risk of ovarian cancer in this high-risk group.[3] While OC use does not appear to increase the risk of breast cancer in unselected women, there has been concern that their use may increase the risk of breast cancer in this particular group.[4] Therefore, it may well be especially advantageous in this clinical situation to minimize the overall dose. The key to doing so will undoubtedly involve tinkering with both the format and the composition of oral contraceptives. Hopefully, there will be a pharmaceutical house with sufficient interest in this difficult undertaking. ❖

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Pregnancy Outcome After Genetic Amniocentesis Complicated by Ruptured Membranes

ABSTRACT & COMMENTARY

Synopsis: *Pregnancies complicated by PPROM after genetic amniocentesis result in significantly better outcomes than pregnancies complicated by spontaneous PPROM.*

Source: Borgida AF, et al. *Am J Obstet Gynecol* 2000; 183:937-939.

To determine the perinatal outcome of pregnancies complicated by preterm premature rupture of the membranes (PPROM) after genetic amniocentesis, these researchers evaluated 11 women who presented within 48 hours after the procedure with PPROM. They compared this group to 11 women who presented with spontaneous PPROM at 17-18 weeks. Women with PPROM after amniocentesis had a significantly longer latency period, 124 days, as compared to women with spontaneous PPROM, 28 days, and delivered at a more advanced gestational age, 34.2 weeks vs. 21.6 weeks. Women were followed with weekly ultrasound examinations and an average of 24 days was required for normal amniotic fluid volume to be restored (range, 8-51 days). Only one perinatal loss occurred in the 11 women with PPROM after genetic amniocentesis, a fetal death associated with chorioamnionitis at 19 weeks, while there was only one surviving infant in the group of 11 women with spontaneous PPROM.

Borgida and colleagues concluded that pregnancies complicated by PPROM after genetic amniocentesis result in significantly better outcomes than pregnancies complicated by spontaneous PPROM.

COMMENT BY STEVEN G. GABBE, MD

Complications after genetic amniocentesis include PPROM, bleeding, infection, miscarriage, and fetal injury. Fortunately, these are extremely rare. Few studies have examined the likelihood of PPROM after genetic amniocentesis in a large population from a single institution. The observation by Borgida et al that only 1% of patients experience leaking of fluid after genetic amniocentesis confirms smaller studies and is reassuring. In this setting, patients are usually advised to maintain pelvic rest, monitor their temperature, and return for periodic ultrasound examinations. In this study, overall pregnancy outcome was excellent in women with PPROM after genetic amniocentesis. Most patients delivered near term, and there was only one perinatal loss. Not surprisingly, perinatal outcome in a control group of patients with spontaneous PPROM was poor, with only one surviving infant in 11 pregnancies. ❖

Oral Contraceptives and the Risk of Breast Cancer

ABSTRACT & COMMENTARY

Synopsis: *Old, no longer used, high-dose oral contraceptives may increase the risk of breast cancer in first-degree relatives of women who had breast cancer.*

Source: Grabrick DM, et al. *JAMA* 2000;284: 1791-1798.

Grabrick and associates from the mayo clinic conducted a follow-up study of the association between oral contraceptive (OC) use and the risk of breast cancer in a cohort of women with a family history of breast cancer. This is a study of families using a cohort first identified between 1944 and 1952 (The Minnesota Breast Cancer Family Study), studied again from 1991-1996, and now in this most recent follow-up, these families were reassessed by telephone interviews. From the original 544 families, a total of 426 families could be updated, yielding a total of 6150 women. In the 6150 women, 153 cases of breast cancer occurred in blood relatives and 86 in marry-ins. In the entire cohort, the relative risk of breast cancer associated with use of oral contraceptives was 1.4 (confidence interval [CI] = 1.0-2.0), not achieving statistical significance. Grabrick et al assessed the effect of inheritance by assessing the risk by relationships to the women initially identified with breast cancer from 1944 to 1952. Sisters and daughters who had ever used OCs had a relative risk of 3.3 (CI = 1.6-6.7) compared with sisters and daughters who were never users. This was not seen with granddaughters, nieces, or marry-ins. No differences were noted for duration of use or age at first use. Among 132 high-risk families (≥ 3 breast or ovarian cancers among blood relatives), even greater relative risks were observed, although the CI was wide because of small numbers. The increased risks were present only in relatives who used OCs prior to 1975, a period during which OCs contained high doses of estrogen (> 50 mg ethinyl estradiol) and progestin. These results remained after adjustments for breast cancer risk factors and for number of mammograms.

COMMENT BY SARAH L. BERGA, MD

This is yet another study attempting to understand who really is at risk for breast cancer if they use exogenous steroids. In this scenario, the exogenous hormones are OCs and the subjects are relatives of women who had breast cancer roughly 50 years ago. Although Grabrick et al chose an interesting approach, the data are nonetheless inconclusive. How, then, does one put this study into perspective? First, the study looked at the incidence of breast cancer, not death from breast cancer. The choice of this end point, however pragmatic, obviously limits the usefulness of the study. Second, Grabrick et al did not ascertain the doses in the OCs and, therefore, used year of use as a surrogate for dose. The customary dose prior to 1975 was 50 µg or more of ethinyl estradiol. No one prescribes this dose of OCs any longer, mostly because of the side effects and the higher risk of venous thromboembolic events. Thus, it is too soon to know if there is any excess risk of breast cancer in women with a family history of breast cancer if they use 20 µg oral contraceptives. Oddly, there was no increase in risk with extended duration of use. This may reflect the difficulty of finding a sample size large enough to allow such relationships to be addressed. There did seem to be a dose relationship, however, between genetic risk and ever use, suggesting that women with a very strong family history of breast cancer appear to more susceptible to agents that are safe to use in everyone else.

Most physicians would not find the above information overly alarming because most women do not have a strong family history of breast cancer. However, most patients would be upset, and many might be tempted to

stop using OCs as their method of birth control. Further, many women harbor fears that they are at excess risk of getting breast cancer, even if they do not have a strong family history. Reassurance sometimes helps in this context. But assuming that there is a kernel of truth in the above data set, the question facing the practicing physician is what to do for the women who truly does have a strong family history, especially the woman who has tested positive for BRCA1 or BRCA2. Should these women be counseled to not use oral contraceptives? Should they be counseled to do something else such as take tamoxifen premenopausally? Should they be offered a medical or surgical oophorectomy, prophylactic bilateral mastectomy, or both? In an era of managed cost, who decides? There are no good answers to these questions. The sad fact is that we have no clue as to what to recommend. All of the choices seem bad. Personally, I do not find the present study of sufficient strength that I would deny the use of very low-dose OCs to women with a family history of breast cancer. But I would also find it difficult to advocate for their use if the family history is compelling.

COMMENT BY LEON SPEROFF, MD

Grabrick et al state in their discussion that "our results suggest that the use of OCs in women with a strong family history of breast cancer may further elevate their breast cancer risk." However, what this study indicates is that high-dose OCs, no longer used, may increase the risk of breast cancer in women with family histories of breast cancer. To be sure, the numbers of users after 1975 were not large and the women were younger, having not experienced yet their entire lifelong risk of breast cancer. Nevertheless, the only positive result is limited to high-dose OCs.

I am especially disturbed by the discussion that refers to the previous study concluding that OC use reduces the risk of ovarian cancer in women with BRCA1 or BRCA2 mutations and argues that the current results indicate that these same women would be at higher risk of breast cancer with the use of OCs.[1] They further support this warning by referring to a study that suggested that OCs increase the risk of breast cancer in carriers of the BRCA mutations.[2] The BRCA ovarian cancer study was performed in women using current low-dose OCs; the current study found an increased risk only with old high-dose pills, not with current low-dose pills. The BRCA breast cancer study involved very small numbers and did not achieve statistical significance. Grabrick et al do not mention these important qualifications. This is yet another example of careless, selective reporting. Therefore, the advice that women with BRCA mutations should avoid low-dose OCs is unfounded and inappropriate, potentially depriving these women of an important benefit.

The conclusions of this study are derived from small numbers. The increased relative risk of 3.3 in sisters and daughters was based on a total of 13 ever users and 25 never users. The accompanying editorial[3] states that the data offer "strong support" for an increased effect in the presence of genetic risk, based upon an increasing relative risk when families had three to five or more members with breast or ovarian cancer. However, these conclusions were based upon 10 users and 16 never users (≥ 3 cancers) and six users and three never users (≥ 5 cancers). Although the conclusions were statistically significant, the confidence intervals were wide, 1.6-6.7 and 2.3-56.4, respectively. Thus, the conclusions are imprecise due to small numbers, hardly robust support as implied by the editorial.

Therefore, I am not convinced that this report is "bad news" for women with a family history of breast cancer, as the editorial suggests. The collaborative re-analysis of the world's data concluded that OC use does not further increase the risk of breast cancer with positive family histories of breast cancer.[4] I believe that low-dose OCs should continue to be offered as an appropriate choice for women with family histories of breast and ovarian cancers. ❖

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Treatment of GDM with Oral Hypoglycemic Drugs

ABSTRACT & COMMENTARY

Synopsis: *In women with gestational diabetes, glyburide is a clinically effective alternative to insulin therapy.*

Source: Langer O, et al. *N Engl J Med* 2000;343: 1134-1138.

To determine if glyburide, a second-generation sulfonylurea drug could be safely and effectively used to treat gestational diabetes mellitus (GDM), these researchers conducted a prospective, randomized trial, with 201 women

receiving glyburide and 203 insulin. All patients had failed diet therapy as evidenced by fasting glucose concentrations greater than 95 mg/dL or postprandial glucose levels greater than 120 mg/dL. Treatment was initiated at approximately 25 weeks gestation, and the average dose of glyburide was 9 mg/d with a maximum dose of 20 mg/d. Women receiving insulin took three injections with an average dose of 85 u/d.

Based on capillary glucose measurements performed seven times each day, all patients achieved excellent glucose control with an average glucose level of 105 mg/dL. No differences were noted in glycosylated hemoglobin levels. Hypoglycemia, defined as a glucose less than 40 mg/dL, occurred in only four women in the glyburide group but was noted in 41 women receiving insulin, a significant difference. Only eight women in the glyburide group (4%) failed to maintain good glucose control on the maximal dose of this drug, and they were switched to insulin. No differences were noted in perinatal outcome in the glyburide and insulin treatment groups, including large for gestational age infants, 12% vs. 13%, and birth weights greater than 4000 g, 7% vs. 4%, respectively. Cord blood insulin concentrations were similar in both groups, and glyburide was not detected in the cord blood of any infant.

Langer and colleagues concluded that, in women with gestational diabetes, glyburide is a clinically effective alternative to insulin therapy.

COMMENT BY STEVEN G. GABBE, MD

For decades, insulin has been the treatment of choice for women with GDM who fail diet therapy. Oral hypoglycemic agents were said to be contraindicated and understandably so. The first-generation sulfonylurea drugs crossed the placenta and stimulated the fetal pancreatic beta-cells producing hyperinsulinemia and excessive fetal growth. Furthermore, profound neonatal hypoglycemia was observed after delivery. In earlier studies, Langer et al demonstrated that glyburide was different. Using a perfused placental model, they found that glyburide did not cross the placenta and decided to try this therapy in women with GDM.[1] Excellent maternal glucose control was achieved, and maternal hypoglycemia was reduced when compared to women using insulin. Perinatal outcome was no different. We have begun to give glyburide to selected patients in our clinic, particularly in women who have difficulty counting and measuring an insulin dose. A word of caution is warranted. Other oral hypoglycemic agents should not be used until carefully performed studies comparable to this one have been conducted. ❖

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Special Feature

Screening for Domestic Violence: Who, What, When, Why, and How?

By Ellen L. Sakornbut, MD

The Scope of the Clinical Problem

Although the reported incidence of domestic violence varies, the literature indicates that violence issues are a common problem in women's health, as common (or more so) than other lifestyle and health problems that are a part of routine health screening. Despite this, domestic violence remains an area of silence between most patients and their physicians. A study of female patients in a Veterans' Administration ambulatory setting found 40% of women had experienced emotional or physical abuse by a partner and 7% were currently in abusive relationships, yet only 12% report being asked about violence by their physicians.[1] The majority of these women reported a willingness to talk about partner violence with their physician and an expectation that the physician would be an advocate.

Domestic violence is not confined to urban or low-income settings. Studies of women seen at family practice clinics in rural and medium-sized communities in the Midwest find a 34-39% lifetime rate of physical abuse, with 8-23% reporting abuse within the past year.[2,3] Although domestic violence may be more common in young women of low educational background, a relatively high rate (25%) of violence with the current partner has been found in an older population of women in a rural area.[4] Other identified risk factors are partner violence in the family of origin and substance abuse by the partner.[5] Domestic violence is a common finding in women treated for depression.[6]

Pregnancy health is affected by domestic violence. A study of women in public prenatal clinics found a 17% incidence of physical or sexual abuse during pregnancy; abused women were twice as likely as nonabused women to enter prenatal care in the third trimester.[7] Physical abuse during pregnancy has also been associated with poor outcomes such as preterm birth and placental abruption.

Acute injuries from domestic violence constitute from 15-35% of all emergency room visits by women. Up to 50% of all homicides in women are committed by a current or former partner. Many of these women have been seen in an emergency room setting within a year or

two prior to the homicide.[8]

Physician Awareness and Behavior

Domestic violence education has become a requirement in undergraduate and graduate, medical education (postgraduate in some states), but domestic violence screening is not a routine part of practice for most physicians providing primary care to women. The U.S. Preventive Services Task Force did not recommend universal screening on the basis of clear evidence of benefit.[9] A large study in California suggested that physicians routinely screen injured patients for intimate partner abuse, but that most do not screen during routine checkups, prenatal care, or new patient visits.[10] This study found no difference in screening by gender of physician or recent training in partner violence. A physician survey about factors affecting screening rates cited lack of physician education in screening (34%) as a deterrent. Other factors that may affect the behavior of physicians include a belief that domestic violence is not an issue in one's patients (46%), a lack of time to deal with abuse (39.2%), and frustration at not being able to help victims (34.2%). Physicians may mistakenly believe that domestic violence does not occur in patients of higher socioeconomic status, but a study of medical school students and faculty found that 17% of female faculty and students and 3% of male faculty and students have experienced partner violence during their adult life.[11]

Short-term physician behavior may be altered by education. An educational intervention for internal medicine residents resulted in significant increases of patients being asked about domestic violence.[12] Whether such an intervention will be effective in establishing a change in practice patterns is not clear. At the current time, there is no evidence that mandatory CME affects physician awareness and response to domestic violence. In one study of mandatory CME, the only positive predictor for likelihood of screening was the presence of a female physician in the practice.[13]

What do Patients Want?

The literature indicates that abused and nonabused women believe health care providers should screen for abuse. Less than 50% of victims have been screened by medical providers for partner violence.[14] Patients who have been abused believe that clinicians should ask more specific questions than women who have not experienced abuse.

Screening Methods

Structured screening methods may improve the detection rate of domestic violence. A study of pregnant women screened using a five-question Abuse Assessment Screen found significantly improved rates in detection of domestic violence as compared to standard interview at prenatal intake visits.[15]

A number of brief screening tools have been developed and validated in primary care settings. The HITS questionnaire is a four-item questionnaire that asks how frequently the patient was physically **H**urt, **I**nsulted, **T**hreatened with harm, and **S**creamed at by the partner.[16] Other brief screening tools include the single question "Have you been hit, slapped, kicked, or hurt during this pregnancy?"[17] The WAST (Women Abuse Screening Tool) uses an initial shortened form that asks two questions about how much tension is present in the relationship and how much difficulty is experienced in resolving conflict with the partner. Positive responses to these questions are followed by administration of the other six questions in this screening instrument.[18]

Structure of a Screening and Treatment Plan

Universal screening for domestic violence may be adopted, although no outcome data are available on the effect of screening. If a strategy of selective screening is used, multiple clinical problems, including depression, unexplained symptoms, injuries, delayed prenatal care, and other psychosocial red flags should prompt more thorough inquiry. A screening tool is likely to be helpful, used in the same way that the CAGE instrument has been used in screening for alcoholism. Clinicians and office personnel should develop routine signals for separating patients and their partners briefly to facilitate screening. The first step in dealing with partner violence is to create a safe environment where patients may tell their story.

A study of physicians working with abuse victims identified these key components of care: giving validating messages that identify abuse as abuse; acknowledging that abuse is not justified; labeling abuse as wrong; listening in a nonjudgmental way to the woman's story; and documenting the history and physical signs of abuse.[19] Patients benefit from referral to community resources; it is unlikely that an individual physician has as much to offer as a team approach. A small business card with important contact numbers should be provided to patients (and may be displayed discreetly in the women's bathroom). In settings where the physician treats both the woman and her partner, ethical and strategic considerations may make it advisable for the physician to refer the partner to another clinician. ❖

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CME Questions

23. Initial management of postoperative ileus should include all the following measures *except*:
a. no oral intake.
b. intravenous hydration.
c. placement of nasogastric tube.
d. antiemetics.
e. None of the above

24. Which of the following does *not* reduce the risk of ovarian cancer?
a. Pregnancy
b. Lactation
c. Ovulation suppression
d. Ovulation induction
e. Lower dose oral contraceptions containing 30-35 µg ethinyl estradiol

25. Which of the following statements are true regarding the association between oral contraceptive (OC) use and the risk of breast cancer?
a. OCs of any kind, taken for long durations, increase the risk of breast cancer.
b. High-dose OCs may increase the risk of breast cancer in daughters and sisters of women who have had breast cancer.
c. OCs do not increase the risk of breast cancer in granddaughters of women who have had breast cancer.
d. Detection/surveillance bias did not affect the conclusions based upon adjustment for number of mammograms.

26. Which of the following statements is *false*?
a. Women who use OCs have an increased risk of breast cancer.
b. The stronger the family history, the greater the risk of developing breast cancer.
c. The stronger the family history, the greater the risk of developing breast cancer from oral contraceptive use.
d. Use of OCs containing 20 mg of ethinyl estradiol reduces the long-term risk of breast cancer.
e. To determine if oral contraceptive use does increase the risk of breast cancer in predisposed women, one would need a very large sample size.

27. In the study by Langer et al, which of the following complications was more common in insulin-treated patients with GDM when compared to the glyburide-treated group?
a. Preeclampsia
b. Cesarean delivery
c. Hypoglycemia
d. Ketoacidosis
e. Weight gain

28. What is the likelihood of PPROM after genetic amniocentesis?
a. 1/1000
b. 1/100
c. 3/100
d. 5/100
e. 10/100

Readers are Invited. . .

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In Future Issues:

Psychosocial and Sexual Functioning in Women with Vulvodynia