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Neurologic Outcome in the Surviving Twin

ABSTRACT & COMMENTARY

Synopsis: *Studies using registries of this type are open to criticism. For example, while different-sexed twins are dizygotic, not all same-sexed twins are monozygotic. Nevertheless, this information will be important in counseling patients when one twin has died in utero, an event that complicated 2.4% of the more than 25,500 twin pregnancies in this registry.*

Source: Pharoah POD, Adi Y. *Lancet* 2000;355:1597-1602.

To determine the prevalence of cerebral palsy in the surviving co-twin of a fetus that had died in utero, these investigators performed a cohort study of all registered twin births in England and Wales between 1993 and 1995. A questionnaire was sent to the general practitioners of all surviving co-twins to determine if that child had a neurologic disability. Pharoah and Adi contrasted outcome in same-sex twins vs. different-sex twins to reflect the risks associated with monozygotic vs. dizogotic twins. Follow-up information was obtained for 241/353 surviving same-sexed twins (68%) and 102/146 surviving different-sexed twins (70%). Among same-sexed twins, the prevalence of cerebral palsy was 106/1000 and for cerebral impairment 114/1000. Cerebral impairment included language, hearing, and motor problems. The prevalence of cerebral palsy was significantly lower in different-sexed surviving twins, 29/1000 but the rate of impairment was not different, 118/1000.

Overall, the prevalence of cerebral palsy in the live-born co-twin of a fetus that has died in utero was 83/1000 infant survivors, a 40- fold increase over the background population prevalence for cere- bral palsy. Furthermore, the risk of serious neurologic morbidity was 20% for the surviving co-twin.

COMMENT BY STEVEN G. GABBE, MD

Twin gestations are well known to be associated with

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INSIDE

increased perinatal morbidity and mortality and, among twin gestations, monozygotic twins are at the highest risk. This cohort study by Pharoah and Adi reports a marked increase in both cerebral palsy and cerebral impairment in the surviving co-twin after the death of one twin in utero. The mechanism responsible for the increased neurologic morbidity is not clear. It has been suggested that emboli from the dead twin may cause cerebral infarction in the surviving twin or that hypotension in the surviving twin causes cerebral ischemia. If these mechanisms are responsible, as Pharoah and Adi point out, early intervention after the death of one twin is unlikely to prevent neurologic injury in the surviving co-twin.

Studies using registries of this type are open to criticism. For example, while different-sexed twins are dizygotic, not all same-sexed twins are monozygotic. Nevertheless, this information will be important in counseling patients when one twin has died in utero, an event that complicated 2.4% of the more than 25,500 twin pregnancies in this registry. ❖

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Comparing Endocervical Curettage and Endocervical Brush at Colposcopy

ABSTRACT & COMMENTARY

Source: Dunn TS, et al. *J Lower Genital Tract D* 2000;4:76-78.

Synopsis: *The endocervical brush can be used in place of the endocervical curettage to evaluate the endocervix.*

Evaluation of the endocervix is a routine part of the practice of colposcopy. In the past, either an endocervical curettage (ECC) or visualization of the entire transformation zone on the portio of the cervix were the most common methods to perform this evaluation. Several papers have now been published that have shown that the ECC has low sensitivity for the detection of disease in the canal (many "false negatives") and that the endocervical brush (ECB) misses far less disease. On the other hand, there are more "false positives" with the ECB.

In order to study which technique is superior, Dunn and colleagues reviewed the charts of 369 consecutive patients referred for colposcopic examination. All patients had an ECB sample taken before colposcopy and an ECC performed at the end of the procedure. Those 105 women who had cervical conization (either by scalpel or loop excision) served as the study sample.

The results of this review showed that the ECB was considerably more sensitive than the ECC for the detection of endocervical disease, but that the specificity was lower. The ECC missed 38% of the endocervical neoplasia that was present in the cone specimen while the ECB missed only 7%. These findings are similar to other studies.

COMMENT BY KENNETH L. NOLLER, MD

This is certainly not the first study to compare ECC to the brush. I have previously reviewed at least some of these articles and have written one editorial about them. Why then would I abstract yet another paper on the same subject?

The answer lies in the fact that, despite multiple articles showing that ECC misses more disease than the brush, the ECC remains a routine part of many colposcopic examinations. When I ask "Why?" the usual response is either, "That's the way I learned" or "I don't want to be sued."

Medicine is an ever-changing field. We must learn from the literature and change the way we do things. In my view, there is now ample evidence to state that the brush is superior to the ECC and the latter abandoned (with the possible exception of the evaluation of an AGUS smear). Likewise, the data are so convincing that I would worry more about being sued if I used a technique (ECC) that has been shown to miss up to 50% of the disease it is supposed to detect than using a technique (brush) that has been shown to be more sensitive. ❖

A Prospective Study of Diet Quality and Mortality in Women

ABSTRACT & COMMENTARY

Synopsis: *A dietary pattern characterized by consumption of foods recommended in current dietary guidelines is associated with decreased risk of mortality in women.*

Source: Kant AK, et al. *JAMA* 2000;283:2109-2115.

This study explores the effects of dietary patterns on health outcomes. The study population was 42,254 women between the ages of 35 and 74 who completed a 62-item food questionnaire between 1987-1989. The women were then followed until 1993-1995 as part of the Breast Cancer Detection and Demonstration Project (BCDDP) sponsored by the National Cancer Institute and the American Cancer Society. There were 2065 deaths. Dietary patterns were scored according to the extent to which they conformed to current dietary recommendations to eat a diverse diet containing fruits, vegetables, low-fat dairy products, lean meats, and whole grains. The diet scores were divided into quartiles. Those with the highest intake of recommended foods had a 30% lower risk of all-cause mortality. There was a nonlinear dose response curve, such that women with scores in the top two quartiles exhibited similar health benefits when contrasted with women with scores in the bottom quartile.

COMMENT BY SARAH L. BERGA, MD

In many ways, this study confirms what many would view as common sense. Any decent course in nutrition introduces many of the key concepts tested in this study. These key concepts include the recognition that whole foods contain many beneficial substances other than those currently identified as important nutrients and the notion that diversity in diet is the best bet if one wants to get enough of recognized and unrecognized micronutrients. Although one might be tempted to dismiss this report as confirming the obvious, there are many reasons why this study is important. First, the sample size is large and the study methods as described are exemplary. As Kant and associates note in the discussion, very few studies have examined the effects of dietary patterns upon health in women. Second, although it is often taken as an article of faith that a good diet promotes health, dietary counseling and nutritional science are often viewed as a lesser clinical art and a lesser science, respectively. For instance, nutritional counseling is often done by practitioners other than physicians, it is generally not reimbursed, and it is rarely given more than a cursory endorsement in the physician's office. Evidence such as that contained in this study is needed if nutritional science and nutritional counseling are to be sanctioned by the medical establishment and payors and introduced into the medical curriculum. Third, patients are prone to gross oversimplifications about what are important nutrients. This leads to the common practice of not eating well and making up for poor food choices with multivitamins and over-the-counter, unregulated "food supplements." Would that things were so easy. I have often wondered if anyone has ever thought about how pompous it is to believe that we can capture in a small pill all that nature has wrought over the eons. As Kant et al point out in the introduction, "complex diets consumed by free-living individuals do not consist of single nutrients or foods, but rather a combination of foods containing multiple nutrients." Based on this insight, current nutritional advice endorses what is commonly termed the "food first paradigm." Supplements are needed only when a nutrient cannot be obtained in sufficient quantities from eating a healthy diet. In general, nutrients are delivered to our bodies in a complex matrix, such as a fruit or vegetable. Therefore, it is difficult and perhaps not scientifically defensible to test the effect of adding a single nutrient to a diet. Nutrients do not come "alone" except when we manufacture them that way and often the reason we manufacture them is to be able to sell them for a profit. Many studies suggest that nutrients interact with one another, leading to synergism among the nutrients, in terms of effects on bodily functions. This is the most compelling rationale for studying dietary patterns rather than the effects of single, isolated nutrients.

People want simple answers. The answer here may seem simple, but in truth it is a complicated recommen-

dation. This study supports the common dictum that one should eat a diverse diet containing fruits, vegetables, whole grains, low-fat meat, and dairy products. This recommendation is simple only if you are not responsible for implementing it or teaching it. It is harder to implement if your nutritional IQ is low, if your budget is meager, or if you don't have much time and energy for shopping and cooking. To some extent, this describes most Americans. I understand that many or most public schools no longer require home economics, so much of what children will know about nutrition must come from their overloaded, harried parents. When one considers how bombarded we are with advertisements from those selling a quick food fix, it is not surprising that many succumb to poor nutritional habits. Kant et al suggest that having a good diet is, at least in part, also a proxy for other lifestyle variables, including not smoking, exercising, and education. Given these considerations, it is easy to see why a good diet may be a surrogate or marker for a set of interlinked behaviors having to do with health awareness and disciplined lifestyle practices. If the agent in this study were a pharmaceutical product conferring a 30% reduction in all-cause mortality, I have no doubt that many would readily endorse its use. Although the recommendation in this study is "simple," I doubt that it will be for most physicians to "prescribe" such a diet in an era of time constraints and productivity expectations. ❖

Diagnosis of Anal Sphincter Tears by Postpartum Endosonography to Predict Fecal Incontinence

ABSTRACT & COMMENTARY

Synopsis: *Sonography of the anal sphincter immediately following delivery can predict later fecal incontinence.*

Source: Faltin DL, et al. *Obstet Gynecol* 2000;95: 643-647.

Fecal incontinence following childbirth is not a rare condition. Postpartum sonography has shown that at least some of these cases are due to unrecognized tears of the sphincter at the time of delivery.

The purpose of this study was to determine whether sonography performed immediately postpartum in the delivery suite could detect rectal sphincter disruption that was undetected by the clinician.

Nulliparous women were recruited for this study. After delivery, eligible cases (vaginal delivery without clinical evidence of sphincter disruption) had sonography before perineal repair. The procedure was said to have been tolerated well by all participants. Three months following delivery, each woman received a mail questionnaire that was designed to determine whether fecal incontinence was a problem for the woman.

At the time of delivery, 42 women were found to have a disruption of part or all of the rectal sphincter that was undetected by the attending staff. On the questionnaire, 22 women reported some type of fecal incontinence. (For this study, flatus incontinence was considered to be a form of fecal incontinence.) This incontinence was associated with three independent variables: birth weight more than 3500 g; fecal incontinence during pregnancy; and occult sphincter tear detected by sonography. Questionnaires were returned from 41 of the 42 women with occult tears and 15 (37%) of them reported fecal incontinence. In this study, instrument delivery was not associated with fecal incontinence.

COMMENT BY KENNETH L. NOLLER, MD

Only within the last few years has there been great attention paid to asking women about fecal incontinence. While many practitioners were (are) at ease asking about urinary incontinence, many did not ask about flatus and stool loss. The large number of studies that are now being reported about this common problem have improved our knowledge, but we still need more research.

This article is interesting for several reasons. First, it is clear that we cannot always tell, clinically, if the sphincter has been disrupted. Can you imagine how hard the delivering physicians looked for tears in this study since they knew that sonography was going to be done as soon as they said there was no tear? In the past when rectal incontinence occurred when we had not seen a sphincter tear at delivery, we had no explanation for it. Now we know that at least in some cases we missed the defect.

Second, there must be other mechanisms for fecal incontinence besides sphincter tears. This article documented an intact sphincter in several women who later reported incontinence. Nerve damage may well be the cause.

There are also problems with this study. We are never told how the sample of 150 was chosen from the 486 eligible women. We are not told if multiple gestations were included. The follow-up was performed

only three months after delivery when healing and nerve regeneration might not be complete. Despite these shortcomings, the article is well done and contains useful information. However, I certainly hope that no one suggests that rectal endosonography become routine post-delivery. Overall, few of the women in this study had fecal incontinence. It would be much more clinically useful (and more cost effective) to reserve such studies for those women who report problems at perhaps six months postpartum. Of course, we have to remember to ask about symptoms. ❖

Psychotherapy and Nefazodone for Treatment of Chronic Depression

ABSTRACT & COMMENTARY

Synopsis: *The combination of psychotherapy and an antidepressant was significantly more efficacious than either treatment alone.*

Source: Keller MB, et al. *N Engl J Med* 2000;342: 1462-1470.

Chronic depression accounts for an inordinate proportion of the enormous burden of illness associated with depression. At any one time, at least 3% of the U.S. population suffers from a chronic form of depression. The majority of these are women. Chronic forms of depression are associated with increased health care use and more frequent suicide attempts than acute depression. Professionally formulated treatment algorithms specify that the combination of psychotherapy and psychotropics is more efficacious than either psychotherapy or the use of antidepressants alone, but this is not what patients are generally offered. This recommendation is buttressed by a limited number of small clinical trials. The present study was undertaken to determine if the recommendation for combination therapy applied to those with chronic depression. A total of 681 adults participated, roughly 65% of whom were women. Most were married. The mean age of participants was approximately 43 years, with mean onset of illness at 26 years. At the time of randomization, subjects met a number of rigorous inclusion and exclusion criteria and were required to withdraw from other psychotropic medications. To receive the diagnosis of chronic depression, a given subject had to have a score on the Hamilton Rating Scale for Depression of at least 20. Only outpatients were included, and they had to have had a diagnosis of depression of at least two years' duration. Subjects were randomized in a 1:1:1 ratio to receive nefazodone (Serzone), psychotherapy, or a combination of both. The intent of psychotherapy was to teach patients how their cognitive and behavioral patterns produce and perpetuate their interpersonal problems, so that they could learn to remedy maladaptive behavioral patterns. Responses were categorized as remission if the Hamilton Rating Score fell to at least 8, favorable if the score fell by 50% and was less than 15, and no response if the above response criteria were not fulfilled.

Although most participants had undergone treatment in the past, the results of the present interventions were encouraging. Of those who completed the trial, the rates of remission or favorable response were 55% for those who received only nefazodone, 52% for those who only received psychotherapy, and 85% for those who received both. Dropout rates were comparable in all arms, although those receiving nefazodone reported more symptoms such as headache, somnolence, and dry mouth.

COMMENT BY SARAH L. BERGA, MD

This is a well-done study with interesting results. Since depression is so common in women, I thought it worthwhile to bring it to your attention. The patient with chronic depression is a challenge to all physicians. Because of the tendency to experience concomitant somatic and psychiatric symptoms, these patients, who are likely to be women, frequently seek the attention of obstetricians-gynecologists and family physicians. It can be difficult to determine which patients have symptoms that are at least partially attributable to physiological processes such as perimenopause and which have symptoms mostly reflecting chronic depression and, thus, need the care of a mental health specialist. For those not trained in psychiatry, there is a tendency to attribute symptoms to physiologic, somatic processes, but it is important to consider the diagnosis of chronic depression should therapies aimed at somatic complaints not ease the symptom complex. Nonetheless, recognizing chronic depression in a general practice is easier said than done. While many patients with chronic depression also have a co-existing personality (approximately 60%) or anxiety (approximately 33%) disorder, this pattern of presentation may serve more to confuse than clarify. In a better world, there would be more liberal access to trained specialists who can perform the appropriate diagnostic maneuvers and who have the clinical experience to confidently render a diagnosis. The main point of this

report, however, is to alert us to the fact that these patients do much better if given combined psycho- and pharmaco therapy. It is commonplace to offer those with chronic depression an antidepressant and to then "let them go" without access to more than monitoring for side effects. As this study points out, this is better than nothing, but far from ideal. Patients with chronic depression need an opportunity to develop more adaptive coping patterns. It is this type of cognitive-behavioral intervention that most ob-gyns and family doctors are less adept at providing. One can only hope this study comes to the attention of those who make policy for health insurance providers as well as the physicians charged with helping these desperately unhappy people. As the study reveals, with proper therapy, there is hope for an improved quality of life. This is an important result that counters the usual clinical nihilism about the prospects for those so afflicted.

This study is also important because it highlights what I predict will be a sea change in the way we approach chronic illness. Gone are the days of monotherapy. Herald the dawn of polypharmacy. The difficult task confronting us now is to determine which combinations make the most sense. I suspect it will be a busy century. ❖

Maternal Mortality in Japan

ABSTRACT & COMMENTARY

Synopsis: *Preventable material deaths in Japan could be reduced if the obstetrician had the assistance of another clinician.*

Source: Nagaya K, et al. *JAMA* 2000;283:2661-2667.

To determine the causes of maternal mortality in Japan, Nagaya and colleagues conducted a cross-sectional study of maternal deaths between Jan. 1, 1991, and Dec. 31, 1992. Maternal death was defined using the International Classification of Diseases, 9th revision (ICD-9), as "the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration of pregnancy or its management, but not from accidental or incidental causes." Death certificates and case records were examined by a 42-member panel of medical specialists to determine if the deaths were preventable. The resources available for patient care and staffing patterns of the facilities where the deaths occurred were characterized. Of 230 maternal deaths, 197 occurred in a hospital, 22 outside a medical facility and, in 11 cases, medical records were not available. The overall maternal mortality rate was 9.5/100,000 births. A total of 86 out of 219 maternal deaths (39%) were due to hemorrhage, making it the most common cause of maternal mortality. Of the 197 deaths that occurred in a hospital, 74 (38%) were due to hemorrhage including uterine rupture (n = 14), atony (n = 11), and placental abruption (n = 10), followed by intracranial hemorrhage (n = 27; 14%), hypertensive disorders of pregnancy (n = 17; 9%), pulmonary embolism (n = 17; 9%), and amniotic fluid embolism (n = 7; 4%). A total of 72 of 197 deaths (37%) occurring in medical facilities were thought to be preventable with another 32 (16%) possibly preventable. The greatest number of preventable deaths were observed in facilities with only one obstetrician, and 49 of the 72 preventable deaths resulted when a single physician was functioning as both the obstetrician and the anesthesiologist. These facilities were also characterized by limited obstetric coverage at night, on weekends and holidays, and limited laboratory support. Smaller facilities that transferred complicated patients to larger centers had a 14-fold higher preventable maternal death rate.

Nagaya et al note that 40% of Japan's deliveries occur in clinics with 19 or fewer beds where staffing is provided by a single physician who sees all outpatients, all inpatients, and performs deliveries. They propose that preventable maternal deaths, particularly those due to hemorrhage, could be reduced if the obstetrician had the assistance of another clinician. They recommend that regional partnerships be established with smaller medical facilities providing ambulatory care and designated regional medical centers providing delivery services.

COMMENT BY STEVEN G. GABBE, MD

Japan has one of the lowest infant mortality rates in the world (3.6/1000). Yet its maternal mortality rate in 1990 was 8.6/100,000, higher than the rates in the United States, the United Kingdom, and Canada. This paper by Nagaya et al and an accompanying editorial by Ikegami and Yoshimura[1] provide important insights into obstetric care in Japan and propose strategies to reduce maternal mortality. In Japan, approximately 11,000 medical facilities provide ambulatory or inpatient obstetric care, but there are only 14,000 obstetricians, including residents. Most facilities have only one physician who serves as both an obstetrician and an anesthesiologist. Family physicians do not provide obstetric care in Japan, and only about 1% of nurse midwives perform deliveries. The fee for obstetrical care is not regulated by the national fee schedule that applies to most healthcare, making obstetric practice profitable. A physician may

own his or her local clinic or small hospital and provide obstetric care in this setting. Furthermore, few hospitals have a quality assurance and improvement program, and recertification is not required by any of the specialty boards. As documented by Nagaya et al, this pattern of practice may contribute to maternal mortality when obstetric emergencies such as hemorrhage occur and the obstetrician must manage the patient alone without adequate anesthetic or laboratory support. The proposal to centralize deliveries in facilities with adequate staffing and ancillary support makes good sense. ❖

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Special Feature

The Word 'Replacement' Is Not Appropriate

By Leon Speroff, MD

I am on a small (and somewhat lonely) campaign to replace the word "replacement" as used with postmenopausal hormone therapy. "Hormone replacement therapy" contains the not so subtle message that we are replacing something missing or that we are restoring the hormonal state to that of the earlier reproductive years. It seems to me that the use of replacement is tied to the notion that menopause and the postmenopause are disease states, specifically estrogen deficiency disease states.

Modern data do not support the concept of menopause and the postmenopause as disease states, and furthermore, the notion of hormone therapy as treatment of a disease is an obstacle to good patient continuation rates (compliance is another word that I try not to use.)

Data from longitudinal studies uniformly indicate that most women experience menopause without difficulty as a normal physiologic event in their lives. The view that menopause has a deleterious effect on mental health is not supported in the psychiatric literature, or in surveys of the general population.[1-4] The concept of a specific psychiatric disorder (involutional melancholia) has been abandoned. Indeed, depression is less common, not more common, among middle-aged women, and menopause cannot be linked to negative mental health changes. [5-12] A negative view of mental health at the time of the menopause is not justified; many of the problems reported at the menopause are due to the vicissitudes of life.[13,14] Men and women at this stage of life both express a multitude of complaints that do not reveal a gender difference that can be explained by a hormonal cause.[15]

Part of the reason for our negative stereotypical views of menopause is that the initial characterization of menopause was derived from women presenting with physical and psychological difficulties. A study of 2001 Australian women aged 45-55 focused on the use of the health care system by women in the perimenopausal period of life.[16] Users of the health care system in this age group were frequent previous users of health care, less healthy, and had more psychosomatic symptoms and vasomotor reactions. These women were more likely to have had a significant previous adverse health history, including a past history of premenstrual complaints. This study emphasized that perimenopausal women who seek health care help are different from those who do not seek help, and they often embrace hormone therapy in the hope it will solve their problems. Similar findings have been reported in a cohort of British women.[17] It is this population that is seen most often by clinicians, producing biased opinions regarding the menopause among physicians. We must be careful not to generalize to the entire female population the behavior experienced by this relatively small group of women.

In my view, it is time to stress the normalcy of this life event. It is important to educate women and clinicians about the normal events of this time period. Changes in menstrual function are not symbols of some ominous "change." There are good physiologic reasons for changing menstrual function, and understanding the physiology will do much to reinforce a healthy, normal attitude. Menopausal women do not suffer from a disease (specifically a hormone deficiency disease). Hormone therapy should be viewed as specific treatment for symptoms in the short term and preventive pharmacology in the long term.

It is well-recognized that continuation rates with postmenopausal hormone therapy are low. The proponents of the "menopause is a disease" concept argue that this approach yields better motivation and continuation. Unencumbered by data, I challenge that argument, and offer an explanation that is at least a contributing factor for the low continuation rates with hormonal treatment. Postmenopausal hormone therapy is a preventive health care decision. It is a decision to undergo daily long-term treatment in order to gain the long-term benefits at a time when an individual is feeling well and in good health. There is an absence of the powerful motivating

forces of pain, sickness, and the threat of disability or death. To make such a strong, long-term decision when the clinician insists an estrogen-deficiency disease is present, when the patient herself (as the longitudinal data tell us) believes menopause is a normal physiologic event, viewed without negative connotations, is very difficult because of the inherent conflict between the clinician's and the patient's views on menopause.

I believe that I have learned this from the women who have revealed what they believe and what they know in the longitudinal studies of the last decade. It only makes sense that trying to convince a woman she has a disease, when she does not believe it, will have a negative effect on the clinician-patient relationship. Postmenopausal hormone therapy is an option that should be offered to most women as they consider their paths for successful aging, but the attitude and beliefs of the clinician have a major influence on the decisions made by patients.

A willful, strong preventive health care decision must originate from an understanding derived from education regarding physiology and health. A clinician who provides such education and who promotes hormone therapy as preventive pharmacologic therapy will help patients generate lasting and firm preventive health care decisions. I believe this approach and attitude will ultimately yield better continuation rates with hormone therapy.

Thus, I believe the use of the word "replacement" is not consistent with a preventive health care approach. I believe the word replacement is rooted in the notion that menopause and postmenopause are disease states. Even the word therapy is not totally satisfactory, denoting treatment of a condition or problem. Nevertheless, "postmenopausal hormone therapy" is a step forward and an improvement over replacement therapy, and the word "replacement" never appears in my textbook. Other possibilities include "substitution, normalization, replenishment, or supplementation." I believe it is time to find a new phrase that appropriately and accurately represents postmenopausal hormone use in the 21st century. ❖

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CME Questions

1. Based on the data of Nagaya et al, which of the following is the most common cause of maternal mortality in Japan?

a. Hemorrhage
b. Hypertensive disorders of pregnancy
c. Intracranial hemorrhage
d. Pulmonary embolism
e. Amniotic fluid embolism

2. Which of the following is *not* recommended as part of a healthy diet?

a. Whole grains
b. Fruits and vegetables
c. Alcohol
d. Low-fat diary products
e. Not smoking

3. According to the article by Faltin et al which of the following was *not* found to be an independent variable for the occurrence of fecal incontinence?

a. Occult sphincter tear
b. Birth weight more than 3500 g
c. Fecal incontinence during pregnancy
d. Instrument delivery

In Future Issues:

Clinicopathologic Features of BRCA-Linked and Sporadic Ovarian Cancer