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A monthly update of developments in female reproductive medicine

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The Clinical Breast Examination: Are You Doing it Right?

ABSTRACT & COMMENTARY

Barton and colleagues conducted a pooled analysis of the English literature on the effectiveness and techniques of clinical breast examination. Clinical breast examination screening was compared to a combination of clinical examination and mammography. The reduction in breast cancer mortality rate was similar. This is a strong argument that clinical breast examination alone can have a beneficial effect on the risk of breast cancer mortality. Importantly, all studies have reported a proportion of breast cancers detected by clinical examination alone (3-45% of breast cancers missed by screening mammographies). In other words, a clinical breast examination can detect cancers missed by mammography. The literature on clinical breast examination is plagued by variability. To a significant degree, this is due to the lack of an unstandardized method of clinical breast examination. The accuracy of clinical breast examination is further reduced by not spending sufficient time at the examination, reduced sensitivity in younger more dense breasts, large breasts, and lumpy breasts. Barton et al concluded that there is sufficient evidence to warrant screening clinical breast examination in every woman older than 40 years of age, and that approximately 50% of asymptomatic breast cancers can be detected by a well-performed breast examination. (Barton MB, et al. *JAMA* 1999;282:1270-1280.)

■ COMMENT BY LEON SPEROFF, MD

This is an article that every clinician who cares for adult women should read. I have always taken pride in my technique for breast examination and, I suspect, this is true for most clinicians. However, this article revealed to me that my technique is not good enough. After making a convincing argument that the literature supports the value of clinical breast examination for the detection of breast cancer, Barton et al provide a detailed description of a technique based upon the research literature, especially that regarding the development and standardization of the clinical examination. There are five vital parts to the correct technique for clinical breast examination:

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- A systematic search pattern
- Thoroughness with adequate duration
- Varying palpation pressure
- The use of three fingers and the pads of the fingers
- A circular motion of the finger pads

In excellent diagrams, this article describes the best patient position to achieve flattening of the lateral and medial parts of the breast, a requirement that is essential for adequate examination. A circular boundary for the examination is inadequate. A complete examination requires covering a rectangular area, bordered by the clavicle, the mid-sternum, the bra line, and the mid-axillary line. The most effective examination pattern is not the circular pattern I have used but, in fact, a vertical strip pattern or lawn mower technique, beginning in the axilla, moving to the bra line, and then back and forth, overlapping rows. The three middle fingers are held together. Palpation is performed by the pads of the fingers, rotating in small dime-sized circles. Most important, at each position, three levels of pressure should be exerted (light, medium, and deep) to complete palpation of all levels of tissue. The duration of examination

affects the accuracy. Studies have demonstrated that a careful examination of an average size breast requires at least three minutes. I know I have not been spending six minutes examining both breasts of patients. In one study, it was documented that the average time equaled 1.8 minutes. Of note is the lack of data supporting inspection in various positions. Thus, it is recommended that careful breast palpation should be combined with careful visual examination simultaneously.

Because of this article, I have already changed the technique of my breast examination, especially changing the pattern of palpation and the duration of examination. I urge you to obtain a copy of this article. Not only are the numbers important, but the description of technique with the excellent diagrams will affect your practice. The numbers tell us that doing it right makes clinical breast examination effective and important. The pictures show us the right way to do it. ♦

Early Discharge After Abdominal Surgery

A B S T R A C T & C O M M E N T A R Y

Synopsis: Early hospital discharge following gynecologic surgery does not lead to significant complications.

Source: Rardin CR, et al. *Gynecol Oncol* 1999;75: 47-50.

Despite the fact that managed care organizations have placed great pressure on physicians to discharge patients from the hospital early after surgical procedures, few studies have examined the effect of such mandated early discharges. In fact, there are virtually no data in the literature to support the use of prolonged hospital stays following gynecologic surgery prior to the imposition of cost-contained measures.

Rardin and colleagues implemented aggressive, standardized practices for the early dismissal of patients from the gynecologic oncology service, and reported the results of this practice for the 266 consecutive patients who were discharged from the service between December 1994 and June 1996. All patients on the service were included in the study with no exclusions. The patients ranged in age from 18 years to 96 years, and greater than half had malignant disease.

Rardin et al identified 19 demographic, clinical, and surgical variables that they believed might affect length of stay and readmission. These included such things as

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type of incision, diagnosis (22% had ovarian cancer), ASA Class (only 30% were Class 1), prior laparotomy (36%), major adhesions (23%), lymph node sampling (21%), use of prophylactic antibiotics and analgesics, time of oral feeding, etc. The mean length of stay for all patients was 2.94 days.

After multivariate analysis, only three variables predicted the need for a prolonged hospital stay—coronary artery disease, type of surgical procedure, and bowel surgery. Patients with radical hysterectomy, and those who underwent extensive debulking procedures required extended hospital stays. There were no patient deaths during hospitalization or during the next 30 days. Seven patients (2.6%) were readmitted during the first month following discharge. Four of these seven had developed wound cellulitis.

In the discussion section, Rardin et al identified “key points” that they believe are necessary to develop a short-stay postsurgical program. These include preoperative patient counseling, early ambulation, and early oral intake. Rardin et al point out that, despite the fact that it has been common practice in the United States to withhold oral feeding until the patient exhibits bowel sounds or passage of flatus, “There are no data to support this practice, in fact, recent studies suggest that some patients undergoing major bowel resections may be fed immediately.”

■ COMMENT BY KENNETH L. NOLLER, MD

This article represents another in a growing list of papers that support the early discharge of patients following major abdominal surgery. While all papers agree that exceptions to short stay are appropriate (e.g., patients with other serious medical diseases, intraoperative complications, general debilitation, etc.), the vast majority of patients may be discharged safely far sooner than was done in the past.

I have been following this growing body of literature closely during the past several years. Despite my preconceived ideas, it has become clear that early discharge is both safe and readily accepted by patients. Indeed, most patients in general good health prefer to be at home rather than in the hospital during the postoperative recovery period.

All of the articles agree that there is one key piece that is essential to early discharge following abdominal surgery: early oral feeding. Indeed, it appears that the practice of waiting for audible bowel sounds prior to initiating oral feedings might, in the future, be looked upon as one of the great mistakes of the second half of the 20th century. The practice does not prevent the occurrence of ileus, causes patients to remain hungry and

underfed for long periods of time, and adds significantly to hospital stay. Perhaps it is time to ban stethoscopes from the postoperative ward. ♦

Prophylactic Oophorectomy and Screening Use in Women at Increased Risk for Breast/Ovarian Cancer

ABSTRACT & COMMENTARY

Synopsis: *Breast/ovarian cancer anxiety rather than objective risk is the major factor that determines a woman's attitude toward prophylactic oophorectomy.*

Source: Meiser B, et al. *Gynecol Oncol* 1999;75: 122-129.

Meiser and colleagues have reported a study in which 95 unaffected women, who approached one of 14 familial cancer clinics for advice about their breast/ovarian cancer risk and surveillance and prophylactic options, were assessed in a cross-sectional design when they attended the clinic. The aim of the study was to evaluate ovarian cancer screening uptake and attitudes toward prophylactic oophorectomy in women at risk of developing hereditary breast/ovarian cancer. Among high-risk women ages 30 and older who had not had a prophylactic oophorectomy, 48% reported ever having had an ovarian ultrasound and, among women ages 50 and older, 23% had taken a serum CA 125 test. Twenty-three percent of women would consider, and 27% of women would not consider, a prophylactic oophorectomy should the genetic test indicate a germline mutation associated with hereditary breast/ovarian cancer, while 38% were uncertain. Twelve percent had already undergone a prophylactic oophorectomy. Interest in prophylactic oophorectomy was associated with increased breast/ovarian cancer anxiety but not objective cancer risk. Meiser et al conclude that the findings demonstrate that breast/ovarian cancer anxiety rather than objective risk is the major factor that determines women's attitude to prophylactic oophorectomy. Furthermore, they conclude that women are likely to benefit from interventions aimed at reducing breast/ovarian cancer anxiety and recommend further research on the use of prophylactic oophorectomy to develop educational strategies

and decision aids to assist women who are trying to make a decision with conditions of uncertainty.

■ COMMENT BY DAVID M. GERSHENSON, MD

There still is no effective screening test for ovarian cancer. Current strategies being studied include a panel of serum tumor markers and combined modality screening (e.g., the use of a combination of CA 125 testing and transvaginal ultrasound based on an algorithm). Several groups and centers have focused on so-called "high-risk" women, who are defined by their family history of ovarian or breast cancer or a personal history of breast cancer. Other possible factors include age and ethnicity. I strongly believe that high-risk women should consider enrolling in a comprehensive screening/genetics program that offers pedigree analysis, risk assessment, genetic counseling, psychological counseling, and selective genetic testing and interventions in addition to the usual CA 125 and sonogram. Such programs should be research-driven so that we can learn how best to improve outcomes for high-risk women. The most interesting finding of this article is that women's attitudes about prophylactic oophorectomy are determined more by anxiety than by objective information. Other recent studies have noted similar findings. I agree with Meiser et al that such information will allow us to develop appropriate interventions to reduce anxiety so that greater objective decision making can occur. Of course, as Meiser et al point out, we don't know whether such attitudes will translate into actual behavior. In addition, we still have a lot to learn about the effect of prophylactic oophorectomy in reducing the incidence of ovarian or peritoneal cancer in high-risk women. ♦

nition that DHEA and DHEAS are synthesized and secreted predominantly by the adrenal glands, the common practice is to replace only glucocorticoid and mineralocorticoid levels in those with either primary or secondary adrenal insufficiency. To better understand the role of DHEA in women, Arlt and colleagues performed a double-blind, placebo-controlled, crossover trial in 24 women with documented adrenal insufficiency. Women were given either DHEA 50 mg daily orally or placebo for three months, followed by a one-month wash-out period, and then three months treatment with whichever product they did not receive initially. As needed, women were on stable doses of glucocorticoids, mineralocorticoids, and gonadal steroids. Outcome measures included hormone levels, cholesterol and lipoprotein profiles, and psychometric inventories. During treatment, serum concentrations of DHEA, DHEAS, androstenedione, testosterone, and dihydrotestosterone increased to the low-normal range. Serum levels of the primary peripheral metabolite of DHEA, androstanediol glucoronide, increased to the upper limit of normal for women. Estrogen levels did not change significantly. Cholesterol levels decreased slightly, as did HDL-cholesterol during treatment with DHEA. Sense of well-being and sexuality as measured by psychometric inventories also improved during treatment with DHEA but not placebo. Five of 24 women reported androgenic side effects such as acne and increased body hair. One woman developed hair loss that resolved when the dose was decreased to 50 mg every other day.

■ COMMENT BY SARAH L. BERGA, MD

The adrenal hormone DHEA is sold in the United States as a food supplement. The common belief is that it restores declining vitality associated with normal aging. This attribution is based in part on the recognition that the adrenal production of DHEA declines steadily with advancing age. In the accompanying editorial, Oelkers points out that by age 70-80 years, the circulating levels of DHEA and its sulfate are roughly 20% of peak in men and 30% of peak in women.¹ It is not surprising that DHEA is touted as an anti-aging compound. However, no long-term studies of its use have been conducted in humans, so we are left with only inferential data from short-term studies to gauge the veracity of this claim. The present study also studied only the short-term use of what was intended as a replacement dose, but the outcome variables are interesting and different from those previously studied. Also, to determine the physiological role, Arlt et al wisely studied women with adrenal insufficiency rather than those with DHEA levels that were normal for age. In the short-term, only about 20% of women given a dose of 50 mg daily by

DHEA Replacement in Women with Adrenal Insufficiency

A B S T R A C T & C O M M E N T A R Y

Synopsis: When given to women with documented adrenal insufficiency, the androgenic precursor DHEA improves well-being and sexuality.

Source: Arlt W, et al. *N Engl J Med* 1999;341: 1013-1020.

The exact physiological roles of dehydroepiandrosterone (DHEA) and its sulfate (DHEAS) remain uncertain. In humans and other primates, the adrenal glands secrete large amounts. Despite the recog-

mouth experienced androgenic side effects. Given the promising data, Oelkers et al felt the data were of sufficient merit to recommend that a daily dose of 25-50 mg be given to any woman with adrenal insufficiency due to adrenal and pituitary causes.¹ Women who are receiving glucocorticoids for other conditions may also develop DHEA insufficiency due to the suppressive effects. They too would be candidates for DHEA replacement.

It is important to point out that physiological replacement of DHEA would be best achieved by a transdermal patch, but such a product is not currently available and has not been studied. Compounding pharmacists can make 25 mg and 50 mg tablets or creams to be applied topically, but even creams will not mimic the physiological secretory pattern. Some of the untoward side effects of oral DHEA may be due to the oral route of administration, so we await an adequate replacement product. Arlt et al attribute the psychological benefits to the developing recognition that DHEA is a "neurosteroid" (i.e., that the brain can use DHEA as a precursor). Also, DHEA appears to alter central serotonergic action. In addition to androgenic side effects, Arlt et al caution that the long-term effect is unknown and there is some concern about using this product in women with breast cancer. Anticipated benefits, however, would include improved well-being, greater energy and increased libido, and increased bone mass and muscle strength. Both Oelkers and Arlt et al stop short, however, of recommending DHEA for the generic chemoprevention of aging. ♦

Reference

- Oelkers W. *N Engl J Med* 1999;341:1073-1074.

Evaluation of Langerhans' Cells in the Cervical Epithelium of Women with CIN

ABSTRACT & COMMENTARY

Synopsis: In patients with HPV/CIN, there is a decrease in immune-competent cells in the epithelium.

Source: Connor JP, et al. *Gynecol Oncol* 1999;75: 130-135.

For some time it has been known that both human papillomavirus (HPV) infection and high-grade cervical intraepithelial neoplasia (CIN) are more common in patients who are immunosuppressed. Iatrogenic suppression in organ transplant patients as well as HIV-induced suppression in patients with AIDS are both known to be associated with markedly increased rates of CIN.

Several studies have attempted to identify the cause for the increased attack rate of HPV/CIN in immunosuppressed patients. Several prior studies have focused on the immunocompetent cells in the cervical squamous epithelium. By general agreement, the most important cell appears to be the Langerhans' cell (LC). This cell appears to be a tissue macrophage which is responsible for recognizing foreign antigens and presenting them to the lymph nodes where an appropriate response can be developed. While some studies have shown a decrease in LC in patients with CIN, other studies have not found a decrease in this cell population.

Connor and colleagues used paired cervical biopsies in both normal patients and patients with CIN to determine the number of LCs in each specimen. In order to identify the LCs, the specimens were prepared using a method that identifies the S-100 antibody, which is thought to be the important protein in the cell-mediated immune system of the cervix. The samples were also prepared for identification of HPV using the hybrid capture technique.

Connor et al determined that immune-competent LCs were significantly reduced in cases of cervical dysplasia, and were also reduced in samples positive for HPV DNA. As an unexpected result, Connor et al found that in both control women and in those with HPV/CIN, S-100 proteins were markedly increased in women with an acute inflammatory process. They postulate that HPV/CIN might decrease the immune competence of the cervical squamous epithelium thus allowing malignant transformation to occur.

■ COMMENT BY KENNETH L. NOLLER, MD

When I entered medical school almost 35 years ago, the whole topic of immunology was covered during one long lecture. The subdivisions of lymphocytes, the production of antibodies, and the results of alterations of the system were largely unknown. During the intervening years, it has become clear that many human diseases are due either to underexpression or overexpression of the immune response. Significant advances have been made in the understanding of the various components of both cell-mediated and humoral responses to outside stimuli, and perhaps most importantly, it has become clear that the development of malignancy may well "always" represent a malfunction or inadequacy of the immune response.

For more than a decade, it has been known that immunocompromised patients often develop cervical

neoplasia than normal individuals. Yet only recently have techniques become available that can focus on specific elements of the immune response in the cervical epithelium. Connor et al have done an excellent job of demonstrating that cases of CIN are associated with a marked decrease in the tissue macrophages (Langerhans' cells) that are responsible for the cell-mediated antibody response of the cervical epithelium. They conclude that HPV (or CIN) causes a reduction in these immune-competent cells by an unknown mechanism. However, because there are not "before and after" samples, an equally plausible explanation would be that the patients had a decrease in immune competent cells to begin with, and, thus, were more susceptible to attack by HPV.

This information may be of more than academic interest to the practicing clinician in the future. We have known for a long time that recurrences of CIN are less frequent in patients who have developed infection following cold knife conization, or who have been treated by techniques that cause an intense tissue reaction. In the future, we may be treating cervical neoplasia medically by the application of topical medications that modify (enhance) tissue immune response. These so-called "immune response modulators" are just beginning to be studied in detail. While early studies suggest that these drugs may be used to treat numerous diseases, their specific effect on the cervical epithelium will need to await extensive study. ♦

The Use of Adjuvant Radiation Therapy by Members of the Society of Gynecologic Oncologists

A B S T R A C T & C O M M E N T A R Y

Synopsis: Complete surgical staging in endometrial cancer appears to decrease the recommendation for postoperative adjuvant radiation therapy.

Source: Naumann RW, et al. *Gynecol Oncol* 1999; 75:4-9.

Naumann and colleagues have reported the findings of a survey of the members of the Society of Gynecologic Oncologists to determine their attitudes about the use of adjuvant radiation therapy in women with endometrial cancer. Of the 767 listed members, 325 (42%) responded. Less than 20% of respondents recom-

mended adjuvant radiation therapy in stage IA, grade 1 or 2, and stage IB, grade 1 endometrial cancer. Adjuvant radiation is recommended by 40-50% of respondents for women with stage IA, grade 3, and stage IB, grade 2 tumors. Most recommend adjuvant radiation for all women with greater than 50% myometrial invasion or grade 3 tumors with any myometrial invasion. Except in stage IA, grade 1 tumors, the chance of recommending further therapy in women with all stages and grades was significantly less if a complete staging procedure, including lymph node dissection, had been performed. Naumann et al conclude that complete surgical staging appears to decrease the chance that postoperative therapy will be recommended. They further recommend that future studies in women with endometrial cancer that do not require lymph node sampling should evaluate the frequency of adjuvant therapy in the absence of complete staging.

■ COMMENT BY DAVID M. GERSHENSON, MD

For the past several decades, adjuvant radiation therapy has been used extensively in patients with endometrial cancer. Historically, radiation was delivered in a variety of schedules—preoperatively, postoperatively, or both, and with a variety of methods—external-beam, brachytherapy, or combinations thereof. Unfortunately, practice patterns were not evidence-based. With the advent of comprehensive surgical staging and revision of the FIGO staging system in the 1980s, preoperative radiation in any form was deleted quickly from our armamentarium. The overarching principle was individualization of the use of radiation based on surgicopathologic findings. Clinical investigators are now focusing on the use of postoperative radiation, as reflected by the results of this survey report. Although not yet published yet, the results of GOG Protocol #99 have been presented in a national forum. In that study, patients with surgical stages IB-IIIB (occult) were randomized to pelvic radiation vs. observation. Although the patients in the radiation arm had a significantly lower rate of vaginal recurrence (1.7% vs 12%), there was no difference in overall survival between the two groups. In addition, there is mounting evidence that patients who have negative retroperitoneal lymph nodes on extended surgical staging do not require any external pelvic radiation, regardless of the presence of unfavorable pathological factors—high-grade, deep myometrial invasion, vascular invasion—in the endometrial tumor. Of course, most experts would still recommend postoperative pelvic radiation for those patients with positive pelvic nodes or extended field radiation for those patients with positive paraaortic nodes (concomitant chemotherapy would also

be recommended by several experts). In summary, the story of the implications of surgical staging for endometrial cancer is still unfolding. Future prospective, randomized trials will hopefully address some of these second-generation questions. ♦

Special Feature

In Utero Programming— Birthweight and Future Health

By Steven G. Gabbe, MD

Obstetricians have long been concerned about the implications of abnormal fetal growth as related to complications during labor and delivery and in the immediate neonatal period. Intrauterine growth restriction, commonly defined as a birthweight below the 10th percentile, has been associated with a higher risk for nonreassuring fetal heart rate patterns during labor and neonatal complications including meconium aspiration, hypoglycemia, and hyperviscosity. Investigators have recently begun to explore the long-term consequences of abnormal growth in utero as a cause for cardiovascular disease and diabetes mellitus later in life.

Dr. David Barker, an epidemiologist from Southampton, England, first proposed that intrauterine conditions could program the development of the cardiovascular system later in life—the so-called Barker hypothesis.¹ Barker and colleagues took advantage of meticulous birth records maintained in several areas of England and Wales. They observed that those areas in which infant mortality was highest in 1901-1910 correlated with areas in which there was also an increased risk for coronary artery disease in men aged 35-74 during the 1960s and 1970s.² They realized that the infant mortality would be highest in low birthweight infants and proposed that low birthweight survivors might be at greater risk for coronary artery disease. Examining birth records, which included not only the infant's birthweight but its birth length, abdominal and head circumference measurements, and placental weight, Barker et al found that infants with a birthweight less than 5.5 pounds had a three-fold increase in death due to coronary artery disease later in life.² The risks for stroke and hypertension were also greater. The infants at greatest risk were those who were not only low birthweight but had a smaller head circumference,

were shorter, and had an increased placenta/birth-weight ratio.

Martyn and colleagues studied singleton babies born in Sheffield, England, between 1922-1926.³ They were able to perform follow-up studies including ultrasonic examination of the carotid arteries and measurements of the ankle-brachial pressure index to assess atherosclerosis in the arteries of the lower limb. They found that the risk of carotid stenosis was more than five times increased for individuals who weighed 6.5 pounds or less at birth than for those who weighed more than 7.5 pounds, after adjusting for cardiovascular risk factors and gestational age at birth. The presence of atherosclerotic disease in the lower limbs was highest in individuals with the lowest recorded birthweights, but this relationship was not significant. These observations support other studies demonstrating an increased risk of hypertension, increased cholesterol and fibrinogen, and impaired glucose tolerance in low birthweight infants. Martyn et al suggest that fetal adaptations in utero may increase the risk of atherosclerotic disease. For example, it is well known that the growth-restricted fetus responds to decreased nutrient flow from its mother by increasing perfusion in the cerebral circulation. Perhaps this change in blood flow leads to a greater risk for atherosclerosis in these vessels later in life.

Why should the low birthweight infant be at greater risk for type 2 diabetes mellitus decades after birth? Insulin is the most important fetal growth hormone. The growth restricted fetus is known to have a reduced level of insulin that may be due to fewer pancreatic b cells.⁴ It might be that these abnormalities in insulin secretion and insulin action persist into adult life. Plante and colleagues recently reported that women who were below the 10th percentile at birth had a 3.6-fold increased risk of a pregnancy complicated by diabetes mellitus at age 20-22.⁵ It could also be that the fetus grows poorly because it has a genetic insulin resistance that is manifested in the adult as type 2 diabetes mellitus.⁶ Phillips, working with Barker et al, has demonstrated that the morning fasting plasma cortisol concentration in men who weighed less than 5.5 pounds at birth is 25% higher than the cortisol level in men who weighed more than 9.5 pounds at birth.⁷ These elevated cortisol concentrations were related to a higher systolic blood pressure and a higher fasting and two-hour plasma glucose concentration. Phillips has proposed that alterations in the fetal hypothalamic-pituitary-adrenal axis in response to intrauterine stress may be associated with insulin resistance and type 2 diabetes later in life.

Recently, two studies have examined long-term neurologic function in the poorly grown fetus. Martyn

et al performed intelligence testing on English men and women born in the same towns studied by Barker et al.⁸ This study of more than 1500 people between 48 and 74 years of age revealed no relationship between body size or proportions at birth and intelligence or cognitive decline in adult life. Martyn et al hypothesized that fetal adaptation in utero appears to be successful in maintaining normal brain development. However, in a recent study of Dutch men born in urban areas during the German Army blockade of food supplies to the Netherlands, psychiatric examinations at the time of military induction revealed that men exposed prenatally to severe maternal nutritional deficiency during the first and/or second trimesters had a significantly increased risk for antisocial personality disorders, which included aggression, unlawful behavior, and disregard for the truth.⁹ The prevalence of antisocial personality disorder in fetuses not subjected to severe prenatal nutritional deficiency was 11.1/10,000 but rose to more than 20/10,000 in men whose mothers were nutritionally deprived. Severe nutritional deficiency was defined as a caloric intake of less than 1000-1500 kcal. Recognizing that many social factors could contribute to their findings, Neugebauer and associates propose that nutritional deficiency early in pregnancy may increase fetal susceptibility to obstetric insults.

In utero programming is an exciting new area of research. Barker et al's unique observation, that low birthweight is associated with an increased risk of cardiovascular disease, has been confirmed in studies in many other countries including Finland, Chile, India, and Sweden. As obstetricians, whenever possible, we should recognize those factors that may impair fetal growth prior to pregnancy, counsel our patients about the associated risks, and make every effort, in cooperation with the patient, to lessen their effect. This effort should include a discussion of the patient's nutrition as well as smoking, substance abuse, and alcohol consumption. ♦

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CME Questions

- 28. All of the following statements about clinical breast examination are true except:**
 - a. The research literature indicates that clinical breast examination can have an effect on breast cancer mortality even in women younger than 40.
 - b. The duration of clinical breast cancer duration should be at least three minutes per breast.
 - c. The accuracy of clinical breast examination is reduced in young women, especially when the breasts are large and lumpy.
 - d. A significant number of breast cancers missed by mammography are detected by clinical breast cancer examination.
- 29. In the article by Rardin et al concerning early discharge, the following variables were found to be associated with prolonged hospitalization after abdominal surgery except:**
 - a. coronary artery disease.
 - b. surgical procedure.
 - c. patient age.
 - d. bowel surgery.
- 30. Effective ovarian cancer screening for high-risk women consists of:**
 - a. transvaginal ultrasound.
 - b. serum CA 125.
 - c. transvaginal ultrasound plus serum CA 125.
 - d. operative laparoscopy.
 - e. None of the above
- 31. Which of the following illnesses is increased in adults who were low birthweight infants?**
 - a. Coronary artery disease
 - b. Type 1 diabetes
 - c. Impaired cognitive performance
 - d. Epilepsy
 - e. Asthma
- 32. Which of the following cells is responsible for the cell-mediated immune response in the cervical epithelium?**
 - a. Basal cell
 - b. Intermediate cell
 - c. Tissue macrophage
 - d. NK lymphocyte

In Future Issues:

Influence of Gestational Age and Smoking Habits on the Risk of Subsequent Preterm Deliveries