



Women's Health & Reproductive Nutrition Report

Volume 5 Issue 4 Spring 2005

Improving Outcomes in Multiple Pregnancies with Nutritional Interventions

Barbara Luke, ScD, MPH, RD

Pregnancy is a state of accelerated starvation, resulting in lower fasting glucose levels and an exaggeration of the insulin response to eating. In twin pregnancies, these changes are magnified, particularly during the second half of pregnancy, with significantly lower maternal serum glucose and insulin concentrations, and higher plasma concentrations of β -hydroxybutyrate compared to maternal concentrations in singleton pregnancies, indicating more rapid depletion of glycogen stores and resultant metabolism of fat between meals and during an overnight fast¹. Both fasting and ketonuria have been linked to an increase in preterm labor and preterm delivery, a phenomenon termed the "Yom Kippur effect"². A reduced glucose stream from mother to fetus results in slower fetal growth, smaller birth size, and an increased risk of fetal growth restriction³. The diet therapy we have used successfully in both twin and triplet pregnancies^{4,4a} is based on the diabetic regimen of three meals and three snacks per day (**Table 1**). In studies with both twins and triplets^{4,4a}, diet therapy with 20% of calories from protein, a lower percentage of calories from carbohydrate (40%) for better glycemic control, and a higher percentage of calories from fat (40%), to provide additional calories with less bulk, is most effective. The emphasis is also on the use of low glycemic index carbohydrates to prevent wide fluctuations in blood glucose concentrations.

Iron Status

Iron-deficiency anemia is also significantly associated with preterm delivery^{5a-b}. Serum ferritin levels, which are lowered with iron-deficiency and elevated in the presence of infection, have also been linked to prematurity. Extremes of maternal serum ferritin levels measured early in the second trimester (15-17 weeks), as well as elevated levels at 24, 26, or 28 weeks have been associated with preterm birth^{6,6a}. It has been shown when elevated third trimester serum ferritin levels reflect a failure to decline from entry to care, they are significantly associated with preterm and very preterm birth, with iron-deficiency anemia and poor maternal

Table 1. BMI-Specific Dietary Recommendations for Twin Gestations*

BMI Categories	Under Weight	Normal Weight	Over Weight	Obese
	<19.8	19.8-26.0	26.1-29.0	>29.0
Kilocalories	4,000	3,500	3,250	3,000
Protein (20% of calories)	200 g	175 g	163 g	150 g
Carbohydrate (40% of calories)	400 g	350 g	325 g	300 g
Fat (40% of calories)	175 g	175 g	175 g	175 g
Exchanges (Servings) per day				
Dairy	10	8	8	8
Grains	12	10	8	8
Meat/meat equivalents	10	10	8	6
Eggs	2	2	2	2
Vegetables	5	4	4	4
Fruits	8	7	6	6
Fats/Oils	7	6	5	5

*Adapted from reference⁴.

nutritional status underlying the relationship⁶. The few studies with evaluated iron status in multiple pregnancies have reported lower hemoglobin levels in the first and second trimesters, higher rates of iron-deficiency anemia, and even residual iron-deficiency anemia in the infants, up to six months of age^{7,7a}. Dietary sources of iron are preferable-particularly heme-iron-rich sources such as red meat, pork, poultry, fish, and eggs-because of better absorption and utilization, their positive effect on nonheme iron bioavailability, and their high quality and quantity of protein and other nutrients. The inclusion of

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Women's Health & Reproductive Nutrition Report



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ABOUT THE AUTHORS

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Barbara Luke, ScD, MPH, RD is Professor of Nursing and Health Studies, with joint appointments in the Department of Obstetrics and Gynecology and the Department of Pediatrics at the University of Miami, Florida. She is the author of numerous books, including *When You're Expecting Twins, Triplets, or Quads* (HarperCollins, second edition 2004), and is the 2005 recipient of the March of Dimes Agnes Higgins Award for lifetime achievement in maternal nutrition.

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Rachelle Lessen, MS, RD, IBCLC is a pediatric nutritionist and lactation consultant who has worked with mothers and babies for 10 years at The Children's Hospital of Philadelphia. She specializes in feeding difficulties, failure to thrive and food allergies.

***Pregnancy 101 Laboratory Assessment*Page 6**

Nancy Turnier-Lamoureux, MA completed the Alternative Dietetic Internship Program, sponsored by the New Jersey Department of health and Senior Services in September 2004. As part of her rotation with our past-chair Alyce Thomas, Nancy researched the basics of pregnancy lab interpretation and submitted this article for our readers. Nancy is currently working as an outreach nutritionist at St. Joseph's Regional Medical Center WIC program, where she has worked for over 15 years!

Jeanne Blankenship, MS, RD is a senior dietitian and clinical researcher at the University of California, Davis Medical Center. Jeanne edited and revised Nancy's original article as a part of our experimental "writer mentorship program." For more about Jeanne, see page 4 "2005-06 WHRN Officers."

***Diet and Ovarian Cancer*Page 8**

Karen M. Gil, PhD is the Resident Research Director, Department of Obstetrics and Gynecology, Akron General Medical Center, Akron, OH and Assistant Professor of Behavioral Sciences, Northeastern Ohio Universities College of Medicine. Her recent research interests have focused on clinical outcomes and preventive health care, including quality of life in gynecologic oncology.

Vivian E. von Gruenigen, MD is an Assistant Professor in Department of Reproductive Biology at Case School of Medicine, in Cleveland, Ohio and the Department of Obstetrics and Gynecology, Division of Gynecologic Oncology at University Hospitals of Cleveland. During her career, Dr. von Gruenigen's research efforts have focused on clinical outcomes and gynecologic cancer patients.

Editors Notes:

- WHRN apologizes for an error made in the Winter 2005 issue in the article Nutritional Guidelines for HIV in Women. The CD4 guidelines box should read "diagnosis of AIDS < 200 cells/mm³" (instead of "diagnosis of HIV").
- Other note: Due to space limitations, the reference lists included for this issue's articles on ovarian cancer and nutrition in multiple gestations are abbreviated. You can request a copy of the full reference list by e-mailing the editor at kscalzo@lij.edu, or going to the members only section of the website.

Darlene Husch, MA RD CDE

Happy Spring! Since our work as a dietetic practice group centers around women and their health throughout the lifespan, I want to share with you some important websites and recent news headlines.

- The Department of Health and Human Services (DHHS), Agency for Healthcare Research and Quality (AHRQ) has developed a series of evidence-based practice reports regarding women's health, including clinical categories with corresponding reports. To view these reports visit www.ahrq.gov. The DHHS has created another site that provides reliable health information to women. Browse the data base at www.4woman.gov.
- The Kaiser Family Foundation's State Health Facts provide state-level and U.S. data regarding many women's health topics including healthcare and health policy. Visit their website: www.statehealthfacts.kff.org.
- The 2005 Dietary Guidelines, published jointly every 5 years by the DHHS and the USDA, are accessible at www.healthierus.gov/dietaryguidelines.

Important news headlines have addressed women's health issues since the beginning of the year. U.S. Surgeon General, Richard H. Carmona, rolled out his 2005 agenda- The Year of the Healthy Child. The agenda focuses on improving the body, mind, and spirit of the growing child. A healthy child begins before birth so his office has highlighted steps women should take to keep themselves healthy, especially when they are considering pregnancy. These steps include eating a healthful diet,

exercising, and eliminating tobacco and alcohol use. They also include taking a folic acid vitamin supplement. Every woman of childbearing age should supplement her diet with 400 micrograms of folic acid each day, even if she is not planning a pregnancy. However, women whose family history shows a high risk of neural tube defects should take ten times the amount: 4 mg. It is important this increased dosage be taken specifically from folic acid supplements, to avoid the risk of Vitamin A poisoning if taken by multivitamins.

In addition to the Surgeon General's agenda, research on preeclampsia has been highlighted in the news headlines. According to research from the National Institute of Child Health and Human Development of the National Institutes of Health, women with low levels of a substance known as placental growth factor (PIGF) in their urine were highly likely to develop preeclampsia. PIGF works in combination with a substance called vascular endothelial growth factor (VEGF). Together, they foster the growth of new blood vessels, and maintain the health of cells lining the inside of blood vessels, including those in the placenta supporting the developing fetus. The researchers believe high blood pressure and other symptoms characteristic of preeclampsia result from low levels of the two substances. They are planning to refine the results into an accurate test.

In closing, I would like to thank Xanodyne Pharmaceuticals for sponsoring this spring newsletter. Xanodyne Pharmaceuticals are a trusted prenatal vitamin manufacturer that has been taking care of moms and babies for more than 25 years! Duet[®]DHA is the latest innovation from StuartNatal[®], which is a prenatal vitamin with the added benefits of DHA. In addition, I would like to thank the USA Rice Federation for providing our bilingual educational insert to this newsletter. This insert will help all of us spread the word about the importance of folate for healthy babies!

Calendar of Events

Compiled by Jamillah Hoy-Rosas, MPH, RD
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June 6 - 10, 2005 Columbia University Institute of Human Nutrition Obesity Conference
<http://www.ascn.org/obeistysummerinstituteschedule.pdf>

ADA Certificate of Training in Adult Weight Management
June 23-25, 2005 Atlanta, GA. **September 8-10, 2005** Alexandria, VA.
<http://www.dcrnet.org/whatsnew/CertificateOfTraining.htm>

June 23 - 26, 2005 American Association of Family and Consumer Sciences (AAFCS) Annual Meeting Sizing Up America: Obesity Causes, Effects and Solutions Minneapolis, Minnesota
<http://www.aafcs.org/meetings/05/index.html>

July 11-13, 2005 National Maternal Nutrition Intensive Course University of Minnesota, West Bank Campus Hubert H Humphrey

Institute <http://www.epi.umn.edu/let>

July 23-27, 2005 Society for Nutrition Education Leading the Way in Nutrition and Health, Orlando, Florida
<http://www.sne.org/conference/index.html>

August 1 - 7, 2005 World Breastfeeding Week World Alliance for Breastfeeding Action and La Leche League International <http://www.lalecheleague.org>

September 12 - 14, 2005 FNS National Nutrition Education Conference 2: Nutrition Connections: People, Programs, Science, Community Arlington, VA
<http://www.fns.usda.gov/oane/menu/nneconnec.htm>

September 28, 2005 National Women's Health and Fitness Day Health Information Resource Center
<http://www.fitnessday.com>

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nonheme-iron sources is encouraged as well, such as iron-fortified breads and grains, vegetables, and nuts.

Calcium, Magnesium, and Zinc Supplementation

Calcium, magnesium, and zinc have been identified by the World Health Organization as having the most potential for reducing pregnancy complications and improving outcomes^{8,8a}. Results of calcium supplementation trials among high-risk women have been promising, with significant reductions in preterm deliveries among teenagers and women with low calcium diets^{9,9a}. Other studies have shown inconsistent results in lowering the rates of pregnancy-induced hypertension, and no effect on preterm delivery and small-for-gestational age births^{10,10a}. The ability of supplemental calcium to decrease preterm delivery risk may be confined to high-risk populations where there is either a severe dietary restriction of calcium or, as in the case of adolescents and multiple gestations, an increased physiologic demand for calcium.

Similar inconsistent results have been reported in studies of magnesium supplementation, which may have been due to differences in study design, study populations, and the concurrent use of other medications. Magnesium, though, may have a neuroprotective role, particularly for the premature infant, in addition to being an effective therapy for preeclampsia.

Although maternal zinc nutriture has been significantly related to length of gestation, infection, and risk of premature rupture of membranes^{11,11a}, clinical trials of zinc supplementation have yielded equivocal results¹². One trial randomly supplementing only women with plasma zinc levels below the median reported an increase in length of gestation of approximately 0.5 week and an increase in birthweight (about half of which was explained by the longer duration of gestation)¹³. To date, there have been no mineral supplementation trials with twin pregnancies. Scholl, Hediger, et al¹⁴ reported a low dietary zinc intake during singleton pregnancy (=6 mg/day or <40% of the RDA for pregnancy) was associated with an increased incidence of iron-deficiency anemia at entry to care, a lower use of prenatal supplements during pregnancy, and a higher

incidence of inadequate weight gain during pregnancy and an increased risk of LBW, preterm delivery, and early preterm delivery. The joint effect of iron-deficiency anemia at entry to care and a low dietary zinc intake during pregnancy increased risk of preterm delivery fivefold.

Multivitamin and Multimineral Supplementation

Ideally, pregnant women should get the level and range of required nutrients through a balanced diet. Recent national dietary surveys indicate, though, adult women fail to meet the RDAs for five nutrients: calcium, magnesium, zinc, and vitamins E and B₆¹⁵. In addition, prenatal use of vitamin-mineral supplements among low-income women has been shown to reduce the risks of preterm delivery and low birthweight, particularly if initiated during the first trimester¹⁶. Supplementation in excess of twice the recommended dietary allowance (RDA) should be avoided, due to the potential for birth defects. The fat-soluble vitamins, particularly vitamins A and D, are the most potentially toxic during pregnancy. The pediatric and obstetric literature includes case reports of kidney malformations in children whose mothers took between 40,000 and 50,000 IU of vitamin A during pregnancy. Even at lower doses, excessive amounts of vitamin A may cause subtle damage to the developing nervous system, resulting in serious behavioral and learning disabilities in later life. The margin of safety for vitamin D is smaller for this vitamin than for any other. Birth defects of the heart, particularly aortic stenosis, have been reported in both humans and experimental animals with doses as low as 4,000 IU, which is ten times the RDA (Recommended Dietary Allowance) during pregnancy.

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2005-2006 WHRN Officers

By Claire Dalidowitz, MS, MA, RD, CD-N

Congratulations to our newly elected WHRN leaders. We are fortunate to have such well-qualified and experienced officers to lead WHRN!!

Chair-Elect: Jeanne Blankenship, MS, RD Jeanne works as a senior clinical bariatric dietitian and nutrition coordinator for the bariatric surgery program at University of California Davis Medical Center - Sacramento. She also has a private practice where she works extensively with special needs populations including low-income and developmentally disabled infants, children and adults. She has been the Nominating Chair-Elect for WHRN DPG but will now move onto the Chair-elect position.

Treasurer: Jamillah Hoy-Rosas MPH, RD, CDN Jamillah works as a bilingual dietitian/nutritionist at the Betances Health Center in New York, New York. She has been the Calendar of Events Coordinator from 2002 to the present as well as WHRN's membership Co-Chair for the past year.

Nominating Committee, Chair: Ginger Carney RD, LDN, IBCLC Ginger is the Clinical Nutrition Manager and Lactation Consultant for Le Bonheur Children's Medical Center in Memphis. She currently represents WHRN as the Professional Liaison to ILCA (International Lactation Consultant Association).

Chair-Elect Nominating Committee: Barbara Dubois, DTR Barbara is a Diet Technician who works at Saint Mary's Home, a long-term care facility, in West Hartford, CT.

Lactation Case Studies

Rachelle Lessen, MS, RD, IBCLC

The number of women choosing to breastfeed is increasing. In 2001, 70% of women initiated any breastfeeding, approaching the Healthy People 2010 goal of 75%. Breastfeeding exclusivity and duration rates have been much slower to increase. At six months only 33% of women are doing any breastfeeding, and only 17% are doing so exclusively. The following case study presents some challenges new mothers may experience trying to provide optimal nutrition for their newborn.

Elizabeth is a healthy, 30-year-old, primipara who set a six-month breastfeeding goal for herself after attending a prenatal breastfeeding class. She would return to work at 6-weeks and pump milk at work for the dad to feed the baby with at home. Her husband was supportive of the plan, although Elizabeth's mother did not breastfeed and did not encourage her.

Elizabeth had premature rupture of membranes at 36 ½ weeks. Labor was induced with pitocin and lasted 12 hours. Birth weight was 3.5 kg. Baby Matthew was exclusively breastfed every 2-3 hours from birth and discharged home on day 3. On day 5, he was admitted to a pediatric hospital for treatment of dehydration and hyperbilirubinemia² after the follow-up weight check at the pediatrician showed he was 13% below birth weight.

On examination, Elizabeth's breasts were full, tender and lumpy. She expressed 20 cc of milk when Matthew was admitted to the hospital. Observation of breastfeeding showed Matthew successfully latched onto the breast, and was able to maintain the latch with nutritive sucking for ten minutes before falling asleep. He did not wake up to latch on to the second breast. Elizabeth arranged to sleep at the hospital to breastfeed Matthew

every 2 to 2 ½ hours. She pumped after breastfeeding to increase her milk supply with the expressed milk offered by bottle. Test weights were initiated, and the family was instructed on how to weigh Matthew before and after breastfeeding to determine breast milk transfer.

On day 7 (day 3 of the hospital admission), Matthew had gained 100g but was still 11% below birth weight. He breastfed every 2-3 hours, and transferred 6-24 cc at the breast followed by 20-30 cc expressed breast milk by bottle. The family rented a scale for at-home use after discharge for test weights of breastfeeding over a six-hour period. A goal of 480 cc per day was determined to meet his calorie needs. If he transferred <120 cc in 6 hours, he would receive a supplement of expressed breast milk to make up the difference. This would encourage him to be hungry to breastfeed but assure he was receiving adequate hydration and calories. Elizabeth would continue to pump after breastfeeding to further stimulate milk production.

DISCUSSION: Matthew can be classified as a "near-term" baby³. Although he had healthy birth weight of 3.5 kg, at 36 weeks his feeding behavior was immature and he was sleepy at the breast. In addition, a bilirubin of 20 mg/dl compromised his ability to successfully breastfeed. A strategy to preserve breastfeeding while providing adequate nutrition was necessary.

The ultimate feeding plan goal to gradually decrease the need for supplemental feedings as Matthew began to transfer greater quantities directly from the breast was never successfully implemented. Less than 36 hours after Matthew was discharged from the NICU, Elizabeth presented with fever, chills, tender abdomen and back pain. She was admitted to the hospital with a presumed uterine infection where she

waited for over 12 hours before receiving a bedside electric pump with only a single kit for pumping. Although she tried to pump every 3 hours during her nearly 3-day stay in the hospital, she watched her supply decrease from 30-50 cc/pumping to only 10 cc/pumping.

By the time she was home, she had not breastfed in 3 days and had a severely depleted milk supply. She did not want to continue pumping. Other options such as use of a breastfeeding supplementer device, medications to increase lactation, and combining breastfeeding with pumping were discussed but Elizabeth was overwhelmed and exhausted. She was relieved Matthew was taking 3-ounces of formula every 3-hours, eating well by bottle, and gaining weight.

In the event a breastfeeding mother or infant is hospitalized, every effort should be made to maintain breastfeeding either directly or by pumping¹. Although Elizabeth continued to exclusively breastfeed throughout Matthew's hospitalization for jaundice and dehydration, when she herself was readmitted for a uterine infection, she was unable to maintain lactation. She was admitted to a medical unit unfamiliar with lactating mothers and was provided with inappropriate lactation support. If Elizabeth had managed to pump, or even breastfeed, during her hospital stay she may have been more likely to continue breastfeeding. When a mother requires hospitalization after birth, keeping the mother and baby together needs to be a priority.

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PREGNANCY 101

Laboratory Assessment

Jeanne Blankenship, MS RD CLE
Nancy Turnier-Lamoureaux, MA

When assessing the nutritional status of the pregnant woman, laboratory measurements can be utilized to uncover nutritional depletions or deficiencies. Biochemical markers are estimates of nutrient stores; ascertaining exact nutrient levels or metabolites is difficult, and sometimes daunting, partially due to the shifting nutrient needs related to maternal changes in blood volume, metabolism and renal function. Dietetic professionals must learn to recognize the expected hemodynamic and metabolic changes that occur during the various phases of pregnancy, and to consider other clinical findings in the context of these changes.

Anemia Studies

Hemoglobin (Hb) and hematocrit (Hct) measurements are the laboratory tests most commonly used to screen for anemia and relative risk. For women with adequate iron nutrition, Hb and Hct values start to decline during the early part of first trimester, reach their nadir near the end of the second trimester, then gradually rise in the third trimester¹. Both values reflect the physiologic change in which maternal blood volume increases more rapidly than red blood cell mass, therefore the specific stage of pregnancy must be considered during interpretation, as noted in Table 1. High altitude and cigarette smoking increase Hb and Hct levels significantly and cut-off

values should be adjusted². Transferrin is the main transport protein for plasma iron and can be used to monitor liver function and nutrition status. Total iron-binding capacity (TIBC) measures the amount of iron transferrin could potentially carry if all binding sites were fully saturated. TIBC is most useful when viewed with regard to serum iron concentrations. Use it to compare the amount of iron available (serum iron) to the amount bound to the receptor sites (TIBC).

Mean Corpuscular Volume (MCV) is the average size of the red blood cells in a given sample and remains relatively unchanged during pregnancy for nonanemic women. MCV can help distinguish between iron and folate deficiency anemias. Iron depletion leads to a reduction in cell size or a microcytic cell while folate depletion leads to an increase in cell size or macrocytic cell. An MCV <83 cubic microns is consistent with iron insufficiency during pregnancy. Likewise, a pregnant woman with a MCV >94 cubic microns should be considered at risk for folate deficiency and a red blood cell folate test should be performed³⁻⁵.

Serum ferritin is also used to screen for iron status. Hgb and Hct values below the acceptable range along with a blood ferritin level of <12 mcg/dl can be interpreted as iron deficiency anemia⁶.

Folic acid acts as a coenzyme in amino acid metabolism and nucleic acid synthesis. Folate deficiency

increases the risk of neural tube defects, miscarriage, fetal prematurity and low birth weight. Folate deficiency leads to an increase in homocysteine levels

which in turn is linked to miscarriage, placental abruption and preeclampsia⁷. Patients may present with macrocytic anemia (MCVs >100) as a result of poor dietary folate intake, alcohol use, or increased demands, such as multifetal gestation⁸.

Glucose Tolerance

Approximately 7% of pregnant women develop gestational diabetes (GDM). If early glucose results are normal, women should be retested at 24-28 weeks with either a 100-g or 75-g oral glucose tolerance test (OGTT). If hyperglycemia or increased risk for GDM is found in early pregnancy, the OGTT should be done immediately. Fasting plasma glucose values of >95 mg/dl or 2 hour plasma glucose readings >155 mg/dl are consistent with GDM. Insulin therapy is initiated for GDM when medical nutrition therapy fails to keep fasting whole blood glucose levels <95 mg/dl or 2-hour postprandial whole blood glucose levels <120 mg/dl⁹.

Protein Status and Calcium

Albumin is produced in the liver and is the most abundant of all blood proteins, functioning mainly as a transport protein. The marked decline early in gestation may explain why there are decreased concentrations of nutrients, which rely on albumin for transport¹⁰. Low serum albumin levels may reflect inadequate protein intake, compromised liver conditions, or may indicate that acute phase proteins are being employed to resolve metabolic stress rather than functioning as transporters. Because albumin has a longer half-life than pre-albumin (22 days versus 2-4 days), the use of pre-albumin in acute care will more readily reflect immediate changes in protein status¹¹.

Iron Concentration	Non-Pregnant (>18 yrs)	Trimester		
		1	2	3
Hemoglobin (g/dl)	12.0	>11.0	>10.5	>11.0
Iron Concentration (%)	35.7	33.0	>32.0	>33.0

Table 1. Desired values during various stages of pregnancy⁸

Total blood calcium during pregnancy is eight percent below non-pregnant levels, with an upper normal limit of 9.5 mg/dl. This level reflects decreased albumin levels caused by the blood volume expansion. If the albumin value is low, the calcium value should be adjusted because each one gram change in albumin per deciliter changes the serum calcium concentration by 0.8 mg/dl. Levels of ionized calcium are not impacted by pregnancy and are a more reliable measure of serum calcium when protein deficiency is suspected¹¹.

Renal Function

Hyperfiltration in the glomerulus reduces maternal plasma levels of creatinine, blood urea nitrogen (BUN), and uric acid. Serum creatinine drops to 0.7 mg/dl by the end of the pregnancy. BUN also falls, from nonpregnant levels of 13 mg/dl to 9 mg/dl¹².

Thyroid Function

The acceptable range for thyroid function tests changes during pregnancy due to the influence of two main hormones, human chorionic gonadotropin (hCG) and estrogen. High levels of hCG at the onset of pregnancy may result in a slightly low thyroid stimulating hormone, TSH. TSH, produced by the pituitary gland, controls the production of T₃ (triiodothyronine) and T₄ (thyroxine), two sensitive assays to identify thyroid disorders. During pregnancy, the thyroid increases production of T₃ and T₄. If the thyroid is under-active, insignificant amounts of T₃ and T₄ will be produced indicating the need for medication. Usually, TSH will be normal or slightly low during the first trimester then will return to normal for the remainder of the pregnancy¹³.

Conclusion:

Laboratory tests to assess maternal nutritional status are confounded by

Laboratory Test	Normal Value (nonpregnant)	Normal Value (pregnant)
Total protein (gm/dl)	6.8-8.5	6.8
Albumin (gm/dl)	3.5-5	2.5-4.5
Prealbumin (mg/dl)	17-39	19-29
Retinol binding protein (mg/dl)	2.7-7.6	2.5-4
BUN (mg/dl)	5-24	4-12
Creatinine (mg/dl)	0.7-1.3	0.4-0.9
Fasting glucose (mg/dl)	65-115	65-100
2 hr postprandial glucose	<110	<120
Calcium (meq/l)	8.6-10.4	8.4-10.4
Phosphorous (mg/dl)	2.5-4.5	2.3-4.6
Alkaline phos (u/l)	0-95	35-150
Cholesterol (mg/dl)	<200	177-345
Triglycerides (mg/dl)	<250	120-400
Folic acid (ng/ml)	5-21	4-14
Iron (mcg/l)	>50	>60
Ferritin (mcg/l)	35	>20
TIBC (mcg/dl)	250-460	300-600
%TIBC saturation	30	>20
Vitamin B12	199-732	Decreased
Zinc (mcg/dl)	65-115	55-80

Table 2. Laboratory values during pregnancy^{14*}
 *Normal ranges may vary slightly at each institution.

changes in blood levels of nutrients, various enzymes and metabolic processes utilizing nutrients for various functions. A comprehensive medical history, physical exam and evaluation of laboratory evaluations using hematology, biochemical and urine assays help determine if a pregnant woman is suffering from true malnutrition or if she is at risk for developing a nutritional deficiency.

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DIET AND OVARIAN CANCER

Impact on Prevention and Survival

Adapted from "Diet and Ovarian Cancer: Impact on Prevention and Survival", *Oncology Nutrition Connection*. 2004;12(1). and reprinted with permission from the Oncology Nutrition Dietetic Practice Group of the American Dietetic Association

Karen M. Gil, Ph.D., and Vivian E. von Gruenigen, M.D.

Introduction

Approximately 22,220 women will be diagnosed with ovarian cancer in the United States during 2005 and 16,210 will die from this disease.¹ There are currently no screening tests for ovarian cancer in the early stages and it tends to present at an advanced stage. A small percentage (approximately 10%) of ovarian cancers have a hereditary basis, primarily from mutations in the BRCA1 and BRCA2 genes.^{2,2a} The disease occurs primarily in perimenopausal and postmenopausal women; 80% to 90% of cases are diagnosed in women over 40.²

Treatment

The goal of surgical staging and tumor debulking with total abdominal hysterectomy and bilateral salpingo-oophorectomy is to reduce the tumor size to the smallest residual disease.³ First line adjuvant therapy is platinum-based chemotherapy (Carboplatin/Paclitaxel). Patients who respond to the platinum-based therapy with a remission lasting for at least six months have a "platinum sensitive" disease. If they have a recurrence of disease they are treated with the first line platinum-based therapies again. Patients who have a disease recurrence within six months belong to the group termed "platinum resistant." These patients receive non-platinum based chemotherapies if they either do not demonstrate a complete response or have a disease recurrence within six months.

In women who are responsive to treatment, recurrent ovarian cancer can become treatment of a chronic disease as chemotherapeutic regimens with different mechanisms of action are being used in the clinical setting. The most important determinants of survival are stage of disease, and residual tumor after surgical debulking. Although five-year survival rates are approximately 53%, rates differ in women diagnosed at an early vs. late stage¹. If the disease has spread to distant locations, five year survival is only 31%¹.

Prevention

Most ovarian cancers are sporadic and result from environmental contributions to gene-environment interactions^{2,4}. Environmental factors known to decrease the risk of ovarian cancer are parity, lactation, hysterectomy, tubal ligation and oral contraceptive use^{5,5a-5e}. Large differences in incidence rates of ovarian cancer around the world have contributed to the drive to identify

other possible modifiable environmental contributions^{6,6a}. Rates used to be much higher in Northern Europe than Southern Europe⁶, but differences are decreasing and, currently, over half of ovarian cancer occurs in the developing world⁷. A problem with determining which factors may be involved in ovarian cancer risk, however, is many of the environmental factors examined when comparing industrialized with developing countries, such as intake of saturated fat, change in parallel with other factors known to affect ovarian cancer, such as parity. Thus, increasing urbanization of Japan is strongly associated with both increasing intake of fat and mortality from ovarian cancer, but is also associated with a decrease in the number of pregnancies⁸. While recognizing multiple factors may play a role in the etiology of ovarian cancer, geographical differences in consumption of saturated fat, vegetables and unsaturated fats often parallel incidence rates of ovarian cancer. These observations have led to a drive to determine if dietary modifications could lead to a decrease in the incidence of a disease tending to present at an advanced stage and with a relatively poor outlook.

Dietary Fat

Rose et al. examined international differences in mortality from ovarian cancer and found rates were positively correlated with a higher per capita availability of total fat (primarily animal fat)⁹. Future studies have examined intake of fat but have not been able to arrive at a clear consensus.

While several case control studies have found an increase in risk associated with intake of animal fat, saturated fat or red meat¹⁷⁻²³, two large cohort studies did not find an association^{24,25}. Fat from plant sources does not appear associated with an increased risk²⁰⁻²² and intake of monounsaturated fat or olive oil may be protective^{26,27}. Further research is needed to determine if olive oil has a protective role^{28,29}. Results of these studies are consistent with recommendations proposed by the American Cancer Society to limit consumption of red meats, especially high-fat and processed meats³⁰.

Vegetables

The international study also found a strong negative correlation between mortality from ovarian cancer and per capita vegetable availability⁹. Studies examining the effect of vegetables have generally demonstrated a reduction in risk^{10, 10b, 10c, 11, 15, 15a}. Identification of compounds exerting this effect would not only be of value in preventing ovarian cancer, but would also provide information concerning the mechanism by which ovarian cancer occurs. One class of compounds extensively studied is the carotenoids. Beta (β) carotene is the major dietary source of vitamin A and is present in green leafy vegetables, carrots and sweet

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potatoes¹⁶. β carotene and vitamin A are associated with a variety of anti-cancer roles including anti-oxidant activity, inhibitors of tumor promotion, and inhibition of ovarian cell line growth^{16,16a}.

A recent case control study specifically examined the relationship between selected nutrients and ovarian cancer¹⁷. A significant reduction in estimated risk was found for the highest vs. the lowest level of intake of vegetables (OR=.47, 95% CI, .23-.97) and carotenoids (OR=.33, 95% CI, .16-.68). While other case control studies have also found an estimated risk reduction with high intake of carotenoids^{15a,18a-c}, two prospective studies did not^{11,19}.

Additionally, a study examining intake of vitamin A and β carotene from diet and supplements also did not find an effect on ovarian cancer risk²⁰. In this study high consumption of vitamins C and E from supplements (but not from diet) was associated with a reduced risk.

One of the prospective studies did, however, find women who reported consuming at least 2.5 servings of fruits and vegetables a day in high school had a 46% reduction in risk of ovarian cancer²⁰. This study suggests the time during life vegetables are consumed may be important, and that diet consumed in adolescence may have an effect on risk of cancer in later years. These studies also suggest vegetables may exert a protective effect, even if there have not been any consistent data demonstrating which nutrient may be involved, and provide even more incentive to follow guidelines to increase intake of vegetables (and fruit) to at least five servings/day¹⁴.

Effect of diet on survival

A recently published study examined the outcome of 609 women with invasive epithelial ovarian cancer who were enrolled in a case control study during 1990-1993²¹. During the time of the study, which ended in 1999, 372 (61%) of the women died from ovarian cancer. Outcome was evaluated in terms of women's reported usual diet pre-diagnosis. There was an inverse association (improved survival) with increasing intake of vegetables overall (greater than 5.5 servings/day vs. less than 3.9 servings/day) and with cruciferous vegetables and also with vitamin E from foods. Cruciferous vegetables include cabbage, broccoli, Brussel sprouts, cauliflower and other member of the genus Brassica, and chemopreventive agents from this class of vegetables have been found to influence carcinogenesis at multiple levels²². Although this

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The Dietetics Educations Task Force Report represents sweeping changes in dietetics education to meet the professional challenges of the future. The report is posted for your review in the member's section of the ADA website (eatright.org).

Recommendations made in the report will be voted on at the Spring House of Delegates meeting.

Although a summary does not do the report justice, here are the major recommendations:

1. CDR to require a graduate degree for registration and entry into practice. The educational preparation should be seamless providing both academic and supervised practice. Degree-granting program entry should provide opportunities for students with diverse educational backgrounds.
2. CADE to re-evaluate the core competencies for entry level practice to allow programs to emphasize a particular area.
3. CADE to include additional knowledge and performance competencies such as: nutrition

diagnosis/implementation; behavior management; business management; practice management; genetics and others.

4. Expand the supervised practice hour requirement.
5. Develop a plan for accreditation of advanced level education programs.
6. Gradual phase-out of the DTR credential and accreditation of DT education programs.

No currently practicing RD or DTR will be required to go back to school to obtain a graduate degree. Susan Laramee, ADA President, urges us to focus our thoughts and attention on what will work for the future of dietetics. As an educator participating in an excellent Coordinated Program at the University of Illinois at Chicago, these changes have profound consequences for my academic department. I am keeping an open mind and I solicit comments from your various perspectives so my participation in the decision process can reflect our combined wisdom.

Please review the report and send your comments to me at pbowen@uic.edu.

study does not address whether women changed their diet after their diagnosis, the authors speculate the apparently beneficial effects observed may reflect a propensity for change in some women to a healthier diet. A recent study examining the effect on the amount of green tea consumed post-diagnosis found a significantly higher proportion of tea drinkers survived for at least three years longer than did non-tea drinkers²³. Since other dietary information was not collected, it is possible women who drank more green tea also made other dietary modifications. These data do suggest, however, dietary modification made after diagnosis may alter outcome.

Conclusion

There is a strong drive to identify environmental factors women may modify to alter their risk of ovarian cancer. One issue emerging in research studies is whether diet early in life can influence later likelihood of cancer; another issue is whether pre- and

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There is an established maternal drain of the essential fatty acids during pregnancy, particularly during multiple gestation¹⁷. Additional supplementation with omega-3 fatty acids, which are vital for neurological and retinal development, may be particularly beneficial during pregnancy for both the mother and her developing baby. Because many of the concerns that food sources of omega-3 fatty acids may be contaminated with environmental pollutants such as lead or mercury, supplements may be a safer alternative. Now there are prenatal supplements which incorporate them. Populations with a higher intake of omega-3 fatty acids have significantly lower rates of preterm delivery and low birthweight¹⁸. Infants whose mothers had higher omega-3 fatty acid levels at birth demonstrated better cognitive development¹⁹.

Maternal Weight Gain

The pattern of maternal weight gain has been shown to be as important as total weight gain in its effect on birthweight in both singleton and twin pregnancies. Although the increase in fetal weight is greatest during the third trimester (after 28 weeks), gains during mid-gestation (either second trimester or 20-28 weeks) have the strongest association with birthweight. In singletons, Abrams and Selvin²⁰ demonstrated birthweight increased in each trimester by 18 grams, 33 grams, and 17 grams, respectively, per kilogram per week of maternal weight gain. Scholl, Hediger, et al²¹ reported weight gains to 20 weeks and to 28 weeks were most strongly related to birthweight, contributing 22-24 grams to birthweight per kilogram per week of maternal weight gain. In addition, a low rate of weight gain or a poor pattern of weight gain is associated with an increased risk of preterm birth. Studies in twins by our research team have shown similar results, with low weight gains

Table 2. Optimal Rates of Maternal Weight Gain and Cumulative Gain by Pregravid BMI Status *Adapted from reference 39

Pregravid BMI	Rates of Weight Gain (lbs/week)			Cumulative Weight Gain (lbs)		
	0-20 weeks	20-28 weeks	28 weeks delivery	to 20 weeks	to 28 weeks	to 36-38 weeks
Underweight (BMI <19.8)	1.25-1.75	1.50-1.75	1.25	25-35	37-49	50-62
Normal Weight (BMI 19.8-26.0)	1.0-1.50	1.25-1.75	1.0	20-30	30-44	40-54
Overweight (BMI 26.1-29.0)	1.0-1.25	1.0-1.50	1.0	20-25	28-37	38-47
Obese (BMI >29.0)	0.75-1.0	0.75-1.25	0.75	15-20	21-30	29-38

BMI is body mass index. Results are from models controlling for diabetes and gestational diabetes, preeclampsia, smoking during pregnancy, partly, placental membranes, and fetal growth before 20 wks.

consistently associated with reduced birthweights. Early- and mid-gestation weight gains seem to exert an even greater effect on twin birthweights, with gains to 20 weeks, between 20-28 weeks, and from 28 weeks to birth increasing birthweights by 65 grams, 37 grams, and 16 grams, respectively, per kilogram per week of maternal weight gain^{22,a-b}.

BMI-specific weight gain guidelines are associated with the best intrauterine growth and subsequent birthweights, and longer length of gestation^{23,23a}. Advice regarding weight gain and target weight gain goals are important underlying factors strongly associated with actual weight gain. But studies among women pregnant with singletons^{24,24a} and twins²⁵ have reported more than one-fourth of women receive no advice regarding weight gain. Among women who do receive guidance, more than one-third of them receive inappropriate advice²⁴. In a study by our research team of 928 women who delivered twins²⁵, women who received nutrition advice from a registered dietitian were the most likely to have the highest weight gains (60% gained >40 lbs, with an average gain of 46.3 lbs) and the lowest proportion of very low birthweight infants (2% versus 12% for women not receiving any advice). We have developed BMI-specific guidelines for twins based on optimal rates of fetal growth birthweights between

the singleton 50%ile and twin 90%ile at 36-38 weeks (2,700-2,800g)²⁶ (Table 2).

Conclusion: Multiple pregnancy presents special challenges, and dietary interventions may be particularly effective in promoting optimal growth and length of gestation, as well as minimizing complications. Women pregnant with multiples should receive specialized prenatal care that includes targeted diet therapy.

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menopausal ovarian cancers have the same risk factors or whether dietary factors selectively affect risk of cancers in different life cycles. Finally, the effects of long-term diet on survival from cancer, as well as the possibility of increasing survival by modifying diet post-diagnosis, are research questions beginning to be addressed in ovarian cancer. Following guidelines to minimize saturated and animal fat, increase plant-based foods, and increase the amount of fruits and vegetables would be consistent with observations made in many studies of ovarian cancer risk.

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Congratulations!

We want to acknowledge and congratulate one of our practice group members, Jamie Stang, PhD, MPH, RD, who has been elected to the Commission on Dietetic Registration. The complete 2005 ADA National Elections results are posted on the ADA website: www.eatright.org

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