

The clinical content of preconception care: nutrition and dietary supplements

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At the time of conception, maternal nutritional status is an important determinant of embryonic and fetal growth.¹ Placental and fetal growth is most vulnerable to maternal nutrition status during the preimplantation period and the period of rapid placental development, which occurs during the first few weeks of development typically before pregnancy has been confirmed.² Most organs form 3–7 weeks after the last menstrual period and any teratogenic effects may occur by this time.³ Evidence is emerging that a mother's diet and lifestyle influence the long-term health of her children.^{2,4} Recent research suggests that inadequate levels of maternal nutrients during the crucial period of fetal development may lead to reprogramming within the fetal tissues that predisposes

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Women of child-bearing age should achieve and maintain good nutritional status prior to conception to help minimize health risks to both mothers and infants. Many women may not be aware of the importance of preconception nutrition and supplementation or have access to nutrition information. Health care providers should be knowledgeable about preconception/pregnancy-related nutrition and take the initiative to discuss this information during preconception counseling. Women of reproductive age should be counseled to consume a well-balanced diet including fruits and vegetables, iron and calcium-rich foods, and protein-containing foods as well as 400 μg of folic acid daily. More research is critically needed on the efficacy and safety of dietary supplements and the role of obesity in birth outcomes. Preconception counseling is the perfect opportunity for the health care provider to discuss a healthy eating guideline, dietary supplement intake, and maintaining a healthy weight status.

Key words: folic acid, health risks, pregnancy-related nutrition, reproductive-age women

the infant to chronic illnesses in adulthood.⁵ A woman's nutritional status is influenced by numerous variables including genetics, environment, lifestyle habits, the presence of disease or physiological stressors, and drug-toxicant exposures.⁶

Nutritional assessment and recommendations are important components of preconception counseling. The key components of the nutrition care process include:

- A nutrition assessment, including analysis and interpretation of anthropometric data and adequacy and quality of dietary habits (including dietary supplements).
- A nutrition diagnosis, which will identify and label any nutrition-related problems or risk factors such as obesity or eating disorders.
- The nutrition intervention, at which time the individual's dietary goals and plan of action are established and care is delivered with the emphasis on appropriate weight gain, consumption of a variety of foods according to the Dietary Guidelines 2005, appropriate dietary supplement use, and physical activity.

- Nutrition monitoring, evaluation, and referrals to dietitians occur as needed, depending on the individual's needs.^{7,8}

In this manuscript, we review the evidence for safety and efficacy of nutrition, dietary supplements, and maternal weight during the preconception period.

Dietary intake prior to conception

Background: The quality of a woman's diet during pregnancy has an influence on positive fetal and maternal outcomes; therefore, a healthy, balanced diet is important before as well as during pregnancy.^{1,9} Many women of child-bearing age in the United States do not maintain a healthy diet prior to, during, and after pregnancy. Not all women have financial or logistical access to a high-quality diet.¹⁰ Furthermore, several studies have shown that most women of reproductive age are not getting enough vitamins A, C, B6, and E, folic acid, calcium, iron, zinc, and magnesium in their diet.^{11–13} This underscores the importance of encouraging healthy eating behaviors early in a woman's child-bearing years because improving dietary habits requires long-term effort.

Clinical studies have shown a positive association between a healthy diet during the preconception period and pregnancy and improved birth outcomes.^{14,15} For example, a case-control study on the risk of orofacial clefts by Krapels et al¹⁶ concluded that the preconception energy-adjusted intake of vegetable protein, fiber, beta-carotene, vitamin C, vitamin E, iron, and magnesium were all significantly lower in cases compared with controls. Additionally, there have been a number of reviews written on the importance of a healthy diet prior to and during pregnancy.^{7,10,17-19} In 1992, the Institute of Medicine (IOM) published *Nutrition during Pregnancy and Lactation: An Implementation Guide*.²⁰ The IOM has also published a series of reports establishing the dietary reference intakes (DRIs).²¹ Throughout this review, we will state the DRI for each supplement we discuss.

Finally, the US Department of Agriculture's (USDA) Food Guide Pyramid and Dietary Guidelines for Americans have resources for patients to consume foods that meet the nutritional requirements of pregnancy.²² USDA has released the MyPyramid food guidance system, which includes MyPyramid Plan for Moms, which helps women identify the appropriate food plan according to pregnancy status, age, weight and height, and physical activity level (www.mypyramid.gov/mypyramidmoms).

MyPyramid identifies an appropriate food plan that covers the individual's energy needs and dietary reference intakes in the perinatal period.^{1,7}

Dietary supplements

Background: Although many of our required vitamins, minerals, amino acids, essential fatty acids, and other constituents are found in food, the physiologic demands of the woman during preconception and pregnancy may require additional dietary supplementation. Requirements for folic acid, calcium, iron, zinc, vitamin D, vitamin C, and vitamin B increase substantially during pregnancy.²² In the United States, dietary supplements are regulated differently than prescription medications by the Food and Drug Administration (FDA).

This difference in regulation may influence the quality of products on the market, and our knowledge of dietary supplement safety and efficacy prior to conception and during perinatal period. There exist serious concerns about dietary supplement safety and efficacy, quality control, misidentification, adulteration, contamination, adverse events, and interactions with medications.²³

Various national surveys estimate that 18-52% of the US population use dietary supplements and women use more supplements than men.²⁴⁻²⁶ Many women use multivitamins, single vitamins, herbal products, traditional medicines, folk remedies, weight loss or sport supplements, and other dietary supplements prior to and during pregnancy.²⁷⁻²⁹ Unfortunately, many women do not discuss their dietary supplement use with their health care professionals.^{30,31} It is critical that all health care professionals ask their patients which vitamins, minerals, herbs, traditional remedies, and other dietary supplements they are using. Women should be encouraged to bring in the labels or bottles of all dietary supplements (pills, powders, teas, etc) to determine whether excessive levels of specific nutrients (or other bioactive compounds) are being consumed on a daily basis.^{8,32}

Evidence for efficacy: Although many health care professionals do recommend certain dietary supplements prior to, during, and after pregnancy (eg, folate, iron, and calcium), the safety and efficacy of many dietary supplements (eg, sport supplements and weight loss products) have not been well established. For example, there are few clinical trials evaluating the safety and efficacy prior to and during pregnancy on herbal products.³³⁻³⁵ Today much data available on herbal products are based on case reports, animal studies, and retrospective studies.^{36,37} Because of the high prevalence of dietary supplement use among women, more research on the safety and efficacy of dietary supplements prior to and during pregnancy is urgently needed. Future studies should focus on subject characteristics that may influence our ability to meet maternal and in-

fant demands (genetic and environmental), sensitivity, and selectivity of measured outcomes and proper use of proxy measures.³⁸

Recommendation. All women of reproductive age should be asked about their use of dietary supplements (vitamins, minerals, traditional/home remedies, herbal products, weight loss products, etc) as part of preconception care plan and should be advised about what is or is not known about their impact, safety, and efficacy. *Strength of recommendation: C; quality of evidence: III.*

Vitamin A

Background: Vitamin A is a fat-soluble vitamin found in several forms. Vitamin A found in foods that come from animals (liver, whole milk) is called preformed vitamin A. It is absorbed in the form of retinol, which is made into retinal and retinoic acid (other active forms of vitamin A) in the body. Vitamin A that is found in fruits and vegetables is called provitamin A carotenoid, which is made into retinol in the body. There is also a synthetic analog (13-cis retinoic acid) isotretinoin (Accutane; Roche Pharmaceuticals, Nutley, NJ), a medication used to treat severe, cystic acne, and related dermatoses. Adequate vitamin A is essential for proper visual functioning, fetal growth, reproduction, immunity, and epithelial tissue integrity.³⁹ Because vitamin A is lipid soluble, it crosses the placenta easily and has a long half-life. Although normal fetal development requires sufficient vitamin A intake, very high levels of preformed vitamin A (retinoic acid) supplementation has been associated with miscarriage and birth defects that affect the central nervous system and craniofacial, cardiovascular, and thymus development.³⁹

Currently the recommended dietary allowance of preformed vitamin A for women is 700 retinol activity equivalents (RAEs) per day, with a tolerable upper intake level of 3000 RAEs/day or 10,000 IU/day.⁴⁰ Dietary sources of vitamin A and beta-carotene (leafy vegetables, carrots, eggs, and dairy products) do not pose a risk of excessive intakes and should be included in a healthy diet. Vitamin A from beta-carotene is not

known to increase the risk of birth defects.⁴¹

Evidence of efficacy: During pregnancy, evidence in humans suggests that more than 10,000 IU of vitamin A per day may be teratogenic, resulting in cranial/neural crest defects.⁴² However, other studies have shown that periconceptional vitamin A exposures greater than 10,000 IU/day were not associated with increased risk for cranial neural crest defects or neural tube defects.⁴³ Although animal data clearly show that high dose vitamin A is teratogenic, such data are difficult to obtain in humans as human clinical trials are not ethically possible.⁴¹

Vitamin A also appears to be protective in pregnant women with human immunodeficiency virus/acquired immunodeficiency syndrome.⁴⁴⁻⁴⁷ There is growing evidence from clinical trials in developing countries that vitamin A may protect against maternal morbidity, although more research is needed.^{44,48-50}

Current recommendations: A World Health Organization expert group consultation concluded that daily doses of up to 10,000 IU (equivalent to 3000 μg retinol) or weekly 25,000 IU (7500 RAEs) are probably safe, especially in areas in which vitamin A deficiency is thought to be common.⁵¹ The half-life of the main metabolite of retinoic acid is 50 hours, so most of the drug and biotransformation products are gone within 10 days of the last dose. Etretinate and isotretinoin (Accutane), synthetic derivatives of retinol, are known to cause serious birth defects and should not be taken during pregnancy or if there is a possibility of becoming pregnant. The current recommendation is to discontinue such medications such as at least 1 month prior to attempting pregnancy.

Recommendation. Currently the recommended dietary allowance of preformed vitamin A for women is 700 RAEs per day, with a tolerable upper intake level for pregnancy is 3000 RAEs/day or 10,000 IU/day; *Strength of recommendation:* B; *quality of evidence for toxicity:* III.

Folic acid

Background: Folic acid, a water-soluble B-complex vitamin required for deoxyribonucleic acid synthesis and cell division, is a nutrient currently recognized as important prior to and during pregnancy because of its proven preventive properties against neural tube defects (NTDs).⁵² Neural tube defects are serious birth defects of the spine (spina bifida) and brain (anencephaly). NTDs affect approximately 3000 pregnancies each year in the United States and are the second most common major congenital anomaly worldwide.⁵³ Populations at increased risk for NTDs or folic acid deficiency include Hispanic women, obese women, diabetic women with poor glycemic control, women with prior NTDs, and women with seizure disorder taking antiepileptic medications.^{12,54,55}

Folate levels can be increased by consuming folate-rich foods or ingesting folic acid, a synthetic compound available through dietary supplements and through fortified foods. The major dietary sources of naturally occurring folate are legumes, green leafy vegetables, citrus fruits and juices, and breads and cereals that contained folic enriched flour. Folic acid is approximately 1.7 times more bioavailable than folate and therefore has a greater efficiency in impacting folate levels.⁵⁶ Supplementing dietary intake with folic acid has been recommended by many professional organizations because of the difficulty for woman to obtain the extra folate required periconceptionally through the diet alone. The current recommended daily intake (RDI) for folic acid is 400 μg for women of preconception age and 600 μg during pregnancy.⁵⁷ The recommended dose is higher (4000 μg) for women who have had a infant with an NTD.⁵⁸ Numerous studies have reported that women in the United States do not consume the recommended 400 μg of folic acid.⁵⁹⁻⁶¹ Furthermore, inadequate folate levels have been linked to increased risks of stroke, cancer, and dementia.^{62,63}

Evidence of efficacy: There is clear scientific evidence that folic acid protects against neural tube defects. Numerous

observational and randomized controlled studies culminate in an estimate that at least 70% of NTDs could be prevented if the embryo were exposed to protective amounts of folic acid during the critical window of organogenesis.^{52,64-66}

Current recommendations: The US Public Health Service, American Academy of Pediatrics, American Dietetic Association, American College of Obstetricians and Gynecologists (ACOG), and American Academy of Family Medicine recommend that women consume 400 μg of folic acid daily.^{7,67-69} The USDA recommends women of child-bearing age who may become pregnant and those in the first trimester of pregnancy consume adequate synthetic folic acid daily (from fortified foods or supplements) in addition to food forms of folate from a varied diet.⁷⁰

Recommendation. All women of reproductive age should be advised to ingest 0.4 mg (400 μg) of synthetic folic acid daily, obtained from fortified foods and/or supplements. In addition, all women should be advised to consume a balanced, healthy diet, which includes folate-rich foods. *Strength of recommendation:* A; *quality of evidence:* I-a.

Multivitamins

Background: Multivitamins are typically the most commonly used dietary supplements reported in surveys in the United States.^{71,72} Willett and Stamfer⁷³ concluded that there is greater benefit than harm in recommending a daily multivitamin that does not exceed the daily recommended intake of its component vitamins for most adults. In their review, Willett and Stamfer⁷³ noted that a multivitamin is especially important for women who might become pregnant, persons who regularly consume 1 or 2 alcoholic drinks per day, those who tend to absorb vitamin B12 poorly, vegans, and those with limited resources to afford adequate fruits and vegetables.

Evidence of efficacy: There is substantial evidence showing that taking multivitamins with at least 400 μg of folic acid daily may also reduce the incidence of other malformations such as orofacial cleft, limb deficiencies, cardiac defects,

urinary tract defects, and omphalocele.⁷⁴⁻⁸⁰ A recent metaanalysis of 41 trials reported that multivitamin supplements provide consistent protection against neural tube defects, cardiovascular defects, limb defects, and other birth defects.⁷⁴ In this metaanalysis, both case control studies (odds ratio [OR], 0.76; 95% confidence interval [CI], 0.62-0.93) and cohort and randomized controlled studies (OR, 0.42; 95% CI, 0.06-2.84) showed lower incidence of cleft palate when women took multivitamins.

For oral cleft with or without cleft palate, case control studies (OR, 0.63; 95% CI, 0.54-0.73) and cohort and randomized controlled studies (OR, 0.58; 95% CI, 0.28-1.19) followed the same pattern. For urinary tract anomalies and congenital hydrocephalus, only the case controls studies showed a statistically significant decrease in anomalies. Finally, for congenital hydrocephalus there was an OR of 0.37 (95% CI, 0.24-0.56) in case control studies and 1.54 (95% CI, 0.53-4.50) for cohort studies, and randomized controlled studies.⁷⁴ Although multiple micronutrient supplementation is theoretically preferable to supplementation with iron and folic acid alone, especially in developing countries in which multiple deficiencies are prevalent, more data need to be collected to determine the advantages of different multiple micronutrient formulations for pregnant and lactating women.⁸¹

Recommendation. All women of reproductive age should be encouraged to take a folic acid-containing multivitamin supplement for the purpose of supporting healthy pregnancy outcomes and preventing congenital anomalies. *Strength of recommendation: A; quality of evidence: II2.*

Vitamin D

Background: Vitamin D is a lipid-soluble vitamin important in the metabolism of calcium and phosphorus. It promotes calcium absorption and bone mineralization. It may be obtained from either endogenous production from sun exposure or dietary sources. The major dietary sources are fortified items, particularly milk, orange juice, and some

breakfast cereals. Other dietary sources include fatty fish (salmon, mackerel, tuna, sardine), egg yolks, beef liver, and cheese.

Vitamin D is essential for the health of pregnant women and their infants. Currently there is an increasing prevalence of vitamin D insufficiency and deficiency in pregnant women and infants in the United States and internationally.⁸²⁻⁸⁷ Vitamin D deficiency is common among pregnant women in ethnic minority groups.⁸⁸ Vitamin D deficiency during pregnancy is reflected in lower maternal weight gain; biochemical evidence of disturbed skeletal homeostasis in the infant; and in extreme situations, reduced bone mineralization, radiologically evident rickets, and fractures.^{89,90} Additionally, vitamin D insufficiency has also been associated in some studies with other health outcomes that affect women, including asthma, diabetes, autoimmune diseases, and certain cancers.^{83,91-93}

Women at risk for vitamin D deficiency include women who are not exposed to enough sunlight; whose dietary vitamin D intake is low (no dairy or lactose intolerant); who wear head coverings.

Evidence of efficacy: The optimal dose of vitamin D for the preconception period and during pregnancy is unknown. Observational studies and vitamin D supplementation trials among pregnant women at high risk of vitamin D deficiency showed improved neonatal handling of calcium with improved maternal vitamin D status. Results concerning the effects of vitamin D on maternal weight gain and fetal growth in these high-risk populations are conflicting and inconclusive.^{94,95} Despite taking prenatal vitamins, vitamin D deficiency has been demonstrated in pregnant women.⁸³ Most experts agree that the current DRI of 200-400 IU is too low and that based on current evidence, daily requirements may be closer to 1000 IU or higher and that more research is needed on the optimal vitamin D dose and blood concentrations for several health outcomes.⁸³

Current recommendations: The American College of Obstetricians and Gynecol-

ogists recommend daily consumption of 400-800 IU.⁹⁶ In the United States, the current DRI is 200 IU/day with 200 IU/day in pregnancy. The USDA guidelines note that people with dark skin and people exposed to insufficient ultraviolet band radiation (ie, sunlight) consume extra vitamin D from vitamin D-fortified foods and/or supplements.²²

Recommendation. The evidence is insufficient to recommend for or against routine screening or vitamin D supplementation during preconception counseling. Based on the emerging data of the importance of vitamin D for women and infants; however, clinicians should be aware of the risk factors for vitamin D deficiency. Additionally, for women with vitamin D deficiency, education on vitamin D in the diet and supplementation should be a part of preconception care. Currently we do not have data for the optimal dose prior to and during pregnancy. More data are urgently needed. *Strength of recommendation: B; quality of evidence: I b.*

Calcium

Background: Calcium is essential for bone development and health and maintenance throughout life and in pregnancy, yet many women in the United States do not consume the recommended amount of calcium prior to and during pregnancy.⁹⁷⁻⁹⁹ During pregnancy, the growing fetus receives its total nourishment from maternal sources. The dynamic balance between skeletal calcium storage and fetal nutritional needs can affect the maternal calcium equilibrium adversely. Therefore, if adequate bone has not been built before pregnancy and adequate calcium is not part of the maternal diet, bone can be degraded as calcium is taken from the maternal skeleton.¹⁰⁰ When completing a diet history during preconception counseling, it is important to ask about dietary calcium consumption (milk, fortified orange juice, etc), calcium supplementation, and use of antacids to assess the woman's overall calcium intake. Vitamin D intake is necessary to facilitate calcium absorption.

Evidence of Efficacy: Studies indicate that increases in calcium intake during pregnancy improve maternal bone health of mother and neonate. Higher birthweight babies, a reduced risk of preterm delivery, and lower infant blood pressure have all been linked with a high calcium intake during pregnancy.^{100,101} More research is needed to assess the optimal dose of calcium prior to and during pregnancy.^{100,102-106} A 2008 metaanalysis of 12 good-quality clinical trials reported that the risk of high blood pressure was reduced with calcium supplementation rather than placebo (11 trials, 14,946 women: relative risk (RR), 0.70; 95% CI, 0.57-0.86). There was also a reduction in the risk of preeclampsia associated with calcium supplementation (12 trials, 15,206 women: RR, 0.48; 95% CI, 0.33-0.69). There was no overall effect on the risk of preterm birth or stillbirth or death before discharge from the hospital.¹⁰⁷ Many reviews have concluded that the lack of available evidence restricts the ability to form strong conclusions, especially with respect to supplementation's effect on maternal bone health during pregnancy. More research is needed to assess the optimal dose of calcium prior to and during pregnancy.^{100,102-106}

Current recommendations: The Institute of Medicine currently recommends 1000 mg/day of calcium for pregnant and lactating women who are 19-50 years old and 1300 mg/day for pregnant and lactating women who are younger than 19 years old.¹⁰⁸

Recommendation. Women of reproductive age should be counseled about the importance of achieving the recommended calcium intake level through diet or supplementation. Calcium supplements should be recommended if dietary sources are inadequate. *Strength of recommendation: A; quality of evidence: I b.*

Iron

Background: Iron deficiency is the most common nutritional deficiency worldwide and is the most common cause of anemia in pregnancy. The prevalence of iron deficiency and iron deficiency ane-

mia in the United States is significant among vulnerable populations. For example, the National Health and Nutrition Examination Survey 1999-2000 reported iron deficiency prevalence among women aged 12-49 years was 9-16%. Among minority females in the same age group, the prevalence of iron deficiency was approximately 3 times higher than the Healthy People 2010 objective of 5%.¹⁰⁹

Reproductive-aged women are at risk of iron deficiency because of blood loss from menstruation, poor diet, and frequent pregnancies.¹¹⁰ In a study of fertile women, only 20% had iron reserves of greater than 500 mg, 40% had iron stores of 100-500 mg, and 40% had virtually no iron stores.¹¹¹ Potential fetal complications secondary to anemia include spontaneous prematurity and intrauterine growth restriction.¹¹² The mechanism(s) by which this occurs are not clear. Prior to conception and during pregnancy, women should eat iron-rich foods (lean meat, poultry, and iron fortified cereals). Foods that inhibit iron absorption, such as whole-grain cereals, unleavened whole-grain breads, legumes, tea, and coffee, should be consumed separately from iron-fortified foods. The Centers for Disease Control and Prevention (CDC) recommends 18 mg/day for women and 27 mg/day for all pregnant women.¹¹³

Evidence of efficacy: There are several systematic reviews reporting the benefits of iron combined with folate prior to and during pregnancy. The Cochrane collaboration completed a systematic review on 20 randomized controlled trials of iron supplementation in pregnancy with normal hemoglobin levels (> 10 dL) at less than 28 weeks of gestation.¹¹⁴ Iron supplementation raised or maintained the serum ferritin level above 10 mg/L and reduced the number of women with low hemoglobin levels late in pregnancy. The reviewers concluded that iron supplementation had no detectable effect on any substantive measures of either maternal or fetal outcomes.¹¹⁴ One review looked at 8 trials involving 5449 women.¹¹⁵ Routine supplementation with iron or folate raised or maintained

serum iron and ferritin levels and serum and red cell folate levels. Supplementation resulted in a substantial reduction of women with a hemoglobin level below 10 or 10.5 g in late pregnancy.

A more recent prospective study done by Ronnenberg et al¹¹⁶ in 2004 examined the relation between preconception hemoglobin concentration and pregnancy outcomes in 405 healthy Chinese women who were planning pregnancy. This study showed an association between preconception maternal anemia status and adverse pregnancy outcomes. The odds of low birthweight and fetal growth restriction were 6.5 and 4.6 times higher, respectively, in women with moderate anemia (hemoglobin < 95 g/L) compared with nonanemic controls. Anemia attributed to iron deficiency was significantly associated with decreased birthweight.

A recent randomized controlled trial of 867 pregnant women (less than 20 weeks) was assigned randomly to receive prenatal supplements with 30 mg of iron as ferrous sulfate or placebo until 26-29 weeks of gestation. The mean birthweight was higher by 108 g ($P = .03$), and the incidence of preterm delivery was lower (8% vs 14%; $P = .05$) in the 30 mg group compared with the control group. Iron supplementation did not affect the prevalence of small-for-gestational-age infants or third-trimester iron status.¹¹⁷

In another recent clinical trial, 513 low-income pregnant women were randomly assigned to receive a monthly supply of ferrous sulfate or placebo until 28 weeks of gestation. Compared with placebo, iron supplementation from enrollment to 28 weeks of gestation did not significantly affect the overall prevalence of anemia or the incidence of preterm births but led to a significantly higher mean birthweight ($P = .010$), a significantly lower incidence of low-birthweight infants ($P = .003$), and a significantly lower incidence of preterm low-birthweight infants ($P = .017$).¹¹⁸ Additional studies on the effectiveness of preconception iron supplementation on preventing prenatal iron depletion are needed.¹¹⁹

Current recommendations: The CDC issued guidelines in 1998 for preventing

iron deficiency based on age and sex. They state that for girls aged 12-18 years and nonpregnant women of child-bearing age, iron status screening should occur every 5-10 years during a routine examination. Annual iron screening should be conducted for women with existing risk factors for iron deficiency. If anemia is confirmed with a second test, a trial of oral iron is warranted. Other sources recommend confirmation of iron deficiency as a cause of the anemia prior to initiation of therapy.¹²⁰ The American College of Obstetricians and Gynecologists recommend all pregnant women should be screened for anemia and those with iron deficiency anemia should be treated with supplemental iron, in addition to prenatal vitamins.¹¹⁰ The USDA food guidelines recommend that women of child-bearing age who may become pregnant eat foods high in hemeiron and/or consume iron-rich plant foods or iron-fortified foods with an enhancer of iron absorption, such as vitamin C-rich foods²²

Recommendation. At a preconception visit, screening should be conducted for women with risk factors for iron deficiency for the purposes of identifying and treating anemia. There is evidence to recommend that all women should be screened at a preconception visit for iron deficiency anemia for the purpose of improving perinatal outcomes. *Strength of recommendation: A; quality of evidence: IB.*

Essential fatty acids

Background: The essential fatty acids (EFA) linoleic and alpha-linolenic acid, and their long-chain derivatives arachidonic acid and docosahexaenoic acid (DHA) are important structural components of cell membranes, the central nervous system, and retinal cell membrane structure.^{121,122} EFAs cannot be synthesized in the body and must be ingested by food. Essential fatty acids are found in such foods as oily fish, flax seeds, walnuts, and vegetables oils.

In 2005, the FDA and Environmental Protection Agency, because of high mercury levels detected in fish, issued warnings that advise young children, pregnant women, nursing women, and

women of child-bearing age to avoid consuming swordfish, king mackerel, shark, and tilefish. The warnings also recommend that those groups eat no more than 12 ounces of fish weekly and no more than 6 ounces of canned albacore tuna weekly.¹²³ Concerns have been raised that eating oil-rich fish exposes the fetus to dioxins and polychlorinated biphenyls, which are environmental pollutants.

Several studies have shown an association between maternal dietary intake of oily fish or oils providing n-3 EFA during pregnancy and visual and cognitive development, maturity of sleep patterns, and motor activity in infants.¹²⁴⁻¹²⁷ Whether all women should be supplemented and at what dose of EFAs (eg, fish or fish oil supplements during preconception and pregnancy) has been the subject of much debate and recent research³

Evidence of efficacy: There is mixed evidence for the efficacy of essential fatty acids such as fish oil against adverse pregnancy outcomes for mother and child during preconception and pregnancy.^{128,129} For example, epidemiological evidence suggests an association between fish intake and birthweight. Another study showed a positive correlation with low fish consumption in early pregnancy and increased risk for preterm delivery and low birthweight.¹³⁰ A metaanalysis of 6 randomized controlled trials demonstrated that supplementation with omega-3 fatty acids was associated with a significantly greater length of pregnancy than in control subjects; however, there was no evidence that supplementation influenced the percentage of preterm deliveries, the rate of low-birthweight infants, or the rate of preeclampsia.¹³¹

In a review, the results of several randomized clinical studies have indicated that supplementation with fish oils may lead to modest increases in gestation length, birthweight, or both.¹³² The Cochrane collaboration review of 6 clinical trials found women randomized to a fish oil supplement had a mean gestation that was 2.6 days longer than women allocated to placebo or no treatment. Birth-

weight was slightly greater in infants born to women in the fish oil group compared with controls. However, there were no overall differences between the groups in the proportion of low birthweight or small-for-gestational-age babies.¹³³

Current recommendations: There are several recommendations and guidelines about omega fatty acid consumption for women. The Institute of Medicine set adequate intake for linoleic acid (N-6) 3 g/day for pregnant women and 12 g/day for women 18-50 years old. The adequate intake for α -N-3 is 1.4 g/day for pregnant women and 1.1 g/day for women 18-50 years old, respectively.¹³⁴ The USDA recommends to keep total fat intake between 20-35% of calories, with most fats coming from sources of polyunsaturated and monounsaturated fatty acids, such as fish, nuts, and vegetable oils.⁷⁰

The International Society for the Study of Fatty Acids and Lipids recommends adequate intakes of 4.44 g of linoleic acid and 2.22 g of α -N-6, with 0.22 g or more of DHA and 0.22 g of EFA for adults and 0.3 g or more of DHA daily for pregnant women.¹³⁵ The Perinatal Lipid Intake Working Group recently released guidelines for maternal dietary fat intake in Europe. After reviewing the literature, they report that intakes of up to 1 g/d DHA or 2.7 g/day n-3 long-chain polyunsaturated fatty acids have been used in randomized clinical trials without significant adverse effects. These guidelines recommend that pregnant and lactating women should aim to achieve an average dietary intake of at least 200 mg of DHA per day. The guidelines note that women of child-bearing age should aim to consume 1-2 portions of sea fish per week, including oily fish.¹³⁶

Recommendation. During the preconception period, women should be encouraged to eat a diet rich in EFAs including omega 3 and omega 6 fatty acids. To achieve this, women should be advised to consume at least 12 ounces of fish weekly and no more than 6 ounces of canned albacore tuna weekly. More research is critically needed to assess the risks and benefits of fish and fish oil con-

sumption during the preconception period. *Strength of recommendation:* B; *quality of evidence:* I-b.

Iodine

Background: Worldwide iodine deficiency is the single most important preventable cause of brain damage. In 2005 the World Health Organization estimated 2 billion people, 35% of the world population were iodine deficient.¹³⁷ Iodine is necessary for the production of thyroid hormones, thyroxine, and triiodothyronine, and it must be provided in the diet. Inadequate iodine intake leads to inadequate thyroid hormone production and to a spectrum of disorders, iodine deficiency disorders, including abortion, stillbirth, mental retardation, cretinism, increased neonatal and infant mortality, goiter, and hypothyroidism. Iodine is readily transferred to the fetus, and the fetal thyroid concentrates iodine and synthesizes thyroid hormones by 10-12 weeks' gestation. Iodine deficiency in pregnancy negatively affects the normal maturation of the developing fetal central nervous system, particularly myelination, and is responsible for cognitive impairment, permanent mental retardation, and in its most severe form, cretinism.¹³⁸

Iodine deficiency disorders are among the easiest and least costly of all disorders to prevent. Adding a small amount of iodine in the form of potassium iodate or potassium iodide to dietary salt is effective for prevention. Salt iodization is the recommended, preferred strategy to control and eliminate iodine deficiency. Sufficient dietary iodine throughout the life cycle, especially during the preconception period, can minimize the risk of iodine deficiency during critical, early fetal development. Studies of the impact of iodine supplementation specifically before pregnancy have not been done. Identification and treatment of iodine deficiency disorders before pregnancy is an effective preventive public health strategy.

Current recommendations: The Institute of Medicine's Food and Nutrition Board recommend minimum daily intake of iodine in the United States of 150 μg for

nonpregnant adults, 220 μg for pregnant women, and 290 μg for lactating women.¹³⁹ The World Health Organization, United Nations Children's Fund, and the International Council for Control of Iodine Deficiency Disorders recommend daily iodine intake of 150 μg for adults (≥ 12 years of age) and 200 μg for pregnant and lactating women.¹⁴⁰

Recommendation. Women of reproductive age with iodine deficiency should be counseled on the risks of this condition to pregnancy outcomes and the importance of maintaining adequate daily dietary iodine intake of 150 μg during preconception and at least 200 μg when pregnant or lactating. Public health efforts to implement salt iodization programs should be encouraged for all women residing in regions with endemic iodine deficiency. *Strength of recommendation:* A; *quality of evidence:* II-2.

Preconception weight and body mass index

Overweight

Background: Approximately one third of all women in the United States are obese, and obesity is identified as the fastest-growing health problem in the country.¹⁴¹ Obesity, defined as a body mass index (BMI) of 30 kg/m^2 or greater, is associated with elevated risks of type 2 diabetes; hypertension; infertility; heart disease; gallbladder disease; immobility; osteoarthritis; sleep apnea; respiratory impairment; social stigmatization; and a variety of cancers, including breast, uterine, and colon.¹⁴²⁻¹⁴⁵ Adverse perinatal outcomes associated with maternal obesity include neural tube defects, preterm delivery, stillbirth, gestational diabetes, hypertensive and thromboembolic disorders, macrosomia, low Apgar scores, postpartum anemia, cesarean delivery, and shoulder dystocia.^{142,143} Furthermore, women who are obese before conception tend to gain and retain more weight during pregnancy.¹⁴⁶

The risks associated with high BMIs are best addressed before conception because weight loss during pregnancy is not recommended. Health risks are better established for obese persons than for overweight individuals (BMI 25-29.9 kg/m^2). However, even mild to moderate

overweight in young adults predicts subsequent obesity.^{144,147} Weight retained from previous gestations is an important contributor to higher-than-optimal BMIs in child-bearing women.

Evidence of efficacy: Counseling to support improvements in diet and physical activity are considered first-line interventions.¹⁴⁷ In a systematic evidence review, the US Preventive Services Task Force concluded that counseling alone or with pharmacotherapy can promote modest sustained weight loss.^{144,147} The most successful nonsurgical approaches to weight loss were intensive, weight-focused counseling consisting of more than 1 session per month or multicomponent, intensive interventions that combine nutrition and exercise counseling with supportive, skill-building behavior interventions. Evidence from randomized controlled trials of long-term improved health with weight loss is limited.

Interventions about gestational weight from randomized controlled trials in pregnant obese women have mixed results. In a review by Guelinckx et al¹⁴⁸, only 2 of 7 trials, using nutrition and physical activity as an intervention, reached a significant decrease in gestational weight gain. There is a growing literature of clinical trials on the safety and perinatal outcomes for women who have undergone gastric bypass surgery.¹⁴⁹⁻¹⁵⁵

ACOG suggests that utilizing the stages of change model as adapted for overweight and obesity may help determine patient motivation and interest in weight loss. ACOG recommends setting an initial goal of losing 5-10% of total body weight over a 6 month period as realistic and achievable.¹⁴⁷ Weight loss is not recommended during any pregnancy, irrespective of pregravid weight. Therefore, to minimize the risks of obesity on reproductive outcomes, interventions must occur before pregnancy.

Current recommendations: In an ACOG Committee Opinion on obesity issued in October 2005, the following recommendations were made: (1) BMI should be calculated for all women and (2) appro-

appropriate interventions or referrals to promote a healthy weight and lifestyle should be offered.¹⁴⁷ Relative to non-pregnant populations, the US Preventive Services Task Force found that counseling and pharmacotherapy can promote modest sustained weight loss and that pharmacotherapy appears to be safe in the short term; however, long-term safety has not been established. The task force also noted that, in selected patients, surgery promotes large amounts of weight loss with rare but potentially severe complications.¹⁴⁴

In 1990, the IOM published a report that reevaluated the evidence regarding optimal weight gain during pregnancy. The report concluded that prepregnancy body weight should be taken into account when advising on optimal weight gain. For women with a normal prepregnancy BMI, a weight gain of around 0.4 kg/week during the second and third trimesters is recommended. For underweight women, a weight gain of 0.5 kg/week is the target, whereas for overweight women, 0.3 kg/week is recommended.¹⁵⁶

Recommendation. All women should have their BMI calculated at least annually. All women of reproductive age with a BMI of 25 kg/m² or greater should be counseled about the risks to their own health, the additional risk associated with exceeding the overweight category, and the risks to future pregnancies, including infertility. All women with a BMI of 25 kg/m² or greater should be offered specific strategies improve the balance and quality of the diet, decrease caloric intake, and increase physical activity, and be encouraged to consider enrolling in structured weight-loss programs. *Strength of recommendation: A; quality of evidence: I-b.*

Underweight

Background: Although most discussions of health risks associated with weight status focus on overweight and obesity, a 2005 analysis estimating the number of excess deaths in adults are associated with various BMI levels revealed that 33,746 deaths were associated with BMIs less than 18.5 kg/m.¹⁵⁷ Health risks of being underweight include nutrient defi-

ciencies, heart irregularities, osteoporosis, amenorrhea, and infertility. For women who become pregnant, low pregravid weight is associated with increased risks for preterm birth and low birthweight, which are all major contributors to poor pregnancy outcomes.¹⁵⁷⁻¹⁶⁰

Evidence of efficacy: A low prepregnancy BMI may also increase the risk of birth defects such as gastroschisis. A study by Lam et al¹⁶¹ found that infants born to underweight mothers (pregnancy BMI < 18.1 kg/m²) were more than 3 times as likely to have gastroschisis compared with infants of normal-weight mothers (pregnancy BMI 18.1-28.3 kg/m²). In this study, every unit increase in BMI was estimated to decrease the risk for gastroschisis by about 11%.

Weight gain in pregnancy cannot overcome the risks associated with a low pregravid weight. Therefore, women should be counseled during the preconceptional period on the potential risks of their weight on fertility and on pregnancy outcome.

Recommendation. All women should have their BMI calculated at least annually. All women of reproductive age with a BMI 18.5 kg/m² or less should be counseled about the short- and long-term risks to their own health and the risks to future pregnancies, including infertility. All women with a low BMI should be assessed for eating disorders and distortions of body image. *Strength of recommendation: A; quality of evidence: III.*

Eating disorders

Background: Women with eating disorders such as anorexia nervosa and bulimia nervosa may have higher rates of miscarriage, low birthweight, obstetric complications, and postpartum depression. Eating disorders are associated with nutritional, metabolic, endocrine, and psychological changes that have potentially negative effects on fetal development. Pregnancy was thought to be a rare occurrence among women with anorexia nervosa; however, women who are below threshold for clinical symptoms or are in remission may not have compromised fertility. Women with bulimia nervosa may have less difficulty

conceiving, but they may experience significant difficulty during the pregnancy related to binge eating, purging, and laxative or diuretic use.¹⁶²

Women with eating disorders may be reluctant to disclose symptoms, and there are no reliable laboratory indicators for eating disorders, so clinicians need to be aware of warning signs and use effective assessment techniques.¹⁶³ Assessment should be done for conditions such as bulimia and anorexia; once identified, nutritional counseling and in some cases treatment of an underlying emotional condition should be initiated. A multidisciplinary approach is most effective in treating a woman with an eating disorder in pregnancy.^{163,164}

Recommendation. All women of reproductive age with anorexia and bulimia should be counseled about the risks to fertility and future pregnancies and should be encouraged to enter into treatment programs before pregnancy. *Strength of recommendation: A; quality of evidence: III.*

Conclusion

Good nutrition is an essential component of attaining a healthy pregnancy and birth outcome. Women of reproductive age should be advised that the quality of a woman's diet may influence her pregnancy outcomes. Women of reproductive age, especially those who are planning a pregnancy, should be counseled to consume a well-balanced diet including fruits and vegetables, calcium-rich foods, and protein-containing foods daily and increase their consumption of iron-rich or iron-fortified foods in conjunction with vitamin C-rich foods to enhance iron absorption. Women should consume folate-rich foods daily including 400 µg of folic acid daily. More research is critically needed in the area of the safety and efficacy of fish consumption and dietary supplements. Health care professionals should address optimal weight gain, healthy diet, and the use of dietary supplements as a part of preconception care. ■

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