Optimal Nutrition for Improved Twin Pregnancy Outcome

William Goodnight, MD, MSCR, and Roger Newman, MD, for the Society of Maternal–Fetal Medicine

Twin pregnancies contribute a disproportionate degree to perinatal morbidity, partly because of increased risks of low birth weight and prematurity. Although the cause of the morbidity is multifactorial, attention to twin-specific maternal nutrition may be beneficial in achieving optimal fetal growth and birth weight. Achievement of body mass index (BMI)-specific weight gain goals, micronutrient and macronutrient supplementation specific to the physiology of twin gestations, and carbohydrate-controlled diets are recommended for optimal twin growth and pregnancy outcomes. The daily recommended caloric intake for normal-BMI women with twins is 40–45 kcal/kg each day, and iron, folate, calcium, magnesium, and zinc supplementation is recommended beyond a usual prenatal vitamin. Daily supplementation of docosahexaenoic acid and vitamin D should also be considered. Multiple gestation-specific prenatal care settings with a focus on nutritional interventions improve birth weight and length of gestation and should be considered for the care of women carrying multiples. Antepartum lactation consultation can also improve the rate of postpartum breastfeeding in twin pregnancies. Twin gestation-specific nutritional interventions seem effective in improving the outcome of these pregnancies and should be emphasized in the antepartum care of multiple gestations. This review examines the available evidence and offers recommendations for twin pregnancy-specific nutritional interventions. (Obstet Gynecol 2009;114:1121–34)

The increasing rate of twin gestations is well-documented. Twin gestations account for a disproportionate share of neonatal morbidity, with increased risks of preterm birth, low birth weight, and intrauterine growth restriction. Infants of multiple births represent 3% of all deliveries but account for 15% of preterm birth, 20% low birth weight (LBW; less than 2,500 g), and 19–24% of very low birth weight (less than 1,500 g) neonates born in the United States. Optimal twin survival has been demonstrated to be associated with birth weights more than 2,850 g and delivery after 36 weeks gestational age.1–3 Unfortunately, twins often deliver with average birth weights between 2,300 g and 2,600 g at a mean gestational age of 35 weeks to 36 weeks. Impaired fetal growth is also associated with long-term complications, including an increased lifetime risk of cardiovascular disease and obesity. Neonatal body composition in appropriately grown twin gestations is similar to singleton neonates, whereas small for gestational age twins have a lower lean body mass, a lower fat mass, and a trend to lower bone density compared with small for gestational age singleton neonates.4

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Maternal pregestational and gestational nutritional status in singleton pregnancies without question is associated with pregnancy outcome. The nutritional demands of pregnancy are magnified by the presence of multiple fetuses, and the potential beneficial impact of optimal nutrition on pregnancy outcomes should not be underestimated. Thus, the nutritional recommendations for singleton pregnancy require specific adaptation for a multifetal gestation. The nutritional competition engendered by the presence of multiple fetuses results in the accelerated depletion of maternal nutritional reserves. Although monochorionic twin pregnancies carry a greater risk of the above adverse pregnancy outcomes than dichorionic twins, there are similar rates of selective intrauterine growth restriction between monochorionic and dichorionic twins. The overall risk of fetal growth restriction in twin pregnancies creates a situation where modification of nutritional intake has a greater opportunity to positively influence the outcome for twins compared with singleton gestations. This article will suggest specific maternal nutritional recommendations for twin pregnancy based on available scientific evidence.

The goals for optimization of maternal nutrition in multiple gestations therefore include

1. optimizing fetal growth and development,
2. reducing incidence of obstetric complications,
3. increasing gestational age at delivery, and
4. avoiding excess maternal weight gain that could result in unnecessary postpartum weight retention.

**PHYSIOLOGIC ADAPTATIONS TO TWIN PREGNANCY**

Multifetal gestations undergo significant maternal physiologic adaptations beyond the usual pregnancy changes, including increased plasma volume, increased basal metabolic rate, and increased resistance to carbohydrate metabolism. The blood volume in a twin gestation increases by 50–70% by 20 weeks of gestation, with only a 25% increase in erythrocytes. This plasma volume expansion results in decreased concentrations of hemoglobin, albumin, and watersoluble vitamins, whereas increases in fat-soluble vitamins, triglycerides, cholesterol, and free fatty acids have been demonstrated. The relatively greater increase in plasma volume in a twin pregnancy also results in a dilutional effect on red blood cells in the second and third trimesters of pregnancy.

The resting energy expenditure is an indicator of maternal basal metabolic rate that can be used to estimate energy requirements. The maternal resting energy expenditure increases each trimester in both singleton and multiple gestations. Singagawa et al demonstrated that compared with singleton pregnancies, maternal resting energy expenditure increased by 10% in twin pregnancies, independent of changes in minute ventilation. The increase in resting energy expenditure can also be seen as a result of the increased mass of maternal tissues, including the breast, uterus, body fat, and muscle as well as the increase in blood volume. Such an increase in resting energy expenditure can result in a 40% increase in caloric requirements for twin gestations.

The relatively larger placental mass in multiple gestations results in an increase in placental steroid and hormone production. As a result, multifetal gestation has been described as a state of “accelerated starvation,” in which the development of starvation ketosis occurs at a more rapid rate in twin gestations than in a singleton pregnancy. These hormonally driven metabolic changes result in remarkable maternal carbohydrate use, resulting in a greater propensity for depletion of maternal hepatic glycogen stores and the development of maternal ketonemia. Casele et al demonstrated that women with twin gestations fed a diet of 40 kcal/kg ideal body weight, divided into three meals, are more susceptible to the development of ketosis after fasting, as evidenced by elevated β-hydroxybutyrate serum levels after an evening fast compared with singleton gestations. Classically, the United States Department of Agriculture (USDA), Institute of Medicine (IOM), and American Dietetic Association (ADA) recommendations for reproductive age women suggest that 43–65% of calories daily be derived from carbohydrates, a diet that has been suggested to result in poor glycemic control and excess weight gain in twin gestations. Luke et al demonstrated that a diet composed of 40% carbohydrates and a greater percentage of fats and protein with an appropriate caloric intake (3,000–4,000 kcal/d in underweight to normal weight women) achieved a greater degree of euglycemia during pregnancy. Other limited trials also suggest that a lower proportion of carbohydrates in the diet in women with gestational diabetes is associated with improved glycemic control, as evidenced by lower insulin utilization.

**DIETARY COMPOSITION**

Although no established nutritional guidelines exist, an estimate of individual macronutrient requirements for twins is described in Table 1. These recommendations are based on extrapolation of the singleton recommended dietary allowances (RDA) published...
by the Food and Nutrition Board of the National Research Council and body mass index (BMI)-specific recommendations for twin gestations published by Luke and coworkers. Luke et al\(^{12}\) have proposed a dietary composition for twins in which energy intake is derived 20% from protein, 40% from low-glycemic index carbohydrates, and 40% from fat (Table 1). Due to the increased nutritional demands of the fetus and maternal metabolism, these recommendations equate to a daily intake of 3,500 calories, composed of a diet with 175 g protein, 350 g of carbohydrate, and 156 g of fat per day for women of normal prepregnancy BMI. Adequate protein intake is essential to normal fetal growth in twin gestations. In singleton pregnancies, the protein storage during pregnancy has been estimated to be 925 g, distributed as 400 g to the fetus, 100 g to the placenta, and 425 g additional stored in the mother.\(^7\) Inadequate protein intake can occur secondary to insufficient dietary intake, intake of poor quality protein (high fat meats), or inadequate caloric intake, which results in dietary protein being diverted to meet maternal energy requirements.\(^{12}\) Reduced amino acid availability to the fetus not only affects fetal growth but may also restrict placental growth, further compounding the effect of protein deficiency.\(^{12}\) Additionally, Moore et al\(^{13}\) evaluated maternal diet composition and the effect on neonatal weight and ponderal index. The percentage of energy from protein (14.4–18.1% in this study) in early pregnancy had the best positive association with neonatal weight, whereas the percentage of energy from carbohydrates (45.3–53.2% in this sample) was inversely proportional to the ponderal index (increased carbohydrates resulted in neonatal thinness).\(^{13}\) Ideal protein sources include lean meat, fish, and skin-free poultry, eggs, dried beans, peas, and tofu. An emphasis on low to medium glycemic index carbohydrates (such as brown rice, whole wheat/multigrain bakery products and pastas, boiled potatoes, green vegetables, beans, and lentils) is also suggested to further reduce the potential for wide serum glucose fluctuations. To gain the necessary calories, the proportion of caloric rich fats is substituted for carbohydrates.\(^{14}\) Table 2 suggests the number of serving suggestions daily to achieve this diet composition and caloric requirements.\(^{14}\) This dietary intake should be divided into three main meals with three smaller snacks interposed in the usual meal schedule to help reduce the development of hypoglycemia and transient ketosis.\(^{14}\) In underweight women (BMI less than 19.8 kg/m\(^2\)) and those with poor weight gain in pregnancy, addition of higher fat, calorie-dense foods, including nutritional supplement drinks, whole or 2% milk, fruit juices, and the change to five balanced meals per day can achieve the necessary weight gain. Similarly, excessive weight gain in pregnancy should lead to a reduction in these high fat, calorie-dense foods.

**WEIGHT GAIN**

Total maternal weight gain and the timing of weight gain are crucial to optimal fetal growth in twin gestations. The preponderance of the evidence in singleton gestations is that there is a relationship between increasing maternal weight gain and in-

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### Table 1. Suggested Daily Diet Composition for Twin Gestation by Maternal Prepregnancy Body Mass Index\(^{14}\)

<table>
<thead>
<tr>
<th></th>
<th>Underweight</th>
<th>Normal Weight</th>
<th>Overweight</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories (kcal)</td>
<td>4,000</td>
<td>3,000–3,500</td>
<td>3,250</td>
<td>2,700–3,000</td>
</tr>
<tr>
<td>Protein (g)*</td>
<td>200</td>
<td>175</td>
<td>163</td>
<td>150</td>
</tr>
<tr>
<td>Carbohydrate (g)*</td>
<td>400</td>
<td>350</td>
<td>325</td>
<td>300</td>
</tr>
<tr>
<td>Fat (g)†</td>
<td>178</td>
<td>156</td>
<td>144</td>
<td>133</td>
</tr>
</tbody>
</table>

\* 4 kcal/g.  
† 9 kcal/g.

### Table 2. 2002 American Dietetic Association Serving Suggestions for Multiple Pregnancy of Normal Body Mass Index

<table>
<thead>
<tr>
<th></th>
<th>Milk/Yogurt/ Cheese</th>
<th>Meat/Poultry/ Fish/Eggs</th>
<th>Vegetable</th>
<th>Fruit</th>
<th>Bread/Cereal/ Rice/Pasta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily servings</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Serving suggestion</td>
<td>1 cup milk; 1 oz cheese</td>
<td>2–3 oz lean meat, fish, poultry; 1 egg</td>
<td>1 cup raw/cooked vegetables; 2 cups raw green leafy vegetables</td>
<td>1 cup fruit; cup dried fruit</td>
<td>1 slice bread; 1 cup ready to eat cereal; cup cooked rice/pasta</td>
</tr>
</tbody>
</table>
creases in birth weight, with a corresponding reduction in the incidence of low birth weight. The published literature also suggests that low maternal weight gain superimposed on a low maternal pregravid weight compounds the adverse effects of each, resulting in high rates of both low birth weight delivery and premature birth. The effect of low maternal weight gain is diminished in women with higher pregravid weights. Historically, weight gain recommendations were made to reduce the risk of LBW, with contemporary recommendations made to achieve optimal fetal growth without excess maternal weight gain. Early retrospective studies attempted to define the appropriate maternal weight gain for twin gestations based on optimal neonatal outcomes. Pederson et al demonstrated that optimal twin pregnancy outcome, defined as two living infants, each more than 2,500 g, born after 37 weeks estimated gestational age, and 5-minute Apgar score more than 7 was associated with a maternal weight gain of 20 kg (44 lb). Less than optimal outcomes were seen with maternal weight gains less than 16.8 kg (37 lb). The timing and the rate of maternal weight gain also affect both birth weight and prematurity. Midgestational maternal weight gains seem to have the greatest effect on fetal growth and ultimate birth weight. Optimal twin outcomes (birth weight more than 2,500 g) have been associated with maternal weight gain of 24 lb by 24 weeks of gestation. Even when there is appropriate catch-up maternal weight gain after 24 weeks, a low rate of weight gain before 24 weeks (less than 0.85 lb/wk) was strongly associated with poor intraterine growth and earlier delivery. In studies making use of serial ultrasonographic measures of fetal growth in relation to maternal weight gain, it has been demonstrated that early maternal weight gain (less than 20 weeks) and midpregnancy weight gain (20–28 weeks) significantly enhanced the rates of fetal growth between 20 weeks and 28 weeks and from 28 weeks until birth. As noted in singleton gestations, this influence of early maternal weight gain on subsequent fetal growth was most pronounced in underweight women. Physiologically, this relationship suggests that early weight gain results in improved maternal nutrient stores that become important later in pregnancy as a nutrient reserve when fetal demands begin to increase. Adequate early maternal weight gain may also enhance placental growth, which helps to sustain an adequate nutrient supply to the twins later in pregnancy.

Byer et al suggested weight gain goals for twin pregnancy based on maternal prepregnancy BMI. Optimal maternal weight gain and timing of weight gain were modeled based on ideal fetal growth and newborn birth weights determined to be between the singleton 50th and twin 90th percentiles by 38 weeks of gestation. Among twins achieving these optimal fetal growth and birth weights, the associated maternal BMI-specific weight gains were found to be described by the maternal weight gain curves noted in Figure 1. In a follow-up study of the effects of using these BMI-specific weight gain recommendations, twin gestations that failed to achieve BMI-specific weight gain goals demonstrated a lower birth weight by nearly 200 g (P<.001) and a 1.04-week shorter length of gestation (P=.02) (Goodnight W, Hill E, Newman R, Rowland A. Achieving maternal BMI-specific weight gain goals improves birthweight and gestational age at delivery in twin pregnancies [abstract]. Am J Obstet Gynecol 2006;195:S121). Based on this new data, the 2009 IOM guidelines for weight gain in twin pregnancy now recommend BMI-specific weight gains for normal weight women of 17–25 kg (37–54 lb), overweight women, 14–23 kg (31–50 lb), and obese women, 11–19 kg (25–42 lb). The small differences from Luke et al are based on different BMI categories used in the IOM recommendations. In practice, we continue to use the graphs created by Luke et al to track and recommend maternal weight gain during pregnancy.

Determinants of maternal weight gain in pregnancy have not been extensively studied in multiple gestations but are likely influenced by multiple biological, behavioral, cultural, and psychosocial factors. Wells et al demonstrated in a retrospective analysis that maternal obesity and hypertension are associated with a greater risk for weight gain above the IOM recommended weight gains, whereas diabetes was not associated with excessive or below IOM weight gain goals, and prior live births was associated with lower risk of excessive maternal weight gain in pregnancy. Initial physician counseling is thus necessary to determine maternal perceptions of weight gain goals, review potential maternal risk factors for excessive or poor weight gain, and provide education and support to achieve optimal weight gain goals. Although it is well established that increased maternal weight gain in pregnancy increases birth weight in twins, the long-term effects of retained maternal weight after delivery remains of concern. Although not extensively evaluated in multiple gestations, excessive maternal weight gain in pregnancy may be associated with increased risks of gestational hypertension, cesarean delivery, and birthweight more than 4,000 g (rare in twins). The weight gain recommendations for twin pregnancy have been criticized for potentially contributing to the risk of maternal obesity through postpartum
retention of the weight gain. Luke et al (Luke B, Hediger ML, Min L, Nugent C, Newman RB, Hankins GD, et al. The effect of weight gain by 20 weeks’ gestation on twin birthweight and maternal postpartum weight [abstract]. Am J Obstet Gynecol 2006;195:S85), however, demonstrated that the mean weight retention for those who gained within the recommended BMI specific weight gain goals was only 1.5 lb at 6 weeks postpartum, minimally above the 0.9 lb weight retention seen in those with maternal weight gain below the BMI-specific weight gain goals. In singleton pregnancy, long-term maternal weight (15 years postpartum) was equivalent among women who gained below or within IOM recommendations, with excessive maternal weight gain in pregnancy associated with higher long-term weight gain.25 Thus, in the multiple gestation clinical situation, attention should be given to both achievement of the recommended maternal weight gain goals and serial assessment of weight gain and equal intervention to prevent or slow excessive weight gain.

MICRONUTRIENTS
Recommendations for micronutrient intake are determined by the Food and Nutrition Board of the Institute of Medicine. Dietary Reference Intakes have replaced the RDA estimates. The RDA recommendations were determined to estimate the intake needed to meet the needs of 97–98% of the population, whereas an Adequate Intake is estimated to cover the needs for all individuals in a specific group. These estimates are supplemented by the Tolerable Upper Intake Levels, an estimate of the maximal intake level that should not cause harm. Nutrients such as magnesium, calcium, and zinc are often lacking in women’s diets and may have effects on fetal growth and preterm delivery. In a randomized, pla-
demonstrated that micronutrient supplementation (vitamin C 60 mg, B-carotene 4.8 mg, vitamin E 10 mg, thiamin 1.4 mg, riboflavin 1.6 mg, niacin 15 mg, pantothenic acid 6 mg, folic acid 200 microgram, cobalamin 1 microgram, zinc 15 mg, magnesium 87.5 mg, and calcium carbonate 100 mg) in pregnancy resulted in a 10% improvement in birth weight (3,300±474 g compared with 3,049±460 g, P=.03) and a reduction in birth weight below 2,700 g among singleton pregnancies. There are fewer data available on micronutrient supplementation in twin pregnancies. However, the expectation would be that similar or greater benefits may be expected because micronutrient needs are greater and deficiencies may be more common in multiple gestations. Because twin gestations are at increased risk for poor fetal growth and preterm birth, small improvements from benign interventions such as micronutrient supplementation may have significant benefits.

Although the majority of micronutrient supplements have a wide safety margin, notable potentially adverse complications may arise from excessive micronutrient supplementation. Excessive doses of vitamin A (at least more than 10,000 international units/d and probably more than 25,000 international units/d) in pregnancy have been associated with fetal anomalies, including anomalies of the cardiovascular system, face and palate, ears, and genitourinary tract; thus, the maximal recommended vitamin A supplement in pregnancy is 8,000 international units/d. Excessive supplementation of most other vitamins can result in gastrointestinal disturbances but seem without teratogenic effect.

**CALCIUM AND VITAMIN D**

During in utero life, the fetus accumulates 25–30 g of calcium, the majority of which occurs in the third trimester. Calcium is made available to the fetus by extraction from maternal bone mass and through increased maternal intestinal absorption. Maternal calcium is also lost in pregnancy because of an increase in urinary calcium excretion. An estimated 200–300 mg/d increase in calcium intake above prepregnancy requirements is thus required to meet the fetal demands and maintain maternal calcium homeostasis. During lactation, there is a reduction in urinary calcium excretion. However, the majority of pregnant women do not consume diets with an adequate calcium intake. Food sources for calcium are primarily milk and dairy products, with some calcium in green leafy vegetables such as kale and turnip greens, with approximately one third of ingested calcium being absorbed. The IOM recommends a calcium intake in pregnancy of 1,000–1,300 mg daily (Tolerable Upper Intake Levels 2,500 mg). A Cochrane review of calcium supplementation of at least 1,000 mg daily in pregnancy, not specifically describing twin gestations, demonstrated significant reductions in the risks of hypertension (relative risk [RR] 0.7, 95% confidence interval [CI] 0.57–0.86) and preeclampsia (RR 0.48, 95% CI 0.33–0.69) in both low- and high-risk populations. The effects of calcium supplementation were most beneficial in high-risk women and in those with low dietary calcium intake. These findings are likely applicable to twin pregnancies because of the increased fetal demands for calcium and the increased baseline risk of preeclampsia in these gestations. Calcium supplementation may also have fetal programming effects that persist into childhood. In a trial by Belizan et al, children of mothers who received calcium supplement in pregnancy had lower rates of hypertension (RR 0.59, 95% CI 0.39–0.9). The presence of maternal contraindications to calcium supplementation (eg, nephrolithiasis) may require reductions in the daily supplement.

Vitamin D is also necessary for the appropriate metabolism of calcium, and deficiency is common in pregnancy. Fetal vitamin D is dependent on maternal vitamin D levels, and low maternal vitamin D is the dominant risk factor for neonatal rickets. The active metabolite of vitamin D is 1,25-dihydroxyvitamin D \([1,25 \text{(OH)}_2 D]\), which facilitates intestinal calcium absorption and calcium mobilization from bone, and decreases renal calcium excretion. The serum concentration of 1,25 \((\text{OH})_2 D\) increases 50–75% in the second trimester (mean 176±36 pmol/L) and doubles by the third trimester (mean 212±83 pmol/L), compared with the nonpregnant state (100±32 pmol/L). The current Dietary Reference Intake recommendation for vitamin D is 400 international units/d based on estimated adequate intakes; however, supplementation at this dose in adults does not result in increased circulating 25(OH)D levels. Adults require sun exposure daily for conversion of vitamin D to 1,25 \((\text{OH})_2 D\), with whites requiring 0.5 hours per day and African Americans requiring 5 times this amount. For those with minimal sun exposure, supplementation during pregnancy should approach 1,000 international units/d. Wagner and Greer report that vitamin D supplementation of levels more than 1,000 international units/d are necessary to achieve normal vitamin D levels (more than 50 nmol/L 25-OH-D). This supplement, plus appropriate sun exposure, will not result in high levels...
associated with hypervitaminosis D (hypercalciumia, hypercalcemia, and extraskeletal calcifications with symptoms of nausea and vomiting and arthralgias), but will provide adequate vitamin D levels for maternal and fetal development. Vitamin D supplementation during pregnancy has been associated with an increase in birth weight as well as an increase in newborn weight gain, whereas deficiency has been associated with an increased risk of preeclampsia. Thus, vitamin D supplementation may be beneficial in twin gestations. The Dietary Reference Intakes/Tolerable Upper Intake Levels for calcium and Vitamin D are 1,300 mg/2,500 mg and 200 international units/2,000 international units daily, thus the diet recommendation for twin gestations includes 2,000–2,500 mg/d of calcium and 1,000 international units of vitamin D daily. Due to the variations in sun exposure and vitamin D levels, assessment of maternal vitamin D levels in twins should be considered in first and early third trimester to allow alterations in the supplement dosage. Attention to vitamin D supplement is especially important given the frequent occurrence of complications resulting in bedrest in twin pregnancy.

ANTIOXIDANTS, VITAMIN C AND E

The role of antioxidant supplements to reduce the risk of preeclampsia and preterm birth has been investigated in pregnancy. Early studies demonstrated a reduction in the recurrence of preeclampsia and an improvement in the plasminogen-activator inhibitor PAI-1 to PAI-2 ratio (favorable antioxidant measure) with vitamin C (1,000 mg) and vitamin E (400 micrograms) supplementation during pregnancy. The VIP trial, however, did not reveal any reduction in preeclampsia either in the overall at-risk population or in a subgroup of twin gestations. Nevertheless, analysis of serum vitamin C levels was noted to be lower in the supplemented group who developed preeclampsia compared with those who did not receive supplementation. The VIP trial, however, demonstrated an increased risk of LBW in those with vitamin C and E supplementation (RR 1.15, 95% CI 1.02–1.30, \( P_{\text{adj}} = .02 \)). Vitamin C has also been suggested to provide protection against preterm premature rupture of membranes in singleton pregnancy. Antioxidant trials to date have examined primarily singleton gestations and demonstrate the most significant benefit in pregnancies with nutritional deficiencies. The current Dietary Reference Intakes/Tolerable Upper Intake Levels for vitamin C and E, respectively, are 80/1,800 mg/d and 15/800 micrograms/d, making suggested intakes of 500–1,000 mg/400 micrograms/d vitamin C/vitamin E reasonable for twin gestations, whereas specific trials in twin pregnancy await. Vitamin C and E have not been associated with toxicities at very high doses, with the exception of gastrointestinal disturbances, and no adverse fetal effects have been noted. Vegetable oils are the primary source of vitamin E, whereas vitamin C is found in citrus fruit and green vegetables.

ZINC AND MAGNESIUM

Zinc is necessary in several biologic systems, including protein synthesis and nucleic acid metabolism as well as prevention of free radical formation. Meats, seafood, and eggs provide the optimal dietary sources of zinc. Zinc deficiency, although rare, may be associated with fetal neurologic malformations and growth restriction, and late pregnancy deficiency may also be associated with impaired brain function and behavior abnormalities due to abnormal neuronal growth. Zinc supplementation in pregnancy may improve several pregnancy outcomes, including reducing preeclampsia and preterm birth, and result in improved birth weight in deficient populations. Hininger et al demonstrated that maternal zinc levels were not different between supplemented or placebo groups in a multinutrient supplement trial, but zinc levels did correlate well with neonatal length \( r = 0.58, \quad P_{\text{adj}} = .03 \). Although there are few data in twin gestations, a systematic review of zinc supplementation of 15–44 mg daily in pregnancy was associated with a 14% reduction in preterm birth (RR 0.86, 95% CI 0.76–0.98), with the majority of the effect seen in nutritionally deficient populations. However, no effect on birth weight was seen. Although zinc metabolism has not been systematically studied in multiple gestations, zinc supplementation could theoretically be beneficial in this population at high risk for preterm birth and LBW. The Dietary Reference Intakes/Tolerable Upper Intake Levels for zinc is 12 mg/40 mg/d respectively. Zinc is not stored in the body and virtually nontoxic; rare cases of leukopenia and anemia have been reported with prolonged intake of more than 50–300 mg/d. Based on National Health and Nutrition Examination Survey III data, 59% of pregnant women achieve adequate intake (supplement and diet) of zinc, with a mean dietary intake of 9.2 \( \pm 2.1 \) mg. Thus achievement of daily intake of zinc of 14–45 mg/d is recommended for twin gestations, often requiring supplement.

Although individual trials of variable quality and design demonstrate conflicting results regarding the effects of magnesium supplementation on preterm birth and fetal growth, a systematic review by
Iron deficiency is the most common nutritional deficiency worldwide, and has been associated with preterm birth and low birth weight. In the United States, estimates of iron deficiency anemia in pregnancy range from 5–17%, whereas estimates of low maternal ferritin (less than 15 micrograms/L) with normal hemoglobin are seen in up to 20% of pregnant women. Fetal and neonatal iron deficiency, as measured by cord blood ferritin level less than 30 micrograms/L is associated with severe maternal anemia (hemoglobin less than 6.0 g/dL). Both mild maternal anemia (hemoglobin less than 8.5 g/dL) and a maternal ferritin level less than 12 micrograms/L are associated with poor fetal iron supply. Scholl et al demonstrated an association between iron deficiency and poor maternal weight gain (adjusted odds ratio [AOR] 2.67, 95% CI 1.13–6.3). Additionally, iron deficiency anemia was also associated with an increased risk of preterm birth (AOR 2.66, 95% CI 1.15–6.17) and LBW (AOR 3.10, 95% CI 1.16–4.39). Cogswell et al demonstrated that iron supplementation with 30 mg elemental iron daily resulted in a significant increase in birth weight (200 g) compared with placebo even in the presence of normal serum ferritin levels in the first trimester.

Twin pregnancies have lower maternal hemoglobin levels in the first and second trimesters and higher rates of iron deficiency anemia, and the resulting infants have increased risk of residual iron deficiency anemia for up to 6 months of age. The rate of iron deficiency anemia is 2.4–4 times higher than in singleton pregnancies. The iron requirement for twin pregnancy is estimated to be nearly twofold that of a singleton pregnancy. Rosello-Soberon et al reported an estimated 869 mg elemental iron requirement for twins compared with 476 mg for singleton pregnancies. Iron supplementation during the first and second trimesters has been associated with reductions in both preterm birth and LBW. In women with iron deficiency (serum ferritin less than 15 micrograms/L), daily replacement with 60–120 mg of elemental iron will increase the hemoglobin concentration by 1g/dL over 4 weeks.

The ideal source of iron supplementation is from an adequate diet that includes heme iron–rich food sources such as red meat, pork, fish, and eggs. These sources of dietary iron are ideal in that they not only provide iron that is more easily absorbed but also represent a higher quality and quantity of protein. Nonheme iron sources, such as iron fortified bread, leafy green vegetables, and nuts, should also be encouraged both for their iron content as well as for the presence of folate. The Dietary Reference Intake/ Tolerable Upper Intake Levels for iron are 27 mg/45 mg daily, respectively. Supplementation of nonanemic twin gestations of 30 mg daily of elemental iron would be appropriate to meet the increased maternal and fetal needs of the pregnancy.

Folic acid is also an important micronutrient in pregnancy because it is essential in DNA synthesis and cell division. Folate is required for the increase in maternal red blood cells as well as for the growth of the fetus. Hyperhomocysteinemia is associated with deficiency in folate and has been associated with intrauterine growth restriction, preeclampsia, and placental abruption through vascular endothelial injury. Anemia due to folate deficiency is eight times more common in twins than in singleton pregnancy. Trials of folic acid supplement in pregnancy have not demonstrated consistent improvements in pregnancy outcome, with one meta-analysis demonstrating a reduction in the risk of low birthweight (RR 0.73, 95% CI 0.53–0.99) and a retrospective review demonstrating a reduction in the risk of preterm birth with preconception folic acid supplementation. The current recommendation for folic acid in the preconception period and during pregnancy include 400 micrograms/d, whereas the Dietary Reference Intake/ Tolerable Upper Intake Levels for folate are 600 micrograms/1,000 micrograms daily. Based on these recommendations, 1mg daily folic acid is suggested for twin gestations.

**OMEGA-3-FATTY ACIDS**

Essential fatty acids (EFA) are lipids that cannot be synthesized in the body and thus require appropriate dietary intake. Essential fatty acids are involved in many metabolic processes, including energy storage, cell membrane function (including neuronal development), control of inflammation, and control of thrombosis. Two groups of EFA exist: omega-6 (ω-6FA: linoleic acid, derived from cereals, grains, processed foods, meat, milk, eggs, and oils, including corn,
sunflower, safflower, and sesame) and omega-3 (ω-3FA: α-linolenic acid, only found in selected seeds, nuts, and fish oils). Because plant sources may not contain the necessary docosahexaenoic acid (DHA) component of ω-3FA, the optimal nutritional source is fish oils. Optimal homeostatic inflammatory and thrombotic states have been theorized to result from a balance between ω-3FA and ω-6FA, with ideal diets having a ratio of ω-6 to ω-3 of 1–2:1. A deficiency in ω-3 results in a prothrombotic and proinflammatory state that has been associated with an increased risk of cardiovascular and inflammatory diseases. A typical Western diet currently has an ω-6 to ω-3 ratio of 16:1.

In comparison with singleton pregnancies, neonates born of twin pregnancies have lower levels of ω-3FA in the walls of their umbilical veins and arteries, indicating an inadequate dietary supply. An in vitro trial of singleton and twin pregnancies demonstrated that DHA concentration in fetal erythrocyte membrane was directly related to maternal concentration and that lower concentration of ω-3FA was associated with increased membrane rigidity and increased resistance to flow. In this study, the mean erythrocyte DHA concentration was significantly lower in twin gestations, leading the authors to conclude that fetal demand for DHA in multiple pregnancies may not be satisfied by typical dietary intake.

Epidemiologic data from the Faroe Islands, where diets are rich in marine oils, suggest that diets with a more favorable ω-6 to ω-3 ratio increase birth weight through either prolongation of pregnancy or by optimizing the fetal growth rate. In prospective trials, fish oil supplementation of 2.7 g of ω-3FA daily has been shown to prevent recurrent preterm birth in singleton pregnancies (OR 0.54, 95% CI 0.3–0.98), with a trend toward a reduction in preterm birth among twins. Smuts et al also demonstrated an increase in length of gestation by 6.0 ± 2.3 days among singleton gestations randomized to receive supplemental DHA (133 mg daily) in the third trimester. Trends for increased neonatal length and head circumference were also noted.

Controversy exists as to the risk of contaminants, notably methyl mercury (MeHg) and polychlorinated biphenyls, found in fish that are rich in ω-3FA. Exposure to extremely high levels of MeHg is associated with microcephaly, seizures, cerebral palsy, and learning deficiency. Such exposures have occurred as a result of toxic environmental spills and deliberate poisoning. However, epidemiologic studies from the Seychelles, in which 83% of the population consume ocean fish containing MeHg levels comparable to fish consumed in the United States (0.05–0.25 ppm methylmercury) on a daily basis, have not demonstrated adverse neurodevelopmental delay in the offspring to 66 months of life. Maternal consumption of seafood in a large epidemiologic study in England demonstrated that low maternal consumption (less than 340 g/ wk) was associated with an increased risk of their children being in the lowest quartile for verbal IQ, as well as more common suboptimal social behaviors, fine motor and communication skills, and social development scores, suggesting low ω-3FA exposure being associated with an increased risk of adverse neurologic development.

The World Health Organization currently recommends 300–500 mg per day of ω-3FA (such as DHA and eicosapentaenoic acid) in an effort to promote fetal and early childhood mental development. Consumption of at least two meals (12 oz total) weekly of low-mercury–containing fish (eg, shrimp, canned light tuna, salmon, pollock, and catfish) by pregnant women, those planning pregnancy, or breastfeeding women, contributes to an adequate ω-3FA intake for optimal fetal neurodevelopmental and obstetric outcomes. It remains wise to follow the U.S. Environmental Protection Agency recommendations to avoid highly contaminated fish (eg, shark, swordfish, king mackerel, tilefish) during pregnancy. Purified nutritional supplements of fish oil can be used to achieve the goal of 300–500 mg daily of DHA. Other sources of ω-3FA include sunflower, safflower, corn, and soybean oil, as well as egg yolk, meat, and spinach.

Although most nutritional supplement trials in pregnancy have shown modest effects on the rates of preeclampsia and preterm birth, at best, these outcomes have usually been improved when deficient populations received supplementation. These findings are likely applicable to twin pregnancy, in which the added demands are typically not met by routine dietary intake. Even among middle- to upper-income women with advanced education, Turner et al demonstrated that pregnant women (singleton gestations) remain at risk for suboptimal intake of some micronutrients. In this study, the probability of intake less than the estimated average requirement for iron was 91%, zinc 31%, magnesium 53%, and vitamin B6 21%. Given the likelihood of increased micronutrient requirements in twin gestations, high risk of micronutrient deficiency, and the potential benefit of micronutrient supplementation in deficiency states, our practice is to recommend the supplement described in this review for twin pregnancies.
SPECIALIZED TWIN NUTRITIONAL PROGRAMS AND PROVIDER INTERVENTIONS

Given the importance of attention to nutrition in multifetal gestations, consultation with a registered dietitian is encouraged if available. The constraints associated with traditional prenatal care visits usually do not allow adequate time for in-depth counseling and education regarding the importance of diet and adequate nutrition. Nutritional consultation can also result in the development of individualized BMI-specific weight gain recommendations, ongoing tracking of maternal weight gain, and interventions to modify maternal diet when women either exceed or fail to meet their recommended weight gain goals. Surveys of women carrying twins reveal that more than 25% receive no advice at all regarding weight gain and that among those who do receive nutritional counseling, the guidance is often incorrect. Clinical studies have suggested that prenatal care for twin pregnancies provided through specialized, multidisciplinary multiple-gestation programs or clinics results in improved maternal and neonatal outcomes. A mainstay of these interventions is the grouping of women with multiple gestations into specialty clinics that have a strong emphasis on nutritional evaluation and education in addition to the provision of prenatal care.

In the Michigan Multiples Clinic, women with multiple gestations received prenatal care in a setting that provides twice monthly dietitian and nurse practitioner visits for dietary counseling, along with physician-directed prenatal care visits. Nutritional modifications emphasized in this program included multimineral supplementation with daily calcium carbonate (3 g), magnesium oxide (1.2 g), zinc oxide (45 mg) in addition to a multivitamin with 100% RDA for nonpregnant recommendations (increased to 200% RDA at 20 weeks). The recommended diet composition included 3,000–4,000 kcal/d, composed of 20% protein, 40% carbohydrates, and 40% fat, divided into three meals and three snacks daily. Compared with nonparticipants, Nutritional Intervention Program mothers were more likely to meet weight gain goals at 20 and 28 weeks and had fewer pregnancy complications (Fig. 2). Program participants also demonstrated an increase in the length of gestation (13.1 days \( P<.001 \)), increased birth weight (435 g, \( P<.001 \)), 7.4 fewer hospital admission days (\( P<.001 \)), and reduced rates of preterm labor and LBW. These reductions in adverse pregnancy outcomes resulted in a cost savings of $52,553 in hospital charges per twin pair.

Follow up of the twins at 8, 18, and 36 months demonstrated that children of program nonparticipants were more likely to have lagging growth (AOR 1.76, 95%CI 1.26–2.45) and more likely to be classified as developmentally delayed (AOR 1.55, 95% CI 1.04–2.31).

A similar program was conducted as part of the Higgins Nutritional Intervention Program conducted by the Montreal Diet Dispensary, emphasizing individualized nutrition assessment and similar diet recommendations as the Michigan Multiples Clinic. The Higgins Program demonstrated a 27% reduction in LBW (OR 0.73, 95% CI 0.54–0.99) along with a reduction in early pregnancy low weight gain (OR 0.49, 95% CI 0.26–0.93) in those receiving the intervention compared with a matched control population. Similar trends toward a reduction in very low birth weight and preterm birth were also noted in the intervention group. Although these studies lacked a randomized prospective design, they suggest that establishment of twin pregnancy-specific nutritional recommendations, together with intensive education and continued maternal assessment and counseling, can improve birth weights and prolong the length of gestation in twin pregnancies in a cost-effective manner.

Finally, does physician input into nutritional education influence the patient’s attention to proper
nutrition? Although evaluated in few clinical trials in twin gestations, several clinical trials demonstrate that provider input into nutritional education is able to affect maternal weight gain and nutritional status in pregnancy.\(^{65,66}\) and antenatal consultation improves initiation of lactation in twin pregnancy.\(^{67}\) Tools available for provider counseling include individual counseling at prenatal care visits, nutrition or dietitian referrals, placement and serial review of maternal weight gain graphs during the pregnancy in the obstetric record, and review of dietary recall surveys, which are commercially available.

**POSTPARTUM AND BREASTFEEDING**

The importance of nutrition for twin gestations does not end after delivery, because proper nutrition is necessary to support breastfeeding. Rates of initiation of breastfeeding in twins can range from 40–90\%, with wide population variation.\(^{68}\) Complications such as prematurity, low birth weight, and neonatal sepsis can adversely affect rates of twin breastfeeding. There are few evidence-based recommendations for specific diet modifications for breastfeeding twins; however, some suggestions may be beneficial. Milk production may be 1.2–2 L per day by the second month of life and require an excess maternal caloric intake of 1,200–1,500 kcal/d.\(^{68}\) A diet similar to that during pregnancy is recommended (20\% of calories from protein, 40\% from carbohydrates, and 40\% from fat), and continuation of a prenatal vitamin supplement, including DHA is recommended.\(^{68}\) Diets with total daily caloric intake during lactation of less than 2,700 cal/d may also be at risk for micronutrient deficiency in calcium, magnesium, zinc, vitamin B\(_6\), and folate. Until further specific research is completed, continuation of micronutrient supplementation as in the antenatal care of twins into the lactation period is reasonable to prevent such micronutrient limitations.

**FUTURE RESEARCH**

Several unanswered questions remain regarding the role of maternal nutrition in improving outcomes in twin gestation. The effects of specific diet composition on maternal weight gain and neonatal birth weight

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**Table 3. Twin Pregnancy Nutritional Recommendations**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>First Trimester</th>
<th>Second Trimester</th>
<th>Third Trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal weight/weight gain</td>
<td>Assess maternal pregravid BMI, determine BMI-specific weight gain goals</td>
<td>Assess/counsel re: maternal BMI-specific weight gain (each prenatal care visit)</td>
<td>Assess/counsel re: maternal BMI-specific weight gain (each prenatal care visit)</td>
</tr>
<tr>
<td>Caloric requirements (kcal·kg(^{-1})·d(^{-1}))</td>
<td>Normal BMI: 40–45 Alter as necessary for weight gain goal</td>
<td>Alter as necessary for weight gain goal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Underweight: 42–50</td>
<td>Alter as necessary for weight gain goal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Overweight: 30–35</td>
<td>Alter as necessary for weight gain goal</td>
<td></td>
</tr>
<tr>
<td>Micronutrient Supplement (daily total intake)</td>
<td>MVI with iron (30 mg elemental tablets)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>1,500</td>
<td>2,500</td>
<td>2,500</td>
</tr>
<tr>
<td>Vitamin D (international units)</td>
<td>1,000</td>
<td>1,000</td>
<td>1,000</td>
</tr>
<tr>
<td>Magnesium (mg)</td>
<td>400</td>
<td>800</td>
<td>800</td>
</tr>
<tr>
<td>Zinc (mg)</td>
<td>15</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>DHA/EPA (mg)</td>
<td>300–500</td>
<td>300–500</td>
<td>300–500</td>
</tr>
<tr>
<td>Folic Acid (mg)</td>
<td>500–1,000/400</td>
<td>500–1,000/400</td>
<td>500–1,000/400</td>
</tr>
<tr>
<td>Vitamin C/E (mg/ international units)</td>
<td>500–1,000/400</td>
<td>500–1,000/400</td>
<td>500–1,000/400</td>
</tr>
<tr>
<td>Nutritional consultation</td>
<td>Yes</td>
<td>Repeat if not at weight gain goal, anemia, GDM</td>
<td>Repeat if not at weight gain goal, anemia, GDM</td>
</tr>
<tr>
<td>Laboratory nutritional assessment</td>
<td>Hemoglobin ferritin folate/ B12 early screen for GDM (risk factors) vitamin D</td>
<td>Follow up abnormalities from first trimester</td>
<td>Hemoglobin ferritin GDM screen with or without vitamin D</td>
</tr>
<tr>
<td>Risk Factor appropriate exercise or reduction in activity</td>
<td>Screen</td>
<td>Screen</td>
<td>Screen</td>
</tr>
</tbody>
</table>

BMI, body mass index; MVI, multivitamin; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; GDM, gestational diabetes mellitus.
and body composition can be explored. Systematic reviews of nutrient use throughout the twin gestation are lacking. Research into the maternal nutrient levels associated with optimal fetal growth in early and late pregnancy may determine baseline values for screening and supplementation as necessary. Evaluation of the effect of supplements such as zinc, magnesium, and \( \omega-3 \) FA on neurodevelopmental outcomes are also needed. Further evaluation of maternal calcium homeostasis and vitamin D metabolism in multiple pregnancies and the effect on bone mineral density of the offspring are also warranted. If optimal nutrition can result in increases in twin birth weights, modest prolongations of pregnancy, or neurobehavioral benefits as has been suggested in retrospective trials, then future prospective controlled trials of nutritional interventions in twin pregnancies are needed.

**CONCLUSION**

We have discussed the nutritional recommendations and evaluation used in our institutions for twin pregnancies, summarized in Table 3. The current literature supports the benefits of BMI-specific weight gain guidelines specific for twin gestations for improved twin birth weight. Thus our practice is to track maternal weight gain through the pregnancy and provide nutrition consultation to achieve these goals. Twin pregnancy is also at risk for micronutrient deficiency and thus supplementation with iron, calcium, and folate, beyond a typical prenatal vitamin, is recommended. Finally, \( \omega-3 \) FA dietary intake or supplementation is also encouraged for potential neurodevelopmental benefits. Although nutritional intervention may not reduce all perinatal morbidity associated with twin pregnancy, increased attention to specific nutritional needs in twin-specific prenatal care settings have been associated with improved neonatal outcomes and should be incorporated into the prenatal care of twins.

**REFERENCES**


