



Nutritional assessment and support during pregnancy

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One of the most significant developments in clinical nutrition is the promulgation of the recommended dietary allowance (RDA) for various nutrients [1–3]. Since the first set of RDAs was published in 1941 and through the last revision in 1989, the goal has been to identify the nutrient amount sufficient to prevent the deficiency syndrome associated with that nutrient. Beginning in 1997 and continuing to the present, the Food and Nutrition Board of the National Academy of Sciences has been reviewing all nutrient recommendations to define not only the minimum required to avoid deficiency disease, but also the optimal amount for long-term health—termed “adequate intake” (AI). The Board also is defining a tolerable upper intake level (UL), above which toxicity may occur, and an estimated average requirement (EAR), which meets the needs of half (the median) of healthy individuals. The RDA continues to be used for those nutrients for which the new recommendations are not yet available. These four nutrient levels, the AI, UL, EAR, and RDA, constitute the dietary reference intakes (DRI).

Perhaps the most important application of this new approach to nutrient recommendations is in pregnancy. The nutritional goal is no longer merely to provide enough for the mother so that she does not run short while sustaining herself and the growing fetus. In light of recent epidemiologic evidence that strongly suggests certain chronic adult diseases are correlated with nutritional conditions in utero [4], the new goal is to set the nutritional foundations for a healthy adult life while the individual is still in utero.

This article thoroughly updates the authors’ previous review [5]. After briefly reviewing nutrient metabolism and requirements, the authors discuss the nutritional assessment of the pregnant woman and review the nutritional

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support principles in hyperemesis gravidarum (HG) and other conditions that can compromise the nutritional health of mother or fetus.

Nutrient metabolism and requirements during pregnancy

Nutritional requirements during pregnancy are dictated by maternal and fetal growth needs. Of the 25 to 35 pounds that a woman of normal weight optimally should gain during pregnancy [6], approximately 40% consists of fetus, placenta, and amniotic fluid, whereas the remainder represents an increase in maternal tissues, including the uterus, breasts, blood, interstitial fluid, and body fat [7]. Fetal survival is correlated strongly with birth weight, up to an optimal weight of 3000 to 4000 g [8]. A low birth weight increases the risk of neonatal complications [9]. Low-birth-weight infants (less than 2500 g) have a fortyfold greater mortality than normal-weight infants [10]. Birth weight, in turn, depends largely on adequate maternal nutrition, as represented by prepregnancy weight and by weight gain during pregnancy [10–12]. Although nutrition is critically important in obstetric care, nonnutritional conditions, such as those caused by smoking, alcohol, teratogenic drugs, or genetic aberrations, are not prevented by nutritional intervention.

This section reviews the requirement of macronutrients (energy and protein) and micronutrients that play a critical role in pregnancy. Table 1 compares the RDAs for the pregnant with those of the nonpregnant patient. Table 2 summarizes the risks of nutrient deficiency or excess during pregnancy.

Energy

The theoretic energy cost of pregnancy in a well-nourished woman gaining 12.5 kg during gestation and delivering a 3.3-kg baby was calculated by Hytten and Leitch to be approximately 80,000 kcal [13], of which approximately 35,000 kcal is required for the deposition of approximately 3.5 kg of fat, and approximately 36,000 kcal represents the increase in basal metabolic rate during pregnancy. Others have, however, estimated energy costs ranging from 45,000 kcal to 110,000 kcal based on measurements of energy intake and expenditure in various populations [14–16]. This wide range of estimates apparently is related partly to variations in maternal fat storage, ranging from an average of 1.3 kg of fat in rural Thai women [17], at an estimated cost of 14,340 kcal, to 5.8 kg in Swedish women [15], at an estimated cost of nearly 64,000 calories. The high end of maternal fat accumulation is not recommended because excessive maternal fat accumulation does not correlate with fetal birth weight [15] and may be detrimental to the mother by increasing the risk of dystocia, cesarean section, and by contributing to residual obesity [11].

Table 1
Dietary reference intakes: vitamins and selected elements

Nutrient	Group	RDA/AT* UL	Selected food sources
Biotin	Females:	(µg/d)	
	14–18 y	25*	ND
	19–30 y	30*	ND
	31–50 y	30*	ND
	Pregnancy:		
	≤18 y	30*	ND
	19–30 y	30*	ND
31–50 y	30*	ND	
Choline	Females:	(mg/d)	(mg/d)
	14–18 y	400*	3000
	19–30 y	425*	3500
	31–50 y	425*	3500
	Pregnancy:		
	≤18 y	450*	3000
	19–30 y	450*	3500
31–50 y	450*	3500	
Folate	Females:	(µg/d)	(µg/d)
	14–18 y	400	800
	19–30 y	400	1000
	31–50 y	400	1000
	Pregnancy:		
	≤18 y	600	800
	19–30 y	600	1000
31–50 y	600	1000	
Niacin	Females:	(mg/d)	(mg/d)
	14–18 y	14	30
	19–30 y	14	35
	31–50 y	14	35
	Pregnancy:		
	≤18 y	18	30
	19–30 y	18	35
31–50 y	18	35	
Pantothenic acid	Females:	(mg/d)	(mg/d)
	14–18 y	5*	ND
	19–30 y	5*	ND
	31–50 y	5*	ND
	Pregnancy:		
	≤18 y	6*	ND
	19–30 y	6*	ND
31–50 y	6*	ND	
Riboflavin	Females:	(mg/d)	(mg/d)
Also known as:	14–18 y	1.0	ND
Vitamin B2	19–30 y	1.1	ND
	31–50 y	1.1	ND

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Table 1 (continued)

Nutrient	Group	RDA/AT*	UL	Selected food sources
	Pregnancy:			
	≤18 y	1.4	ND	
	19–30 y	1.4	ND	
	31–50 y	1.4	ND	
Thiamin	Females:	(mg/d)	(mg/d)	
Also known as:	14–18 y	1.0	ND	Enriched, fortified, or whole-grain products; bread and bread products, mixed foods whose main ingredient is grain, ready-to-eat cereals
Vitamin B1	19–30 y	1.1	ND	
Aneurin	31–50 y	1.1	ND	
	Pregnancy:			
	≤18 y	1.4	ND	
	19–30 y	1.4	ND	
	31–50 y	1.4	ND	
Vitamin A	Females:	(µg/d)	(mg/d)	
	14–18 y	700	2800	Liver, dairy products, fish
	19–30 y	700	3000	
	31–50 y	700	3000	
	Pregnancy:			
	≤18 y	750	2800	
	19–30 y	770	3000	
	31–50 y	770	3000	
Vitamin B6	Females:	(mg/d)	(mg/d)	
	14–18 y	1.2	80	Fortified cereals, organ meats, fortified soy-based meat substitutes
	19–30 y	1.3	100	
	31–50 y	1.3	100	
	Pregnancy:			
	≤18 y	1.9	80	
	19–30 y	1.9	100	
	31–50 y	1.9	100	
Vitamin B12	Females:	(µg/d)	(µg/d)	
Also known as:	14–18 y	2.4	ND	Fortified cereals, meat, fish, poultry
Cobalamin	19–30 y	2.4	ND	
	31–50 y	2.4	ND	
	Pregnancy:			
	≤18 y	2.6	ND	
	19–30 y	2.6	ND	
	31–50 y	2.6	ND	
Vitamin C	Females:	(mg/d)	(mg/d)	
Also known as:	14–18 y	65	1800	Citrus fruits, tomatoes, tomato juice, potatoes, brussel sprouts, cauliflower, broccoli, strawberries, cabbage, spinach
Ascorbic acid	19–30 y	75	2000	
Dehydroascorbic acid (DHA)	31–50 y	75	2000	
	Pregnancy:			
	≤18 y	80	1800	
	19–30 y	85	2000	
	31–50 y	85	2000	

Table 1 (continued)

Nutrient	Group	RDA/AT*	UL	Selected food sources
Vitamin D	Females:	($\mu\text{g/d}$)	($\mu\text{g/d}$)	
Also known as:	14–18 y	5*	50	Fish liver oils, flesh of fatty fish, liver and fat from seals and polar bears, eggs from hens that have been fed vitamin D, fortified milk products, fortified cereals
Calciferol (1 μg	19–30 y	5*	50	
calciferol = 40	31–50 y	5*	50	
IU vitamin D)	Pregnancy:			
The DRI values	≤ 18 y	5*	50	
assume the	19–30 y	5*	50	
absence of adequate	31–50 y	5*	50	
exposure to sunlight				
Vitamin E	Females:	(mg/d)	(mg/d)	
Also known as:	14–18 y	15	800	Vegetable oils, unprocessed cereal grains, nuts, fruits, vegetables, meats
α -tocopherol	19–30 y	15	1000	
	31–50 y	15	1000	
	Pregnancy:			
	≤ 18 y	15	800	
	19–30 y	15	1000	
	31–50 y	15	1000	
Vitamin K	Females:	($\mu\text{g/d}$)	($\mu\text{g/d}$)	
	14–18 y	75*	ND	Green vegetables (collards, spinach, salad greens, broccoli), brussel sprouts, cabbage, plant oils, margarine
	19–30 y	90*	ND	
	31–50 y	90*	ND	
	Pregnancy:			
	≤ 18 y	75*	ND	
	19–30 y	90*	ND	
	31–50 y	90*	ND	
Calcium	Females:	(mg/d)	(mg/d)	
	14–18 y	1300*	2500	Milk, cheese, yogurt, corn tortillas, calcium-set tofu, Chinese cabbage, kale, broccoli
	19–30 y	1000*	2500	
	31–50 y	1000*	2500	
	Pregnancy:			
	≤ 18 y	1300*	2500	
	19–30 y	1000*	2500	
	31–50 y	1000*	2500	
Chromium	Females:	($\mu\text{g/d}$)	($\mu\text{g/d}$)	
	14–18 y	24*	ND	Some cereals, meats, poultry, fish, beer
	19–30 y	25*	ND	
	31–50 y	25*	ND	
	Pregnancy:			
	≤ 18 y	29*	ND	
	19–30 y	30*	ND	
	31–50 y	30*	ND	
Copper	Females:	($\mu\text{g/d}$)	($\mu\text{g/d}$)	
	14–18 y	890	8000	Organ meats, seafood, nuts, seeds, wheat-bran cereals, whole-grain products, cocoa products
	19–30 y	900	10000	
	31–50 y	900	10000	

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Table 1 (continued)

Nutrient	Group	RDA/AT*	UL	Selected food sources
	Pregnancy:			
	≤18 y	1000	8000	
	19–30 y	1000	10000	
	31–50 y	1000	10000	
Iodine	Females:	(µg/d)	(µg/d)	
	14–18 y	150	900	Marine origin, processed foods, iodized salt
	19–30 y	150	1100	
	31–50 y	150	1100	
	Pregnancy:			
	≤18 y	220	900	
	19–30 y	220	1100	
	31–50 y	220	1100	
Iron	Females:	(mg/d)	(mg/d)	
	14–18 y	15	45	Fruits, vegetables, fortified bread and grain products such as cereal (nonheme iron sources); meat and poultry (heme iron sources)
	19–30 y	18	45	
	31–50 y	18	45	
	Pregnancy:			
	≤18 y	27	45	
	19–30 y	27	45	
	31–50 y	27	45	
Magnesium	Females:	(mg/d)	(mg/d)	
	14–18 y	360	350	Green leafy vegetables, unpolished grains, nuts, meat, starches, milk
	19–30 y	310	350	
	31–50 y	320	350	
	Pregnancy:			
	≤18 y	400	350	
	19–30 y	350	350	
	31–50 y	360	350	
Phosphorus	Females:	(mg/d)	(mg/d)	
	14–18 y	1250	4000	Milk, yogurt, ice cream, cheese, peas, meat, eggs, some cereals and breads
	19–30 y	700	4000	
	31–50 y	700	4000	
	Pregnancy:			
	≤18 y	1250	3500	
	19–30 y	700	3500	
	31–50 y	700	3500	
Selenium	Females:	(µg/d)	(µg/d)	
	14–18 y	55	400	Organ meats, seafood, plants (depending on soil selenium content)
	19–30 y	55	400	
	31–50 y	55	400	
	Pregnancy:			
	≤18 y	60	400	
	19–30 y	60	400	
	31–50 y	60	400	

Table 1 (continued)

Nutrient	Group	RDA/AT*	UL	Selected food sources
Zinc	Females:	(mg/d)	(mg/d)	
	14–18 y	9	34	Fortified cereals, red meat, certain seafoods
	19–30 y	8	40	
	31–50 y	8	40	
	Pregnancy:			
	≤18 y	12	34	
19–30 y	11	40		
	31–50 y	11	40	

Abbreviations: RDA, recommended dietary allowance (bold type); AI, adequate intake (ordinary type followed by an asterisk); UL, tolerable upper intake level; ND, not determined because of insufficient data; y, years old. RDAs are set to meet the needs of 97% to 98% of individuals in a group.

Adapted from Dietary reference intakes for energy, carbohydrates, fiber, fat, protein and amino acids (macronutrients). Washington, DC: National Academy Press; 2002; with permission.

Improved nutrition has been associated with lower maternal fat stores at term, whereas increased fetal growth during the latter months of pregnancy correlates better with increased plasma volume in the mother [18]. This can be explained physiologically. Optimal fetal growth depends on an adequate and balanced supply of nutrients, which ultimately comes from the mother's diet. Insofar as this diet may be deficient in one or more nutrients, greater amounts of this diet may be ingested to achieve sufficiency in these nutrients, but the excess calories add maternal fat without enhancing fetal growth. Indeed, a recent study indicated that pregnant Spanish women consume inadequate amounts of folates, iron, pyridoxine and zinc, yet consume too much lipid [19]. Thus the wide range of maternal fat accumulation during pregnancy probably reflects the variable amount of “empty calories” in the diet.

Although it is important to avoid excess calories, it is equally important to avoid deprivation. Deficient maternal food intake can affect fetal development and lead to specific disease states later in the individual's life [20–23]. Hypertension and coronary artery disease have been linked to insufficient maternal food intake before and during pregnancy.

The RDA is an additional 300 kcal/d during the second and third trimesters but not during the first trimester, unless pregnancy begins in a depleted state [24]. On this diet, a woman at 90% to 110% of standard weight at conception should gain approximately 12 kg, increasing by approximately 400 g/wk during the second and third trimester. An increase in carbohydrate consumption is preferred during pregnancy and lactation, because the fetus and mammary gland tend to use glucose [25].

Depending on the mother's pregestational condition, greater or lower weight gains are recommended [11]. Obese (>120% of standard weight)

Table 2
Selected nutrient requirements during pregnancy and risk of maternal and fetal deficiency or excess

Nutrient	Risks of deficiency in mother and infant	Risks of excess
Protein	Present but not conclusively defined	
Folic acid	Megaloblastic anemia in mother; neural tube defects, prematurity, spontaneous abortion, low birth weight	May mask vitamin B12 deficiency
Vitamin B6	Mental depression in mother; decreased Apgar score	
Vitamin C	Possible association with preeclampsia and premature rupture of the membranes	“Rebound scurvy”
Vitamin A	Teratogenic in lower animals, but not in humans	Teratogenic effects: congenital obstructive lesions of the ureter and other malformations of the urinary tract, neural tube defects; isotretinoin causes craniofacial, CNS, cardiac, and thymic malformations
Vitamin D	Hypocalcemia or enamel hypocalcemia	Fetal hypercalcemia, fetal growth retardation, aortic stenosis, deposition of calcium in brain and other organs
Vitamin E	Low birthweight, intrauterine growth retardation when occurring with protein calorie malnutrition	
Vitamin K	Neonatal bleeding tendencies including neonatal intracranial hemorrhage, maxillonasal hypoplasia, spontaneous abortions	
Thiamine		Parenteral doses >400 mg cause nausea, anorexia, lethargy, mild ataxia, heaviness in limbs and diminution of gut tone
Calcium	Reduced fetal bone density	Pregnancy-induced hypertension, preeclampsia, eclampsia
Phosphorus	Leg cramps	
Zinc	Intrauterine growth retardation, malformations, premature and postmature births, low birth weight, perinatal death, abnormal delivery with dystocia and placental abruption	
Iron	Maternal anemia; fetal anemia, low birth weight, and preterm babies	Increased maternal hypertension; increased perinatal death, low birth weight, and preterm delivery

Table 2 (continued)

Nutrient	Risks of deficiency in mother and infant	Risks of excess
Copper	Placental insufficiency and intrauterine death	
Chromium	Gestational diabetes and hyperglycemia	
Selenium	Neural tube defects, sudden infant death syndrome, first trimester miscarriages	Toxicity and possible death
Iodine	Miscarriages, stillbirths, congenital anomalies, goiter cretinism, impaired brain function, and hypothyroidism	

patients should gain 7 to 8 kg at a rate of no more than 300 g/wk. Underweight (<90% of standard weight) patients should gain 14 to 15 kg at a rate of 500 g/wk. Adolescent (<5 years past menarche) patients should gain 14 to 15 kg at a rate of 500 g/wk. The growing adolescent woman must gain almost 4 g for every gram of fetal weight because of her own growth needs, whereas the biologically mature woman needs to gain only 3 g for every gram of baby weight [26].

Women carrying twins should gain 35 to 45 pounds or approximately 150 kcal a day more than for a singleton pregnancy [27]. Women pregnant with twins should gain approximately 4 to 6 pounds during the first trimester and 1.5 lb/wk thereafter. This weight gain is associated with a decreased risk of preterm delivery and low-birth-weight infants. Only two studies have assessed weight gain in triplet pregnancies. A weight gain of 50 pounds in total, or approximately 1.5 lb/wk throughout pregnancy, may be appropriate.

Protein requirement

The RDA for protein for the average adult is 0.8 g/kg/d. During pregnancy, additional protein is required for deposition in fetal, placental, and expanding maternal tissues. The mother and fetus accrue a total of approximately 1 kg of protein during pregnancy, although the rate of accretion is not constant. The requirement for additional protein is 1.3, 6.1, and 10.7 g/d for each of the three trimesters of the pregnancy, respectively. The RDA for pregnancy is an additional 10 g/d throughout the pregnancy [24]. Whereas protein deficiency during pregnancy causes adverse effects in animals and humans [28], it has not been studied independently. Protein deficiency during pregnancy usually occurs with limited intake of energy. Comparisons providing the mother with additional energy versus additional energy and protein show similar effects on pregnancy outcome.

Folic acid

Folates function metabolically as coenzymes that aid in the transport of single carbon fragments from one compound to another in amino acid metabolism and nucleic acid synthesis [24]. During pregnancy, which is a state of increased maternal and fetal cell proliferation, the requirement is greater [11,29] and the risk of deficiency is correspondingly higher. Folic acid deficiency leads to impaired mitosis and altered protein synthesis [24]. These effects are profound during pregnancy. In addition to causing maternal megaloblastic anemia (a sign of advanced deficiency [30]), folate deficiency is associated with neural tube defects, prematurity, spontaneous abortions, and low birth weight [31–35]. A new study notes that folate deficiency also is associated with an increase in homocysteine levels [36], which is correlated with an increased risk of recurrent spontaneous abortions, placental abruption, and preeclampsia. Epileptic patients taking anticonvulsants have an even greater risk [37], because of drug-induced reductions in folate levels [38]. Although folic acid supplementation reduces the risk of these disorders [34,39], the prevention of neural tube defects requires that supplementation be given before conception or early during pregnancy [40], especially during the first four weeks of pregnancy, which are the most critical period for neural tube closure [11].

The 1989 RDA was 180 $\mu\text{g}/\text{d}$ for the average adult nonpregnant female and 400 $\mu\text{g}/\text{d}$ for the average pregnant female. Recent studies, however, suggest a greater requirement. Researchers in Ireland [41] reported that the excretion of folate catabolites peaked in the third trimester at twice the rate in nonpregnant controls. The Irish researchers suggested that the RDA should be raised to 250 μg for nonpregnant women and for pregnant women should be raised to 430 μg during the second trimester and to 540 μg during the third trimester. The Institute of Medicine advocates an RDA of 600 μg dietary folate equivalent/d [42].

The United States Centers for Disease Control (CDC) recommends that women of childbearing years increase their intake of folic acid to 0.4 mg/d [24]. Although some recommend adding folate supplements to certain foods for the entire population, others discourage this practice because excessive folic acid administration may mask vitamin B12 deficiency [11,43]. Nevertheless, the CDC recommends that a pregnant woman who has previously had a neural tube defect– (NTD-) affected child take folate 4 mg/d (10 times the RDA) under medical supervision. Canadian researchers recommend that women with epilepsy who wish to become pregnant take 5 mg/d of folic acid three months before conceiving and during the first trimester [44].

The problem, however, is less in the science of folate nutrition than in its practical application. Given that dietary folate intake tends to be marginal and that pregnancy increases this requirement, it is not surprising that the incidence of folate deficiency generally increases as pregnancy advances

[31]. In fact, even the old RDA frequently was not met without supplementation [37].

Which women take folate supplements? Irish researchers reported that relatives of women who gave birth to infants with neural tube defects were more likely than the general public to take folate supplements [45], but American researchers reported contrary results [46]. Of 21 women interviewed, none took the recommended prenatal 4.0 mg/d of folic acid at least one month before conception. The investigators called for effective education by health care workers about folic acid supplementation. One study indicated that previous pregnancies, unplanned pregnancies, and younger maternal age were associated with failure to take folic acid supplements [47]. The investigators of this study called for improving health education, improving the dietary intake of the entire population, and fortifying common foods.

More and better education is needed to inform women of the importance of folic acid supplementation before and during pregnancy [48–52]. Canadian researchers reported that only one third of well-educated, English-speaking women took vitamin supplements before conception. They believed this represented a failure in education and called for a comprehensive campaign involving the media, public health agencies, physicians, and schools. Dutch health authorities organized a campaign in 1995 to inform women of the importance of folic acid supplementation [53]. The percentage of women who heard about folic acid supplementation rose from 28% to 78%, and the percentage of women taking the supplements increased from 7.8% to 26%.

Vitamin B6

Vitamin B6 is involved in amino acid metabolism. The current RDA for the adult woman is 1.3 mg/d. With the increased intake of protein during pregnancy and the synthesis of nonessential amino acids in growth, this amount is raised to 1.9 mg/d during pregnancy, whereas the safe upper limit is set at 100 mg/d [54].

Biochemical signs of vitamin B6 deficiency occur in a significant number of pregnant women [55], particularly in low socioeconomic groups [56,57] and adolescent women [58]. Effects attributed to this deficiency include mental depression [59] and a decrease in the neonatal Apgar scores [58].

In one study, women who received 2 or 3 mg of pyridoxine supplementation per day had significantly higher maternal and cord plasma concentrations of pyridoxal phosphate and delivered larger infants than women who received 0 or 1 mg/d of supplements. The investigators noted that a daily supplement of 2 mg of pyridoxine ensures adequate maternal and infant vitamin B6 levels and improves fetal growth [60].

Although no correlation has been found between vitamin B6 status and morning sickness, one randomized, placebo-controlled, double-blind study documented significant relief of the nausea by pharmacologic doses of

pyridoxine (25 mg every 8 hours for 72 hours) [61]. A recent review of the treatments for nausea and vomiting during pregnancy also concluded that vitamin B6 was effective in reducing nausea [62].

Vitamin C—ascorbic acid

The 1989 RDA for vitamin C in the adult female was 60 mg/d. A recent study, however, has shown that an intake of 90 to 100 mg of vitamin C per day in nonsmoking men and women decreases the risk of chronic diseases including cancer, heart disease, and cataracts, presumably through antioxidant mechanisms [63]. Based on these data, the investigators recommended a daily intake of 120 mg of vitamin C [63].

The RDA for vitamin C for pregnant women was 70 mg/d [24], 10 mg higher than for the nonpregnant female to compensate for the 10% to 15% decline in plasma levels of ascorbic acid [8]. The National Academy of Sciences promulgated guidelines in 2000 of 80 to 85 mg/d as the AI for pregnancy and 2000 mg/d as the UL [64].

Except for isolated [65–67] but unconfirmed [68–70] reports linking low plasma levels of vitamin C with preeclampsia or premature rupture of the membranes, there were no recognized adverse effects of vitamin C deficiency on pregnancy. Recent research, however, indicates that the association between low vitamin C levels and preeclampsia is based on an excess of lipid peroxides relative to the antioxidants vitamins C and E [71] and that supplementation with vitamins C and E may reduce the risk of these pregnancy complications. In one study [72], 283 women at increased risk for preeclampsia were randomized to receive 1000 mg/d of vitamin C and 400 IU/d of vitamin E or placebo starting at 16 to 22 weeks of gestation. The women who received the vitamin supplementation showed a 21% decrease in plasma markers for preeclampsia during gestation. In addition, preeclampsia occurred in 24 (17%) of the placebo group versus 11 (8%) of the vitamin group. The investigators proposed supplementation with vitamin C and E to prevent preeclampsia in women at increased risk of the disease. Others found that increased consumption of vitamins C and E, through foods or supplementation, might reduce the risk of premature rupture of membranes [73].

Alternatively, excessive vitamin C intake may condition the fetus to require high quantities of this vitamin, by inducing rapid vitamin C degradation, so that the neonate develops “rebound scurvy” soon after birth despite an adequate vitamin intake [74].

A recent recommendation is to obtain 200 mg/d of vitamin C from five servings of fruits and vegetables or 100 mg/d of pharmaceutical vitamin C, and to consider 1 g or more as potentially toxic [75]. Although the new guidelines allow up to 2000 mg/d as safe, a recent study [76] showing that maximal antioxidant protection is attained at an intake of 500 to 1000 mg/d argues against exceeding 1000 mg/d.

Finally, regardless of the level of vitamin C that ultimately is recommended, public education is required, given that a surprisingly high percentage of Americans have vitamin C deficiency. In one study, 6% of almost 500 healthy, middle-class outpatients, including 350 females, had vitamin C deficiency, and 30.4% were vitamin C depleted [77].

Vitamin A

Vitamin A is required for growth, cellular differentiation, and normal fetal development [24]. The recently issued DRI for vitamin A set the RDA for the nonpregnant adult female at 700 RE and for the pregnant woman at 750 to 770 retinol equivalent (RE), whereas the UL is set at 2800 to 3000 RE/d [78]. Despite its importance, this vitamin can be toxic when taken in excess and may be teratogenic when taken in excess shortly before or during early pregnancy [79–81]. Several cases of adverse pregnancy outcome have been associated with ingestion of 25,000 IU (7500 RE) or more per day of vitamin A [81]. Excessive intake has been linked with congenital obstructive lesions of the ureter and urinary tract malformations [82–84] and may be associated with neural tube defects [85]. The drug isotretinoin, a vitamin A analog used to treat cystic acne, causes major congenital malformations involving the cranium, face, central nervous system, heart, and thymus [81,86,87].

Although deficiency of this vitamin is not uncommon in third world countries, and experimental vitamin A deficiency is teratogenic in lower animals, no teratogenic effects have been documented in humans. One study [88] reported that nine otherwise healthy primigravidas with low plasma levels of retinol and vitamin E (but not of betacarotene) subsequently developed preeclampsia, although the causation was unclear.

Unlike water-soluble vitamins, plasma levels of vitamin A do not decline during pregnancy, despite fetal uptake [89]. This perhaps is because of fat mobilization, which typically occurs from the end of the first through the third trimester in pregnancy [8] and usually causes hyperlipidemia.

The effects of vitamin A on pregnancy have been studied throughout the world. One study of pregnant Indian women found that almost 15% had moderate vitamin A deficiency, whereas 4% had severe vitamin A deficiency [90]. The deficiency was associated with poor general maternal nutritional status, low dietary intake of vitamin A during pregnancy, poor literacy, and multiparity. In another study, addition of vitamin A to iron supplementation in Indonesian pregnant women improved the hemoglobin level [91]. In a study of more than 15,000 Nepali women, weekly supplementation of vitamin A resulted in a lower risk of nausea, fainting, and night blindness during the latter months of pregnancy [92]. Vitamin A also shortened the length of labor and reduced puerperal symptoms.

Two studies have investigated the relationship between vitamin A deficiency and impaired dark adaptation during pregnancy. In a laboratory

setting, pregnant Nepali women taking vitamin A supplements experienced improved pupillary adaptation to the dark [93]. In another study, pregnant Nepali women with night blindness experienced a fourfold improvement of night vision compared with women who received other nutritional supplements [94].

Vitamin D

Vitamin D is necessary for mineral homeostasis and skeletal growth [24]. During pregnancy, vitamin D functions to maintain a positive calcium balance and to deposit calcium in the growing fetus [24]. Maternal deficiency during pregnancy may lead to adverse effects in the newborn [95], including hypocalcemia or enamel hypocalcemia [10]. Whereas increased serum levels of vitamin D are normal during pregnancy, levels may be twice as high during the second and third trimesters as after parturition [57]; hypervitaminosis D may cause fetal hypercalcemia, which may lead to fetal growth retardation, aortic stenosis, and calcium deposition in the brain and other organs. Severe infantile hypercalcemia, however, is believed to be the result of fetal hypersensitivity to vitamin D rather than high maternal intake [84].

The recently issued DRI for vitamin D sets the AI at 5 µg/d for pregnant and nonpregnant females up to age 50, whereas the UL is set at 50 µg/d [96]. According to recent research, several groups of women are at increased risk of vitamin D deficiency and consequent fetal toxicity. One study reported that 80% of veiled or dark-skinned pregnant women had serum 25-hydroxyvitamin D₃ values below normal levels, and their offspring had an increased risk of rickets and hypocalcemia [97]. Other authorities recommend maternal vitamin D supplementation during pregnancy in countries where dairy products do not contain supplemental vitamin D [98]. A Finnish study concluded that a balanced diet meets the nutritional requirements of a pregnant woman, except for vitamin D, folate, and iron [99]. This study also found that pregnant women were taking dietary supplements incorrectly and that young, uneducated women need nutritional guidance.

Other women at increased risk for vitamin D deficiency include Arabic and northern Canadian women. One study reported that Saudi women had significantly lower bone mineral densities than American women because of vitamin D deficiency resulting from a high number of pregnancies and long periods of breast-feeding [100]. Another study found that native north Canadian mothers, including Inuits and Indians, had significantly lower intake of vitamin D than non-native mothers [101]. These researchers recommended vitamin D supplementation for northern Canadian mothers during pregnancy and for their children during infancy. Lastly, a case report described that all the infants of five mothers with vitamin D deficiency had vitamin D deficiency, poor sunlight exposure, and were

breast-fed or had vitamin D–poor diets [102]. The researchers noted that regardless of race, infants who receive inadequate sun exposure or inadequate intake of vitamin D are at risk for vitamin D deficiency. Vitamin D supplementation of breast-feeding women and their infants is recommended.

Vitamin E

The current RDA for vitamin E is 15 mg alpha-tocopherol equivalents for pregnant and nonpregnant females, whereas the UL has been set at 800 to 1000 mg/d [64]. Although vitamin E deficiency has been associated with spontaneous abortion in experimental animals, no such association has been observed in humans, and vitamin E supplementation has not been shown to prevent spontaneous abortions [10]. Conversely, one study showed that maternal serum levels of vitamin E are significantly lower in mothers with low-birth-weight infants and in smokers [103]. In another study, vitamin E deficiency together with protein calorie malnutrition was associated with intrauterine growth retardation [104].

Recent research points to an association between vitamin E deficiency and preeclampsia. In one study, normotensive pregnant women had significantly higher serum vitamin E levels than women with mild or severe preeclampsia [105]. The investigators suggested that vitamin E, as an antioxidant, prevents excessive accumulation of lipid peroxides that cause the vascular endothelial damage and vasoconstriction of preeclampsia [106–108]. Others have confirmed these clinical findings [106,107,109,110]. Hypovitaminosis C and E also have been associated with premature rupture of membranes [73], because these antioxidants prevent an accumulation of reactive oxygen radicals that result in premature rupture of membranes. A study demonstrated a reduced risk of preeclampsia with supplementation of 1000 mg/d of vitamin C and of 400 mg/d of vitamin E, amounts that are far above their RDA levels, but below their ULs.

Some spontaneously aborting women have high serum vitamin E levels (> 0.50 mg/100 ml), but no causal relationship was apparent [111]. Excessive vitamin E intake in pregnant rats resulted in high concentrations of vitamin E in their pups, but no teratogenicity. Plasma tocopherol levels normally rise 40% to 60% starting in the second trimester of the pregnancy, a phenomenon probably related to the elevations in plasma lipids observed during pregnancy [8,112].

Vitamin K

The RDA for the pregnant and nonpregnant adult female for vitamin K is 65 μ g/d [24]. The new DRI guidelines set 90 μ g as the AI [78]. Maternal deficiencies of this vitamin have been associated with neonatal bleeding tendencies [113], including neonatal intracranial hemorrhage [114], maxillofacial hypoplasia, and perhaps frequent spontaneous abortions when the

deficiency occurs during the first trimester [115,116]. Japanese researchers reported a case in which an ultrasound at 28 weeks of gestation showed an intracranial mass in the fetus of a young woman with Crohn's disease [117]. The researchers diagnosed and treated maternal vitamin K deficiency. At birth, the neonate was normal but had a chronic subdural hematoma detected by magnetic resonance imaging. Thus Crohn's disease may result in vitamin K deficiency during pregnancy that can cause fetal hemorrhage. The investigators recommended monitoring the prothrombin time in pregnant patients with Crohn's disease.

Vitamin K deficiency typically occurs with use of anticonvulsant drugs in epileptic patients [55,118], fat malabsorption, prolonged antibiotic therapy, prolonged parenteral nutrition without vitamin K supplementation [8], and chronic coumadin anticoagulation (most commonly for artificial heart valves) [116]. Pregnant women administered carbamazepine, phenobarbital, or phenytoin for epilepsy should be supplemented with phytomenadione starting four weeks before the expected date of delivery [119].

In all these conditions, vitamin K supplementation is recommended at least during the first trimester and the ninth month of pregnancy; in patients requiring anticoagulation, heparin should be used instead of coumadin during these high-risk periods [120,121]. Vitamin K antagonists, however, were more effective than heparin in patients with cardiac valve devices [122]. Vitamin K deficiency most simply is diagnosed by observing the correction of the prothrombin time following the vitamin's administration [8,123].

Thiamine (B1)

The RDA for thiamine is 0.5 mg for each 1000 kcal intake per day. As such, the usual recommendation for the adult female has been 1.0 mg/d, with 0.4 mg added during pregnancy to match the additional 300 kcal/d during pregnancy [24]. The new guidelines are nearly the same: 1.1 mg/d for the adult nonpregnant female and 1.4 mg/d for the pregnant female.

Urinary thiamine excretion typically decreases during the second and, particularly, third trimesters possibly as a result of increased metabolic requirements. The erythrocyte transketolase assay is a more sensitive indicator of thiamine status. An erythrocyte transketolase stimulation of less than 15% reflects adequate thiamine stores [8,124].

Using nonpregnant standards, Heller and associates [125] found a 25% to 30% incidence of deficiency in pregnant women, but no correlation between thiamine status and pregnancy outcome. Dutch researchers reported, however, that thiamine supplementation increases intrauterine fetal growth in women treated for gestational diabetes mellitus, whereas conventional treatment of this condition, without thiamine, increases the risk of low birth weight [126]. They suggest that thiamine supplementation is an effective, preventive measure in women with gestational diabetes mellitus.

Several cases have been reported of Wernicke's encephalopathy complicating HG, usually when the vomiting was prolonged [127–129]. Two recent articles reportedly four further cases of HG associated with Wernicke's encephalopathy and emphasized the importance of administering thiamine to women with severe gestational vomiting [15,379,380]. Another pregnant, alcoholic patient with hyperemesis had a high anion-gap acidosis, lactic acidosis, and thiamine deficiency [26]. The patient's symptoms resolved after treatment with thiamine. The medical team cautioned physicians to suspect lactic acidosis related to thiamine deficiency when a pregnant patient presents with a high anion-gap acidosis.

Although there is no evident toxicity from large doses of orally administered thiamine, parenteral doses of greater than 400 mg cause nausea, anorexia, lethargy, mild ataxia, heaviness in the limbs, and diminished gut tone [130].

Calcium

The RDA for calcium is 1200 mg/d for males and females through age 24 to promote bone growth, after which the RDA is reduced to 800 mg/d. During pregnancy, approximately 30 g of calcium is accumulated, mostly during the third trimester, at an estimated rate of 200 to 250 mg/d during that period [24]. Accordingly, the RDA during pregnancy rises to 1200 mg/d [24]. The new DRI guidelines set 1000 mg/d as the AI for adult males and females and recommend no increase during pregnancy, although the UL is set at 2500 mg/d [96]. Calcium fluxes during pregnancy seem to be controlled more by hormonal levels than calcium intake [57,131,132]. The key factor is believed to be an increase in 1,25-dihydroxyvitamin D levels (up to twice postpartum values), which leads to an increase in intestinal calcium absorption [57]. The increase is so large that it exceeds the calcium needs and results in 2.5-fold higher urinary calcium excretion during pregnancy than postpartum [57].

Although women in some cultures have successful pregnancy outcomes with less dietary calcium, they typically have less dietary protein and consequently less urinary calcium loss. Multiparous women with poor calcium intake may develop clinical osteomalacia, and the fetal bone density may be similarly affected [10]. Leg cramps during pregnancy may reflect altered calcium or magnesium metabolism [133].

Calcium supplementation of 1 to 2 g/d during pregnancy may reduce the risk of developing the hypertensive disorders of pregnancy, including pregnancy-induced hypertension, preeclampsia, and eclampsia [134–136]. The mechanism is unclear, especially because supplemental calcium can aggravate an already elevated cytosolic free calcium concentration in hypertensive pregnancy [137]. Other research showed a reduced risk of preterm delivery when women at high risk for hypertension took calcium supplements during pregnancy [138,139]. Women with low baseline calcium intakes benefited most from the supplementation. A large retrospective study failed to

find a difference in the incidence of pregnancy-induced hypertension between patients with high versus low calcium intakes [140], although this study does not negate the effect of pharmacologic supplementation. Some investigators have recommended calcium supplementation (1 to 2 g/d with 400 IU of vitamin D/d) for pregnant women who require prolonged bed rest or who are administered heparin prophylaxis to prevent demineralization [141]. The patient, however, may then require monitoring for nephrolithiasis [142].

Phosphorus

The RDA for phosphorus currently is set at 1250 mg/d for males and females up to age 19. Thereafter, it remains fixed at 700 mg/d, including during pregnancy. Because of the widespread presence of this mineral, deficiency is rare [24]. The UL is set at 3500 mg/d during pregnancy. Although more phosphorus is required during pregnancy, gestational hormones obviate any need to increase dietary phosphorus intake: the rise in calcitriol [57,143] and reciprocal decline in parathyroid hormone [57] result in increased renal retention of phosphorus [143].

Nocturnal leg cramps during pregnancy have been attributed to a decline in serum calcium levels related to an imbalance in calcium versus phosphorus levels. A reduction of the intake of milk, which is high in calcium and phosphorus, coupled with supplementation with nonphosphate calcium salts, has been recommended to relieve this symptom [10].

Zinc

The RDA for zinc for pregnant women is 11 mg/d, three grams more than that allotted for the nonpregnant woman, although up to 40 mg/d is considered safe [78]. The RDA is doubled for vegetarians because less zinc is absorbed with this diet [78]. Without supplementation, zinc levels normally decrease during pregnancy, especially between weeks 14 and 35 [144,145]. Even with adequate supplementation, zinc levels decrease by 20% to 35% below prepregnancy levels, possibly the result of increases in blood volume, gestational estrogens, fetal needs, and the gestational decrease in albumin, which binds zinc. Plasma zinc concentrations decline more precipitously when iron is supplemented orally as a result of competition for absorption by these two ions. It is, therefore, suggested that iron supplementation be used only when required. Zinc absorption also was reduced by 50% when a calcium supplement was added at mealtimes in one study [146]. Current recommendations are to maintain plasma zinc levels at 50 µg/100 ml or higher [8]. A recent study found that pregnant females consumed less zinc than recommended [147]. The investigators called for monitoring food intake during pregnancy and for educating pregnant females about food sources for deficient nutrients.

Populations at risk for zinc deficiency include vegetarians, alcoholics, smokers, teenagers, multigravidas with impaired intestinal absorption of zinc,

women receiving diuretics, and those with an acute stress response to infection or trauma [148–151]. Zinc deficiency has been associated with fetal intrauterine growth retardation, congenital malformations, premature and postmature births, low birth weight, perinatal death, and abnormal delivery with dystocia and placenta abruption [148,152,153]. Gestational zinc deficiency can impair the development of the fetal immune system [154] and impair neurogenesis and subsequent cognitive development, thereby influencing activity, attention, and neuropsychologic performance [155]. High zinc levels have been associated with fetal neural tube defects and spina bifida [156,157], although this was attributed to a disturbance in zinc metabolism or maternal-to-fetal transfer, rather than excessive intake [158–160].

Iron

The RDA for the average adult woman for iron is 18 mg/d [78]. Because of increased iron use during pregnancy for the increase in maternal red cell mass, for fetal erythropoiesis, and for replacing blood lost during delivery, approximately 1040 mg of iron is needed during pregnancy, 840 mg of which is lost from the body during delivery and 200 mg of which is returned to storage as blood volume decreases postpartum. Although iron needs increase little during the first trimester because of cessation of menses, an RDA of 27 mg/d is recommended throughout pregnancy to fulfill the new needs and prevent depletion of maternal iron stores. The UL is set at 45 mg/d [78]. An iron supplement, usually the 30 mg included in the prenatal mineral/vitamin tablet, is recommended because the typical American diet provides only 6 to 7 mg/1000 kcal of iron.

Iron deficiency has been documented throughout the world, particularly in developing countries [161–169]. Iron deficiency results in maternal anemia, defined by a hematocrit of less than 32% and hemoglobin level less than 11 g/dl, and fetal iron deficiency anemia [170]. The anemic mother is less able to tolerate hemorrhage during labor and is more prone to infection [171]. Iron deficiency anemia, when present in early pregnancy, also causes a higher incidence of low birth weight (but not small for gestational age) and preterm babies [172,173].

For established iron deficiency, as reflected by a serum ferritin level below 12 µg/L or a hypochromic microcytic anemia, some recommend taking 120 to 150 mg/d of elemental iron, in divided doses, until the hemoglobin level is more than 12 g/dl and the serum ferritin level is more than 35 µg/L [11]. Others recommend a routine prophylactic iron supplementation of 65 mg/d from 20 weeks of gestation to prevent iron deficiency anemia [163]. Others caution against routine iron supplementation in nondeficient patients to avoid iron overload in those with the mutation for hereditary hemochromatosis, who compose approximately 10% of Caucasians [174]. High ferritin concentrations also have been associated with an increased risk of preterm birth and neonatal asphyxia [175].

Finally, subjects in a study of pregnancy-induced hypertension had higher levels of serum iron than did controls [176], although the pathogenesis was unclear.

Most researchers believe female adolescents need routine iron supplementation [141]. One study noted that iron requirements in teenage women rise from 7 to 9 mg/d of iron to as much as 22 mg/d of iron [177]. Because teenage women are unlikely to consume these amounts, they are at increased risk of iron deficiency anemia during pregnancy.

Copper

The RDA for copper is 1 mg/d for the pregnant woman. Up to 10 mg/d is considered safe (UL) [78]. During pregnancy, the serum copper level normally increases progressively up to as high as 1.5 to 4 times prepregnancy levels, paralleling the increase in ceruloplasmin, the copper binding protein [177]. The National Research Council suggests that in the absence of hypoproteinemia, serum levels during pregnancy below the normal range for nonpregnant women indicate copper deficiency or abnormal copper metabolism [178]. Low serum copper levels are associated with placental insufficiency and intrauterine death [179]. Copper retention towards the end of pregnancy, the period of greatest fetal accumulation, normally averages approximately 0.28 mg/d [8]. One patient with untreated Wilson's disease developed copper toxicity that caused hepatic injury and placental copper accumulation during pregnancy [180].

Chromium

Chromium is a cofactor for insulin. Its deficiency can cause impaired glucose tolerance despite normal insulin levels [24]. Deficiency of chromium (and of magnesium, potassium, and pyridoxine) has been associated with gestational diabetes [181]. Recently issued DRI guidelines [78] set 30 µg/d as the AI for chromium during pregnancy. The UL was not determined because of insufficient data, leading to the general recommendation that sources of chromium intake be foods rather than supplements to prevent excessive intake. The previous 1989 edition of the RDA suggested 50 to 200 µg/d as a "safe and adequate" range for chromium [24].

Although high chromium intake can be toxic [182,183], several recent studies have documented clinical benefits from chromium supplementation at levels above the current AI [184–187]. In a double-blind, placebo-controlled crossover study conducted in Saudi Arabia, type 2 diabetic patients who received supplements of either Brewer's yeast, containing 23.3 µg/d of chromium, or CrCl₃, containing 200 µg/d of chromium, had significant declines in mean serum glucose, fructosamine, and triglyceride levels and were able to decrease their insulin doses [184]. In another study [185], type 2 diabetics who were administered 500 µg of chromium twice a

day in the form of chromium picolinate showed benefits in their serum glucose, insulin, and cholesterol levels.

Chromium also has been used and abused for weight loss. In a study of obese African American women following a dietary and exercise regimen, 600 µg of niacin-bound chromium taken for two months was associated with significant fat loss [188]. In another study of 44 women enrolled in a 12-week exercise program, 400 µg/d of chromium picolinate did not, however, significantly affect serum glucose and lipid concentrations or body composition [189]. One 33-year-old white woman, who took 1200 to 2400 µg/d of over-the-counter chromium picolinate for four to five months in an effort to lose weight, presented with weight loss associated with anemia, thrombocytopenia, hemolysis, and hepatic dysfunction. It is unknown whether or not lower dose supplements, for example, 500 to 1000 µg/d, taken chronically or taken during pregnancy, also might be toxic [182,187].

Selenium

The RDA for the average adult woman is 55 µg/d. During pregnancy, it increases to 60 µg/d [64]. Because the average American diet contains 103 µg/d, deficiency is unlikely in the United States and has occurred only in patients receiving long-term total parenteral nutrition (TPN) that did not include selenium [24]. Studies from other countries have reported an association between maternal serum selenium deficiency and neural tube defects [190], sudden infant death [191], and first trimester miscarriages [192], but further studies are needed to confirm that low selenium level causes, rather than results from, abnormal gestation and that selenium supplementation could prevent these toxic effects.

In one study, selenium deficiency was associated with an increased risk of intrahepatic cholestasis of pregnancy [193]. Another report indicated that selenium deficiency, as determined by hair samples, was linked to recurrent miscarriages [194]. In a third study, selenium concentrations were significantly lower in women with preterm deliveries [195]. This finding might explain the occurrence of retinopathy and respiratory distress syndrome in these infants.

Recent research notes selenium excess is associated with pathologic pregnancies, including preeclampsia [196,197]. One report indicated that selenium supplementation given to very low-birth-weight infants did not improve their status [198]. Excessive ingestion of selenium in “health store” supplements can cause toxicity or death [24,199].

Iodine

The current RDA for iodine is 150 µg/d in nonpregnant females, increasing to 220 µg/d during pregnancy [78]. Maternal deficiency can cause miscarriage, stillbirth, congenital anomalies, goiter, cretinism, impaired

brain function, and hypothyroidism [200–202]. Iodine deficiency is estimated to cause a reduction of 10% to 15% on scores in intellectual tests [203]. The extent of cognitive damage correlates with the severity of the deficiency. Moreover, maternal deficiency might compromise neonatal neurologic development even when it does not cause cretinism [204].

Iodine has become more widely available during the past decade, but pockets of insufficiency exist, even in developed countries. Sixty-eight percent of people around the world now have access to iodized salt, compared with 10% in 1991 [205]. A study conducted in Sydney, Australia, however, indicated that healthy adults, pregnant women, and schoolchildren had urinary iodine excretion (UIE) levels below the normal minimum of 100 µg/L [206]. Decreased levels of iodine in milk and a decline in the use of table salt have led to reduced iodine intake.

Treatment of iodine deficiency during the first trimester may prevent fetal toxicity from iodine deficiency. Later supplementation may improve brain growth and development slightly, but does not improve neurologic status [207]. During pregnancy, iodine deficiency cannot be diagnosed by a low plasma inorganic iodide level, because the iodide level is normally depressed during gestation as a result of a higher renal clearance and more rapid extraction, up to 2 to 3 times normal, by the thyroid. Tri-iodothyronine and thyroxine levels, however, normally are elevated during pregnancy, and low levels of tri-iodothyronine and free thyroxine may be used to diagnose iodine deficiency during pregnancy. Radioiodine studies are contraindicated during pregnancy because of radiation teratogenicity.

Nutritional assessment

Although malnutrition has severe adverse effects on pregnancy, nutritional therapy, when delivered invasively by intravenous nutrition or tube feeding, also entails risks [208,209]. The purpose of nutritional assessment is to guide the nutritional therapy and to maximize the benefits while reducing the complications.

Several excellent reviews discuss the various methods and techniques—clinical versus research, bedside versus laboratory—of nutritional assessment [11,199,210–218]. This review focuses on parameters and tests pertinent to the clinical evaluation of the pregnant patient.

Nutritional assessment must answer the following basic questions:

- With what nutrient reserves has the woman entered pregnancy?
- What are the baseline physiologic needs and what are the added requirements during pregnancy?
- Does the pregnant woman have any diseases or receive any therapy that might affect her nutritional requirements or nutrient tolerance?
- Is the current intake meeting the nutritional needs?

These questions usually are answered during a routine, but comprehensive, medical history, physical examination, and standard laboratory evaluation including hemogram, blood chemistry, and urinalysis.

Most patients do not require extensive nutritional assessment. To facilitate and expedite the assessment, all patients should undergo screening tests to identify patients who suffer from malnutrition or are at risk of developing a nutritional deficit. Further investigations are then appropriate to confirm a suspected nutritional problem and to determine its pathogenesis and define its severity, so as to devise the appropriate therapy. Although agreeing that all women should undergo a nutritional assessment before pregnancy to identify their specific needs, Menard [219] recommended all women receive folic acid supplementation before conception and iron supplementation during the second and third trimesters. Menard also recommended a multivitamin and mineral supplement for women who consume an inadequate diet.

In addition to individual assessment, community-wide assessment of pregnant women can identify nutritional deficiencies. Swenson et al [220] studied more than 100 women enrolled in the Special Supplemental Program for Women, Infants and Children in a Midwestern city. Each woman underwent a one-hour interview, provided a venous blood sample, and completed a dietary questionnaire. This study indicated that the women consumed only 85% of the RDA for energy. Iron-deficiency anemia was identified in 22% of the women, whereas more than 90% of the subjects reported consuming less than two thirds of the RDA for iron. Ngare [221] developed a four-factor model, including BMI, hemoglobin level, mid-upper arm circumference, and socioeconomic status, to assess risk factors for low birth weight in a rural area of Kenya. This model allows clinicians to identify women at increased risk for low birth weight deliveries at the community level. A study from India found that women from slum areas have a high incidence of micronutrient deficiencies [222]. A community-wide intervention program in Montreal designed to identify high-risk pregnant adolescents showed that individual dietary prescriptions significantly improved outcomes [223]. The treated group had a 39% lower rate of low birth weight than untreated controls.

A study comparing the diets of pregnant adolescents with those of adults during the second and third trimesters found that teenagers ate more than adults, but both groups consumed below the recommended amounts of calcium, folate, vitamins D and E, magnesium, iron, and zinc [147]. Pregnant adolescents are at high nutritional risk because they often are poor and have an insufficient food intake. Thus, young pregnant mothers compete with their fetuses for nutrients [224]. Another recent study indicated that pregnant women in Spain consume inadequate amounts of folates, iron, pyridoxine, and zinc, but consume too much lipid [19].

Women safely may follow a vegetarian diet during pregnancy. A recent report indicated that energy and protein intakes are similar for a vegetarian

compared with a standard diet, but vegetarians may lack adequate iron and vitamin B12. The investigators concluded that meat is an optional part of a pregnant woman's diet and that a well-rounded vegetarian diet is safe for mother and fetus [225].

Pregestational nutritional status

Women with very high or very low prepregnancy body mass indexes (BMIs) face increased gestational and fetal risks. Higher BMIs increase the risk of hypertensive disorders during pregnancy [226,227], antepartum stillbirth [228], and dystocia [229]. The investigators suggested that overweight women should not give birth at home or in an alternative birth center.

Low prepregnancy maternal BMI causes fetal undernutrition that is associated with the insulin resistance syndrome [230]. The investigators of this study suggested that improving food intake in young women might result in healthier infants. Infants of women with low prepregnancy BMIs tend to be smaller than other infants [231]. Underweight women should try to achieve adequate BMIs before conceiving. Another study found that low late-pregnancy maternal BMI increases the risk of a neonate subsequently developing schizophrenia [232].

BMI also affects female fertility. High and low BMIs adversely affect hormone levels and processes involved with in vitro fertilization [233]. A Danish study found that women with BMIs greater than 25 kg/m² were less fertile than women with BMIs of 20 to 25 kg/m² [234]. Another study reported that an average BMI and optimal weight gain reduced complications before and after birth and promoted an ideal birth weight [235].

Although much has been written on the regulation of body weight, most people eating normally according to taste and appetite, with no inkling of RDA guidelines, maintain a remarkably steady body weight and body composition (ie, a normal nutritional state). Malnutrition of one or more nutrients eventually results in a structural or functional deficit (Table 3). An asymptomatic person who eats freely from an unrestricted diet without recent weight gain or loss is unlikely to have any nutrient deficiency. Extensive testing is unwarranted in this situation, but the levels of folate and iron, which often are at borderline levels, should be tested. Conversely, when the medical history suggests interference with nutritional homeostatic mechanisms, by disease or therapy causing anorexia, by a fad diet, or by recent planned or unplanned weight change, a focused evaluation of nutrient stores often is required.

Although body weight is the most popular indicator of nutritional status, proper interpretation of a weight measurement or a weight change requires an assessment of three major body compartments: fat, muscle mass, and extracellular water [213,236] (Fig. 1). These compartments easily are evaluated at the bedside without costly instrumentation.

Table 3
Clinical findings with selected vitamin and mineral deficiencies

Vitamin	Clinical findings
Vitamin A	Night blindness, xerophthalmia, Bitot's spots, follicular hyperkeratosis
Vitamin D	Osteomalacia, tetany, bone pain
Vitamin E	Peripheral neuropathy, ophthalmoplegia, hemolysis, possible anemia
Vitamin K	Bleeding tendency, echymoses, prolonged prothrombin time
Vitamin B1	Beriberi, Wernicke's encephalopathy, peripheral neuropathy, congestive heart failure, lactic acidosis
Vitamin B2	Cheilosis, angular stomatitis, magenta tongue
Niacin	Pigmented dermatitis of exposed skin, glossitis, diarrhea, dementia
Pantothenic acid	Burning feet, peripheral paresthesias, sleep disturbances, impaired coordination, nausea
Vitamin B6	Epileptiform convulsions, glossitis, acneform rash on forehead, anemia
Biotin	Nausea, depression, hyperesthesia, glossitis, alopecia, dry scaly dermatitis, elevated serum cholesterol
Folic acid	Macrocytic anemia, atrophic tongue papillae
Vitamin B12	Macrocytic anemia, atrophic tongue papillae, impaired position and vibratory sense, ataxia, anorexia
Vitamin C	Perifollicular petechiae, ecchymoses, swollen gums, delayed wound healing
Iron	Microcytic anemia, fatigue, koilonychia, glossitis
Zinc	Ageusia, dysgeusia, anorexia, perioral/perineal dermatitis, delayed wound healing, low alkaline phosphatase activity
Magnesium	Weakness, arrhythmias, seizures, hypocalcemia, hypokalemia
Iodine	Thyroid enlargement

Data from Refs. [8,24,199,212,213,218,237].

Because half of body fat is subcutaneous, pinching the skin to estimate skinfold thickness provides a qualitative categorization of energy stores as adequate, depleted, or excessive. Precise measurement of skinfold thickness using skinfold calipers generally adds little to this assessment during pregnancy, except perhaps as a baseline measurement for postpartum weight reduction efforts. A useful observation pertains to the looseness of the skin: easily pinchable loose skin suggests previous weight loss (although remaining subcutaneous fat may still be excessive), whereas a difficult to pinch skinfold suggests that the patient is at her maximum weight (E. Hamaoui, unpublished observation).

Muscle mass helps estimate "protein stores," even though the body does not contain any storage form of protein as it does for fat (adipocyte lipid) or carbohydrate (glycogen). Rather, during stress, the body sacrifices dispensable structural proteins in muscle to supply the amino acids required to synthesize urgently needed proteins (eg, acute phase proteins, immunoglobulins, and collagen) for wound healing. Muscle mass is assessed clinically by inspection and palpation of various muscles including temporal, biceps, triceps, quadriceps, and calf muscles. Muscle mass can be measured semiquantitatively by midarm circumference (MAC) at the level where the triceps skinfold was measured, to derive the midarm muscle circumference (MAMC), or by the 24-hour urinary creatinine or

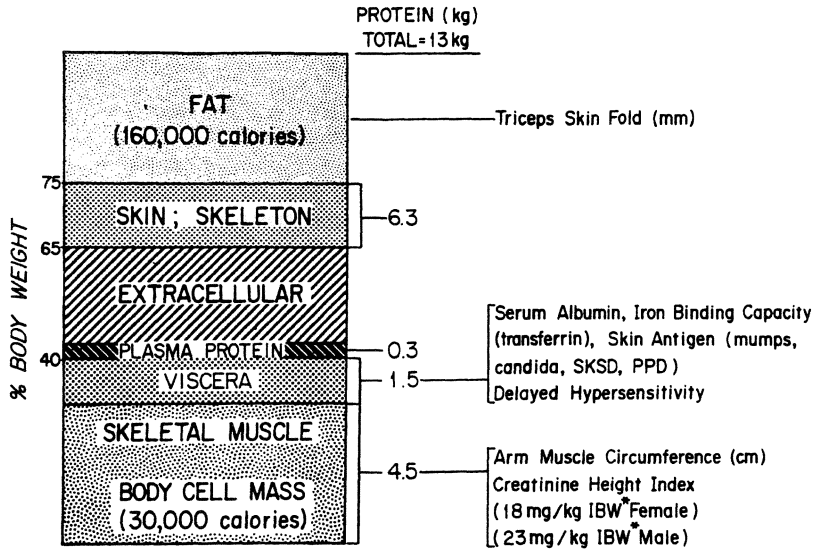


Fig. 1. Nutritional assessment for protein-calorie malnutrition. Body compartments are illustrated with some of the clinical tests used to assess malnutrition affecting these compartments. IBW, ideal body weight; PPD, purified protein derivative; SKSD, streptokinase streptodornase. (From Blackburn GL, Bistrian BR, Maini BS, et al. Nutritional and metabolic assessment of the hospitalized patient. *J Parenter Enteral Nutr* 1977;11:22; with permission.)

3-methylhistidine excretion. The greater precision of these laboratory assessments, however, adds little to the clinical care of the pregnant woman, although such measurements may be useful in clinical research.

Large rapid increases in body weight in excess of the growth expected from a positive energy balance (eg, more than 1 kg/wk) predominantly reflect increases in extracellular water [11]. This compartment easily is assessed clinically by checking for dependent edema and by monitoring body weight. These changes need to be monitored closely to guide fluid and electrolyte therapy properly and to avoid overfeeding or underfeeding.

A fourth compartment, the viscera, including visceral organs, nerves, and blood cell mass, is not easily measurable but is believed to be assessable by measurement of serum proteins synthesized by the liver, such as albumin, transferrin, total iron-binding capacity (TIBC), prealbumin, or retinol binding protein. The levels of these transport proteins, however, do not reflect visceral mass as creatinine or 3-methylhistidine reflect muscle mass. These proteins rather are general monitors of hepatic protein synthesis, affected by nutrient intake, hepatic function, and metabolic stress. Thus, a low serum albumin level may reflect inadequate protein intake, hepatic insufficiency, or redirection of hepatic protein synthesis to produce acute phase proteins that is required during metabolic stress, instead of transport proteins. Nevertheless, except for hepatic insufficiency, hypoalbuminemia generally indicates an increased need for protein, either to compensate for

previously inadequate intake or to avoid excessive protein loss during hypercatabolic stress.

Nutrient reserves can be assessed by direct measurements, such as the measurement of weight, body fat, red blood cell folate, and serum ferritin, or by measurement of dependent functions. For example, a normal serum albumin suggests adequate protein intake, and a normal prothrombin time reflects sufficient vitamin K. Some dependent parameters serve as indicators of several nutrients. For example, muscle strength reflects protein and calorie intake and the adequacy of micronutrients, including iron, magnesium, potassium, and phosphorus. Similarly, skin and mucosal integrity presume adequate supplies of protein, zinc, group B vitamins, and essential fatty acids. Table 3 provides a comprehensive list of signs of nutrient deficiencies [237].

A reasonable screen for pregestational nutrient reserves includes a medical history, including at least cursory information on appetite, diet, and weight; a physical examination, including measurement of height and weight; and standard clinical laboratory tests, including a complete blood count (CBC), serum chemistries including albumin, and serum ferritin, folate, and thyroid function tests of T3, T4, and TSH. Unfortunately, the pregestational nutritional state must be deduced from the findings in midpregnancy in the 25% to 30% of pregnant women who initially present for prenatal care in the second trimester [11].

To avoid a misdiagnosis of malnutrition, physiologic changes occurring in normal pregnancy should be appreciated, including

1. Expansion of plasma volume by up to 50%, reaching a plateau in the middle of the third trimester [11]. This reduces the concentration of plasma constituents by one third, unless counterbalancing mechanisms occur. Serum albumin declines by approximately 1 g/100 ml, almost one third [8]. The hematocrit, however declines by only 12% to 15%, because erythrocyte cell mass increases by 20% (peaking at the time of delivery).
2. Active transport of certain nutrients from the maternal circulation across the placenta that further reduces the concentration of these nutrients, such as amino acids, iron, zinc, and water-soluble vitamins except niacin (Table 4) [11].
3. Gestational hormone-induced fat mobilization that increases triglycerides and cholesterol levels by approximately 40% [11] or more [8] and fat soluble vitamins (betacarotene, vitamin D, and vitamin E, but not vitamin A) levels by 30% to 120% [11].

Physiologic nutritional needs

In addition to the nutritional needs related to pregnancy, the pregnant patient has needs unrelated to the pregnancy that are a function of body size (more precisely, body cell mass), physical activity, and metabolic activity.

Body mass

Larger subjects require more calories to maintain a larger mass, although an obese person burns fewer calories on a per kilogram basis, because adipose tissue adds weight but consumes relatively little energy. Excessive extracellular fluid, recognized as pitting edema, adds weight but does not consume energy.

The Harris-Benedict formula estimates basal energy expenditure (BEE) in healthy individuals based on height and weight (with adjustment for obesity), age (which is associated with an increasing percentage of body fat and a reduction in energy need), and gender (women generally have a higher percentage of body fat). The formula for women is

$$\text{BEE} = 655.10 + 9.56 W + 4.85 H - 4.68 A$$

where W is body weight in kilograms, H is body height in centimeters, and A is age in years.

BEE is the energy use of a person lying recumbent in bed after an overnight fast. It does not include the energy required for digesting and metabolizing food or for such minimal activity as going from bedroom to bathroom. Resting energy expenditure (REE) that includes these additional energy requirements is estimated by adding 10% to the BEE.

Physical activity

Caloric expenditures for physical activity, such as activities of daily living or exercise, are difficult to estimate because they vary from subject to subject and from day to day even for the same subject. Fortunately, subjects who are healthy enough to engage in significant physical activity usually do not need these energy needs determined because they usually do not require nutritional support and can adjust their oral intake spontaneously by homeostatic modulation of appetite. In those rare situations when an active pregnant woman depends on parenteral or enteral nutrition, the nutritional prescription needs to be adjusted empirically to achieve the desired rate of weight gain.

Exercise is safe and beneficial during pregnancy [238–240]. Exercise is associated with fewer symptoms during late pregnancy, shorter labor, and a reduced risk of a large-for-gestational-size infant [241]. Exercise also was associated with a lower risk of chromosomally normal spontaneous abortions [242]. In addition, investigators found that women who exercise during pregnancy may lower their risk of developing gestational diabetes mellitus [243]. The American College of Obstetricians and Gynecologists recommends that pregnant women, in the absence of complications, engage in 30 or more minutes of moderate exercise on most days, if not every day, of the week [244]. Pregnant women who exercise should drink an adequate amount of water and have appropriate ventilation to prevent overheating and possible fetal danger [245]. Strenuous physical activity may be detrimental to mother and fetus and may be associated with a lower birth weight [238].

Metabolic activity

In addition to the metabolic activity required to support fetal growth in utero and the growth of maternal tissues needed to sustain the pregnancy, other metabolic functions compete for nutrients. A growing pregnant adolescent is at greater risk of nutrition-related complications than a pregnant adult of the same height and weight because the adolescent must satisfy her own growth needs and those of the fetus [11]. In this context, adolescence is defined as the five years following the beginning of menarche. After this time, her nutritional demands become similar to that of any other pregnant adult, even if she is still in her teens [11]. One study noted that pregnant women deal with the increased energy demands by reducing their activities [246].

Effect of disease or therapy on nutrient requirement or tolerance

The metabolic response to severe physical injury or major sepsis, which includes synthesis of acute phase reactants, mounting an immune response, and healing wounds, may increase the REE by up to double and the nitrogen requirement by up to fourfold [247]. In these situations, however, early fetal demise more likely results from inadequate fluid resuscitation leading to vasoconstriction and impaired placental perfusion [248,249]; the increased protein and caloric requirements must be addressed after hemodynamic stability is achieved to optimize the maternal recovery and fetal growth.

Some disease states affect nutrient tolerance more than nutrient requirements. For example, phenylalanine intolerance occurs in phenylketonuria (PKU), carbohydrate intolerance occurs in diabetes, protein intolerance occurs in renal disease, and fat intolerance occurs in hypertriglyceridemia. These conditions necessitate dietary modification. Acute pancreatitis, inflammatory bowel disease (IBD), and HG temporarily may preclude oral intake. Severe depression or other psychiatric disease can severely affect appetite and require nutritional intervention.

Sometimes, the therapy, rather than the disease, has an impact on the nutritional state. Anticonvulsants adversely affect folate and vitamin D metabolism. Antacids and sucralfate interfere with phosphate absorption resulting from aluminum binding and can cause hypophosphatemia. Diuretics can cause excessive losses of potassium, magnesium, and zinc. Excessive iron supplements can reduce zinc absorption by competitive inhibition.

Intake versus nutritional needs

The relationship between intake and nutritional needs dictates whether or not nutritional intervention is indicated and, if already started, if it should be continued. Regardless of the presence of malnourishment, high or low nutrient needs, and concomitant diseases, the only indication for nutritional intervention during pregnancy is that the intake (of one or more

nutrients) is not matching the needs and the deficit is likely to have an adverse effect. Controls on nutritional therapy are designed to prevent risks from unnecessary intervention. The indication for nutritional therapy should be reviewed before starting the therapy and periodically thereafter. Therapy should be discontinued as soon as it is unnecessary.

Nutritional support in pregnancy

Detailed review of the various modalities of enteral and parenteral nutrition is beyond the scope of this article, which highlights those therapies that pertain to the pregnant patient. Materials and methods, indications, complications, and cost effectiveness of nutritional support are reviewed in several textbooks [250–253]. The American Society for Parenteral and Enteral Nutrition recently has published evidence-based guidelines for parenteral and enteral nutrition in various conditions, including pregnancy [254].

Correction of hypovolemia

A pregnant woman who presents with chronic vomiting and weight loss or recent acute blood loss requires urgent attention. Fluid resuscitation, usually administered intravenously, and correction of intravascular depletion are the first priorities for preventing compensatory vasoconstriction and uterine hypoperfusion. During traumatic stress, the uterus is treated as a nonvital organ and hypoperfused [255].

Significant hypovolemia can develop in a pregnant woman before it becomes clinically obvious. The pregnant patient may withstand an acute blood loss of 10% to 20% or a gradual loss of 35% of circulating blood volume before showing signs or symptoms of shock because of the 50% increase in blood plasma volume in pregnancy [248,249,255]. Maternal hypovolemia, however, triggers release of catecholamines, which cause peripheral and uterine vasoconstriction. As a result, uterine perfusion may decline by up to 20% without any changes in maternal blood pressure. The fetus therefore is likely to be jeopardized in a mother with borderline hemodynamic stability [248].

Maternal blood pressure, pulse, and oxygen saturation are unreliable signs of maternal and fetal well being [256]. Other clinical signs that follow include skin color and temperature, character of the peripheral pulse, urine output, and degree of agitation. Acidosis, bicarbonate, and lactate levels are useful indicators of maternal hypoperfusion and under-resuscitation [257]. Because of the difficulty in diagnosing hypovolemia and hypoxia, supplemental oxygen should be administered during maternal resuscitation and evaluation until maternal hypoxia and hypovolemia, and fetal distress are excluded [248].

For the patient in shock, fluid resuscitation is generally followed. Ringer's lactate is more physiologic and effective in restoring fetal oxygen levels than other plasma expanders [248,255]. Recent research has shown that crystalloids are preferable to colloids [258]. Crystalloid fluid should be used to replace blood loss at a ratio of at least three to one [248,249]. Large quantities of normal saline solution should not be used because they can cause hyperchloremic acidosis in the mother and fetus [248]. For blood loss of more than 1 L, or hypovolemia not corrected after 2 L of crystalloid, blood transfusion usually is indicated [248]. Central venous pressure (CVP) readings are difficult to evaluate in the pregnant patient because they are normally depressed during pregnancy. Failure of the CVP, however, to rise after treatment or a further decline despite fluid resuscitation indicates persisting hypovolemia, even if the pulse and blood pressure are normal [248]. Once the patient is hemodynamically stable, the micronutrient and macronutrient nutritional needs, discussed previously, should be addressed.

Correction of anemia

Iron deficiency anemia is a serious health problem in the United States and world wide [259]. In the United States, an estimated 7.8 million adolescent girls and premenopausal women have low iron stores [260]. Approximately 20% of pregnant women in industrialized countries [261] and more than 50% of pregnant women in developing countries have low iron stores [262]. Anemia during early pregnancy increases the risk of preterm birth [263,264]. A thorough diagnostic evaluation is recommended. Serum ferritin should be used to screen for iron deficiency early in pregnancy.

The role and efficacy of iron supplementation during pregnancy is controversial. Allen [265] advocates routine iron supplementation during pregnancy, even in women who begin pregnancy with sufficient iron levels. Iron supplementation during one pregnancy can provide protection during a subsequent pregnancy. In addition, low iron stores during pregnancy can affect the neonate during his first year of life. Haram et al [261] argues that the effect of iron supplementation on birth weight is unsubstantiated but agrees that supplementation may improve the neonatal iron levels during the first year of life. Lynch [262] advocates iron supplementation during adolescence before pregnancy, so that female adolescents can begin their pregnancies with adequate iron stores. In a study comparing intravenous iron sucrose with oral iron sulfate, iron sucrose was found to be an effective treatment for iron deficiency anemia without serious side effects [266].

Routes of nutritional support

The route of nutritional repletion depends on the degree and the anticipated duration of gastrointestinal dysfunction, the severity of nutritional depletion, and patient acceptance. The greater the maternal or fetal

nutritional risk, the more invasive intervention is justified, despite potential iatrogenic complications. Conversely, when oral supplementation is sufficient, the discomfort and risks of tube feeding are unwarranted. When tube feeding will do, the risks and cost of TPN are unjustified.

Enteral versus parenteral nutrition

Enteral nutrition should be used whenever the gastrointestinal tract is usable, even if only by tube, for the physiologic advantages of enteral alimentation and to avoid the risks and expense of parenteral nutrition [246,267]. In addition to defensive barriers provided by the mucous layer, gastric acidity, and secretory immunoglobulins against infections and toxic factors that accompany food and drink, the gastrointestinal tract modulates the absorption of certain nutrients, such as calcium, iron, and magnesium, to meet changing needs while avoiding toxic excesses [268]. Furthermore, the portal funneling of absorbed nutrients to the liver allows additional homeostatic regulation of glucose, amino acids, vitamins, and other nutrients before they enter the systemic circulation [269,270].

Parenteral nutrition is fraught with dangers because it bypasses these protective and regulatory mechanisms. Besides the potential complications associated with central venous catheter insertion of pneumothorax, hemothorax, air embolus, and thoracic duct injury, parenteral nutrition, even when administered via a peripheral vein, can cause serious septic complications and various metabolic derangements, including hyperglycemia, hypoglycemia, acid-base disturbances, electrolyte abnormalities, and, in long-term TPN, hepatobiliary disease and metabolic bone disease [209,271,272]. Food within the gastrointestinal tract normally exerts a trophic influence on gut mucosa [268,273]. Loss of enteral feeding can result in mucosal atrophy, failure of cytoprotection, mucosal ulcerations, disintegration of barrier functions, bacterial overgrowth, and enterogenic sepsis. To reduce these risks, parenteral nutrition, when necessary, should be provided by strict protocol under the close supervision of knowledgeable staff, preferably a trained multidisciplinary team consisting of a physician, dietitian, nurse, and pharmacist [274]. The mere capacity to catheterize a subclavian vein or knowledge of the composition of a standard TPN solution is inadequate for the provision of safe parenteral nutrition.

A study of 562 patients randomized to receive either enteral or parenteral nutrition, however, showed that the enteral route was associated with a higher rate of inadequate nutrient intake [275] and complications. A literature review of prospective randomized studies comparing enteral to parenteral nutrition concluded that enteral nutrition was not necessarily superior, except in acute abdominal trauma, where it reduces septic morbidity and costs less [276]. The clinical choice of enteral versus parenteral nutrition may pit truth against reality. Undoubtedly the gastrointestinal tract is nature's preferred and the physiologically most effective route of nutrient acquisition, but a patient's refusal of an enteral tube or a

clinician's greater competence in managing parenteral feeding may dictate a pragmatic decision.

Central versus peripheral vein nutrition

Parenteral nutrition can be administered through a large central or peripheral vein. Central venous nutrition (CVN) offers the advantage that the high volume of blood flow in a central vein results in immediate dilution of the necessarily hypertonic nutrient solutions and avoids the phlebitis and thrombosis, which typically occurs in peripheral veins. Thus CVN can deliver an adequate nutrient intake within a reasonable fluid volume, for example, 2400 kcal including 100 g amino acids within 2000 ml, for as long as necessary. Alternatively, peripheral vein nutrition (PVN) avoids the mechanical risks of central vein catheterization, but cannot provide such support. Even though half as concentrated as CVN, in that PVN contains approximately 0.6 kcal/ml versus 1.2 to 1.4 kcal/ml in CVN, PVN usually cannot be administered beyond one to two weeks because of an associated phlebitis. Nevertheless, the potentially more dangerous CVN is not justified when PVN meets the nutritional needs of a given patient and is not expected to be required for more than a few days.

Peripherally inserted central catheters (PICC) increasingly are used to combine the advantages of peripheral and central nutrition while reducing the risk [277,278], although some, perhaps earlier on the learning curve, found that PICCs were more difficult to insert than subclavian catheters and were more frequently associated with thrombophlebitis [279].

Tube feeding complications

Tube feeding is not risk free [208]. The most dreaded complication is aspiration pneumonia, which typically occurs when gastric contents are regurgitated and the patient cannot protect her airway because of conditions such as unconsciousness or stroke. It also can occur if the trachea is inadvertently intubated and feeding is then directly infused into the respiratory tract. This erroneous intubation can occur without eliciting violent coughing in the comatose or heavily sedated patient. The risk of aspiration thus is mainly a problem in the neurologically impaired patient. To reduce this risk, the use of continuous rather than bolus feeding is recommended, as is monitoring gastric residual periodically in order to avoid gastric distention and regurgitation. Elevation of the head of the bed to 30° may also help prevent gastroesophageal reflux and regurgitation.

Another complication of tube feeding is diarrhea, although in most cases the diarrhea is to the result of concomitant medications rather than the tube feeding. Common offenders include magnesium containing antacids or supplements, phosphate supplements, sorbitol-dissolved drugs (including elixirs of theophylline, acetaminophen, and vitamins), antibiotics (resulting in suppression of normal gut flora and in overgrowth of enteropathogenic bacteria), prokinetic drugs (including metoclopramide and cisapride), and,

sometimes, laxatives given for prior constipation and not discontinued. Tube feeding–related diarrhea may occur if a hypertonic formula is infused directly into the small bowel, especially if given as a bolus (causing a dumping syndrome), if a polymeric formula is used in a patient with impaired digestion, or if tube feedings have been contaminated by bacteria as a result of improper handling.

Treatment of the diarrhea requires a workup to identify the cause and to guide the therapy. The problem should not be addressed simply by diluting the tube feedings, especially if the administered formula already is isotonic, in which case the only achievement is reduced nutrition and increased water intake. Similarly, routine addition of an antidiarrheal agent to the tube feeding is inappropriate, because this may lead to toxic megacolon in a patient when the diarrhea is the result of pseudomembranous colitis.

Despite these dangers and concerns, parenteral feeding can be administered long term without complications. Spanish clinicians reported that one 30-year old pregnant woman with severe chronic intestinal pseudo-obstruction was maintained on parenteral nutrition from conception to delivery [280]. Pregnancy and labor were uneventful, and no metabolic complications occurred. In another case, a 34-year old pregnant patient lapsed into a vegetative state after undergoing brain surgery at 22 weeks of gestation [281]. Enteral feeding was administered through a nasoduodenal feeding tube without complications. The patient delivered a 2150-g viable male infant at 33 weeks of gestation. Occupational and physical therapy led to improved mental status and the patient was discharged one month postpartum.

Two more patients with either severe HG or chronic intestinal pseudo-obstruction conceived while receiving gastrostomy feedings [282,283]. The patient with severe HG was fed via a self-propelled, blindly placed nasojejunal tube. The pregnant woman with chronic intestinal pseudo-obstruction wore a portable feeding pump and received nutrition through a gastrostomy. The investigators reported that the techniques were cost effective with few complications. Both women received the nutritional support at home and delivered healthy babies.

Formulas for enteral nutrition

The choice of formula for enteral feeding presents difficulties not found with TPN. Whereas in TPN nutritional requirements are directly met by prescription of specific amounts of amino acids, glucose, fat emulsion, electrolytes, vitamins, and trace elements in a desired fluid volume, enteral nutrition involves choosing among dozens of brand-name formulas [284]. A dietician can assist in this selection after the patient's gastrointestinal pathology has been defined. The available categories of formulas are as follows.

Meal-replacement formulas

These formulas essentially are a liquid alternative to a nutritionally complete, regular diet. They provide approximately 40 g protein and 1000 kcal/L, and deliver the RDA for vitamins and minerals in 1500 to 2000 ml/d. Products formulated for oral consumption are flavored, which slightly increases their osmolality, whereas those formulated for tube feeding are not. These formulas rarely used to contain fiber; now, many do because fiber may help prevent constipation and diverticular disease, and fiber, particularly soluble fiber, is converted by gut flora to short-chain fatty acids, the preferred fuel substrate for colonocytes. These meal-replacement formulas are appropriate oral supplements for patients whose intake is insufficient and who, for some reason, perhaps esophagitis, tolerate liquids better or as tube feeding for patients who are unable or unwilling to swallow because of endotracheal intubation, coma, neurogenic dysphagia, or anorexia nervosa, but whose gastrointestinal tract is otherwise functional.

Concentrated formulas

These formulas are similar to the meal-replacement formulas in composition except they contain less water and deliver 1.5 to 2.0 kcal/ml. These formulas are indicated for the fluid-restricted patient.

High-protein formulas

These formulas provide approximately 60 g/1000 kcal of protein, approximately 1.5-fold the standard formula concentration. As an oral supplement, such formulas are useful when the caloric intake is almost acceptable, but the protein intake is poor. They also can be used as exclusive feeding either orally (using flavored formulas) or by tube for metabolically stressed patients, in whom the nitrogen requirement increases more than the caloric requirements, and for obese diabetics, in whom a combination of adequate protein intake with caloric restriction is often desirable.

Elemental and semielemental formulas

These formulas are designed for patients with impaired digestion. The proteins have been hydrolyzed to elemental single amino acids or semi-elemental small peptides. The long-chain triglycerides (LCT) largely have been replaced by medium-chain triglycerides (MCT), retaining only a small amount of the LCT required as essential fatty acids. Such formulas also have been used in acute pancreatitis to minimize pancreatic stimulation from enteral feeding and in patients with lower gastrointestinal disease to maintain nutritional intake while reducing fecal residue because the formula is absorbed by the upper gut, leaving little or no residue for excretion; the rationale for these indications recently has been questioned [285].

Modular formulas

These products contain only one macronutrient (protein, carbohydrate, or fat) used to boost the corresponding ingredient in the patient's diet or

tube feeding. These products are supplements that are not nutritionally complete.

Disease-specific formulas

These are nutritionally complete products formulated to either exclude or to be fortified in specific nutrients that compensate for a metabolic disorder or achieve a pharmacconutrient effect. Examples of these products include formulas containing a high ratio of branched-chain amino acid (BCAA) to aromatic amino acids (AAA) in order to normalize the concentration of these amino acids in the blood of patients with hepatic encephalopathy; formulas excluding nonessential amino acids to reduce the nitrogen load in uremic patients; formulas with reduced carbohydrate content to facilitate glucose control in diabetics or reduce carbon dioxide production in patients with hypercapnia; and formulas fortified with certain nutrients, such as arginine, nucleotides, and Ω -3 fatty acids, for immune function potentiation. The indications, efficacy, and cost effectiveness of these products are controversial [273,284,286–290].

Refeeding syndrome

Regardless of the nutritional route, a pregnant patient receiving nutritional support, especially after a period of weight loss, should be monitored closely for refeeding syndrome complications [208,290]. The most common manifestation is a triad of electrolyte aberrations: hypophosphatemia, hypokalemia, and hypomagnesemia resulting from rapid uptake of these ions by the expanding maternal and fetal body cell masses. A small increase in body cell mass can cause a significant decline in their serum concentration because potassium, magnesium, and phosphate are the predominant intracellular ions but have a miniscule extracellular concentration. This syndrome can cause muscle weakness, arrhythmias, seizures, respiratory failure, and death. The typically normal laboratory values prior to nutritional repletion should not lull the clinician into a false sense of security because these electrolyte alterations occur after starting the feeding. Close monitoring and careful anticipant therapy bypass these complications. Also in the refeeding syndrome, a sudden increase in carbohydrate intake in a patient with latent thiamine deficiency can precipitate “high output” failure or “wet beriberi” and Wernicke’s encephalopathy [124,290].

Nutritional support in certain conditions

Hyperemesis gravidarum

HG refers to nausea and vomiting during pregnancy that is so severe that the patient loses more than 5% of her pregravid weight [291,292]. HG occurs in approximately 1% to 2% of pregnancies and generally is distinguished from “morning sickness,” which is common in pregnancy and

is considered a sign of pregnancy well being [291]. Risk factors for HG include primigravidas, multiple gestation, prior unsuccessful pregnancy, and prior HG. Women who were 10% or more below their ideal weight before conception have a poorer outcome from this hyperemesis [29].

HG originally was thought to occur only in the Western Hemisphere, but has been described in Asian women with similar characteristics and frequency. HG is not correlated with race, socioeconomic status, or pre-nuptial conception. The incidence of HG decreases in wartime [291].

This condition usually requires treatment in the hospital. This condition can cause inadequate intake of nutrients and calories, dehydration, and electrolyte derangements. Reported complications include Wernicke's encephalopathy (also caused by the administration of glucose without concomitant thiamine supplementation [124]), hepatic and renal dysfunction, depressed immunologic response, and, rarely, maternal or fetal death [293].

Although of unknown etiology, proposed theories include elevated human chorionic gonadotropin (hCG) levels, adrenal dysfunction, hyperthyroidism, hyperparathyroidism, hepatic abnormalities, autonomic nervous system dysfunction, allergy, gastrointestinal dysmotility, peptic ulcer disease from *Helicobacter pylori* infection, abnormal metabolic and nutritional factors, and psychosomatic disorders [61,291,294,295]. This section focuses on the treatment of this condition. Another article in this issue reviews this entire subject.

In the absence of a known etiology, the treatment is symptomatic and empirical, albeit with increasing sophistication in the treatment or prevention of any resultant malnutrition. Reported treatments range from the conservative, including short-term intravenous rehydration, sedation, antiemetic medication, and, sometimes, psychotherapy [296], leading to the resumption of oral intake, to invasive TPN for the remainder of the pregnancy [297]. When intravenous fluids, electrolytes, and antiemetics succeed in controlling the condition, exposure of the patient to the risks of more aggressive modalities is not justified, although some experts do not recommend antiemetic drugs during the first trimester because of possible fetal toxicity [293,298].

TPN has been used effectively in pregnancies complicated by HG in the first [299] and the later trimesters [300–303]. In one study, 10 patients placed on TPN (FreAmine III 4.25% and 25% dextrose with intralipids given once a week administered via a silastic Hickman catheter placed in subclavian vein) during the first trimester for HG experienced rapid relief of nausea and vomiting and stopped losing weight [299]. The patients gradually began eating orally, with overnight supplementation by TPN. All pregnancy outcomes were favorable. Other studies have confirmed the safety and efficacy of parenteral nutrition, including lipids, in providing 50% of non-protein calories for severe HG [304].

In another study, nausea and vomiting subsided within one day after twenty subjects with HG received a ten-day treatment regimen of

intravenous rehydrating saline solution with an intravenous multivitamin supplement without oral fluids or food [293]. Only two patients required readmission for a recurrence of symptoms. Whether or not the beneficial effects were the result of psychologic factors, rehydration, or vitamin therapy is not known. The investigators suggested that a resultant vitamin imbalance might contribute to perpetuation and exacerbation of the hyperemesis because nausea, anorexia, and malaise often are nonspecific signs of vitamin deficiency, especially of group B vitamins [293]. Some have added diazepam to the parenteral fluids to reduce the nausea [305].

The generally preferred enteral route of feeding has been avoided in HG because of the risk of aspiration, especially in light of the already present vomiting [293]. Several recent studies, however, reported successful nasogastric tube feeding [306–308]. In one study, seven hyperemetic women were treated with continuous infusion of full-strength, standard, isotonic formulas through an 8-Fr Dobhoff nasogastric tube beginning at 25 ml/h, with the rate of infusion increased as tolerated by 25 ml/h/d until the target goal of a maximum rate of 110 ml/h was achieved [306]. Once the target rate was achieved, the total daily volume was consolidated and delivered overnight to provide for the BEE and the added 300 cal/d necessary during pregnancy. The feedings were well tolerated. Nausea and vomiting improved in all seven patients within 24 hours after starting the enteral feedings. All patients were discharged within 8 (mean, 4.6) days after patient stabilization. Six of the women continued enteral feedings at home, self-administered by a portable infusion pump. Patients were instructed to eat normally when able and, eventually, discontinued their enteral feedings when their nutritional needs were met orally. A visiting nurse provided support for the enteral feedings. Enteral feedings were continued on an outpatient basis for a mean of 43 days and a range of 5 to 174 days. Although two women experienced recurrent nausea and vomiting when the tube became clogged or dislodged, symptoms resolved when the tube was replaced. All patients subsequently gave birth to full-term, normal-weight babies.

For patients unable to tolerate a nasogastric tube and expecting to need tube feeding for several weeks, a tube can be passed percutaneously into the stomach under endoscopic guidance by percutaneous endoscopic gastrostomy (PEG). Godil and Chen reported the first use of PEG in two pregnant women who could not tolerate oral food intake [309]. Both cases resulted in good fetal outcomes. Serrano et al [310] reported the first successful use of percutaneous endoscopic gastrojejunostomy for enteral feeding in two pregnant women with HG without complications. The researchers noted the method was cost effective.

Steroid therapy also has been successfully used to treat HG. Moran and Taylor [311] reported that prednisolone 10 mg three times daily quickly relieved nausea and vomiting, enabling patients to be discharged on average in three days. Safari et al [312] found in a randomized controlled trial that oral methylprednisolone at 16 mg three times daily was more effective for

treating hyperemesis than promethazine. None of the patients receiving methylprednisolone had to be readmitted to the hospital within two weeks, compared with approximately 30% of the promethazine-treated group. In another study, patients administered 40 mg of prednisolone daily for one week improved their appetite, gained weight, and felt better, but the treatment did not completely relieve the nausea and vomiting [313].

The success of a wide spectrum of treatments has led to the hypothesis that perhaps HG is several diseases sharing a final common pathway or expression of severe vomiting [291]. The same data, however, can have another explanation. From the perspective of a clinical nutritionist, the most intriguing aspect of this severe vomiting is its response to tube feeding. In other clinical situations of nausea, including gastric or intestinal obstruction, postoperative ileus, pancreatitis, hepatitis, cholecystitis, gastroenteritis, uremia, cancer chemotherapy, increased intracranial pressure, and so forth, the vomiting is exacerbated, not relieved, by oral or intragastric feeding. In all these circumstances, emptying the stomach, usually by nasogastric suction, not filling it, generally provides relief. The reported symptomatic relief from initiation of tube feedings [306], so much so that patients with HG may request tube reinsertion and feeding resumption [306], is unique. Whereas in any other clinical setting, nausea is highly upsetting to the patient and a cause for concern, in pregnancy it is curiously almost welcomed, at least in popular thinking, as an early sign of pregnancy [254] and even as a sign of pregnancy well being [291]. Furthermore, even though 80% of pregnancies are affected by “morning sickness,” only 7% result in a low-birth-weight baby [11].

The authors hypothesize that the nausea of pregnancy is akin to the nausea that sometimes occurs during fasting. As such, it is best viewed and treated as a manifestation of severe, although masked, hunger. As any fasting person instinctively knows, the best treatment for nausea during fasting is to start eating. As the starved person begins to eat, the sensation of nausea is replaced by a more typical sensation of hunger that leads to sufficient eating to compensate for the starvation and to regain any lost weight. By analogy, the pregnant woman, who must eat enough to increase her weight by approximately 25 lb or more during nine months, must develop the same ravenous hunger as the starved individual, a hunger that might turn to nausea if it is ignored.

This theory explains the intriguing observations noted previously and the success of disparate therapies for this condition. The term “morning sickness” is apt, even though the symptoms may continue through noon and night [314], because the enforced fasting during sleep at night provides more time for hunger to develop and become nausea by the morning than does the fasting between meals. Naturally, if no eating occurs in the morning, the “morning sickness” may continue throughout the day and occasionally become HG. Thus, extreme hunger, which is critical for the well being of pregnancy, may be at the root of “morning sickness” and HG, except that

the chronicity and severity in the latter can result in additional complications of dehydration, electrolyte imbalances, and nutrient deficits that may exacerbate the nausea and compromise the pregnancy.

Because the treatment for hunger is food, almost any food, the delivery of any nutrients by any route may successfully control the nauseating hunger of the hyperemesis patient and allow resumption of a normal oral intake—hence, the success with intravenous saline and vitamins [315,316], TPN, and nasogastric tube feeding. Empiric therapies of “eating small frequent meals” or “having a snack before bedtime or during the night” [297] presumably are effective because they prevent the development of severe hunger.

Although antiemetics provide temporary relief, their primary use should be to facilitate the return of oral intake, which is the ultimate treatment for hunger. Similarly, ginger [317], acupressure [291,318], acupuncture [319], psychotherapeutic techniques [296,320], or electrostimulation of the vestibular apparatus [321] may help by facilitating and encouraging the resumption of oral intake, although they themselves do not satiate hunger.

The authors' preference is to institute peripheral venous nutrition with or immediately after volume repletion to prevent further nutritional deficiency while waiting for antiemetic therapy to work and oral intake to resume. The authors typically administer 63 g of amino acids, 150 g of glucose, and 100 g of fat (total 1762 kcal) with vitamins, minerals, and required electrolytes for a total volume of 2000 ml/day. The authors prepare their patients for the possibility of prolonged parenteral nutrition or tube feeding, but patients usually start tolerating some oral intake within 24 hours and no longer require parenteral nutrition by approximately the third day.

Diabetes mellitus

Poor diabetic control during the first trimester, especially in the first seven weeks, increases the risk of congenital malformations and spontaneous abortion [322]. Women with pregestational or gestational diabetes mellitus need evaluation and intervention to achieve good labor outcomes, because their offspring face an increased risk of congenital malformations from impaired maternal glycemic control. In a meta-analysis of 14 studies [323] of women with pregestational diabetes, prenatal care reduced the risk of congenital malformations. The investigators noted the importance of early intervention because diabetic women often have unplanned pregnancies. For example, folic acid supplementation should be instituted early. One study indicated that women with pregestational diabetes mellitus face an increased risk of caesarean section and gestational hypertension, compared with women who have gestational diabetes [324], but another study reported that fetal, maternal, and neonatal complications were similar in women with pregestational versus gestational diabetes mellitus [325].

Maternal hyperglycemia during the second and third trimesters is associated with fetal overnutrition and hyperinsulinemia; neonatal macrosomia and hypoglycemia; and long-term obesity lasting through childhood and into adulthood [322]. Recent studies indicate poor maternal lipid and glucose regulation in the second and third trimesters is correlated with poor performance on intelligence tests years later [326]. In a multicenter controlled study, rigorous control of blood glucose levels in insulin-dependent diabetic mothers, using either multiple daily insulin injections or continuous subcutaneous insulin infusion with an external pump (aiming for a fasting blood glucose of 70 to 100 mg/dl and a one-hour postprandial level \leq 140 mg/dl), reduced the risk of fetal malformations and spontaneous abortions to that of nondiabetics [376].

For the noninsulin-dependent, obese, gestational diabetic patient, moderate caloric restriction of 1700 to 1800 kcal/d, or 25 kcal/kg of ideal prepregnancy body weight, was associated with lower maternal weight gain and a lower rate of macrosomia [327]. Severe caloric restriction of 1200 kcal/d, however, although resulting in improved glucose levels, causes ketonemia and ketonuria, which should be avoided in pregnancy [327]. Addition of insulin to control gestational diabetes further was reported to produce lower [328,329], higher [330], or unchanged [331] rates of macrosomia in various studies. These conflicting data support Gunderson's hypothesis that good control of the gestational diabetic depends more on intensive dietary therapy with frequent self-blood glucose monitoring (SBGM) than on insulin usage [327].

In a multicenter French study, no large-for-gestational-age infants occurred among pregnant women with gestational diabetes who had consumed more than 210 grams of carbohydrates a day [332]. The study investigators recommended that women with gestational diabetes consume at least 250 grams of carbohydrates per day, eat the carbohydrates throughout the day, and select the carbohydrates in the form of low-glycemic index foods to prevent postprandial hyperglycemia. A literature review concluded that the amount of carbohydrates a pregnant woman with pregestational diabetes consumes is the most important factor in achieving glucose control; the ideal amount provides adequate calories without causing postprandial hyperglycemia or premeal ketosis [333].

Although intravenous feeding can lead to higher blood glucose levels than enteral nutrition, addition of insulin to the parenteral formulation allows easier and more precise matching of insulin dosage with the nutrient intake than is feasible in the orally or tube-fed patient. Control of blood glucose in the tube-fed, insulin-dependent diabetic may be achieved by giving NPH insulin every 12 hours to maintain steady insulin activity during continuous feeding [287]. Hyperglycemia can thwart enteral and parenteral nutrition. Hyperglycemia is associated with gastroparesis [44], which can drastically limit oral intake or nasogastric tube feeding, and it increases by severalfold the rate of catheter sepsis [44], which can complicate TPN delivery.

The uncontrolled diabetic essentially is in a catabolic state that causes loss of intracellular ions just as in starvation. He may present like a patient with the refeeding syndrome [334]. In addition to driving potassium and phosphorus intracellularly with glucose, insulin therapy re-establishes anabolism. Severe hypokalemia, hypophosphatemia, and hypomagnesemia may ensue, requiring close monitoring and therapy.

The American Diabetes Association position statement [335] on evidence-based nutritional principles for the treatment and prevention of diabetes during pregnancy notes that energy needs do not increase during the first trimester. An additional 300 kcal/d are suggested for the second and third trimesters. An adequate protein diet includes 0.75 g/kg/d plus 10 g/d. All women of childbearing age should consume 400 µg of folic acid from fortified food or a supplement. Prepregnancy counseling should include a prenatal food plan to optimize blood glucose control. Women with gestational diabetes should consume carbohydrates throughout the day in three small- to moderate-sized meals and two to four snacks. Regular aerobic exercise is recommended to lower fasting and postprandial glucose concentrations. After delivery, women with gestational diabetes should practice lifestyle changes, including weight loss and physical activity, because of their risk of developing type 2 diabetes.

Monitoring does not end at delivery. Physicians must develop a postpartum nutrition plan designed to enable the patient to achieve glycemic control [336]. Glucose tolerance should be tested postpartum because a significant minority of patients with gestational diabetes develops permanent diabetes.

Inflammatory bowel disease

Although most women with IBD can conceive and deliver a healthy baby [337], they face increased risks of complications if the disease is active, including an increased risk of small and premature babies [338–340]. Clinicians should treat and control the disease during pregnancy. Most drugs used to treat IBD are not harmful to the fetus [341,342] and are safe during lactation [343].

Some patients with Crohn's disease or ulcerative colitis have nutritional deficiencies [344]. Nutritional support in the nonpregnant patient usually is triggered by the need to treat or prevent malnutrition, especially during periods of prescribed "bowel rest." In pregnancy, because of the severe deleterious maternal and fetal effects of malnutrition, nutritional support should be instituted early before malnutrition has developed and continued until adequate oral/enteral intake is re-established. Whereas an attempt at enteral feeding is reasonable in a well-nourished, nonpregnant individual before resorting to parenteral nutrition [344], TPN should be instituted first in a pregnant patient with an acute exacerbation of IBD associated with weight loss, and then, having thus assured an AI, address gut rehabilitation and enteral feeding.

Multifetal pregnancy

With increasing assisted reproduction, the number of multifetal pregnancies is rising. This group of women poses a challenge to the nutrition specialist, because guidelines for singleton pregnancies are not applicable. Nutritional support is known to improve outcomes in multifetal pregnancies [27]. In a study conducted at the Montreal Diet Dispensary, women pregnant with twins who received dietary counseling achieved an average weight gain of 40 pounds, compared with 35 pounds in women pregnant with twins who did not receive counseling, and their infants weighed, on average, 80 grams more than infants of women who did not receive counseling [345].

Recommendations for nutritional support for multifetal pregnancies include, first, a total weight gain of 35 to 45 pounds in twin pregnancies. This amounts to approximately 150 kcal/d more than consumption needs for a singleton pregnancy. Women pregnant with twins should gain approximately four to six pounds during the first trimester and 1.5 lb/wk thereafter. This pattern decreases the risk of preterm delivery and low-birth-weight infants. Second, only two studies have assessed weight gain in triplet pregnancies. A weight gain of 50 pounds may be appropriate. Women pregnant with triplets should gain approximately 1.5 lb/wk throughout pregnancy. Third, women with multifetal pregnancies should eat three or more servings of the following food groups: the meat, poultry, fish, dry beans, eggs and nuts group; the milk, yogurt and cheese group; and the vegetable group. They should eat six or more servings from the bread, cereal, rice, and pasta group; and two or more servings from the fruit group. Fourth, the Institute of Medicine recommends that women with multifetal pregnancies should take a supplement containing 15 mg of zinc, 2 mg of copper, 250 mg of calcium, 2 mg of vitamin B6, 300 µg of folate, 50 mg of vitamin C, and 5 µg (200 IU) of vitamin D. These women also should take a 30-mg iron supplement after the twelfth week of pregnancy. Fifth, women with multifetal pregnancies should consume more essential fatty acids than women with a singleton pregnancy. Sources include sunflower, safflower, corn, and soybean oil; egg yolks; meat; fatty fish; and canola oil.

Celiac disease

One in 70 pregnant women has celiac disease, but the disease often is undiagnosed and untreated [346]. Pregnant women with untreated celiac disease face an increased risk of fetal growth retardation, low birth weights, and miscarriages [347]. Interestingly, men with celiac disease are more likely to father infants with lower birth weights and shorter gestations [348]. Celiac disease results in deficiencies of factors necessary for organogenesis, including folic acid, iron, and vitamin K [349] and also is associated with vitamin B12 deficiency [350].

Women with treated celiac disease, however, face no increased risk of pregnancy. In a study of 127 women with celiac disease and 1260 controls, untreated women with celiac disease delivered infants who weighed, on average, 238 grams less than the infants of the controls, but women treated for celiac disease delivered infants who weighed more than the infants of the controls [351]. Infants of untreated mothers with celiac disease faced a threefold increased risk of intrauterine growth retardation compared with no increased risk for infants of treated mothers.

Corrado et al caution that mild gastrointestinal symptoms or anemia during late pregnancy should alert clinicians to the possibility of undiagnosed celiac disease [352]. Rostami et al suggest testing patients with reproductive disorders for celiac disease, because celiac disease reduces female fertility [353].

Acute pancreatitis

Acute pancreatitis is rare during pregnancy [354]. In a retrospective study, Chang et al cite an incidence of one per 6790 pregnancies. Among 16 hospitalized patients, the etiology included primary hyperlipidemia in 56% and gallstones in 38%. The women received low-fat diets and conservative treatment. The mothers all did well and improved postpartum, but the fetal outcomes included eight preterm deliveries and three fetal deaths. Aggressive fluid resuscitation and enteral or parenteral nutrition to reduce pancreatic stimulation might improve the fetal outcome.

Until recently, treatment for acute pancreatitis included placing the patient nothing by mouth to avoid pancreatic stimulation and feeding parenterally to prevent malnutrition [355]. Now, however, enteral feeding is increasingly recommended [356–359]. Lobo et al [356] suggest that enteral feeding may be superior to parenteral feeding, but note that some pancreatitis patients cannot tolerate enteral nutrition. For these patients, parenteral nutrition may be preferred. McClave et al [357] state that enteral feeding may reduce the hypermetabolic stress response and prevent gut atrophy and that feedings entering more distally in the gastrointestinal tract stimulate the pancreas less. They consider jejunal feeding as safe as total parenteral feeding in acute pancreatitis. Abou-Assi and O'Keefe [359] argue that enteral feeding is cheaper, safer, and more effective because it reduces the systemic inflammatory response, but other authorities believe that the data are inconclusive and that further clinical trials are required [360].

In one case report, a woman with lipase-deficient familial hypertriglyceridemia received enteral feedings with a low-fat diet and medium-chain triglyceride supplementation [361]. She did not develop gestational hyperlipidemic pancreatitis and successfully delivered a healthy baby. This patient previously had lost a pregnancy at 32 weeks of gestation as a result of hyperlipidemic pancreatitis.

Epilepsy

Pregnant women with epilepsy constitute 0.5% of pregnancies [18]. Anticonvulsant medications are teratogenic, particularly when combined or when valproate is used [362]. Anticonvulsant medications affect folic acid and vitamin K metabolism and may increase the risk of neural tube defects and neonatal hemorrhage [18]. These women also face a small but significantly increased risk of HG, preeclampsia and eclampsia, premature labor, and vaginal bleeding [362].

Antiepileptic monotherapy is recommended if an epileptic woman is considering pregnancy [363]. Folate and vitamin K supplements also must be given, the folate at 5 mg/d starting three months before conception and during the first trimester and the vitamin K starting one month before the expected delivery date, especially if the patient is taking carbamazepine, phenobarbital, or phenytoin [363]. With proper therapy, 95% of pregnancies in women with epilepsy have a favorable outcome [18].

Morbid obesity and bariatric procedures

Morbid obesity complicates the entire course of pregnancy. Morbidly obese women often are infertile [364]. Those who do conceive are at increased risk of hypertension, diabetes, and other risk factors of pregnancy, resulting in poorer neonatal outcomes [364,365]. Weight loss is, therefore, important in severely obese women who wish to bear children. Surgery is the only proven effective method for weight reduction in the morbidly obese [366–370]. Bariatric surgical procedures are performed with increasing frequency and efficacy and with decreasing morbidity. Between 1987 and 1996, the use of bariatric procedures increased threefold in Switzerland [371]. A group in California reported nearly 400 morbidly obese and superobese patients underwent laparoscopic Roux-en-Y gastric bypass procedures with an average hospital stay of only 1.6 days [372]. Patients often experience significant postoperative micronutrient deficiencies, however, which are particularly relevant during pregnancy.

Bariatric surgical procedures are classified as restrictive (such as gastric banding, which limits gastric capacity and the amount that can be ingested at one meal) or restrictive–malabsorptive (such as the Roux-en-Y gastric bypass, which creates a small gastric pouch and reduces absorptive capacity by anastomosing the pouch to the distal jejunum) [370]. The latter procedures cause greater weight reduction, but can induce multiple nutrient deficiencies. Whereas any procedure may cause nutrient deficiencies from behavioral noncompliance or surgical complications [370], the malabsorptive procedures particularly are prone to causing specific micronutrient deficiencies, including deficiencies of vitamin B12, iron, folate, and calcium from the effects of the malabsorption and from postoperative difficulty in tolerating certain foods, particularly meat products [369,370,373,374]. Some studies have also have reported protein calorie deficiencies

Table 4
Methods of placental transfer of nutrients

Diffusion Simple	Facilitated	Active transport
Gases	Carbohydrates	Amino acids
Free fatty acids		Water-soluble vitamins
Electrolytes		Sodium/calcium/iron
Fat-soluble vitamins		
Plus: pinocytosis, solute drag, breaks in villi		

From McGanity WJ, Dawson EB, Fogelman A. Nutrition in pregnancy and lactation. In: Shils ME, Olson JA, Shike M. Modern nutrition in health and disease. 8th edition. Philadelphia: Lea & Febiger; 1994, p. 712; with permission.

[369,375,377,378]. In the authors' experience, postbariatric surgery patients often voluntarily ingest no more than 500 to 600 kcal/d and often less than 30 g/d of protein, which renders supplementation essential. Byrne recommends that patients undergoing gastric bypass surgery take a multivitamin supplement for life, ferrous sulfate 650 mg/d, and calcium 1200 mg/d [373]. In the authors' experience, malabsorptive postbariatric surgery patients may require higher doses of vitamin supplementation, necessitating the monitoring of micronutrient levels.

Given the sensitivity of the growing fetus to micronutrient deficiencies and the susceptibility of postbariatric surgery patients to such deficits, the nutritional care of these patients during pregnancy is critically important. For the severely obese patient trying to become pregnant, some recommend restrictive rather than malabsorptive surgery, specifically a laparoscopically placed adjustable gastric band, to permit optimal control of maternal weight change during the Table 4 pregnancy [365].

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