



Lectures on Hygiene and Ecology

Nutrition in Different Groups of Population

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Nutrition in Pregnancy and Lactation

Optimal maternal nutrition during pregnancy and lactation is vitally important to the health of mother and infant. Nutritional needs rise during pregnancy in response to the metabolic demand of the developing embryo as well as to changes in maternal physiology.

There is definitive evidence that periconceptional folate supplementation decreases the incidence of neural tube defects. The maternal diet is often deficient in calcium, iron, and other micronutrients, and supplementation with a prenatal vitamin throughout pregnancy is indicated. Vitamin A at doses of about 10,000 IU per day is potentially teratogenic and should be avoided during pregnancy. Carotenoids with vitamin A activity are safe. There is evidence supporting omega-3 fatty acid supplementation, generally in the form of fish oil, during both pregnancy and lactation. Caloric needs rise in pregnancy, and thus energy intake should be increased, but excessive weight gain is potentially disadvantageous to mother and fetus.

Under most circumstances, breast feeding is the preferred nutritional source for neonates. The composition of human milk changes in response to maternal diet. A generous intake of dietary calcium and continued use of prenatal vitamins are indicated throughout the period of lactation. The pattern of macronutrient intake indicated for general health promotion is appropriate during pregnancy and lactation as well. Biologic maturity occurs on average five years after menarche. Before this time, a woman may still be growing herself, creating metabolic demands in conflict with the needs of pregnancy.

Diet

Maternal weight should be nearly ideal at the start of pregnancy to prevent complications that may arise from either maternal obesity or underweight. Underweight in the mother is associated with low birth weight, whereas maternal overweight is associated with increased risks of gestational hypertension, diabetes, and toxemia. Babies of mothers with prepregnancy obesity appear to have an increased risk of spina bifida and other congenital anomalies, as well as increased

incidence of macrosomia, low Apgar scores, shoulder dystocia, and childhood obesity.

Physiologic changes during pregnancy alter nutritional requirements. Plasma volume expands nearly 50% during pregnancy. Total mass of red blood cells increases about 33% over prepregnancy levels. Basal metabolic rate is increased by 15% to 20% toward the end of gestation. These changes require increased intake of energy, nutrients, and fluid. The greater increase in plasma volume than red cell mass will cause the hematocrit to fall during pregnancy; however, the mean corpuscular hemoglobin concentration should remain fairly constant, barring a concurrent anemia. Maternal hemoglobin at sea level during pregnancy should consistently be higher than 11 g per dL to ensure adequate oxygen delivery to the fetus. Nutritional causes of anemia should be considered if the hemoglobin level falls below this value and another explanation is not evident. A microcytic anemia suggests iron deficiency, whereas a macrocytic anemia suggests folate or vitamin B₁₂ deficiency; the former is the more common.

Requirements for folate, calcium, iron, and zinc rise disproportionately during pregnancy. In general, intestinal nutrient absorption is enhanced during pregnancy as an adaptation to increased metabolic demands. Serum lipids tend to rise during pregnancy, due largely to the effects of progesterone.

Whereas electrolytes, fatty acids, and fat-soluble vitamins cross the placenta by simple diffusion, sugars are carried to the fetus by facilitated diffusion so that glucose levels tend to be higher in fetal than in maternal blood. Amino acids, water-soluble vitamins, sodium, calcium, and iron are actively transported across the placenta to the fetal circulation.

In general, pregnancy requires a calorie increase over baseline of approximately 300 kcal per day, and lactation requires 500 kcal per day. Nutrients for which the recommended dietary allowance is specifically raised in pregnancy include total protein, total energy, magnesium, iodine, zinc, selenium, vitamin E, vitamin C, thiamine, niacin, iron, calcium, and folate. Lactation requires additional

increases in protein, zinc, vitamin A, vitamin E, vitamin C, and niacin; requirements for iron and folate decline (Table 1).

Inadequate weight gain during pregnancy is associated with low birth weight and maternal delivery complications, whereas excessive weight gain is associated with macrosomia, fetopelvic disproportion, and attendant complications of labor and delivery.

Maternal weight gain during pregnancy should occur predominantly during the second and third trimesters; total energy expenditure changes little in the first trimester but increases thereafter. Recent evidence suggests that in normal-BMI women, no increase in energy intake is required during the first trimester, while approximately 350 kcal per day should be added to the diet in the second trimester and 500 kcal per day in the third trimester. Pregnancy is thought to require an increase in energy consumption of 45,000 to 110,000 kcal over the level required for weight maintenance in the nonpregnant state; an 80,000 kcal increase is the standard estimate [1].

A total weight gain of 12.5 kg (approximately 27.5 lb) is appropriate during pregnancy, although weight gain will vary with maternal and fetal size. Weight gain recommendations for pregnancy vary with prepregnant weight. For women with a baseline body mass index (BMI) below 20, weight gain of 0.5 kg per week during the second and third trimesters is indicated. For women with a BMI greater than 26, weight gain of 0.3 kg per week during the same period is recommended. Weight gain of more than 1 kg per week at any time is generally excessive, whereas weight loss or weight gain of less than 1 kg per month generally indicates inadequate nutrition. Obligatory weight gain during pregnancy, attributable to fetal growth, placental growth, amniotic fluid production, uterine and breast enlargement, and expansion of the blood volume, accounts for approximately 7.5 kg on average. Weight gain in excess of this amount represents weight the woman will need to lose through a combination of calorie restriction and increased energy expenditure following pregnancy to return to prepregnant weight. Available evidence suggests that biologically immature women—i.e., those less than five years after beginning

menarche—require on average an additional 150 kcal per day and an additional 3 kg weight gain to avoid low birth weight.

Table 1—Recommended Nutrient Intake Changes Associated with Pregnancy and Lactation^a

| Nutrient | Recommended Intake by Subject Category | | | | Average Dietary Intake in Adult Women | Content of Representative Prenatal Vitamin ^b |
|------------------------------|--|--------------------|--------------------|------------------------------|---------------------------------------|---|
| | Female (19-30 yr.) | Female (31-50 yr.) | Pregnancy | Lactation (Initial 6 months) | | |
| Calcium (mg) | 1,000 | 1,000 | 1,000 ^c | 1,000 ^c | 530 | 250 |
| Folate (µg) | 400 ^b | 400 | 600 ^c | 500 ^c | 280–300 | 1,000 |
| Iodine (µg) | 150 | 150 | 220 | 290 ^d | 170 | 150 |
| Iron (mg) | 18 | 18 | 27 ^c | 9 | 10.7 | 60 |
| Magnesium(mg) | 310 | 320 | 350 ^c | 310 ^d | 207 | 25 |
| ω-3 fatty acids (g) | 1.1 | 1.1 | 1.4 | 1.3 | | |
| Niacin (mg NE) | 14 | 14 | 18 | 17 ^d | 16 | 20 |
| Phosphorus(mg) | 700 | 700 | 700 ^c | 700 ^c | 1,000 | — |
| Protein (g) | 46 | 50 | 60 ^d | 65 ^c | 70 | — |
| Riboflavin(mg) | 1.1 | 1.1 | 1.4 ^d | 1.6 ^d | 1.34 | 3.4 |
| Selenium (µg) | 55 | 55 | 60 ^d | 70 ^d | 108 | — |
| Thiamin (mg) | 1.1 | 1.1 | 1.4 ^d | 1.4 ^d | 1.05 | 3 |
| Vitamin A (µg RE) | 700 | 700 | 770 | 1,300 ^d | 1,170 | 1,500 |
| Vitamin B ₁₂ (µg) | 2.4 | 2.4 | 2.6 | 2.8 ^d | 4.85 | 12 |
| Vitamin B ₆ (mg) | 1.3 | 1.3 | 1.9 ^d | 2.0 ^d | 1.16 | 10 |
| Vitamin C (mg) | 75 | 75 | 85 | 120 | 77 | 100 |
| Vitamin D (µg) | 5 | 5 | 10 ^c | 10 ^c | 1.5 | 10 |
| Vitamin E (mg TE) | 15 | 15 | 15 ^d | 19 ^c | 7.1 | 22.2 |
| Vitamin K (µg) | 90 | 90 | 90 | 90 | 300–500 | — |
| Zinc (mg) | 8 | 8 | 11 ^d | 12 ^c | 10–15 | 25 |

^a NE, niacin equivalent equal 1 mg of dietary niacin or 60 mg of dietary tryptophan; RE, retinol equivalent; TE, α-tocopherol equivalent.
^b Intake of folate 400 µg per day is now recommended for all women of child-bearing age to ensure adequate stores at the time of conception.
^c Maternal prenatal vitamins.
^d Nutrient intake levels represent a 50% or more increase over recommendations for nonpregnant adult women.
^e Nutrient intake levels represent a 20% or more increase over recommendations for nonpregnant adult women.

Weight gain targets can be tailored to a particular situation. A woman who is overweight before pregnancy (BMI greater than 25) should gain as little over the obligatory 7.5 kg as possible; the rate of weight gain should be approximately 300 g

per week. A woman with BMI below 25 who does not plan on breast feeding should gain approximately 10 kg at a rate of 350 g per week. A woman with BMI between 20 and 25 and planning to breast feed should gain approximately 12 kg at a rate of 400 g per week. Underweight (BMI less than 20) and biologically immature women should gain 14 to 15 kg at a rate of 500 g per week. Women bearing twins generally should gain at least 18 kg at a rate of 650 g per week (8,9). For women in the United States, each pregnancy adds an average of approximately 2.5 kg of permanent weight.

Physical activity during pregnancy offers benefits to the mother at no cost to the fetus, provided that maternal tolerance is not taxed. Extreme exertion will result in elevated fetal temperature. Maintenance of moderate exercise during pregnancy is appropriate unless precluded by complications. Vigorous exercise before pregnancy and at least light-to-moderate activity during pregnancy may reduce risk for abnormal glucose tolerance and gestational diabetes mellitus [85]. Exercise with potential high impact, such as skiing, or at altitude is to be avoided during pregnancy. Postpartum exercise facilitates desired weight loss.

A total of approximately 925 g of protein is incorporated into the developing fetus and other products of conception. Peak requirements during pregnancy add a need for 8.5 g of protein to basal requirements. Protein intake by women is typically about 70 g per day, a figure well in excess of minimal requirements for all stages of pregnancy. Therefore, no particular effort to raise protein intake during pregnancy is indicated unless the diet is atypical. The fetus gains approximately 30 g per day during the third trimester. Interventions to ensure term delivery are essential in maintaining this rate of development. Intensive care of premature infants can rarely sustain more than 20 g of growth per day.

The developing fetus uses glucose as its major energy source, and glucose is especially crucial for use by the fetal brain in the third trimester. Carbohydrate requirements therefore increase to approximately 175 g per day in pregnancy.

Overall, the increased micronutrient requirements of pregnancy exceed the increased energy requirements. Therefore, vitamin supplementation during

pregnancy is universally indicated, and the nutrient density of foods assumes increased importance.

The teratogenicity of vitamin A in high doses was revealed through the use of the vitamin A analogue isotretinoin for acne. Ingestion of 20,000 IU or more of vitamin A per day is thought to be potentially teratogenic. Carotenoid precursors of vitamin A provide adequate retinol while avoiding any known toxicity. Therefore, prenatal vitamin supplements typically provide vitamin A at well below the toxic threshold and generally in the form of the precursor β -carotene.

Successful pregnancy outcomes depend heavily on maternal health and lifestyle but of course are mediated as well by the condition of the fertilizing sperm. Preliminary evidence suggests that vitamin C, which is concentrated in semen, and vitamin E, which is not, may play important roles in protecting the integrity of DNA in sperm from oxidative injury [2,3]. There is also preliminary evidence that folate and zinc, which are highly concentrated in seminal fluid, may influence spermatogenesis [3].

Immediately following birth for a period of approximately 3 to 5 days, the mother's mammary glands produce colostrum, a fluid rich in sodium, chloride, and immunoglobulins that confer passive immunity to the newborn. Colostrum is replaced by milk, which is rich in lactose and protein and comparatively low in sodium and chloride. Milk volume consumed by the neonate is 50 mL per day at birth, 500 mL by day 5, and 750 mL at 3 months.

Milk production is maintained by infant suckling, which suppresses hypothalamic dopamine production, thereby disinhibiting prolactin release. The first 4 months of lactation consume, and convey to the infant, an amount of energy comparable to that of the entire gestational period. Human milk is both appropriate and optimal as the sole source of infant nutrition for the first 6 months of life, barring contraindication (e.g., active tuberculosis, HIV infection). There is uncertainty whether milk meets all the infant's nutritional needs beyond this point. Multiple national and international medical and health organizations recommend exclusive

breast feeding as the preferred method of infant feeding for the first 4 to 6 months, with continued breast feeding with complementary foods for at least 12 months [4].

The fatty acid composition of human milk varies with maternal dietary intake. With the exception of iodine and selenium, there is little evidence that the levels of minerals and trace elements in milk vary with maternal diet. In contrast, vitamin levels in milk are responsive to dietary intake, with the strength of the relationship varying by nutrient. The levels of both fat- and water-soluble vitamins in milk vary in proportion to maternal intake. Calcium and folate, and possibly other nutrients, are preserved in milk at the expense of maternal stores when maternal intake is less than daily requirements.

Breast milk contains more than 100 different oligosaccharides. There is current interest in the influence these carbohydrates have on intestinal flora of the infant and their capacity to play a role in the prevention of infection [5].

As noted previously, maternal diet strongly influences the fatty acid and vitamin composition of breast milk, but it generally exerts a modest influence on minerals. Iodine and selenium are exceptions, varying substantially in response to maternal intake. Vitamins D and K are generally present at low levels in breast milk, and supplementation is recommended [5]; however, there is some evidence that low vitamin D intake in breast-fed neonates may not adversely affect bone metabolism.

Breast feeding is accompanied by a decline in maternal bone density, regardless of maternal calcium intake; however, studies show that bone mineral density is recovered fully after weaning [6].

Breast milk and infant formulas differ substantially in a variety of nutrients. The significance of all of the differences has yet to be established. Although earlier studies suggested an association between breast feeding and greater intelligence, a recent large prospective study [7] found no significant correlation. In same time, results, based on the largest randomized trial ever conducted in the area of human lactation with total of 17,046 healthy breastfeeding infants [8], provide strong evidence that prolonged and exclusive breastfeeding improves children's cognitive development.

Energy requirements to sustain lactation are based on the caloric density of human milk (approximately 70 kcal per 100 mL), the metabolic cost of milk production, and total milk volume. The consensus view that lactation requires 500 kcal per day above the energy required to maintain maternal weight assumes that approximately 200 kcal per day of milk production energy will derive from pregnancy-related fat stores. Loss of 0.5 to 1 kg per month is common during lactation, whereas loss in excess of 2 kg per month implies inadequate nutrition. Weight maintenance and weight gain during lactation are not uncommon. Weight loss of up to 2 kg per month appears to be safe during lactation, with preservation of energy transfer to breast milk. Prolactin levels tend to rise in response to maternal energy restriction during lactation, perhaps serving to preserve energy delivery to the neonate. Evidence suggests that energy restriction beginning one month postpartum can facilitate maternal weight loss without adverse effects on milk production or infant growth, but dietary restriction may lead to inadequate vitamin D and calcium intake. Judicious management of diet and weight throughout the gestational and postpartum periods, rather than a focus on energy restriction during lactation, is therefore clearly advisable [9].

Exercise during lactation, independent of energy restriction, is not known to pose any threat to mother or infant, and it offers a range of benefits. Lactation does not specifically aid in weight loss, despite the suggestion in folklore that it does. Women do tend to lose weight while breast feeding, as is to be expected in the postpartum period. Generally, however, nonlactating women lose weight at least as readily as do their breast-feeding counterparts.

There is interest in the role breast feeding may play in preventing the development of atopy, but the data are preliminary [10,11]. Evidence is convincing that breast feeding confers protection against infections, although the mechanisms by which breast milk influences infant immunity remain under study. Erythropoietin in breast milk is apparently resistant to degradation in the infant gastrointestinal tract and may stimulate the newborn's marrow [12].

The amino acid pattern of breast milk is species specific, suggesting another way in which human milk might make unique contributions to early development. Maternal diet influences the flavor of breast milk and thereby serves as a means of introducing the neonate to a variety of taste experiences.

Strong flavors, and the familiarity or novelty of such flavors, may influence the feeding behaviors of infants. Ingestion of garlic by the mother has been shown to lengthen feeding at first but to shorten feeding when exposure is recurrent. Alcohol ingested by a breast-feeding woman is conveyed to breast milk and generally results in reduced feeding by the infant immediately after exposure to the alcohol, with compensatory increased feeding when alcohol is no longer present in the milk. This effect is not due to the taste of alcohol per se but to some other effect of alcohol on the feeding experience. Contrary to folklore, maternal alcohol ingestion appears to decrease the sleep of a breast-feeding infant rather than increase it [13].

Nutrients and Functional Foods

Folate

The link between adequate folic acid intake and reduced risk of neural tube defects (NTD) is so definitive that mandatory folic acid supplementation of grain products was instituted in 1998; studies show that the incidence of NTD declined by 20% to 30% following this public health measure. Current recommendations suggest that all women capable of becoming pregnant supplement with approximately 400 µg of folic acid per day in addition to consuming a folate-rich diet. Pregnant women should increase supplementation to 600 µg per day. Ingestion of more than 1 mg per day of folate is generally not recommended. However, in women with prior pregnancies leading to NTD, the ingestion of up to 4 mg per day of folate may confer additional benefit.

Fluoride

Breast milk does not provide optimal fluoride levels to term infants, and supplementation is generally recommended.

Iron

Anemia is the most common nutrient-related abnormality of pregnancy and is attributable to iron deficiency nearly 90% of the time, with the remainder due primarily to folate deficiency. Because of the cessation of menses, iron requirements drop during the first trimester. Demands increase over baseline in the second trimester and peak in the third trimester, at 4 mg per day.

Pregnancy consumes approximately 1,040 mg of iron in total, of which 200 mg is recaptured after pregnancy from the expanded red cell mass and 840 mg is permanently lost. The iron is lost to the fetus (300 mg), the placenta (50 to 75 mg), expanded red cell mass (450 mg), and blood loss at parturition (200 mg). Only about 10% of ingested iron is absorbed in the nonpregnant state, but pregnancy may enhance absorption by as much as 30%. Therefore, an intake between 13 and 40 mg per day is required during the third trimester. Multivitamin/multimineral supplements generally contain 30 mg of iron, and the diet provides an additional 15 mg, easily meeting the needs of most women without anemia.

Women with iron-deficiency anemia during pregnancy require increased intake to replenish bone marrow stores and still provide for the metabolic needs of the fetus. In this situation, daily iron intake between 120 and 150 mg is typically required. Iron supplementation before conception will facilitate meeting the iron needs of pregnancy and lactation, which together result in a net loss between 420 and 1,030 mg of elemental iron. Iron supplementation should continue postpartum, both to provide iron for breast milk and to replenish losses due to bleeding at delivery. It is possible that iron supplementation in women with already adequate iron stores may increase risk of gestational diabetes and other maternal complications [13]. Routine iron supplementation for full-term, healthy breast-fed infants does not appear to be necessary [14].

Calcium

There is some evidence that calcium supplementation may reduce the risk of pregnancy-induced hypertension and preterm delivery due to preeclampsia [15].

Vitamin D

Adequate vitamin D intake is important to ensure a healthy maternal response to neonatal calcium handling [16]. Vitamin D supplementation in pregnancy and lactation has come under scrutiny in the past few years as a result of increased prevalence of vitamin D deficiency in darkly pigmented Americans. A recent review of the literature concluded that appropriate doses of vitamin D during pregnancy and lactation are not known but are likely higher than the current recommended intakes, especially in pregnant women and breast-feeding infants with darkly pigmented skin and those who do not live in sun-rich environments [17].

Magnesium

The evidence that magnesium supplementation may prevent preeclampsia is mixed. Alternative medicine sources recommend supplements of about 500 mg per day, which appears to be safe. Conventional prenatal vitamins provide only 25 mg per day; as a result, intake is often below recommended levels.

Selenium

Based on the reported association between selenium deficiency and sudden infant death syndrome, as well as low birth weight, selenium supplementation of 200 µg per day is advocated. The benefits of selenium may be limited to individuals from areas with selenium-deficient soil. Selenium deficiency in countries, where soil levels are high, is not generally considered a problem. Selenium in breast milk is very responsive to maternal intake, which distinguishes it from most other minerals.

Zinc

Studies of zinc nutrition in relation to pregnancy outcome have shown mixed results. There is some evidence that zinc supplementation may extend pregnancy to term among women with low levels of serum zinc. Zinc supplementation may directly contribute to normal birth weight through its effects on protein metabolism, or the influence may be indirect as a result of extended gestation. Zinc levels in breast milk are not thought to vary readily with dietary intake. However, a cohort study in Spain suggests that low dietary zinc intake during the third trimester predicts relatively low levels in breast milk [16].

Caffeine

Data about the consumption of caffeine doses of 300 mg/d (the equivalent of up to five or six cups of coffee) or less do not suggest increased risk of adverse pregnancy, fertility, or neurodevelopmental outcomes. At this time, the data about caffeine consumption of 300 mg/d or greater are limited and conflicting; therefore, it is best to limit caffeine intake to less than 300 mg/d. The amount of caffeine per cup of coffee varies between products, but as a general rule, consuming 1 to 2 cups of coffee a day is not expected to be a concern [17].

Alcohol

Heavy alcohol ingestion during pregnancy is associated with the fetal alcohol syndrome, a condition of fetal developmental delay and cognitive deficits. The incidence of fetal alcohol syndrome in the United States among offspring of women consuming 1.5 to 8 drinks per week is approximately 10%. A “drink” contains on average 17 g of ethanol. An occasional alcoholic drink during pregnancy is not known to be harmful, but recommendations favor abstinence.

The analysis of prospectively collected data of a British cohort has demonstrated that low levels of maternal alcohol consumption, in particular in the first trimester, have a negative association with fetal growth and gestational age and greatly increase the odds of babies being born small for gestational age and preterm. Pregnant women and women planning to become pregnant should be advised to abstain from drinking, as even those women who adhered to the UK guidelines of 1–2 units once or twice a week in the first trimester were at risk of having babies with reduced birth weight and born preterm when compared to mothers who abstained from alcohol [18].

ω -3 Fatty Acids

Available data suggest that high consumption of marine oils is associated with longer gestation [19,20] and that dietary supplementation with docosahexaenoic (DHA) via n-3 polyunsaturated oils may increase the proportion of term births in diverse populations [21]. The summarize evidence suggests that the addition of n-3 LC-PUFA to the mother may reduce the risk of early preterm labor for > 34 weeks and is very promising for the primary prevention of allergies in children [22].

Because a mother actively transfers DHA to her fetus and nursing infant [23], a deficiency may result if dietary intake is not adequate. Observational studies suggest an association between a low maternal DHA status after pregnancy and the occurrence of postpartum depression. Because a mother actively transfers DHA to her fetus and nursing infant [23], a deficiency may result if dietary intake is not adequate. Observational studies suggest an association between a low maternal DHA status after pregnancy and the occurrence of postpartum depression. A recent analysis found lower breast milk DHA content and lower seafood consumption to be associated with higher rates of postpartum depression in mothers across several countries [24]. Preliminary evidence from several small open-label trials suggests beneficial effects of ω -3 supplementation on symptoms of depression during pregnancy and the postpartum period [25].

There is evidence that n-3 fatty acids are important in the normal development of eye and brain function [26]. One recent randomized trial found that the children born to mothers who had taken cod liver oil (rich in n-3 fatty acids) during pregnancy and lactation scored higher on a battery of intelligence tests at 4 years of age than children whose mothers had taken a non- ω -3 oil supplement [27]. A case-control study in Greece supports the hypothesis that ω -3 fatty acids may be especially important in fetal brain development and that low maternal fish consumption may elevate risk of cerebral palsy [28]. A recent trial showed an association between fish and seafood intake during pregnancy and enhanced neurodevelopmental milestones and IQ in the offspring [29]. Benefits were seen with up to 340 g of seafood intake per week as compared to none; higher intake levels showed neither decisive benefits nor harms compared to more moderate intake.

The ω -3 content of breast milk is mediated by maternal intake. Maternal supplementation with ω -3 fatty acids instead of ω -6 fatty acids during pregnancy and lactation has been shown to provide more DHA to the infant and decrease maternal plasma lipid levels [30]. Increased consumption of ω -3 fatty acids may therefore confer health benefits to both mother and baby. Relative to the prehistoric

dietary pattern, the modern diet is deficient in ω -3 fatty acids, lending the support of an evolutionary context to the hypothesis that increased intake may be beneficial.

Of note, while marine foods may provide n-3 fatty acids, several varieties are commonly contaminated with mercury, a potential neurotoxin. As a result, the US Food and Drug Administration advises pregnant women to avoid swordfish, tilefish, king mackerel, and shark [31]. These species are all large predators, and they concentrate in their bodies the mercury accumulated by the smaller fish on which they feed. The FDA also cautions against albacore tuna, another large predatory fish; canned light tuna, made from smaller fish, contains much less mercury. The FDA recommends a total fish intake during pregnancy of up to 340 g, or two to three meals, per week [32]. Fish oil supplements can provide n-3 fatty acids while avoiding the risk of heavy metal contaminants.

Pyridoxine (Vitamin B₆)

Other than its role in metabolism, supplemental B₆ is recommended for treatment of pregnancy-induced nausea based on the results of small randomized double-blind trials. Systematic reviews of randomized and/or controlled trials have shown that pyridoxine (vitamin B₆) improves mild to moderate nausea [33]. A dose range from 50 to 100 mg per day is advised, and this level exceeds the content of diet and prenatal vitamins combined.

The mechanism for the therapeutic effect is unknown. Hypotheses include prevention/treatment of vitamin B₆ deficiency, intrinsic antinausea properties, and/or synergy with the antinausea properties of antihistamines [34].

Gingerroot

Hyperemesis gravidarum, or pernicious vomiting of pregnancy, is a complication of pregnancy that affects various areas of the woman's health, including homeostasis, electrolytes, and kidney function, and may also have adverse fetal consequences. The pathogenesis is not fully understood, but may be attributed to hormones, gastrointestinal dysfunction, thyrotoxicosis, serotonin, hepatic abnormalities, autonomic nervous dysfunction, nutritional deficiencies, asthma, allergies, *Helicobacter pylori* infection, or psychosomatic causes. Hyperemesis itself

is not a risk factor for adverse outcomes, but these outcomes are the consequence of the low weight gain associated with hyperemesis.

Ground gingerroot, at a dose of 250 mg four times daily, has been shown effective in the treatment of hyperemesis gravidarum [35].

Vitamin E and C supplementation during pregnancy

Vitamin E functions as a lipid-soluble antioxidant, protecting cells of the body from damage by harmful free radicals (i.e. reactive oxygen molecules) and may have other physiological functions. Vitamin C has also antioxidant properties, and is additionally involved in the synthesis of collagen and metabolism of iron and folate.

As antioxidants, vitamins E and C act synergistically to help prevent oxidative stress, which is an imbalance in the number of free radicals circulating in the body and the availability of antioxidants to counter the free radicals. Vitamin E and C supplementation is thus often given concurrently.

Links have been made between oxidative stress during pregnancy and the development of pre-eclampsia, and increased risk of intrauterine growth restriction and pre-labour rupture of membranes (breakage of the amniotic sac before the onset of labor). Oxidative stress has also been implicated in many disorders common to preterm infants including chronic lung disease, necrotising enterocolitis and others. However, currently available evidence indicates that supplementation with vitamin E and C together likely has little to no effect on relevant outcomes in mothers and infants, and may in fact increase the risk of pre-labour rupture of membranes.

Vitamin E and C supplementation is not recommended by WHO for pregnant women to improve maternal and perinatal outcomes [36].

Clinical Highlights

Dietary recommendations for pregnancy and lactation vary to some extent with the prepregnant weight, age, and nutritional status of individual women. Assuming near-optimal prepregnancy weight and nutritional status and biologic maturity at conception, most women following a prudent diet during pregnancy would be able to meet their macronutrient recommendations. In such a diet, 25% to 30% of calories come from fat, 45% to 60% from carbohydrate, and 15% to 25%

from protein. Energy consumption should be increased approximately 300 kcal per day during pregnancy and 500 kcal per day during lactation.

The use of multivitamin/multimineral supplements beginning several months before conception and throughout pregnancy and lactation is indicated. An omega-3 fatty acid supplement, generally in the form of fish oil at 1 to 2 g per day, is appropriate. Low-fat or nonfat dairy products should be eaten regularly as a source of calcium, and lean red meat should be eaten as a source of heme iron, provided that fat and protein intake is in compliance with guidelines. Vegetarian women may require iron supplementation in addition to a prenatal vitamin; such supplementation is generally not required in omnivorous women. Vegans may require calcium supplementation, as is true of other women without regular intake of dairy products.

Vitamin B6 and gingerroot have been used with success in the management of pregnancy-related nausea and appear to be safe. A graded program of exercise and caloric restriction postpartum is required to restore prepregnancy weight. Most women in the United States retain approximately 2.5 kg after each pregnancy, a factor contributing to the prevalence of obesity among women. Management of diet and the degree of weight gain during pregnancy are thought to be preferable to an exclusive focus on postpartum weight loss; obese women should try to lose weight before pregnancy to minimize adverse outcomes, but dieting to lose weight is not advised during pregnancy. When maternal weight gain is insufficient during pregnancy, the risk of low birth weight is increased; therefore, diet should be managed to ensure that energy intake is neither excessive nor deficient.

Diet and Early Development: Pediatric Nutrition

Physical and cognitive development are rapid during infancy and early childhood, which imposes extreme metabolic demands. The provision of adequate nutrition from birth is fundamental to the maintenance of normal growth and development. Infants are subject to certain specific micronutrient deficiencies, and they have requirements different from those of adults for macronutrients, particularly protein.

The health benefits of breast feeding during the first six months of life are increasingly clear. Although the principal goal of nutrition management in early childhood is the preservation of optimal growth and development, children in the developed countries are increasingly susceptible to the adverse effects of dietary excess, particularly obesity. As a result, there is intense interest regarding the age at which dietary restrictions might first be safely imposed.

In general, restriction of macronutrients (saturated fat being of particular concern) is discouraged before age 2, with increasing evidence that restrictions comparable to those recommended for adults may be safe and appropriate after age 2. The establishment of health-promoting diet and activity patterns in childhood may be of particular importance, as preferences established early in life tend to persist.

Diet

The importance of adequate nutrition to normal growth and development during the neonatal period and early childhood is well established and largely self-evident. Basal metabolic rate is higher in infants and children than in adults; the nutritional needs to support growth are super imposed on the higher basal metabolism, resulting in considerably higher energy and nutrient requirements per unit body weight.

The average-term infant triples in weight and doubles in length during the first year of life. Consequently, energy requirements in early childhood are very high. Newborns require three to four times more energy per unit body weight than do adults: 90 to 120 kcal/kg-day compared to 30 to 40 kcal/kg-day for adults. Inefficiency of intestinal absorption contributes to this difference.

As a result of a child's rapid growth, protein requirements are higher in infancy than in adulthood. Total protein requirement is greater than the additive needs for essential amino acids by a factor of two to three. Protein intake of 2.0 to 2.2 g/kg-day is recommended, compared with 0.8 to 1.0 g/kg-day for adults who engage in moderate levels of physical activity.

Infants require protein of high biologic value to ensure adequate consumption of essential amino acids (leucine, isoleucine, valine, threonine, methionine,

phenylalanine, tryptophan, lysine, and histidine). Cysteine and tyrosine also are recognized as essential dietary proteins in infancy, although not beyond the first six months of life. The reason is unclear in the case of tyrosine, whereas for cysteine, there is a well-characterized delay in the maturity of the enzymatic pathway that converts methionine to cysteine. The minimal intake necessary to provide the indicated amounts of all essential amino acids would provide half or less of total protein requirements, indicating the importance of both quantity and quality of dietary protein.

The protein composition of human milk is ideal for infants. Breast milk provides on average 1 g of protein per 100 mL. Therefore, to achieve the recommended intake of 2.0 to 2.2 g/kg-day, infants need to consume approximately 200 mL of breast milk per kg per day. This level exceeds the intake of many infants, yet protein deficiency generally does not occur in breast-fed infants. Apparently, any limitations in the quantity of breast milk protein consumed are compensated by the digestibility and quality of protein in breast milk. Currently available infant formulas contain all amino acids essential for infants and, therefore, provide protein of comparable quality to that of breast milk.

Need for carbohydrate and fat in infancy is restricted to those levels necessary to prevent ketosis and fatty acid deficiency, respectively. Total intake of carbohydrate and fat generally are adequate whenever total energy intake is appropriate.

Recommended dietary allowances (RDAs) have been established for essential nutrients for both the first and second six-month intervals of life (Table 2). Iron deficiency is the most common nutrient deficiency in early childhood. Iron absorption from breast milk is apparently particularly efficient, as iron deficiency rarely occurs in breast-fed infants despite the lower levels of iron in breast milk than in formula. Exclusive breast feeding after four to six months of age may lead to iron deficiency, so iron-fortified cereal or iron supplementation is recommended at that point. Increased use of iron-fortified infant formula among babies who were not breast fed has substantially reduced the incidence of iron deficiency in this age

group. Iron requirements may be related to vitamin E and polyunsaturated fat content of the diet. Supplementation is recommended in infants who are not breast fed until age 2. Vitamin deficiencies are rare in adequately nourished infants. Vitamin K is provided by injection at or near the time of birth to prevent neonatal hemorrhage; subsequently, deficiency is uncommon.

An intake of 75 to 100 mL fluid per kg per day is considered adequate for the first years of life, but 150 mL is preferred as a defense against dehydration. A well-nourished infant generally easily meets the recommended intake with either breast milk or formula.

The nutrient recommendations for infants 6 to 12 months of age are based largely on extrapolation from the first 6-month period; less is known about the nutrient needs of infants 6 to 12 months old. There is currently debate regarding the optimal level of energy intake, with some recommending a reduction from 95 to 85 kcal/kg-day. Adequate growth apparently is maintained at the lower energy-intake level.

By 6 months of age, gastrointestinal physiology is substantially mature, and infants metabolize most nutrients comparably to adults. Nutrient needs can be met with breast milk or formula, but most authorities advocate the gradual introduction of solid foods beginning at or around 6 months. As infant foods begin to replace breast milk or formula, the nutrient density of the diet is apt to decline, and the introduction of a multivitamin supplement is indicated. Of note, a recent study found an association between early multivitamin supplementation and increased risk for asthma or food allergy in some children. Completion of weaning to solid food by 1 year of age is common practice and is appropriate.

Breast milk is widely considered the optimal means of nourishing newborns, barring contraindications such as communicable disease in the mother. Breast milk has lower calcium and phosphorus than bovine milk.

Table 2—Recommended Dietary Allowances in Infancy/Childhood^a

| Nutrient | Age | | | |
|------------------------------|-------------------|--------------------|----------------|----------------|
| | 0–6 months | 7–12 months | 1–3 yr. | 4–8 yr. |
| Protein (g) | 9.3 | 11 | 13.7 | 21 |
| Vitamin A (µg RE) | 400 | 500 | 300 | 400 |
| Vitamin D (µg) | 5 | 5 | 5 | 5 |
| Vitamin E (mg TE) | 4 | 5 | 6 | 7 |
| Vitamin K (µg) | 2 | 2.5 | 30 | 55 |
| Vitamin C (mg) | 40 | 50 | 15 | 25 |
| Thiamine (mg) | 0.2 | 0.3 | 0.5 | 0.6 |
| Riboflavin (mg) | 0.3 | 0.4 | 0.5 | 0.6 |
| Niacin (mg NE) | 2 | 4 | 6 | 8 |
| Vitamin B ₆ (mg) | 0.1 | 0.3 | 0.5 | 0.6 |
| Folate (µg) | 65 | 80 | 150 | 200 |
| Vitamin B ₁₂ (µg) | 0.4 | 0.5 | 0.9 | 1.2 |
| Calcium (mg) | 210 | 270 | 500 | 800 |
| Phosphorus (mg) | 100 | 275 | 460 | 500 |
| Magnesium (mg) | 30 | 75 | 80 | 130 |
| Iron (mg) | 0.27 | 11 | 7 | 10 |
| Zinc (mg) | 2 | 3 | 3 | 5 |
| Iodine (µg) | 110 | 130 | 90 | 90 |
| Selenium (µg) | 15 | 20 | 20 | 30 |
| Biotin (µg) | 5 | 6 | 8 | 12 |
| Pantothenic acid (mg) | 1.7 | 1.8 | 2 | 3 |
| Copper (mg) | 0.2 | 0.22 | 0.34 | 0.44 |
| Manganese (mg) | 0.003 | 0.6 | 1.2 | 1.5 |
| Fluoride (mg) | 0.01 | 0.5 | 0.7 | 1.0 |
| Chromium (µg) | 0.2 | 5.5 | 11 | 15 |
| Molybdenum (µg) | 2 | 3 | 17 | 22 |

^a NE, niacin equivalent equal 1 mg of dietary niacin or 60 mg of dietary tryptophan; RE, retinol equivalent; TE, α -tocopherol equivalent.

Compared to formula-fed infants, breast-fed infants have a less mineralized skeleton at several months of age, but there is no evidence that this is harmful. Bone density during the first several months of life is lower in breast-fed than formula-fed infants because of the lower calcium and phosphorus of breast milk. Differences in bone density do not persist beyond infancy. Breast feeding is also associated with transient hyperbilirubinemia during the first few days of life; if extreme, phototherapy is indicated to prevent kernicterus.

The protein content of breast milk seems lower than ideal, yet, as noted, breast-fed infants rarely display evidence of protein deficiency. The particular advantages of breast feeding relate to the development of immune function and resistance to infection, development of the intestinal tract, and psychological bonding between mother and infant. There is increasing evidence that breast feeding reduces the risk of infant and childhood infections; a recent study found that full breast feeding for at least the first four months of life was associated with reduced risk of hospital admission for infections in the first year of life.

An increasing body of evidence points to prolonged breast feeding as protective against later obesity. One hypothesized mechanism for this is that mothers who breast feed develop less restrictive feeding behavior and are more responsive to infant cues of hunger and satiety. Breast feeding likely protects against food allergy and intolerance.

The principal hazard of breast feeding is the issue of supply; infants must be followed closely during the first few days to weeks of life to ensure normal growth. The adequacy of breast feeding can be assessed by preprandial and postprandial weighings; every milliliter of milk consumed should add 1 g of weight.

There are concerns about converting from breast milk to bovine milk (rather than formula) as the principal source of nutrition after 6 months. The practice results in protein and sodium intake well above recommendations and iron and linoleic acid intake well below. Deficiency of essential fatty acids is the most significant concern regarding the use of bovine milk (whole or reduced fat) as the staple after 6 months.

Formulas are generally based on either unmodified or modified bovine milk protein. Bovine milk can be modified so that the whey-to-casein ratio approximates that of human milk. There is no clear evidence that either is superior. For infants intolerant of bovine milk protein, the protein can be hydrolyzed, or soy protein can be substituted. Soy-based formulas are appropriate for infants with lactose intolerance.

Formulas based on bovine milk protein typically provide 1.5 g of protein per 100 mL, or 50% more protein than breast milk. The nutrient composition of commercial formulas is otherwise very comparable to that of breast milk (Table 3). Provided that a sanitary water supply is available, the safety of formula generally is not of concern. Properly nourished, a healthy infant should double in weight by 4 to 5 months of age and triple in weight by 12 months. Demand feeding is the preferred method of ensuring adequate energy intake.

Inclusion of cow's milk in the diets of infants 6 to 12 months old appears to be fairly common practice. The result is elevated intake of protein and sodium relative to the RDAs. Protein and sodium consumption is higher still in infants fed reduced-fat milk. There is interest in the role of preventing hypertension in adulthood by restricting sodium intake in childhood, but the data are only preliminary. The substitution of skim or reduced-fat milk for whole milk in this age group does not confer any known benefit, nor does it appear to reduce total energy intake as a result of compensation for the missing calories. The substitution of bovine milk for formula tends to reduce the iron level in the diet, and skim milk will reduce the intake of linoleic acid below recommended levels.

Children over the age of one year tend to eat an appropriate variety of foods/nutrients when provided access to them. Balance may not be achieved on any given day; however, provided that the child continues to be provided reasonable food choices, balance will be achieved over several days' time. Parents should be reassured that a balanced diet need not be measured on a per-meal or even per-day basis. A reasonable approach is to avoid any major distinction between snacks and

meals so that healthy food can be eaten when the child is hungry, and meal size can be adjusted to account for snacking.

Table 3—Composition of Commonly Available Commercial Formulas Compared to That of Breast Milk

| Nutrient (quantity per liter) | Human Milk | Similac | Enfamil | Prosobee^a | Isomil^a |
|--------------------------------------|-------------------|----------------|----------------|-----------------------------|---------------------------|
| Energy (kcal) | 680 | 676 | 680 | 660 | 660 |
| Protein (g) | 10.5 | 14.5 | 14.2 | 19.7 | 16.1 |
| Fat (g) | 39 | 36.5 | 35.8 | 34.8 | 35.8 |
| Percent polyunsaturated | 14.2 | 37 | 29 | 18.8 | 23.5 |
| Percent monounsaturated | 41.6 | 17 | 16 | 37.6 | 38.3 |
| Percent saturated | 44.2 | 46 | 55 | 42.5 | 32.7 |
| Carbohydrate (g) | 72 | 72.3 | 73.7 | 65.6 | 67.6 |
| Calcium (mg) | 280 | 492 | 528 | 690 | 690 |
| Phosphorus (mg) | 140 | 380 | 358 | 540 | 490 |
| Magnesium (mg) | 35 | 41 | 54 | 70 | 50 |
| Iron (mg) | 0.3 | 12.2 | 12.2 | 11.8 | 11.8 |
| Zinc (mg) | 1.2 | 5.1 | 6.8 | 7.9 | 4.9 |
| Manganese (µg) | 6 | 34 | 101 | N/A | 160 |
| Copper (µg) | 252 | 610 | 507 | 490 | 490 |
| Iodine (µg) | 110 | 95 | 68 | N/A | N/A |
| Sodium (mg) | 179.4 | 184 | 184 | 240 | 290 |
| Potassium (mg) | 526.5 | 706 | 729 | 790 | 710 |
| Vitamin A (µg) | 675 | 676 | 630 | 590 | 590 |
| Vitamin D (µg) | 0.5 | 10 | 10.8 | N/A | N/A |
| Vitamin E (IU) | 4 | 20 | 13.6 | 9.7 | 13.2 |
| Vitamin K (µg) | 2.1 | 54 | 54 | N/A | N/A |
| Thiamine (µg) | 210 | 680 | 541 | 530 | 390 |
| Riboflavin (µg) | 350 | 1,010 | 947 | 590 | 590 |
| Pyridoxine (µg) | 205 | 410 | 406 | N/A | N/A |
| Vitamin B ₁₂ (µg) | 0.5 | 1.7 | 2.0 | 2.0 | 3 |
| Niacin (mg) | 1.5 | 7.1 | 6.8 | 6.6 | 8.9 |
| Folate (µg) | 50 | 100 | 108 | 110 | 100 |
| Pantothenic acid (mg) | 1.8 | 3 | 3.4 | N/A | 4.9 |
| Vitamin C (mg) | 40 | 60 | 81.2 | 79 | 59 |
| Biotin (µg) | 4 | 30 | 20.3 | N/A | N/A |

^a Soy-based formulas.

The epidemiology of nutrition-related health problems in children changed dramatically in the latter half of the 20th century. In Ukraine, according to official statistics 2015, in the age structure of obese patients the share of children is 19.3% . Childhood obesity is considerably more common than is growth retardation. Studies show that children today are consuming a significantly greater volume of food and beverages than children did two decades ago, as well as large amounts of soft drinks and fast foods not compensated for by physical activity. Most children still consume saturated and trans-fat in excess of recommendations and fail to consume the recommended quantities of fruits and vegetables. The increased prevalence of overweight and hypertension has also been observed to be disproportionately great among ethnic minority children. A pathology study of adolescents and young adults who died of trauma demonstrated that elevated serum lipids, as well as smoking, influence the development of early signs of atherosclerosis in adolescents; the Bogalusa Heart Study found that childhood measures of LDL cholesterol and body mass index (BMI) were predictive of carotid intima-media thickness, an important predictive measure of future atherosclerotic events. Elevated serum lipids probably contribute to early lesions of atherosclerosis in children 10 to 14 years old and may begin to do so in children between the ages of 3 and 9 years.

Dietary intervention has been shown to lower the high cholesterol levels common among children in Finland, with levels rising again on resumption of the habitual diet. Therefore, from a population perspective, there appears to be little potential harm and considerable potential gain in promoting the dietary pattern recommended for adults to school-age children as well.

The prudence of advocating the same diet for adults and children has been challenged. There is still only limited evidence that dietary restrictions in childhood prevent chronic disease in adults. Obtaining such evidence, however, is a daunting challenge. Indirect, epidemiological, and inferential evidence may be the best guidance available. Over the past decade, there has been controversy over the safety and efficacy of fat restriction after age 2; proponents of the restriction of dietary fat beginning at age 2 cite evidence that atherosclerosis begins in childhood and that a

diet with not more than 30% of calories from fat beginning at age 2 is compatible with optimal growth [42]; others argue for a gradual transition to lower fat intake and attention to the type and distribution of dietary fat, as has been recommended in Canada [43].

Further support for advocating dietary fat restriction in particular for young children comes from epidemiological data in Italy. A rise in the consumption of saturated fat has been noted in a population with a traditionally health-promoting “Mediterranean” diet. A study of 100 Finnish school-age children demonstrated that the intake of several important nutrients tended to be lower among the children with the highest fat intake [43]. Further, this study suggested that the diets of young children are quite diverse, so that offering dietary recommendations was unlikely to “disrupt” a traditional dietary pattern chosen by families for their young children.

Efforts to resolve the debate regarding the safety of fat restriction in early childhood have resulted in controlled intervention studies [44]. One earlier intervention trial (the Child and Adolescent Trial for Cardiovascular Health (CATCH)) examined the effects of a multidisciplinary program emphasizing change in school nutrition on cardiac risk factors in children beginning in third grade. The study lowered fat intake significantly and lowered serum cholesterol minimally. Growth and development were unaffected.

The Dietary Intervention Study in Children (DISC) randomly assigned 8- to 10-year-old children with LDL cholesterol above the 80th percentile to either usual care or a dietary intervention with 28% of energy from total fat, less than 8% from saturated fat, up to 9% from polyunsaturated fat, and less than 75 mg per 1,000 kcal cholesterol per day. After approximately seven years of follow-up, children in the intervention group were found to have greater reductions in LDL cholesterol levels compared to the usual care group, and they had no adverse effects on growth and development.

Data from studies encourage a common eating pattern for families, with the implication that the fat content in the diets of children might decline, and all sources encourage the promotion of regular physical activity and fruit and vegetable

consumption during childhood. There is evidence that the increase in television watching and other sedentary activities has an important role in the rise of childhood obesity.

There is increasing evidence that efforts to modify the diets of children to reduce long-term cardiovascular risk are likely to be safe. Whether such diets reduce long-term risk is less clear. Obviously, evidence of long-term outcome effects is difficult to obtain. To be considered in the debate is the importance of providing a single, consistent dietary pattern for a family, as well as the issue of dietary patterns tracking over time. Data from the Bogalusa Heart Study and the Muscatine Study demonstrate that there is tracking through early childhood and adolescence of dietary pattern, physical fitness, and cardiovascular risk factors [45].

In light of these considerations, it appears that the recommendation to advocate a similar diet for everyone over the age of 2 years is reasonable and safe, and it may offer long-term benefits. Although there is some evidence that a comparable diet may be safe even before age 2, consensus opinion and prudence argue against the imposition of macronutrient restrictions in this age group.

Nutrients and Functional Foods

n-3 Fatty Acids

Long-chain polyunsaturated fatty acids are particularly concentrated in the brain and retina. Eicosapentaenoic acid and docosahexaenoic acid (DHA) are relatively abundant in human breast milk and prominently incorporated into the developing brain. DHA in particular is considered essential to healthy brain development. Impaired cognitive development in premature infants may be related in part to insufficient availability of DHA during a critical period of brain development.

Breast feeding has been associated with enhancement of IQ and visual acuity in infants, though recent evidence suggests that the evidence for an effect on intelligence may have been confounded by maternal IQ. The apparent health benefits of breast feeding relative to formula feeding may be related in part to the DHA content of breast milk. Increasingly, long-chain polyunsaturated fatty acids,

including DHA, are being added to commercial formulas. One recent double-blind, randomized trial compared DHA and arachidonic acid-supplementation of infant formula to breast milk; at 4 years of age, children who had been fed either the DHA and AHA-supplemented formula had visual acuity and verbal IQ scores similar to those who were breast fed, while the control group had poorer visual acuity and poorer verbal IQ scores. Although the essential fatty acid α -linolenic acid is a precursor to DHA as well as to eicosapentaenoic acid, conversion to DHA in particular appears to be limited and variable. The putative benefits of DHA apparently require that it be administered directly in the diet. Although health benefits of DHA supplementation are likely on the basis of confluent lines of evidence, the benefits are not yet conclusive.

Clinical Highlight

The provision of optimal nutrition during infancy and early childhood is of vital importance to growth and development and is likely related to a wide array of health outcomes later in life. The establishment of good nutriture for an infant begins while in utero, during which time maternal dietary practices may influence fetal metabolism.

The most reliable way to ensure optimal nutrition for a newborn is breast feeding. Therefore, clinicians should routinely encourage breast feeding for a period of six months unless the practice is contraindicated by communicable disease. This advice is based on the confluence of multiple lines of evidence.

The maintenance of salutary maternal nutrition during lactation is of importance to the health of both mother and baby. As evidence of the importance of DHA and other essential fatty acids continues to accrue, the composition of most commercial formulas has been revised to mimic levels found in breast milk.

Weaning to solid food generally should begin at approximately 6 months; earlier weaning may increase the risk of food allergies. Weaning from breast milk or formula is generally complete by around 12 months, although such practices are culturally determined; medically, weaning at 12 months is appropriate.

Children generally will self-select foods that meet micronutrient requirements when provided with an array of healthy food choices; this practice is to be encouraged. Children also reliably meet their energy needs, although energy intake may vary considerably by meal and even day. Parents should be reassured in this regard and discouraged from placing too great an emphasis on “plate cleaning”; whether or not such a practice contributes to later obesity is unknown, but an association is plausible.

Controversy persists regarding the optimal timing for approximating adult dietary guidelines in children. There is evidence that adult dietary recommendations are safe for children as young as 7 months of age, although few in the United States would endorse such a practice. Evidence is more definitive that the imposition of such guidelines beginning at age 2 is safe and reasonable. Taking this approach provides the added benefit of unifying family dietary practices earlier. There is evidence that dietary preferences established in childhood tend to persist, highlighting the importance of establishing a prudent dietary pattern early. Therefore, the diet that should be advocated to adults and older children to promote health may be provided promptly, or approximated gradually, in children beginning at age 2. Micronutrient supplementation with a multivitamin/multimineral tailored for children is a reasonable practice. Regular consumption of fish should be encouraged. The consistent intake of DHA may offer considerable health benefits, which is supported by preliminary, but accumulating, evidence.

Diet and Adolescence

The nutritional requirements of adolescence differ from those of childhood by virtue of the adolescent's larger body size and the advent of sexual maturation. They differ as well from those of adulthood because of the metabolic demands of rapid growth. As a result, the recommended dietary allowances (RDAs), and now Dietary Reference Intakes (DRIs), for adolescence differ from those of other periods of the life cycle (Table 6). Nutrients of particular importance to all adolescents appear to

be magnesium, zinc, and calcium. With the advent of menses, adolescent girls become particularly subject to iron deficiency.

Specific aspects of diet, health, and adolescence relate to physical activity patterns and issues of body image. Relatively sedentary adolescents are at risk of obesity because nutrient energy intake exceeds need. Adolescent obesity anticipates adult obesity. Similarly, the combination of inactivity and a diet excessive in processed and fast-food high in saturated fat, sugar, salt, and calories predisposes to elevations of cholesterol, insulin, and possibly blood pressure.

Many adolescents participate in competitive sports and, therefore, are at potential risk of inadequate nutrient intake. Inadequate nutrients and energy are particularly problematic in those participating in sports requiring low body weight, such as wrestling, crew, gymnastics, and ballet.

Body image is of particular importance to adolescents and may result in extreme efforts to control or modify diet. The adoption of vegetarianism by an adolescent may mask a weight-loss effort and, if so, may result in a nutritionally unbalanced diet. Eating disorders, considered psychiatric rather than truly nutritional disorders, are typically manifest in adolescence.

Factors influencing changes in dietary pattern at adolescence are both physiologic and social. Physiologically, energy and nutrient requirements are driven up by increasing body size and the advent of sexual maturation, including menarche in girls. Socially, adolescence affords opportunity for food selection independent of parental guidance, often for the first time. Such choices are often made on the basis of prevailing patterns in peer groups. Adolescents are particularly resistant to health promotion messages, likely a consequence of the need to exercise autonomy. Typical dietary patterns in adolescents are influenced by targeted advertising and industry promotions and, therefore, emphasize commercial products, such as sodas and fast foods, rather than unprocessed foods.

As a consequence, dietary patterns established in adolescence may initiate susceptibility to obesity, hyperlipidemia, hypertension, and other chronic disease. The common preoccupation with body image during adolescence (particularly

among girls), along with the psychosocial pressures of this period, are related to the development of eating disorders.

Topics of importance in the dietary management of health during adolescence include obesity, hypertension, diabetes, osteoporosis, vegetarian diets, athletic activity, and eating disorders, as well as the nutritional demands of rapid growth. Although adolescents' energy requirements are high because of their rapid growth, the recommended dietary pattern is the same as that for adults. Recommendations call for calories predominantly from complex carbohydrates, but adolescents in developed countries tend to have diets particularly high in fat and sugar, a phenomenon that has led to markedly increased prevalence of overweight and obesity in recent years.

Table 3—Dietary Reference Intakes for Adolescents^a

| Nutrient Energy ^b | Ages 9–13 yr. | | Ages 14–18 yr. | | Ages 19–30 yr. | |
|---------------------------------|---------------|---------|----------------|---------|----------------|---------|
| | Female | Male | Female | Male | Female | Male |
| Kcal | 1,600 | 1,800 | 1,800 | 2,200 | 2,200 | 2,900 |
| kcal/cm | 14.0 | 15.9 | 13.5 | 17.0 | 13.4 | 16.4 |
| Protein (g) | 28 | 27 | 38 | 44 | 38 | 46 |
| Sodium (mg) | <2,200 | <2,200 | <2,300 | <2,300 | <2,300 | 2,300 |
| Vitamin A ^c (μg) | 420 | 445 | 485 | 630 | 500 | 625 |
| Vitamin D (IU) | 200-400 | 200-400 | 200-400 | 200-400 | 200-400 | 200-400 |
| Vitamin E (mg) | 9 | 9 | 12 | 12 | 12 | 12 |
| Vitamin K (μg) | 45 | 45 | 55 | 65 | 60 | 70 |
| Vitamin C ^{c,d} (mg) | 39 | 39 | 56 | 63 | 60 | 75 |
| Thiamine (mg) | 0.7 | 0.7 | 0.9 | 1.0 | 0.9 | 1.0 |
| Riboflavin (mg) | 0.8 | 0.8 | 0.9 | 1.1 | 0.9 | 1.1 |
| Niacin (mg NE) | 9 | 9 | 11 | 12 | 11 | 12 |
| Vitamin B ₆ (mg) | 0.8 | 0.8 | 1.0 | 1.1 | 1.1 | 1.1 |
| Folate ^e (μg) | 250 | 250 | 330 | 330 | 320 | 320 |
| Vitamin B ₁₂ (μg) | 1.5 | 1.5 | 2.0 | 2.0 | 2.0 | 2.0 |
| Calcium ^{c,f} (mg) | 1,300 | 1,300 | 1,300 | 1,300 | 1,300 | 1,300 |
| Phosphorus (mg) | 1,055 | 1,055 | 1,055 | 1,055 | 580 | 580 |
| Magnesium (mg) | 200 | 200 | 300 | 340 | 255 | 330 |
| Iron ^{c,g} (mg) | 5.7 | 5.9 | 7.0 | 7.7 | 8.1 | 6.0 |

| | | | | | | |
|------------------------|-----|-----|-----|-----|-----|-----|
| Zinc ^c (mg) | 7.0 | 7.0 | 7.3 | 8.5 | 6.8 | 9.4 |
| Iodine (µg) | 73 | 73 | 95 | 95 | 95 | 95 |
| Selenium (µg) | 45 | 40 | 50 | 50 | 55 | 70 |
| Copper (µg) | 540 | 540 | 685 | 685 | 700 | 700 |

^a NE, niacin equivalents equal 1 mg of dietary niacin or 60 mg of dietary tryptophan; RE, retinol equivalent; TE, α-tocopherol equivalent.

^b Energy intake is expressed as the average daily need assuming average height, and the average need per centimeter of height.

^c Nutrients for which adolescent intake is most likely to fall short of recommendations.

^d The recommended intake of vitamin C has been increased for adults from 60 to 200 mg per day.

^e Daily intake of about 400 µg is recommended before conception to prevent neural tube defects. This intake is advisable in adolescent girls planning on becoming or at risk of becoming pregnant.

^f Calcium supplementation may be particularly important in adolescent girls unless the diet is very calcium dense. An intake of 1,500 mg per day may be better than the RDA of 1,200 mg. During pregnancy and lactation, the calcium requirements of adolescent girls are even higher.

^g Iron intake of 18 mg per day in both sexes is now generally recommended. Supplementation in adolescent girls may be indicated. Monitoring of the complete blood count after menarche is indicated but has low sensitivity for early iron deficiency. If an individual adolescent is believed to be at risk of deficiency, serum ferritin should be assayed.

The short-term risks of such a dietary pattern are modest, but the persistence of this pattern beyond adolescence is common and clearly is associated with the prevailing chronic diseases of adulthood.

The maximal rate of growth in height for girls occurs between the ages of 10 and 13, whereas for boys it is between the ages of 12 and 15. The adolescent growth

spurt contributes approximately 15% to 20% to adult height and 45% to 50% to adult weight. The growth during adolescence reduces the proportion of total body mass contributed by adipose tissue in boys but increases it in girls. Body fat in girls rises during adolescence from 10% to between 20% and 24%. A divergence in adiposity at adolescence contributes to the diverging nutritional requirements of males and females at this stage of life. By the end of adolescence, lean body mass in males on average is double that of females.

In girls, peak calorie intake typically occurs in the year of menarche. In boys, calorie intake continues to rise throughout the growth spurt, generally peaking near 3,400 kcal at about age 16. The divergence in lean body mass results in a marked divergence in macronutrient needs. The average daily caloric requirement per unit height rises during adolescence for boys, and it actually falls for girls because of the increasing proportion and lower metabolic demand of body fat.

The adequacy of energy intake in adolescents can be assessed through determination of body mass index and comparison to age-appropriate reference ranges. Inadequate energy intake in adolescents, if mild, tends to delay the growth spurt rather than prevent attainment of normal height. While RDAs were developed and DRIs are being developed on the basis of chronologic age, the developmental stage is a more reliable index of actual needs. The Tanner scale of sexual maturity is widely used and can guide nutritional recommendations to adolescents.

Protein intake in adolescents is more likely to exceed than to fall short of recommendations. However, if protein deficiency is suspected because of dietary restrictions, prealbumin and retinol-binding protein are useful laboratory assays that provide high sensitivity for subclinical protein malnutrition.

The average adolescent consumes a diet deficient in several key vitamins and minerals, most prominently calcium, iron, folate, vitamins A and E, zinc, and magnesium. Inadequate calcium intake is both common and of great concern in adolescents, as it contributes to the risk of osteoporosis and fractures in later life. Rapid growth and expansion of both blood volume and muscle mass lead to increased iron requirements in adolescence; with the onset of menarche, girls

become further susceptible to iron deficiency. Serum ferritin is the most reliable measure of iron stores. Iron deficiency commonly leads to anemia, defined in adolescents as a hemoglobin level below 11.8 g per dL at ages 12 to 14.9 years and below 12.0 g per dL at 15 years and older. Adolescents have increased requirements for folate; supplementation may therefore be warranted. This is especially true for sexually active young women, given the demonstrated benefits of folate supplementation in reducing risk of neural tube defects if taken early in pregnancy. Nominal zinc and magnesium deficiency are apparently common in adolescents, and inclusion in the diet of foods rich in these minerals is appropriate.

In general, the dietary fiber intake of the population is well below recommendations. Although there has been concern that high fiber intake could interfere with micronutrient absorption and adequate caloric intake among growing children and adolescents, the current recommendation of “age+5”—that is, fiber intake equal to age plus 5 to 10 g per day—is both safe and sufficient for disease prevention.

Excess energy and fat intake is common in children and adolescents, contributing to obesity, type 2 diabetes, and adult risk of cardiac events. Consumption of sugar-sweetened drinks such as soda and increased sedentary activities—particularly television/video and computer use—have also been found to be associated with increased risk of obesity. Many studies have shown that type 2 diabetes has increased dramatically in obese children and adolescents throughout the world in recent years. Cardiac risk factors established in adolescence or earlier are known to track into adulthood. Diabetes screening as well as assessment of tobacco use and serum lipids, body mass index, blood pressure, physical activity level, and habitual diet are indicated in adolescence to reverse or prevent developing risk for cardiovascular disease in adulthood. Hypertension in adolescents poses increased long-term health risks; prompt identification and management are therefore warranted. A recent meta-analysis of controlled trials assessing effects of salt restriction on blood pressure in children found that modest reductions in dietary salt intake resulted in significant reduction in systolic blood pressure.

Translating recommendations into practice may be particularly difficult with adolescent patients. Dietary counseling in adolescence is most likely to be influential if it emphasizes current health, current activities, and/or appearance rather than long-term health effects to which adolescents generally feel relatively invulnerable. Dietary health promotion in the school setting may be particularly important, and there is some evidence that school-based interventions can help modify activity and nutrition behaviors. Home environment may also play a role: an association has been shown between adolescents who eat dinner with their families and more healthful dietary intake patterns, illustrating the importance of parental involvement as well.

In general, physical activity is beneficial to health and complementary to the health-promoting effects of prudent diet. Competitive athletics in adolescent girls, however, can lead to a syndrome known as the female athlete triad, which consists of osteoporosis, disordered eating, and menstrual disorders. Though initially thought to stem from low adiposity, menstrual disturbances in female adolescents are now believed to result principally from inadequate energy availability, which causes hypothalamic-pituitary hormone dysfunction. Amenorrhea in particular is associated with reduced peak bone mass, stress fractures, and increased risk of osteoporosis in later years. In the treatment of adolescent amenorrhea, reductions in training or increases in energy intake or both and use of oral contraceptives may be indicated to restore menses and maintain normal bone mineralization.

Clinical Highlights

In developed countries the average adolescent is at greater risk of nutritional excess and obesity than of macronutrient deficiencies. But even in the context of overnutrition, deficiencies of select micronutrients appear to be quite common. Deficiencies of iron, calcium, zinc, vitamin A, and vitamin C are particularly common, although other nutrients probably are not consumed at truly optimal levels. Omega-3 fatty acids tend to be deficient in the diets of children and adults alike. Although a balanced diet provides needed micronutrients, social pressures at adolescence tend to favor a particular pattern of dietary imbalance, with excessive intake of processed and fast foods and, consequently, sugar, salt, and fat. A

multivitamin/multimineral supplement is an appropriate recommendation although clearly not compensatory for an imprudent dietary pattern.

Energy requirements of athletes may not be met. This is particularly problematic for girls, who as a result may develop endocrinological disturbances and even amenorrhea. The resultant disruption of bone mineralization may be irreversible. Calcium supplementation, control of energy expenditure, and supplemental energy intake are all indicated to maintain menses and protect the bones of female athletes. In extreme cases, oral contraceptives should be used as well. Screening for iron-deficiency anemia is also recommended for menstruating girls.

Eating disorders often emerge at adolescence, and a high level of suspicion facilitates early detection. Management is specialized, relying in particular on expert and often multidisciplinary psychiatric care.

Risk factors for cardiovascular disease often develop during adolescence and, when they do, track into adulthood. Therefore, efforts to identify and modify risk factors for cardiovascular and other chronic disease in adolescents are clearly indicated, as are screening for hypertension, lipid disorders, and diabetes.

Modification of adolescent dietary patterns to promote health will be most effective if environmental as well as behavioral factors are addressed. The same overall dietary pattern recommended for health promotion in adults is appropriate for adolescents, but translating such recommendations into practice represents a particular challenge with this age group.

Diet and Senescence

Nutritional factors play important roles in the process of aging. Requirements for energy and specific nutrients change as a result of altered metabolism, diminished energy expenditure, and changes in behavioral patterns. The optimal adjustments in micronutrient intake for individuals older than 65 or the “older old,” greater than age 80, are uncertain, but progress is being made in this area of study, and new recommendations are being generated.

Even more fundamental than the modified energy needs of older age is the role nutrition appears to play in the physiology of aging. Oxidation is emerging as an important aspect of cellular aging; therefore, dietary pro-oxidants and antioxidants may influence the nature and pace of the aging process itself. Animal studies demonstrate convincing extension of the lifespan with reduced energy intake, provided that micronutrient adequacy is maintained; the implications of this for humans is at present as speculative as tantalizing, but our understanding of the physiology is advancing.

Nutritional recommendations may be made with some confidence both to older patients trying to maintain health and to younger patients seeking ways to forestall the effects of aging. The importance of optimal nutrition for the elderly population continues to increase with the size of this population and the prolongation of life expectancy.

Diet

Life expectancy is steadily increasing and may soon reach 85 to 90 years.

Assigning particular physiologic characteristics to the process of aging is a complex and controversial process. Cellular degradation, the accumulation of oxidative stress, and a putative limit to the replicative capacity of DNA appear to be key components. Recent study into the anti-aging effects of resveratrol, a compound concentrated in the skin of grapes, has suggested the governance of aging processes by a discrete cluster of genes and their products, the SIRT1 enzyme, also known as NAD-dependent deacetylase sirtuin-1, in particular. Whatever the natural pace of aging might be, it is clearly influenced, in humans and other species, by environmental stressors. Among such stressors are not only infectious disease and trauma but also nutrient excess and deficiency, along with psychological stress, sleep quality and quantity, environmental toxins, and an array of other factors both known and unknown.

Daily energy consumption is driven largely by resting metabolic rate (RMR), which accounts for 60% to 75% of the total. An additional 10% is accounted for by postprandial thermogenesis, the thermic effect of food. The energy consumed as fuel

for physical activity can vary by nearly 30-fold, from a low of approximately 100 kcal per day.

Aging is associated with reductions in RMR, postprandial thermogenesis, and physical activity, with declines in activity disproportionately responsible for reduced energy expenditure. People older than 65 initially are subject to weight gain and obesity because they tend to maintain the energy intake of their younger years and reduce their expenditure. The older old are increasingly subject to weight loss and the sequelae of malnutrition as a result of reduced intake. The decline in RMR associated with aging is the result of reduced fat-free body mass, as well as the effects of reduced physical activity. Studies suggest that the association between age and declining RMR begins at around age 40 in men.

The capacity to measure the energy requirements of different age groups has been enhanced by application of the doubly labeled water method, an accurate means of measuring total daily energy expenditure. Use of the method has clarified the importance of variability in physical activity in the variability of energy requirements among the elderly, with physical activity influencing RMR. Use of the doubly labeled water method suggests that energy requirements of the elderly may, in general, have been underestimated. Such methods also suggest that an age-related increase in body fat may be largely attributable to reduced physical activity. The potential hazards of both undernutrition and overnutrition in the elderly have been noted. Energy requirements generally decline with age, predominantly because of a loss of lean body mass and associated change in metabolic rate, as well as reductions in energy expenditure in physical activity. There is evidence that basal metabolic rate declines with age to some degree; some reduction in RMR not attributable to declines in physical activity or fat-free mass is apparent.

A regimen of regular physical activity can, to varying degrees, preserve lean body mass in the elderly and will naturally result in higher energy requirements, while conferring a host of health benefits as is true in younger age groups. A study of 11 healthy women with a mean age of 73 revealed that, with maintenance of physical activity, energy expenditure was not reduced as a product of age. Evidence

suggests that the effects of aging on energy requirements and body composition are quite variable and modified substantially by general health and physical activity. A longitudinal evaluation of elderly subjects found that higher levels of physical activity were associated with higher muscle mass.

Although in general energy requirements decline with age, in part or whole because of diminished physical activity and consequent loss of lean body mass, there is evidence that energy intake goes down disproportionately. Consequently, many elderly, particularly those living alone and homebound, are undernourished. Factors influencing reduced energy intake in elderly individuals include changes in olfaction or taste, poor dentition, dysphagia, constipation, and anorexia.

Aging is associated with a substantial increase in proportional body fat, along with a loss of lean body mass up to age 65 or so, after which body fat content declines as well. Negative energy balance and particularly negative nitrogen balance are common problems in the elderly. As energy intake falls, protein requirements to avoid negative nitrogen balance rise.

Undernutrition in the elderly appears to be secondary not only to underestimates of energy requirements in this age group but also to a relative inability of elderly individuals to maintain a constant energy balance. In a study comparing the adaptive responses of younger and older men to periods of overfeeding and underfeeding, it was reported that compensation occurred only in the younger men. It is not yet fully understood why older adults develop impairment in their ability to accurately regulate energy intake; age-related changes in hormonal and metabolic mediators of energy regulation may play a role, as may alterations in appetite, satiety, and sensory perception.

Protein requirements tend to rise in the elderly, especially those with limited mobility. Both inactivity and reduced muscle mass tend to result in negative nitrogen balance, requiring increased protein consumption to compensate. Protein requirements remain relatively stable in elderly people whose functional status and activity are preserved. Whereas protein deficiency appears not to be a problem in most elderly people who live independently, protein malnutrition is common among

those living in institutions. Increased protein is needed particularly when demands rise in the context of injury or illness, both of which are common in the elderly. There is no evidence that protein intake above 0.8 g per kg accelerates a decline in renal function in elderly people who show no evidence of renal insufficiency. For elderly people in whom renal insufficiency is established, protein restriction may be indicated.

Because many protein-rich foods have a high nutrient content in general, their consumption by elderly should be encouraged. Protein intake in the elderly in developed countries is generally near the recommended 0.8 to 1 g/kg/day. The maintenance of nitrogen balance is strongly influenced by total energy intake. When energy intake is inadequate, negative nitrogen balance occurs even with putatively adequate protein intake. Inadequate protein intake can lead to suppressed immune function, poorer healing, and increased recovery time from illness.

Even when a person's weight stays consistent, energy requirements decline with advancing age, whereas protein requirements remain fairly constant or increase. Therefore, the maintenance of adequate protein nutrition requires the percentage of calories from protein to rise over time. For example, 56 g per day of protein would be required to provide 0.8 g/kg/day to a 70 kg individual. At an energy intake of 2,500 kcal, protein would constitute 9% of calories. At a reduced energy intake of 1,800 kcal, protein would constitute over 12% of calories. Carbohydrate and fat intake guidelines for the elderly do not differ from those for younger adults.

Whereas the maintenance of adequate nutritional intake in the elderly is a priority, calorie restriction over time is associated with longevity in most species studied. In virtually all species studied to date, caloric restriction appears to lower body temperature, reduce basal metabolic rate, and reduce signs of oxidative injury to cells, organelles, and DNA. Although several mechanisms have been proposed, one leading hypothesis is that the reduction in mitochondrial free radical generation underlies the markedly reduced oxidative damage (a major factor in the pathological aging process) seen in caloric restriction.

The effects of restricted energy intake result not only in optimizing survival (i.e., raising mean survival to nearer the predicted maximum) but in extending the natural lifespan as well. Preliminary studies of caloric restriction in primates suggest that the same effects seen in rodents and other species also occur in primates. Studies examining the effects of resveratrol on protein expression and enzymatic activity are beginning to yield insights into the potential mechanisms by which calorie restriction promotes longevity.

Evidence suggests that obesity poses less risk of premature mortality to older subjects than to younger. However, only those individuals who have already avoided early mortality live to experience obesity late in life, and obesity at earlier ages, including middle age, is clearly associated with increased risk of premature mortality. Obesity can cause serious medical complications and exacerbate age-related functional declines in older adults.

There is, to date, no confirmatory evidence in humans that energy restriction directly extends survival, although it does appear to improve biomarkers of longevity. A recent randomized trial found that after 6 months on a very-low-calorie diet, overweight adult male subjects had significantly decreased levels of fasting insulin and body temperature. Nonetheless, there is no evidence that caloric restriction initiated in old age is beneficial. If calorie restriction is beneficial in humans, energy restriction must be accompanied by nutrient supplementation to prevent deficiencies.

As the maintenance of adequate energy and micronutrient intake in the elderly is often of paramount importance, efforts to restrict fat intake in elderly patients whose fat intake was not previously restricted are likely to be justified only when in response to some specific health risk or need. In elderly subjects already adhering to a fat-restricted diet, there is likely to be little reason to increase fat intake, provided that weight maintenance is satisfactory. In either case, supplementation of fat-soluble vitamins is likely to be prudent.

The reduction in physical activity associated with age and resultant decline in energy consumption is leading to reduced intake of micronutrients unless the

nutrient density of the diet is intentionally altered. The decline in micronutrient intake places the elderly at risk of subtle deficiencies, with potentially important implications for health. In the population over 65 years old, 80% have one or more chronic medical conditions requiring use of prescription drugs. Both the disease state and the pharmacotherapy may influence metabolism, and polypharmacy is associated with increased risk of malnutrition. The wide variation in the state of health and the rate of aging, producing extreme heterogeneity among the elderly with regard to energy and nutrient requirements, limits the utility of broad, age-specific recommendations.

In the same individual, skeletal muscle is approximately 40% less at age 70 than during early adulthood, resulting in declines in RMR of 1% to 2% per decade beginning at age 25. Reductions in caloric expenditure made for the sake of avoiding obesity require commensurate reductions in energy consumption but at the risk of reducing consumption of essential micronutrients.

Between ages 25 and 75, a person would have to reduce energy consumption by 25% to maintain energy balance and avoid excessive body fat. But the maintenance of a comparably nutrient-dense diet over time would then result in a corresponding 25% reduction in the intake of micronutrients.

For some nutrients, intake is generally sufficiently abundant so that such a reduction would preserve adequacy. For others, such a reduction might lower intake below the desired threshold. Intake levels of copper, zinc, chromium, calcium, and vitamin D during adulthood typically do not allow for a 25% reduction, thus placing the elderly at risk of deficiency.

The modern nutrition recommendations reflect an emphasis on health promotion and disease prevention. In addition, there are now age-specific recommendations for adults age 51 to 70 and adults over 70 years of age, based on the growing recent literature examining nutritional issues in the elderly. The recommended dietary allowances (RDAs) for these two age groups are shown in Table 7.

There is evidence that deficiencies of vitamins C, B₆, and B₁₂ are fairly prevalent among the elderly.

In general, deficiency of fat-soluble vitamins is infrequent because of large tissue stores. One exception in the elderly appears to be vitamin D, the levels of which decline with age because of decreased consumption, decreased sun exposure, and decreased efficiency of the body's ability to convert pro-vitamin D to the active form. Recent evidence suggests that higher doses of vitamin D than previously advised may confer a range of health benefits.

Although most mineral requirements do not appear to change with aging per se, metabolic disturbances associated with disease or treatment (e.g., diuretic use) may alter certain nutrient needs. Iron requirements tend to decline somewhat with age, especially in postmenopausal women; elderly women in particular may benefit from increased calcium intake. The RDA for vitamin A may be too high for the elderly, as absorption appears to increase with age.

Table 4—Recommended Dietary Allowance and Adequate Intake for Certain Vitamins and Minerals for Males and Females Aged 51 to Over Age 70^a

| Nutrient | Females | | | Males | | |
|--------------------------------|-----------|-----------|---------|-----------|-----------|---------|
| | Age 31–50 | Age 51–70 | Age >70 | Age 31–50 | Age 51–70 | Age >70 |
| Vitamin A (µg/d) | 700 | 700 | 700 | 900 | 900 | 900 |
| Vitamin C (mg/d) | 75 | 75 | 75 | 90 | 90 | 90 |
| Vitamin D (µg/d ^b) | 5 | 10 | 15 | 5 | 10 | 15 |
| Vitamin E (mg/d) | 15 | 15 | 15 | 15 | 15 | 15 |
| Vitamin B ₆ (mg/d) | 1.3 | 1.5 | 1.5 | 1.3 | 1.7 | 1.7 |
| Vitamin B ₁₂ (µg/d) | 2.4 | 2.4 | 2.4 | 2.4 | 2.4 | 2.4 |
| Folate (µg/d) | 400 | 400 | 400 | 400 | 400 | 400 |
| Calcium (mg/d) | 1,000 | 1,200 | 1,200 | 1,000 | 1,200 | 1,200 |
| Chromium (µg/d) | 25 | 20 | 20 | 35 | 30 | 30 |

| | | | | | | |
|--|----|----|----|----|----|----|
| Selenium ($\mu\text{g}/\text{d}$) | 55 | 55 | 55 | 55 | 55 | 55 |
| Zinc (mg/d) | 8 | 8 | 8 | 11 | 11 | 11 |
| ^a The RDA for younger adults is shown for comparison. | | | | | | |
| ^b Each μg of cholecalciferol = 40 IU of vitamin D. | | | | | | |

There are age-dependent changes in gastrointestinal physiology. The principal changes include achlorhydria secondary to atrophic gastritis, almost invariably due to *Helicobacter pylori* infection, and lactose intolerance. The former can impair absorption of iron, folate, calcium, vitamin K, and vitamin B12, whereas the latter may contribute to poor calcium nutriture. With these exceptions, gastrointestinal function is well preserved with aging and generally is not the limiting factor in the maintenance of optimal nutritional status.

Serum glucose levels tend to rise with age, and suggestions have been made for age-specific thresholds for defining fasting hyperglycemia. Age-related glucose intolerance may be compensated by relative restriction of simple sugar intake. Hyperglycemia even in the absence of diabetes may be associated with increased mortality.

Complex carbohydrates should be prioritized as a source of fiber, both soluble and insoluble, and of micronutrients. Dietary fiber intake in elderly is less than the recommended amount, which is 25 to 30 g per day. Reductions of energy consumption by elderly patients are likely to result in low fiber intake as well. The elderly are particularly susceptible to constipation and are apt to benefit from increased consumption of dietary fiber.

The more rapid intestinal transit time that comes with increased fiber consumption, however, may reduce mineral absorption, increasing the risk of deficiencies in the elderly. Therefore, increased nutrient density or supplementation is indicated when fiber intake is augmented. Fruits, vegetables, and cereal grains may offer protection against constipation, diverticulosis, and nutrient deficiencies. Dentition should be assessed in making such recommendations; ability to eat fruit and vegetables may be impaired in elderly patients with poor dentition.

Aging is associated with a decline in immune function, as well as greater susceptibility to an array of micronutrient deficiencies. In a study of institutionalized elderly individuals with evidence of micronutrient deficiencies, multivitamin supplementation (B complex, vitamins C and E, and β -carotene) for a period of 10 weeks significantly enhanced immune function, as gauged by cutaneous hypersensitivity reactions to injected antigens.

Elderly patients are particularly subject to dehydration and its sequelae because of reduced body water, diminished renal concentrating ability, diminished thirst, insensitivity to antidiuretic hormone, and susceptibility to orthostatic hypotension due to reduced autonomic tone. Thirst is not a very reliable index of hydration status among the elderly.

Recommendations to maintain optimal fluid status are for fluid intake of 30 mL per kg of actual weight, 1 mL per kilocalorie consumed, or 1,500 mL per day, whichever is highest; this is generally appropriate under conditions of typical daily activity. A study examining the prevalence of dehydration in community-dwelling older adults reported virtually no evidence of dehydration in those subjects ingesting six or more glasses of fluid per day.

Kerstetter et al. [50] offer a practical approach that does not require patients to measure their fluid intake so precisely. Maximal concentration of urine at age 90 is estimated at 800 mosmol per L, down from 1,200 mosmol per L at younger age. Therefore, in the elderly, fluid intake should be maintained at a level that allows for the excretion of approximately 1,200 mosmol of solute waste per day. This amount would require at least 1.5 L of urine produced per day for the very elderly. At this concentration, the urine appears light yellow. Therefore, a level of fluid intake that results in urine that is consistently light yellow implies adequate hydration status.

In an article on the potential benefits of complementary medicine to an aging population, Bland [51] characterizes the functional declines of aging in discrete categories, such as impaired mitochondrial function related to oxidative stresses, glycation of functional proteins, chronic inflammation, and impaired methylation. Many of the physiologic changes of aging are nutrient responsive. Mitochondrial

function may be influenced by a range of nutrients, including ubiquinone, n-acetylcysteine, lipoic acid, creatine, vitamin E, and n-acetylcarnitine.

Glycation may be reduced by improved glucose tolerance, potentially influenced by intake of chromium, magnesium, and other nutrients. Inflammation may be reduced by augmenting intake of n-3 fatty acids and by other interventions. Methylation is supported by adequate intake of B vitamins and can be tracked by the level of plasma homocysteine. Although the evidence for various nutritional interventions in efforts to curtail adverse effects of aging varies, many “complementary” or “alternative” practices are consistent with the weight of available evidence in the scientific literature.

Nutrients and Functional Foods

Vitamin D

Actual or suspected lactose intolerance, as well as prevailing social patterns, tend to limit milk consumption by the elderly. Fortified dairy products and fatty fish—intake of which tends to be low among the elderly—are the principal dietary sources of vitamin D. The skin's ability to manufacture vitamin D with exposure to sunlight becomes less efficient with age, and the elderly tend to reduce their amount of sun exposure. Therefore, vitamin D deficiency appears to be fairly widespread among the older population, and a study of more than 1,200 independent, community-dwelling older persons found that nearly 50% were vitamin D deficient or insufficient at the onset of the trial. Moreover, those with baseline vitamin D deficiency were at significantly greater risk of future nursing home admission than equivalent individuals with high vitamin D levels. Deficiency of vitamin D leads to impaired calcium absorption, compounding the generally inadequate calcium intake in this age group. Current recommendations suggest supplementation with 400 IU of vitamin D alone or as part of a multivitamin as a prudent precaution against deficiency and accelerated osteopenia. Even higher doses, of 600 to 800 IU, are recommended for adults over the age of 71 and those at high risk of deficiency. High dose supplementation in this range appears to reduce the risk of both falls and fractures. There is some evidence of protection against colon cancer as well.

Vitamin C

The RDA for vitamin C was recently revised upward from 60 to 75 to 90 mg per day. There is no specific evidence that deficiency occurs more commonly among the elderly than among younger people, but specific populations, such as those who have dementia or reside in nursing homes, appear to have reduced intakes of vitamin C, and smokers of any age have increased requirements to compensate for the oxidative damage of smoking. High-dose supplementation is not known to be particularly beneficial, but there is some evidence that maintaining adequate stores of vitamin C (whether through diet or supplementation) may be a valuable preventive health measure. For the same reasons that intake up to 500 mg per day may be beneficial to other age groups, intake in this range may offer benefits to the elderly as well.

Vitamin B₆

The current RDA for vitamin B₆ is 2 mg per day. Recent evidence suggests that even this revised level is too low. Intake of vitamin B₆ among the elderly often fails to meet the RDA. Low intake of vitamin B₆ may contribute to elevations of serum homocysteine and accelerated atherosclerosis. A vitamin B₆ supplement of 2 mg per day is indicated for the elderly; most multivitamins provide this dose.

Vitamin B₁₂

Atrophic gastritis is more prevalent in the elderly than in others and, therefore, so is vitamin B₁₂ deficiency. In individuals with atrophic gastritis, vitamin B₁₂ must be supplemented parenterally because intrinsic factor is lacking. Less severe vitamin B₁₂ deficiency due to poor diet may also occur and may contribute to cognitive impairment, anemia, or elevated homocysteine levels in older people. Vitamin B₁₂ supplementation in a multivitamin is reasonable and appropriate for elderly individuals.

Folate

Folate deficiency does not appear to be a particular problem associated with aging. However, low folate intake will occur when the diet is poor and may contribute to elevations in homocysteine. Folate supplementation in the form of a

multivitamin is appropriate. Note that symptoms of vitamin B₁₂ deficiency, a much more common problem in this population, may be masked by high folate consumption; folate supplements should therefore also include vitamin B₁₂, and the index of suspicion for vitamin B₁₂ deficiency should be high so that it is detected early if it occurs.

Calcium

Calcium intake throughout life tends to be lower than recommended, especially for women. In the elderly, the discrepancy between recommended and actual intake is more pronounced with calcium than perhaps any other micronutrient. Calcium absorption declines with age, particularly after age 60 or so. This decline in function is compounded by vitamin D deficiency. Marginal intake of both vitamin D and calcium contributes to age-related bone loss and the risk of fracture. The elderly are particularly susceptible to osteoporosis and related fracture. Adequate calcium intake may forestall osteoporotic fracture, but it cannot restore bone density already lost. Calcium intake is also associated with reduced risk of colon cancer and reduction in blood pressure. Reduced-fat dairy products are preferable as dietary sources of calcium, but supplementation with up to 1,000 to 1,200 mg per day may offer benefits.

Copper

The current RDA for copper is 0.9 mg per day for both younger and older adults. Copper intake is often inadequate in the elderly due to decreased total caloric intake. Copper is needed for hematopoiesis, and deficiency can result in both anemia and neutropenia, particularly in tube-fed institutionalized elderly patients. Idiopathic myopathy in adults may also be a result of unrecognized copper deficiency.

Chromium

The diet provides approximately 15 µg per 1,000 kcal of chromium. At the prevailing level of chromium density, at least 2,000 kcal per day would be required to meet recommended intake, placing the elderly at particular risk for deficiency. Deficiency of chromium impairs glucose and insulin metabolism, produces elevations of serum triglycerides, and is associated with peripheral neuropathy.

Older adults with, or at risk for, type 2 diabetes may particularly benefit from chromium supplementation.

Zinc

Zinc appears to affect immunity. As immune dysfunction is characteristic of aging and may result in life-threatening infections, efforts to maintain optimal immune function are important.

Consumption of less than 10 mg per day by elderly individuals may impair immunity, wound healing, and the acuity of taste and smell. The average diet provides approximately 5 mg of zinc per 1,000 kcal; therefore, 3,000 kcal would be required to provide the recommended 12 to 15 mg per day.

Zinc is abundant in poultry, fish, and meat, and diets rich in these sources may provide a greater density of zinc. However, increased meat consumption generally is precluded by efforts to limit fat intake and promote fruit and vegetable consumption. Zinc supplementation of 15 mg per day is a reasonable precaution; this level is provided by most multivitamin/multimineral supplements. A recent randomized controlled trial found that daily supplementation of 45 mg of zinc in elderly subjects reduced incidence of infections and levels of oxidative stress markers compared to placebo.

Iron

Iron requirements decline with age for women because of the cessation of monthly blood loss following menopause. Even though iron absorption declines with age, iron stores tend to increase.

Magnesium

Magnesium intake in developed countries is often marginal in all age groups. Whereas intake in the range of 4 mg/kg/day is common, 6 mg/kg/day is considered more appropriate. Deficiency is particularly likely among the elderly, due to reduced intake, depletion associated with chronic disease states such as type 2 diabetes mellitus, and impaired gastrointestinal absorption. Clinical consequences may include sleep disturbance, cognitive impairment, and myalgias. Although the results of trials demonstrating sustained benefit of magnesium supplementation are lacking

to date, the use of diet or supplements to achieve an intake level greater than 5 mg/kg/day appears justified. Of note, use of magnesium-containing laxatives among the elderly may lead to hypermagnesemia.

Resveratrol

Resveratrol is an antioxidant concentrated in the skin of grapes, and thus in red wine. Animal research suggests potent effects on enzyme systems of vital importance to diverse processes of aging, in particular cellular oxygen consumption. High dose administration in rodent models appears to forestall aging, but the relevance for humans remains speculative at this point. Supplementation is not currently advised, but the topic is of clear interest and warrants close attention.

Clinical Highlights

Aging is associated with a loss of lean body mass and an increase in body fat up until the sixth decade. Thereafter, both lean mass and fat mass diminish. Energy requirements tend to decline with age, in part because of reduced physical activity and in part because of the loss of metabolically active tissue. Nutrient and energy intake, however, tend to decline disproportionately to energy needs, so that many elderly are undernourished.

Energy deficiency in the elderly results in negative nitrogen balance with accelerated muscle loss. Deficiencies of micronutrients, particularly of B vitamins, vitamin D, and certain minerals, such as zinc, are very common. Use of prescription medications may compound age-related changes in olfaction, taste, and gastrointestinal motility, contributing to poor dietary intake.

Emphasis in primary care should be on the maintenance of weight and especially preservation of lean body mass. Elderly people should be encouraged to become or remain physically active as their functional status permits. Periodic assessment of dietary intake, informally or via referral to a dietitian, may be helpful in ensuring maintenance of adequate nutrition. A multivitamin/multimineral supplement is a low-cost and safe means of protecting elderly patients against several common micronutrient deficiencies, although specific evidence of benefit from such a practice is lacking.

An effort to increase the nutrient density of the diet is a valid, although more difficult, alternative, and the two practices are complementary rather than mutually exclusive. Common sequelae of aging, such as cognitive and immunologic deficits, may be due in part to nutrient deficiencies and, therefore, are potentially preventable or reversible. There is convincing evidence to support supplementing the diets of elderly patients with zinc, chromium, magnesium, calcium, and possibly copper, along with vitamins. There is some suggestive evidence that nutrients not traditionally included on the RDA lists, such as ubiquinone (coenzyme Q₁₀) and lipoic acid, may offer benefits for elderly patients.

As patients age, the short-term functional benefits of adequate nutrition may need to be compared with any long-term consequences of specific dietary practices. For example, whereas the cholesterol content of eggs may be a relevant consideration in younger adults at long-term risk for coronary disease, the nutrient density of eggs may provide benefits in excess of any risks for elderly patients. A diet rich in a variety of fruits and vegetables offers the same array of benefits to the elderly as to younger age groups.

References

1. Caulfield L.E., Elliot V. Nutrition of Adolescent Girls and Women of Reproductive Age in Low- and Middle-Income Countries: Current Context and Scientific Basis for Moving Forward. Strengthening Partnerships, Results, and Innovations in Nutrition Globally (SPRING); Arlington, VA, USA: 2015.
2. Gernand A.D., Schulze K.J., Stewart C.P., West K.P., Jr., Christian P. Micronutrient deficiencies in pregnancy worldwide: Health effects and prevention. *Nat. Rev. Endocrinol.* 2016; 12:274–289. doi: 10.1038/nrendo.2016.37.
3. Blumfield M.L., Hure A.J., Macdonald-Wicks L., Smith R., Collins C.E. A systematic review and meta-analysis of micronutrient intakes during pregnancy in developed countries. *Nutr. Rev.* 2013;71:118–132. doi: 10.1111/nure.12003. [PubMed] [CrossRef] [Google Scholar]
4. Hollis B.W., Wagner C.L. New insights into the vitamin D requirements during pregnancy. *Bone Res.* 2017;5:17030. doi: 10.1038/boneres.2017.30.

5. De-Regil L.M., Peña-Rosas J.P., Fernández-Gaxiola A.C., Rayco-Solon P. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. *Cochrane Database Syst. Rev.* 2015 doi: 10.1002/14651858.CD007950.pub3.
6. Li J., Zhao H., Song J.-M., Zhang J., Tang Y.-L., Xin C.-M. A meta-analysis of risk of pregnancy loss and caffeine and coffee consumption during pregnancy. *Int. J. Gynecol. Obstet.* 2015;130:116–122. doi: 10.1016/j.ijgo.2015.03.033.
7. Lowensohn R.I., Stadler D.D., Naze C. Current concepts of maternal nutrition. *Obstet. Gynecol. Surv.* 2016;71:413–426. doi: 10.1097/OGX.0000000000000329.
8. Lonnie M., Hooker E., Brunstrom J.M., Corfe B.M., Green M.A., Watson A.W., Williams E.A., Stevenson E.J., Penson S., Johnstone A.M. Protein for life: Review of optimal protein intake, sustainable dietary sources and the effect on appetite in ageing adults. *Nutrients.* 2018;10:360. doi: 10.3390/nu10030360.
9. Elango R., Ball R.O. Protein and amino acid requirements during pregnancy. *Adv. Nutr.* 2016;7:839S–844S. doi: 10.3945/an.115.011817.
10. Ota E., Hori H., Mori R., Tobe-Gai R., Farrar D. Antenatal dietary education and supplementation to increase energy and protein intake. *Cochrane Database Syst. Rev.* 2015 doi: 10.1002/14651858.CD000032.pub3.
11. Morisaki N., Nagata C., Yasuo S., Morokuma S., Kato K., Sanefuji M., Shibata E., Tsuji M., Senju A., Kawamoto T., et al. Optimal protein intake during pregnancy for reducing the risk of fetal growth restriction: The Japan environment and children's study. *Br. J. Nutr.* 2018;120:1432–1440. doi: 10.1017/S000711451800291X. [PubMed] [CrossRef] [Google Scholar]
12. Augustin L.S., Kendall C.W., Jenkins D.J., Willett W.C., Astrup A., Barclay A.W., Bjorck I., Brand-Miller J.C., Brighenti F., Buyken A.E., et al. Glycemic index, glycemic load and glycemic response: An international scientific consensus summit from the international carbohydrate quality consortium (icqc) *Nutr. Metab. Cardiovasc. Dis. NMCD.* 2015;25:795–815. doi: 10.1016/j.numecd.2015.05.005.
13. 27. Qiu C., Coughlin K.B., Frederick I.O., Sorensen T.K., Williams M.A. Dietary fiber intake in early pregnancy and risk of subsequent preeclampsia. *Am. J. Hypertens.* 2008;21:903–909. doi: 10.1038/ajh.2008.209. [PubMed] [CrossRef] [Google Scholar]
14. 30. Markovic T.P., Muirhead R., Overs S., Ross G.P., Louie J.C., Kizirian N., Denyer G., Petocz P., Hyett J., Brand-Miller J.C. Randomized controlled trial investigating the effects of a low-glycemic index diet on pregnancy outcomes in women at high risk of gestational diabetes mellitus: The gi baby 3 study. *Diabetes Care.* 2016;39:31–38. doi: 10.2337/dc15-0572.

15. Middleton P., Gomersall J.C., Gould J.F., Shepherd E., Olsen S.F., Makrides M. Omega-3 fatty acid addition during pregnancy. *Cochrane Database Syst. Rev.* 2018 doi: 10.1002/14651858.CD003402.pub3.
16. Saccone G., Berghella V. Omega-3 supplementation to prevent recurrent preterm birth: A systematic review and metaanalysis of randomized controlled trials. *Am. J. Obs. Gynecol.* 2015;213:135–140. doi: 10.1016/j.ajog.2015.03.013.
17. Saccone G., Berghella V., Maruotti G.M., Sarno L., Martinelli P. Omega-3 supplementation during pregnancy to prevent recurrent intrauterine growth restriction: Systematic review and meta-analysis of randomized controlled trials. *Ultrasound Obstet. Gynecol.* 2015;46:659–664. doi: 10.1002/uog.14910.
18. McCauley M.E., van den Broek N., Dou L., Othman M. Vitamin A supplementation during pregnancy for maternal and newborn outcomes. *Cochrane Database Syst. Rev.* 2015 doi: 10.1002/14651858.CD008666.pub3.
19. Stipanuk M.H., Caudill M.A. *Biochemical, Physiological and Molecular Aspects of Human Nutrition*. 3rd ed. Saunders; St Louis, MO, USA: 2013.
20. Black R.E., Victora C.G., Walker S.P., Bhutta Z.A., Christian P., de Onis M., Ezzati M., Grantham-McGregor S., Katz J., Martorell R., et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet.* 2013;382:427–451. doi: 10.1016/S0140-6736(13)60937-X.
21. Sukumar N., Rafnsson S.B., Kandala N.-B., Bhopal R., Yajnik C.S., Saravanan P. Prevalence of vitamin B-12 insufficiency during pregnancy and its effect on offspring birth weight: A systematic review and meta-analysis. *Am. J. Clin. Nutr.* 2016;103:1232–1251. doi: 10.3945/ajcn.115.123083.
22. Salam R.A., Zuberi N.F., Bhutta Z.A. Pyridoxine (vitamin B6) supplementation during pregnancy or labour for maternal and neonatal outcomes. *Cochrane Database Syst. Rev.* 2015 doi: 10.1002/14651858.CD000179.pub3.
23. Rogne T., Tielemans M.J., Chong M.F.-F., Yajnik C.S., Krishnaveni G.V., Poston L., Jaddoe V.W.V., Steegers E.A.P., Joshi S., Chong Y.-S., et al. Maternal vitamin B12 in pregnancy and risk of preterm birth and low birth weight: A systematic review and individual participant data meta-analysis. *Am. J. Epidemiol.* 2017;185:212–223. doi: 10.1093/aje/kww212.
24. Rumbold A., Ota E., Hori H., Miyazaki C., Crowther C.A. Vitamin E supplementation in pregnancy. *Cochrane Database Syst. Rev.* 2015 doi: 10.1002/14651858.CD004069.pub3.

25. Rumbold A., Ota E., Nagata C., Shahrook S., Crowther C.A. Vitamin C supplementation in pregnancy. *Cochrane Database Syst. Rev.* 2015 doi: 10.1002/14651858.CD004072.pub3.
26. Mousa A., Naderpoor N., Teede H.J., De Courten M.P., Scragg R., De Courten B. Vitamin D and cardiometabolic risk factors and diseases. *Minerva Endocrinol.* 2015;40:213–230.
27. Mousa A., Abell S.K., Shorakae S., Harrison C.L., Naderpoor N., Hiam D., Moreno-Asso A., Stepto N.K., Teede H.J., de Courten B. Relationship between vitamin D and gestational diabetes in overweight or obese pregnant women may be mediated by adiponectin. *Mol. Nutr. Food Res.* 2017;61 doi: 10.1002/mnfr.201700488.
28. Buppasiri P., Lumbiganon P., Thinkhamrop J., Ngamjarus C., Laopaiboon M., Medley N. Calcium supplementation (other than for preventing or treating hypertension) for improving pregnancy and infant outcomes. *Cochrane Database Syst. Rev.* 2015 doi: 10.1002/14651858.CD007079.pub3.
29. WHO . *Guideline: Calcium Supplementation in Pregnant Women.* World Health Organization; Geneva, Switzerland: 2013. [Google Scholar]
30. Harding K.B., Peña-Rosas J.P., Webster A.C., Yap C.M.Y., Payne B.A., Ota E., De-Regil L.M. Iodine supplementation for women during the preconception, pregnancy and postpartum period. *Cochrane Database Syst. Rev.* 2017 doi: 10.1002/14651858.CD011761.pub2.
31. WHO/UNICEF . *Reaching Optimal Iodine Nutrition in Pregnant and Lactating Women and Young Children.* World Health Organization and United Nations Children’s Fund; Geneva, Switzerland: 2007. [Google Scholar]
32. Peña-Rosas J.P., De-Regil L.M., Garcia-Casal M.N., Dowswell T. Daily oral iron supplementation during pregnancy. *Cochrane Database Syst. Rev.* 2015 doi: 10.1002/14651858.CD004736.pub5.
33. WHO. *WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience.* World Health Organisation; Geneva, Switzerland: 2016. [Google Scholar]
34. Popova S., Lange S., Probst C., Gmel G., Rehm J. Estimation of national, regional, and global prevalence of alcohol use during pregnancy and fetal alcohol syndrome: A systematic review and meta-analysis. *Lancet Glob. Health.* 2017;5:e290–e299. doi: 10.1016/S2214-109X(17)30021-9.
35. DeVido J., Bogunovic O., Weiss R.D. Alcohol use disorders in pregnancy. *Harv. Rev. Psychiatry.* 2015;23:112–121. doi: 10.1097/HRP.0000000000000070.

36. Jahanfar S., Jaafar S.H. Effects of restricted caffeine intake by mother on fetal, neonatal and pregnancy outcomes. *Cochrane Database Syst. Rev.* 2015 doi: 10.1002/14651858.CD006965.pub4. [PubMed] [CrossRef] [Google Scholar]
37. Chen L.W., Wu Y., Neelakantan N., Chong M.F., Pan A., van Dam R.M. Maternal caffeine intake during pregnancy and risk of pregnancy loss: A categorical and dose-response meta-analysis of prospective studies. *Public Health Nutr.* 2016;19:1233–1244. doi: 10.1017/S1368980015002463.
38. Rhee J., Kim R., Kim Y., Tam M., Lai Y., Keum N., Oldenburg C.E. Maternal caffeine consumption during pregnancy and risk of low birth weight: A dose-response meta-analysis of observational studies. *PLoS ONE.* 2015;10:e0132334. doi: 10.1371/journal.pone.0132334.
39. Barchitta M., Maugeri A., Quattrocchi A., Agrifoglio O., Agodi A. The role of miRNAs as biomarkers for pregnancy outcomes: A comprehensive review. *Int. J. Genom.* 2017;8067972. doi: 10.1155/2017/8067972.
40. Barchitta M., Maugeri A., La Rosa C.M., Magnano San Lio R., Favara G., Panella M., Cianci A., Agodi A. Single nucleotide polymorphisms in vitamin D receptor gene affect birth weight and the risk of preterm birth: Results from the “mamma & bambino” cohort and a meta-analysis. *Nutrients.* 2018;10:1172
41. Marquina C., Mousa A., Scragg R., de Courten B. Vitamin D and cardiometabolic disorders: A review of current evidence, genetic determinants and pathomechanisms. *Obes. Rev.* 2019;20:262–277. doi: 10.1111/obr.12793.
42. Dietary recommendations for children and adolescents: a guide for practitioners. Gidding SS, Dennison BA, Birch LL, Daniels SR, Gillman MW, Lichtenstein AH, Rattay KT, Steinberger J, Stettler N, Van Horn L; American Heart Association. *Pediatrics.* 2006 Feb;117(2):544-59. doi: 10.1542/peds.2005-2374. PMID: 16452380
43. Christian P, Mullany LC, Hurley KM, Katz J, Black RE. Nutrition and maternal, neonatal, and child health. *Semin Perinatol.* 2015 Aug;39(5):361-72. doi: 10.1053/j.semperi.2015.06.009.
44. Haschke F. Summary--Early Nutrition and Obesity Prevention. *Nestle Nutr Inst Workshop Ser.* 2016;85:111-2. doi: 10.1159/000441079
45. Olson M, Chambers M, Shaibi G. Pediatric Markers of Adult Cardiovascular Disease. *Curr Pediatr Rev.* 2017;13(4):255-259. doi:10.2174/1573396314666180117092010
46. Lartey A. Maternal and child nutrition in Sub-Saharan Africa: challenges and interventions. *Proc Nutr Soc.* 2008; 67(1):105-8. doi: 10.1017/S0029665108006083.

47. Koletzko B. Long-term consequences of early feeding on later obesity risk. Nestle Nutr Workshop Ser Pediatr Program. 2006; 58:1-18. doi: 10.1159/000094838.
48. de Jong N. Nutrition and senescence: healthy aging for all in the new millennium? Nutrition. 2000 Jul-Aug;16(7-8):537-41. doi: 10.1016/s0899-9007(00)00317-8. PMID: 10906548.
49. Shlisky J, Bloom DE, Beaudreault AR, et al. Nutritional Considerations for Healthy Aging and Reduction in Age-Related Chronic Disease. Adv Nutr. 2017;8(1):17-26. Published 2017 Jan 17. doi:10.3945/an.116.013474
50. Kerstetter JE, Kenny AM, Insogna KL. Dietary protein and skeletal health: a review of recent human research. Curr Opin Lipidol. 2011 Feb;22(1):16-20. doi: 10.1097/MOL.0b013e3283419441.
51. Bland JS. The use of complementary medicine for healthy aging. Altern Ther Health Med. 1998 Jul;4(4):42-8. PMID: 9656500.
52. Гігієна харчування з основами нутриціології: підручник; у 2 кн. — Г46/Т.І. Аністратенко, Т.М. Білко, О.В. Благодарова та ін.; за ред. проф. В.І. Ципріяна.— К.: Медицина, 2007. — 528 с.