Can Dietary Amino Acids Prevent Sarcopenia?

Elena Volpi, MD, PhD

Learning Objectives:
After reading this article, the participant should be able to:
1. Define sarcopenia and contrast it with other types of muscle wasting.
2. Explain the role of contractile proteins in maintaining muscle function throughout the lifespan.
3. Recall dietary interventions that may stimulate muscle protein synthesis in elderly persons.

WHAT IS SARCOPENIA?
Sarcopenia is the slow and involuntary loss of muscle mass that occurs with aging and contributes significantly to frailty and functional decline in elders. Sarcopenia is fundamentally different from other types of muscle loss, such as cancer cachexia and muscle wasting of acute injury or infectious disease. These, in fact, are characterized by a rapid decline in muscle mass, which is driven mainly by an excess inflammatory load associated with hypermetabolism and malnutrition.

The rate of muscle loss with aging is much slower, usually spanning decades, although the speed of muscle loss can vary greatly. Evidence is accumulating that sarcopenia is a multifactorial problem in which background factors, such as age and genetics, are compounded by lifestyle changes, such as reduced physical activity and malnutrition, and pathophysiological changes and/or diseases, including metabolic alterations, that may accelerate or precipitate muscle loss, functional decline, and frailty. Functional decline and frailty are fundamental causes of disability and dependence in older adults and, consequently, they are a major focus of geriatric research and clinical practice.

WHAT ARE THE DETERMINANTS OF MUSCLE FUNCTION?
Muscle function depends on mass, strength, and power (work/time). In general, muscle strength is proportional to muscle mass, but this relationship does not always hold in all circumstances. Contraction-induced changes in muscle quality, such as fiber type composition or motor unit recruitment, can improve strength to a degree greater than expected from changes in muscle mass. For example, the increase in muscle strength seen with testosterone treatment is driven basically by the hormone-induced increase in muscle mass, whereas resistance exercise (weight lifting) can induce a strength gain that may be disproportionately larger than the gain in muscle mass.

Changes in muscle mass are fundamentally due to changes in the size of muscle fibers, mainly determined by the contractile protein content, rather than changes in the number of muscle fibers. This also is true for age-related sarcopenia, where changes in muscle fiber type and a reduction in the number of nuclei in each muscle fiber are accompanied by a reduction in the contractile protein.
content of the individual fibers rather than a reduction in the total number of fibers.²

Because the proportion of contractile proteins in the muscle fibers is a fundamental determinant of muscle mass and, consequently, muscle strength, it is important to focus treatment of sarcopenia on those factors that can promote an increase in contractile protein deposition in the muscle.

**WHAT ARE THE DETERMINANTS OF MUSCLE PROTEIN CONTENT?**

Contractile muscle proteins are continuously synthesized and degraded in a dynamic process that allows for the substitution of damaged and malfunctioning proteins with newly synthesized ones. Thus, the amount of contractile proteins in the muscle is determined by the balance between their synthesis and breakdown, so that both muscle loss and gain are due to imbalances in the synthesis and breakdown equilibrium.

The net balance between protein synthesis and breakdown typically is negative in the fasting state, indicating a net protein loss. This is due to the fact that skeletal muscle is the only reservoir of amino acids for the entire body, and these amino acid reserves are mobilized during periods of fasting to support protein turnover in the other organs and tissues and to produce energy through oxidative processes. None of the amino acids are produced in the body, and once oxidized they can be replaced only from nutritional sources; for this reason, these amino acids are referred to as essential. Thus, the meal is the major anabolic time for skeletal muscle proteins, because the essential amino acids absorbed from the gut reach the muscle and are deposited in the muscle as contractile proteins.³

A number of recent studies have demonstrated that amino acids, particularly essential amino acids, can stimulate muscle protein synthesis directly. Among these, leucine appears to function as a major signal for initiation of protein synthesis. Other muscle anabolic stimuli, such as insulin, growth hormone, and testosterone, appear to function via an increase in muscle protein synthesis, and, to a lesser extent, a decrease in muscle protein breakdown. On the other hand, catabolic stimuli can both decrease muscle protein synthesis and increase breakdown, thereby accelerating amino acid output from the muscle and decreasing the protein content in the muscle fiber.

**WHAT IS THE ROLE OF DIETARY AMINO ACIDS IN SARCOPENIA?**

An adequate intake of dietary amino acids is of pivotal importance for the maintenance of muscle mass. In fact, a recent longitudinal study has highlighted that the rate of decline of lean body mass in older adults is inversely proportional to the amount of protein in the diet: the higher the protein intake the slower the lean mass loss.³

Progressive nutritional changes also have been reported with aging, and include reduced food intake and changes in food preference, which, in turn, can predispose to protein malnutrition and accelerate sarcopenia. These changes have been attributed to many causes, including poor dietary protein intake the slower the lean mass loss.³

*Mr. Lomangino and Dr. Gray have disclosed that they have no significant relationships with or financial interests in any commercial organizations pertaining to this educational activity.*
dentine, changes in taste, and social factors, and typically are subtle and slowly progressive.

Other studies have also suggested that the protein requirements of older individuals may be higher than the RDA of 0.8 g/kg/day; and for this reason, there is ongoing discussion in the scientific community regarding the optimal protein intake for older persons. Several reasons have been advocated for such an increase in protein requirements. Our group and others have found resistance of skeletal muscle proteins to the anabolic action of a mixed meal in older individuals. This can be attributed, at least in part, to a reduced response of skeletal muscle proteins to insulin, independent of glucose tolerance (i.e., a defect measurable also in nondiabetic older persons). The specific mechanisms are still unclear, but it appears that they involve both a reduction in the vasodilatory action of insulin, with consequent lack of the physiological increase in muscle perfusion and nutrient flow during the meal, and altered anabolic signaling in the skeletal muscle. This insulin resistance of muscle proteins may be overcome by aerobic exercise, which underscores how this alteration may have some points in common with the insulin resistance of type 2 diabetes.

Another problem, highlighted by other studies, is that whereas muscle tissue in older individuals maintains the capacity to respond to a maximal amino acid or protein load, the response of skeletal muscle proteins to low amino acid intakes is reduced. Interestingly, the resistance of muscle proteins to both amino acids and a mixed meal can be overcome by the administration of excess leucine. Based on the recently published data, it has been estimated that the amount of leucine necessary to induce a muscle protein anabolic response in older subjects is about 3 g, which corresponds to approximately 30 g of a high-quality protein. This roughly corresponds to 4 oz of fish or meat, five eggs, or 1 L of milk. Such an amount of protein typically is eaten only during one of the daily meals, but in many older persons, this level of protein intake is never reached in a single meal.

These recent findings provide a likely explanation for an earlier finding showing that nitrogen retention is enhanced in older individuals when they are given most of their RDA for protein (0.8 g/kg/day) in a single meal. A series of studies also has shown that the rate of digestion of dietary proteins may significantly affect the anabolic response in older muscle. Rapidly digested proteins exert a larger anabolic effect than does the same amount of protein digested slowly. This result seems to be related to the differential effects of the two types of proteins on blood amino acid concentrations, with the protein inducing the larger increase being more effective in stimulating muscle protein deposition.

CLINICAL IMPLICATIONS
From the data available thus far, it is possible to conclude that dietary amino acids play a fundamental role in the maintenance or loss of muscle with aging. The reduced ability of skeletal muscle to respond to the nutritional stimulus with increased protein deposition in older adults may contribute significantly to sarcopenia. However, large increases in blood amino acid concentrations, particularly leucine concentration, can overcome this anabolic resistance of aging and promote protein accumulation in the muscle. Such large increases in amino acid concentrations can be achieved by increasing the total amount of amino acids/proteins provided with each individual meal and using rapidly digested proteins with high leucine content. Another potential avenue is utilizing protein supplements devoid of carbohydrate between meals to provide an additional protein anabolic stimulus. Increasing physical activity also is highly beneficial and may reduce or eliminate the muscle protein resistance to feeding.

However, it is important to underscore that these concepts derive from acute studies. Such studies do not address the more clinically relevant question of whether the RDA for protein in older adults should be increased for prevention of sarcopenia, or whether it would be sufficient to modify the quality and pattern of protein intake within the current recommendations.

One of the major concerns with increasing protein intake in older adults regards its potential effects on renal function. Although no compelling evidence of a direct negative effect of increased amino acid/protein intake on renal function has been reported, it is important to remember that renal function is decreased in a number of older adults and that nitrogen overload in these patients could be harmful. The debate in the scientific community is ongoing, and prospective long-term trials are necessary to establish clearly not...
The current recommended dietary allowance (RDA) values for protein have been widely misinterpreted by the clinical community, according to a recent commentary in the Journal of the American Medical Association. The RDA, by definition, is the minimum amount of protein needed to avoid a deficiency that would lead to progressive loss of lean body mass. However, many clinicians mistakenly view the RDA as an appropriate or optimal daily intake of this macronutrient, say Robert R. Wolfe, PhD, of the University of Arkansas for Medical Sciences, Little Rock, AR, and his coauthor, Sharon L. Miller, PhD.

Guidelines based on this flawed interpretation may substantially underestimate the appropriate amount of protein to consume for optimal health, the authors say. They note that the USDA’s dietary guidelines, as well as the government’s school lunch and Meals on Wheels programs, all use the RDA of 0.8 g/kg/day as the recommended (not the minimum) amount of protein intake. “More persuasively,” they add, “dietary guidelines published in the dietetic literature, the popular press, and various nutritional computer programs promulgate a protein intake of 0.8 g/kg/d,” they say.

While the RDA for protein is thought to be adequate to prevent a negative nitrogen balance and associated muscle loss, it was never intended to serve as a target intake for improving function or decreasing chronic disease risk, according to Wolfe and Miller. To the contrary, “There is ample evidence that the optimal level of protein intake is greater than the RDA,” they comment. “A variety of studies have shown levels of protein intake above the RDA benefiting muscle mass, strength, and function, bone health, maintenance of energy balance, cardiovascular function, and wound healing.”

IS RDA A MISNOMER?

How did so much confusion arise over a seemingly basic nutritional concept? In an interview, Wolfe cast some of the blame on clinicians “for never actually reading the [Dietary Reference Intake (DRI)] report” and understanding what the RDA means. The concept is defined there quite clearly as “an estimate of the minimum daily average dietary intake level that meets the nutrient requirements of nearly all (97 to 98 percent) healthy individuals.”

But perhaps a larger contributing problem may be the fact that the RDA is, in Wolfe’s view, a misnomer. “Recommended Dietary Allowance’ sounds like the recommended amount you should eat,” Wolfe says. “I don’t know how else you would interpret that.” He suggests that the term “minimal daily requirement” would do a better job of expressing the RDA concept and should replace the term “RDA” in future DRI updates.

The misapplication of the RDA probably has led to a distorted view of how much protein, as well as other macronutrients, the general population

REFERENCES
1. Fried LP, Hadley EC, Walston JD, et al. From bedside to bench: research agenda for frailty. Sci Aging Knowledge Environ 2005;2005:e24.
2. Lexell J. Human aging, muscle mass, and fiber type composition. J Gerontol A Biol Sci Med Sci 1995 Nov; 50 Spec No:11-16.
3. Timmerman KL, Volpi E. Amino acid metabolism and regulatory effects in aging. Curr Opin Clin Nutr Metab Care 2008;11:45-49.
4. Houston DK, Nicklas BJ, Ding J, et al. Dietary protein intake is associated with lean mass change in older, community-dwelling adults: the Health, Aging, and Body Composition (Health ABC) Study. Am J Clin Nutr 2008;87:150-155.
5. Paddon-Jones D, Short KR, Campbell WW, Volpi E, Wolfe RR. Role of dietary protein in the sarcopenia of aging. Am J Clin Nutr 2008;87:1562S-1566S.
should be eating, according to Wolfe. “If a dietitian calculates out what your dietary intake should be, and they use 0.8 as a guideline, it’s actually very hard to eat that small of an amount of protein each day,” he says. “And so it’s led to the general perception that we eat too much protein.” When protein intake is restricted, Wolfe adds, people will tend to fill the resulting energy void with other macronutrients that may be less healthy for them in the long run. “The jump that people don’t realize they’re making when they give these recommendations about protein intake is that they’re actually saying, ‘So what you need to do is increase your fat and carbohydrate intake,’” he says.

**IMPACT ON THE ELDERLY**

The effects of too little protein would be felt most keenly by elderly persons. Emerging data suggest that even the RDA is an inadequate amount of protein for this population. Moreover, elderly persons are more likely to rely on government programs that use the RDA as the basis for their menu selection. Wolfe notes that the RDA sometimes is adopted as the maximum amount of protein that such programs will provide to their clients. “At the Meals on Wheels program in Arkansas,” he says, “they’ll absolutely figure out how much protein is there, and if someone wants an extra slice of ham, well, they’re going to stick to that 0.8 guideline.”

The problem may be pervasive but can be easily addressed by a simple shift in emphasis, Wolfe claims. He notes that the DRI report also includes an Acceptable Macronutrient Distribution Range (AMDR) for protein and other macronutrients. This is defined as a range of intakes that provides adequate essential nutrients and is associated with reduced risk of chronic diseases. Noting that the definition for the AMDR is actually quite similar to the widely perceived meaning of the RDA, he suggests that clinicians abandon the RDA and adopt the AMDRs as the recommended target for intake. The RDA could then be discontinued in favor of the more precise “minimal daily requirement.”

“The solution to the dilemma of widespread misinterpretation of the RDA for macronutrients, particularly for protein, would be to accept that a discrete value cannot be assigned to each macronutrient and to use the AMDR to express the recommended intakes,” Wolfe and Miller conclude.

**REFERENCE**

1. Wolfe RR, Miller SL. The recommended dietary allowance of protein: a misunderstood concept. *JAMA* 2008;299:2891-2893.

---

**Choline: Update on an Essential Nutrient**

Kevin Lomangino  
Editor, *Clinical Nutrition Insight*

Learning Objective:  
After reading this article, the participant should be able to state current dietary recommendations for choline and describe which populations may be at risk of inadequate intake.

Although investigators have been studying choline since as far back as the 1860s, it is only within the past decade that we have formally recognized this compound as an essential nutrient requiring a minimum dietary intake. Current adequate intake (AI) recommendations for choline reflect the lowest amounts that were needed to correct liver dysfunction during the tightly controlled administration of a choline-deficient diet (Table 1).

However, higher intake levels may be required to realize other choline-related health benefits that have been hinted at by recent research. These include prevention of neural tube defects, optimization of fetal neurodevelopment, and improved memory and cognition during adulthood. In addition, an emerging body of epidemiologic data suggests a possible role for choline in the prevention of...
chronic diseases associated with inflammation.

**WHAT IS CHOLINE?**

Choline is a basic cell-building block that serves a number of biological functions. It is necessary for production of the phospholipids that are a key component of all human cell membranes. It also is used to make acetylcholine, a neurotransmitter, as well as lipoproteins, which shuttle fat and cholesterol around the body. Choline also is a precursor of betaine, a key methyl group donor that helps keep homocysteine in check by facilitating its conversion to methionine. Elevated homocysteine levels are associated with increased risk of cardiovascular disease and neural tube defects (NTDs). (The source cited in reference 1 provides a detailed review of choline metabolism.)

**CHOLINE AND LIVER FUNCTION**

Acute deficiency of choline results in the impaired synthesis of lipoprotein particles needed to export fat from the liver. This causes a buildup of hepatic triglycerides and the subsequent development of fatty liver. Choline deficiency also can cause liver damage (as indicated by elevated aspartate aminotransferase [AST] levels) and skeletal muscle dysfunction (marked by elevated creatinine phosphokinase [CPK] levels). Some of these signs have been observed clinically in patients receiving total parenteral nutrition (TPN) with no source of dietary choline. The fatty liver associated with TPN was reported to resolve in some patients with choline supplementation, then return again once the original choline-deficient solution was reinstated.

**FETAL GROWTH AND DEVELOPMENT**

Choline requirements are increased during pregnancy to ensure that the needs of the developing fetus are met. In rodents, choline deficiency leads to impaired development of the fetal brain septum and hippocampus, whereas supplementation with choline in utero leads to lifelong improvement in memory and function. In addition, both rodent and human studies suggest that choline is important to ensure closure of the fetal neural tube.

One recent cross-sectional study looked at periconceptional choline intake and its association with fetal NTDs among mothers of 424 children with NTD and mothers of 440 healthy controls. Results show that women in the lowest quartile of choline intake had double the risk of a fetal NTD compared with women in the highest quartile.

**CHRONIC DISEASE PREVENTION**

The relation between choline and chronic disease prevention previously had been difficult to study due to the lack of food composition tables that included this nutrient. The recent publication of these data by the USDA has led to a flurry of epidemiologic studies exploring these links. Increased choline and betaine intake was associated with reduced homocysteine levels in both the Nurses’ Health Study and the Framingham Heart Study. While this result has been widely interpreted as suggesting a prevention benefit for choline with respect to cardiovascular disease, a large body of randomized trial data now indicates that other homocysteine-lowering agents (e.g., B vitamins) have little or no effect on cardiovascular outcomes. These finding cast doubt on the clinical significance of choline’s homocysteine-lowering effects—at least with respect to cardiovascular disease and stroke.

However, other studies suggest additional mechanisms through which choline and betaine may exert a beneficial impact. A recent cross-sectional study from Greece, for example, showed that higher intakes of choline and betaine were associated with lower levels of inflammatory markers such as plasma C-reactive protein, interleukin-6, and tumor necrosis factor-alpha. In addition, findings from the Long Island Breast Cancer Study showed a reduced incidence of breast cancer for women in the highest quintile of choline intake compared with those in the lowest.

**OPTIMIZING INTAKE**

Just how much choline we need for optimum health is a challenging research question that will require further study. However, the Adequate Intake (AI) recommendations for choline are provided in Table 1.

---

**Table 1. Adequate Intake Recommendations For Choline**

| Life Stage | Adequate Intake (mg) |
|------------|----------------------|
| 0–6 mo     | 125                  |
| 7–12 mo    | 150                  |
| 1–3 y      | 200                  |
| 4–8 y      | 250                  |
| **Males**  |                      |
| 9–13 y     | 375                  |
| >13 y      | 550                  |
| **Females**|                      |
| 9–13 y     | 375                  |
| 13–19 y    | 400                  |
| >19 y      | 425                  |
| **Pregnant**|                     |
|            | 450                  |
| **Lactating**|                    |
|            | 550                  |

Data from Food and Nutrition Board, Institute of Medicine. Dietary Reference Intakes: Thiamin, Riboflavin, Niacin, Vitamin B-6, Vitamin B-12, Pantothenic Acid, Biotin, and Choline. Washington, DC: National Academy Press, 1998:390-422.
much more study to establish, according to Leslie Fischer, PhD, MPH, RD, a researcher at the University of North Carolina, Chapel Hill, who works with Steve Zeisel, MD, PhD, the noted choline expert. She says that after current AIs were issued in 1998, their research team spent five years attempting to further refine the dietary requirements for choline and help establish an Estimated Average Requirement (EAR). They assessed how 57 healthy men and women responded to choline intakes at the current AI (550 mg/d) followed by an experimental low-choline diet containing less than 50 mg/d.5

“What we discovered is that there is not a one-size-fits-all requirement for choline; there are, in fact, people who need very little choline because their endogenous production is ample enough to make what they need on their own,” Fischer commented in an interview. “But there are also people out there who need a lot more choline than the current Adequate Intake level and who manifest symptoms of choline deficiency (namely liver and/or muscle dysfunction) when ingesting choline at this level of intake.”

The experimental choline-deficient diet produced organ dysfunction in 77% of the men and 80% of the postmenopausal women, Fischer and her colleagues reported, while only 44% of the premenopausal women developed such symptoms after 42 days of choline restriction. Interestingly, six of the 26 men in the study also developed organ dysfunction after 10 days on the diet that contained the current AI of 550 mg/d of choline. This suggests that the current AI may not provide enough choline for a substantial minority of the male population.

**Figure 1.** Common food sources of choline. (Reprinted from USDA National Nutrient Database for Standard Reference, Release 20; www.nal.usda.gov/fnic/foodcomp/Data/sr20/nutrientlist/sr20w421.pdf.)

**CLINICAL CONSIDERATIONS**

Choline is abundant in the food supply (Figure 1) and is consumed most commonly as phosphatidylcholine (lecithin). Individuals who eat a balanced diet are unlikely to become deficient in this nutrient. Still, Fischer says that there are several populations for whom ensuring adequate intake is a clinical priority. Noting that eggs are an especially rich source of choline, she advises pregnant and lactating women to eat two to three eggs per day to provide adequate quantities of choline to the fetus or infant. She adds that clinicians should consider potential choline deficiency in patients with unexplained elevations in liver function tests or liver fat (e.g. non-alcoholic fatty liver disease) or elevated CPK.

**SUPPLEMENTATION**

Despite a wealth of promising lab data, there is little clinical evidence that choline supplementation provides health benefits beyond the prevention of deficiency-related liver dysfunction. Several small, short-term studies have reported that choline supplementation improved memory in healthy volunteers as well as patients with dementias. But other studies reported no such benefits, and there is no clinical consensus in favor of choline supplementation for this purpose.

Although supplementation trials in adults have been mixed, Fischer and Zeisel hypothesize that increased choline intake could permanently enhance brain function if provided during a critical window of fetal and/or early childhood development. Their team currently is exploring the concept in a supplementation trial involving pregnant and lactating women. The data have not yet been reported, but the supporting animal studies suggest that there is reason to be optimistic, according to Fischer—at least in a subset of individuals who have greater dietary requirements for choline. “It has been shown repeatedly that if extra choline is given to pregnant rodents, the pups born to these dams have enhanced memory and are less susceptible to age-related dementia,” she says. The first report from this study is expected in late 2009.

**REFERENCES**

1. Zeisel SH. Choline: critical role during fetal development and dietary requirements in adults. *Annu Rev Nutr* 2006;26:229-250.
2. Shaw GM, Carmichael SL, Yang W, et al. Periconceptional dietary intake of choline and betaine and neural tube defects in offspring. *Am J Epidemiol* 2004;160:102-109.
3. Detopoulou P, Panagiotakos DB, Antonopoulou S, et al. Dietary choline and betaine intakes in relation to concentrations of inflammatory markers in healthy adults: the ATTICA study. *Am J Clin Nutr* 2008;87:424-430.
4. Xu X, Gammon MD, Zeisel SH, et al. Choline metabolism and risk of breast cancer in a population-based study. *FASEB J* 2008;22:2045-2052. Epub 2008 Jan 29.
5. Fischer LM, daCosta KA, Kwock L, et al. Sex and menopausal status influence human dietary requirements for the nutrient choline. *Am J Clin Nutr* 2007;85:1275-1285.
Children who are at risk of obesity, or who have a family history of cardiovascular disease, should be given reduced-fat milk instead of whole milk between the ages of 12 months and two years, according to recently issued guidelines from the American Academy of Pediatrics (AAP). Previous AAP recommendations had emphasized that whole milk, and the saturated fat it contains, was essential for the neurodevelopment of all children during this critical growth period. But now the organization says that lower-fat milk would be a better choice for toddlers when “overweight or obesity is a concern” or when there is “a family history of obesity, dyslipidemia, or CVD [cardiovascular disease].”

The change was prompted by new research suggesting that a fat-reduced diet does not adversely affect development, according to guideline authors Stephen R. Daniels, MD, PhD, of the University of Colorado School of Medicine, and Frank R. Greer, MD, of the University of Wisconsin School of Medicine and Public Health. They cite data from the Special Turku Risk Intervention Program study from Finland, which was a randomized controlled trial of a reduced fat dietary intervention for children. Members of the intervention group were assigned to a diet in which total fat accounted for less than 30% of calories, saturated fat accounted for less than 10% of calories, and cholesterol intake was below 200 mg/day, using 1.5% cow milk after 12 months of age. The study involved 1062 children enrolled at approximately 7 months of age.

LOW-FAT BENEFITS
Assessment of the children at age five years revealed no adverse effect of the intervention on neurodevelopmental outcomes. Subsequent follow-up showed potential benefits from the intervention, including reduced LDL concentrations among boys at age seven years, as well as decreased prevalence of overweight among girls at age 10 years, compared with controls. These results, combined with those of other studies, “indicate that there is no harm associated with prudent diet changes, even when they are instituted in children soon after weaning,” according to the AAP report. “This includes use of reduced-fat milk in children after 12 months of age.”

The change reflects growing understanding of how cardiovascular disease develops and progresses throughout the lifespan, according to the report. The authors note that many CVD risk factors, including elevated LDL, high blood pressure, and obesity, can be present at an early age and may foreshadow adult disease. They add that rising rates of childhood obesity make early interventions to address these risk factors an urgent public health priority.

“The current obesity epidemic among children has increased the need for pediatric health care professionals to be knowledgeable of the risk factors for CVD and to implement the changes recommended in this report in practice,” the AAP authors conclude.

The milk guidance is part of an overall emphasis on early dietary changes to help prevent...
future cardiovascular disease. All children over the age of two years should follow the healthful diet recommended in Dietary Guidelines for Americans, according to the report, while those at high risk of CVD should take additional steps, including reducing saturated fat to 7% of total calories and dietary cholesterol to 200 mg/day. The report also recommends earlier cholesterol screening (between ages 2 and 10 years) for children with a family history of CVD or dyslipidemia, or with other cardiovascular risk factors such as being overweight or obese, hypertension, diabetes, or smoking.

THE USPSTF PERSPECTIVE
The authors suggest that dietary interventions in childhood can help lower the lifelong risk of CVD and pose little risk of adverse effects. But others who have reviewed the data are more circumspect regarding the potential benefits. A recent U.S. Preventive Services Task Force (USPSTF) report noted that despite the compelling logic of early intervention, “There is no evidence that diet or exercise interventions in childhood lead to improved lipid profiles or better health outcomes in adulthood.” The report also expressed greater concern about the potential for harm from low-fat dietary interventions. Although most studies that have tested low-fat diets in children indicate no adverse effects on growth and development, a few studies have reported that such diets are associated with growth failure in children and adolescents. In one particularly worrisome example cited by the USPSTF, growth failure was observed in eight of 40 (20%) children assigned to a low-fat diet, three of whom had nutritional dwarfing. These findings contributed to the Task Force conclusion that “Adverse effects from lipid-lowering medications and low-fat diets, including potential long-term harms, have been inadequately evaluated in children.”

The AAP report acknowledges what it describes as “anecdotal reports” of nutritional insufficiency during a very low-fat diet intervention, but it notes that the diets were implemented by parents without supervision from nutrition professionals. A dietitian’s involvement can provide assurance that families are “[making] the appropriate changes without compromising good nutrition,” the report states.

REFERENCES
1. Daniels SR, Greer FR. Lipid screening and cardiovascular health in childhood. Pediatrics 2008;122:198-208.
2. Hakanen M, Lagström H, Kaitosaari T, et al. Development of overweight in an atherosclerosis prevention trial starting in early childhood. The STRIP study. Int J Obes (Lond) 2006;30:618-626.
3. US Preventive Services Task Force. Screening for lipid disorders in children: US Preventive Task Force recommendation statement. Pediatrics 2007;120(1):e215-219; www.pediatrics.org/cgi/content/full/120/1/e215.

View past,* current, and future issues of your paid subscription to Clinical Nutrition Insight online for free! Follow these instructions to log on to your account.

1. Locate your 12-digit account number on the mailing label of your current issue.
2. Go to: www.lwwnewsletters.com.
3. From the choices on the top yellow toolbar, select “Sign On.”
4. In the spaces provided, enter your “Username” and “Password.” Your username will be the letters LWW (case sensitive) followed by the 12-digit account number on your address label. We have provided an easy-to-remember “default” password for you. Simply type the numbers 1234. (This password cannot be changed.)
5. Click “Sign On.”
6. Click “Access My Account.”
7. Click “View or Renew Subscriptions.” Click on “Clinical Nutrition Insight,” and select the current or archive issue you wish to view. All issues are posted in PDF format. You will need Adobe Acrobat Reader installed on your computer to view the issues. To download your free copy of Acrobat Reader, visit www.Adobe.com.

If you have any questions or problems regarding your print or electronic account, please call 1-800-787-8981.

* Archive issues are available as far back as 1999.
Clinical Nutrition INSIGHT CME QUIZ

To earn CME credit, you must read the CME articles and complete the quiz and evaluation assessment survey on the other side of this form, answering at least 70% of the quiz questions correctly. Select the best answer and use a blue or black pen to completely fill in the corresponding space on the enclosed answer form. Please indicate any name and address changes directly on the answer form. If your name and address do not appear on the answer form, please print that information in the blank space at the top left of the page. Only two entries will be considered for credit. Make a photocopy of the completed answer form for your own files and mail the original answer form in the enclosed postage-paid business reply envelope by June 30, 2009, for ADA and AAFCS credit or September 30, 2009, for AMA, DMA, and NOA credit. For more information, call (800) 787-8981.

Online quiz instructions: To take the quiz online, go to http://cme.LWWnewsletters.com, and enter your username and password. Your username will be the letters LWW (case sensitive) followed by the 12-digit account number on your mailing label. You may also find your account number on the paper answer form mailed with your issue. Your password will be 1234; this password may not be changed. Follow the instructions on the site. You may print your official certificate immediately. Please note: Lippincott CME Institute, Inc., will not mail certificates to online participants.

Lippincott Continuing Medical Education Institute, Inc., is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. Lippincott Continuing Medical Education Institute, Inc., designates this educational activity for a maximum of 1.5 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

This continuing education program meets the criteria for one hour of credit as established by the Commission on Dietetic Registration of the American Dietetic Association, American Association of Family and Consumer Sciences, and the Dietary Managers Association. The program on which this test is based is part of the Clinical Nutrition Insight curriculum, which is designed to serve the clinical nutrition needs of the Registered Dietitian, Dietetic Technician, Registered Dietary Manager, and the Certified Home Economist. Each issue of the newsletter will contain a test that will count toward continuing education credits.

Clinical Nutrition INSIGHT 2008–2009 curriculum

JUNE 2008
Controversies in Using the Glycemic Index, by Susan Raatz, PhD, Division of Endocrinology and Metabolism, University of Minnesota, Minneapolis

JULY 2008
The Growing Latino Community: New Challenges for Nutrition and Health Professionals in the United States, by Hugo Melgar-Quinonez, MD, PhD, Department of Human Nutrition, The Ohio State University

AUGUST 2008
Viscosity of Dysphagia Diet Foods: Are Published Values Accurate?, by Bruce K. Rubin MEgr, MD, Professor and Vice Chair for Research, Department of Pediatrics, Wake Forest University School of Medicine, and colleagues

SEPTEMBER 2008
Management of Diabetes in the Patient Receiving Nutrition Support, by Else M. Brett, MD, FACE, CNSP, Mount Sinai School of Medicine, New York

OCTOBER 2008
Can Dietary Amino Acids Prevent Sarcopenia?, by Elena Volpi, MD, PhD, Assistant Vice Chair for Research, Department of Internal Medicine, University of Texas Medical Branch

NOVEMBER 2008
Omega-3 Fatty Acids in the Treatment of Cancer Cachexia, by Michael Tisdale, PhD, DSc, of the Pharmaceutical Sciences Research Institute, Aston University, Birmingham, UK

DECEMBER 2008
Low-CHO Diets and Diabetes, by Richard Feinman, PhD, State University of New York Downstate Medical Center

JANUARY 2009
Reasons for Failed Weight Loss Surgery, by Mark D. Rusch, PhD, Medical College of Wisconsin

FEBRUARY 2009
Fish Oil: Magic or Drug?, by Gerard E. Mullin, MD, Division of Gastroenterology and Liver Disease Johns Hopkins Hospital

MARCH 2009
Diet and Fertility, by Elizabeth Ruder, PhD, Penn State University
1. Sarcopenia is defined as
   A. rapid muscle wasting brought on by an inflammatory response to cancer
   B. rapid muscle wasting primarily due to infection
   C. slow and involuntary loss of muscle mass that occurs with aging
   D. none of the above

2. Which of the following factors contribute to sarcopenia?
   A. Age and genetics
   B. Lifestyle changes such as reduced physical activity and malnutrition
   C. Pathophysiological changes and/or diseases, including metabolic alterations
   D. All of the above

3. Intake of which one of the following appears to function as a major signal for protein synthesis in skeletal muscle?
   A. Eicosapentaenoic acid
   B. Leucine
   C. Histidine
   D. Proline

4. According to recent data, approximately what amount of leucine is necessary to induce a muscle protein anabolic response in older subjects?
   A. 1 g
   B. 2 g
   C. 3 g
   D. 4 g

5. Increased protein/amino acid intake may be harmful for older adults who also have
   A. impaired renal function
   B. elevated LDL cholesterol
   C. benign prostatic hyperplasia
   D. cardiomyopathy

6. The current recommended dietary allowance for protein is 0.8 g/kg/day.
   A. True
   B. False

7. The Acceptable Macronutrient Distribution Range for protein is
   A. 20% to 35% of total energy
   B. 10% to 35% of total energy
   C. 45% to 65% of total energy
   D. none of the above

8. The American Academy of Pediatrics recommends reduced-fat cow’s milk for children between 12 months and two years of age with a family history of
   A. casein allergy
   B. dyslipidemia
   C. celiac disease
   D. multiple sclerosis

9. Low maternal intake of choline has been associated with what pregnancy-related outcome?
   A. Higher risk of neural tube defects
   B. Higher risk of preeclampsia
   C. Higher risk of gestational diabetes
   D. None of the above

10. In a study by Fischer et al., six of 26 men developed organ dysfunction after 10 days on a diet that contained the current AI of 550 mg/d of choline.
    A. True
    B. False

---

Omega-3 Fatty Acids in the Treatment of Cancer Cachexia, by Michael Tisdale, PhD, DSc, of the Pharmaceutical Sciences Research Institute, Aston University, Birmingham, UK.
**NEWS BITES**

**STUDY QUESTIONS FREQUENT LIPID TESTING**

Once they reach their cholesterol targets, patients on lipid-lowering therapies should be monitored much less frequently than current guidelines recommend, the authors of a new analysis suggest. Most national lipid management guidelines advise semi-annual testing once treatment goals have been achieved, according to Paul P. Glasziou, MBBS, PhD, of Oxford University, and colleagues. However, tests conducted this often are likely to pick up misleading short-term lipid spikes instead of true increases in cholesterol levels that warrant clinical attention, the researchers say. “Much of current testing will detect only false-positive results—that is, changes that are related to either short-term biological variation or analytic error,” Glasziou et al conclude. (See *Ann Intern Med* 2008;148:656-661.)

The researchers analyzed data on 9,014 patients with coronary heart disease randomized to receive pravastatin or placebo. Lipids levels were checked at randomization, 6 and 12 months later, and then annually for five years. The authors used mathematical modeling to estimate short-term within-person variation as well as longer-term “true” variability in cholesterol levels. The results show that short-term within-person variation in total cholesterol was 7%, or approximately ±31 mg/dL, whereas true long-term variation in cholesterol levels was considerably smaller. It took about three years for changes in the true cholesterol levels to equal those attributable to short-term changes, the researchers found.

Frequent testing of patients with well-controlled cholesterol levels (i.e. at least 19 mg/dL under target) identified many more false-positives than true increases in LDL, the researchers say. Based on these findings, “retesting adherent patients every 3 to 5 years may be sufficient once adequate response has been attained,” Glasziou et al conclude.

**DIET WARS CONTINUED**

Consistent with a growing body of clinical trial data, results from a new study suggest that three different diet approaches—low-fat, low-carbohydrate, and the Mediterranean diet—produce similar, relatively small amounts of weight loss and have similar beneficial effects on lipid profiles. The researchers studied 322 participants (277 men and 45 women) who worked in an isolated nuclear research facility in Israel and ate lunch (the largest meal of the day in Israel) in a communal cafeteria. The researchers randomly assigned the participants to one of the three diet plans, which respectively called for the consumption of 30% of calories from fat and no more than 10% from saturated fat (low-fat group); 35% of calories from fat with an emphasis on monounsaturated sources (Mediterranean diet); or 20 g of carbohydrate per day during induction followed by an increase to 120 g per day (low-carbohydrate). The authors provided regular nutrition counseling, as well as color-coded foods in the cafeteria, to assist with compliance. The research was partially funded by the Atkins Research Foundation. (See *N Engl J Med* 2008;359:229-241.)

After two years, participants in the low-fat group lost 2.9 kg, compared with 4.4 kg for the Mediterranean-diet group and 4.7 kg for the low-carbohydrate group. In addition, all three diets produced a modest beneficial effect on lipid profiles—although the changes observed in the low-carbohydrate group were significantly larger for HDL cholesterol, triglycerides, and the ratio of total to HDL cholesterol, compared with the low-fat group. The researchers conclude that low-carbohydrate and Mediterranean diets are “effective alternatives to the low-fat diet for weight loss and appear to be just as safe.” Adding that the low-carbohydrate and Mediterranean diets appeared to have superior metabolic effects compared with the low-fat diet, they said that these dietary strategies “might be considered in clinical practice” and should be “individualized according to personal preferences and metabolic needs.”

Reaction to the study has been predictably heated, with low-fat advocates such as Dean Ornish noting in *Newsweek* that the low-carbohydrate dieters in the study “were counseled to choose vegetarian sources of fat and protein” and were not eating a traditional Atkins diet. Others, such as the nutrition writer Gary Taubes, point out that that the low-carbohydrate group ate more saturated fat, and yet had better lipid profiles, compared with the low-fat group. “Why does the [American Heart Association] continue to insist that saturated fat should be avoided, if these trials repeatedly show that high saturated fat diets lead to better cholesterol profiles than low-saturated fat diets?” Taubes wondered in an interview in *The New York Times.*

---

**DIET WARS CONTINUED**

Consistent with a growing body of clinical trial data, results from a new study suggest that three different diet approaches—low-fat, low-carbohydrate, and the Mediterranean diet—produce similar, relatively small amounts of weight loss and have similar beneficial effects on lipid profiles. The researchers studied 322 participants (277 men and 45 women) who worked in an isolated nuclear research facility in Israel and ate lunch (the largest meal of the day in Israel) in a communal cafeteria. The researchers randomly assigned the participants to one of the three diet plans, which respectively called for the consumption of 30% of calories from fat and no more than 10% from saturated fat (low-fat group); 35% of calories from fat with an emphasis on monounsaturated sources (Mediterranean diet); or 20 g of carbohydrate per day during induction followed by an increase to 120 g per day (low-carbohydrate). The authors provided regular nutrition counseling, as well as color-coded foods in the cafeteria, to assist with compliance. The research was partially funded by the Atkins Research Foundation. (See *N Engl J Med* 2008;359:229-241.)

After two years, participants in the low-fat group lost 2.9 kg, compared with 4.4 kg for the Mediterranean-diet group and 4.7 kg for the low-carbohydrate group. In addition, all three diets produced a modest beneficial effect on lipid profiles—although the changes observed in the low-carbohydrate group were significantly larger for HDL cholesterol, triglycerides, and the ratio of total to HDL cholesterol, compared with the low-fat group. The researchers conclude that low-carbohydrate and Mediterranean diets are “effective alternatives to the low-fat diet for weight loss and appear to be just as safe.” Adding that the low-carbohydrate and Mediterranean diets appeared to have superior metabolic effects compared with the low-fat diet, they said that these dietary strategies “might be considered in clinical practice” and should be “individualized according to personal preferences and metabolic needs.”

Reaction to the study has been predictably heated, with low-fat advocates such as Dean Ornish noting in *Newsweek* that the low-carbohydrate dieters in the study “were counseled to choose vegetarian sources of fat and protein” and were not eating a traditional Atkins diet. Others, such as the nutrition writer Gary Taubes, point out that that the low-carbohydrate group ate more saturated fat, and yet had better lipid profiles, compared with the low-fat group. “Why does the [American Heart Association] continue to insist that saturated fat should be avoided, if these trials repeatedly show that high saturated fat diets lead to better cholesterol profiles than low-saturated fat diets?” Taubes wondered in an interview in *The New York Times.*