

# Therapeutic Diets in Clinical Practice: An Anti-Inflammatory Diet and Other Dietary Approaches

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## Educational Goals:

1. Appreciate the role that diet plays in the prevention and adjuvant treatment of diseases, especially cardiovascular disease (CVD), diabetes, gastrointestinal disorders, cancer, neurodegenerative diseases and others.
2. Identify characteristics of therapeutic diets that are important, and the mechanisms through which dietary guidelines may have beneficial effects.
3. Understand the composition of therapeutic diets and the specific foods included (eg. for meals, as snacks and beverages), which may have clinical benefits.
4. Understand what constitutes an anti-inflammatory diet.

## Introduction: Overview of Dietary Guidelines and Research

The increase in the prevalence of overweight, obesity, Type 2 Diabetes Mellitus (T2DM) and related diseases has led to the renewed recognition that diet and exercise are essential parts of an effective medical management program for these disorders. In order to understand what dietary guidelines can be helpful, it is important to understand what dietary research has been done over the last 30-40 years, as well as the factors and influences that have guided this process. Consistent throughout these years, has been the inclusion of natural and healthy foods, with balanced dietary guidelines that include significant servings of vegetables, whole grains, beans/legumes, fruit, nuts/seeds and other foods. This dietary pattern could be called a vegetarian-based diet.

Dietary choices can increase nutrient and phytonutrient intake, as well as limit the intake of foods/beverages that can impair health and well-being. To the extent that dietary guidelines may maximize benefits and minimize potential adverse effects, therapeutic diets and nutrition can be considered for most, if not all, chronic diseases. The following outline and the lecture will review and analyze dietary guidelines, therapeutic considerations, research and related issues.

### Vegetarian Diets

The two primary types of vegetarian diets are: (a) lacto-ovo vegetarian (includes dairy products and eggs; excludes fish, poultry and meat); and (b) vegan or strict vegetarian (excludes all animal products). Dietary practices are often not rigid, however, so many people will include fish.

The Lifestyle Heart Trial published in the Lancet in 1990 was a landmark study that showed that the Ornish Diet (10% kcal from fat; largely vegetarian) and lifestyle factors could reverse CVD (Ornish, 1990). This led to a large shift in dietary recommendations toward high carbohydrate and low fat guidelines. A primary problem is that it is very difficult to follow such a low fat diet, so compliance and generalizability are important concerns. It was also not well acknowledged that the lifestyle factors (regular exercise and daily relaxation techniques) had significant benefits as well.

## Therapeutic Diets

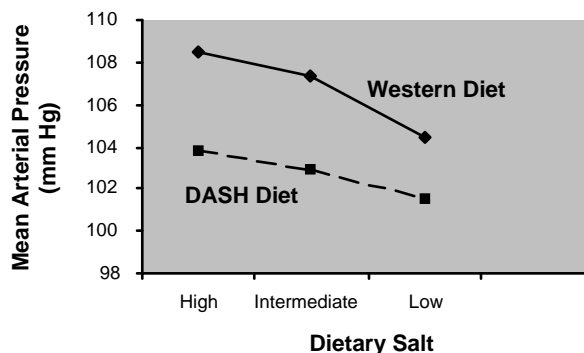
- Vegetarian diets (Seventh Day Adventist research) / Ornish diet / Macrobiotic diet
- DASH (Dietary Approaches to Stop Hypertension) diet / NCEP (National Cholesterol Education Program) Adult Treatment Panel (ATP) III – (#2) diet, exercise and weight control or therapeutic lifestyle change

- Carbohydrate regulation dietary approaches
  - Glycemic index and glycemic load
  - Lower carbohydrate diets – Atkins, South Beach, Zone
- Anti-Inflammatory diet – described in the web-based module from University of Arizona and below
- Elimination diets – described below for GI disorders, headaches, and others
- Dietary patterns – Mediterranean diet, Healthy Eating Index

## DASH DIET

FOOD GROUP	SERVINGS	SERVING SIZES	IMPORTANCE TO DIET
Grains and grain products	7-8	1/2 c dry cereal 1/2 c cooked rice, pasta, or cereal	Major sources of energy and fiber
Vegetables	4-5	1 c raw leafy vegetables 1/2 c cooked vegetables	Rich sources of potassium, magnesium, and fiber
Fruits	4-5	1 medium fruit 1/4 c dried fruit	Important sources of fiber, potassium, and magnesium
Low-fat or fat-free dairy foods	2-3	1 c yogurt 1.5 oz. Cheese	Rich sources of calcium and protein
Meats, poultry, and fish	≤ 2	3 oz. Cooked meats, poultry, or fish	Rich sources of calcium and protein
Nuts, seeds, and dry beans and peas	4-5/wk	1.5 oz. or 1/3 c nuts 1/ c cooked dry beans	Rich sources of energy, magnesium, potassium, protein, and fiber
Fats and oils	2-3	1 Tbsp low-fat mayonnaise 2 Tbsp light dressing	Adds satiety, but DASH diet has only 27% energy as fat
Sweets	5/wk	1 Tbsp sugar 1 Tbsp jelly or jam	Sweets should be low in fat

**Figure 1. The Effect of the DASH Diet and Dietary Sodium Level on Mean Arterial Blood Pressure (average of systolic and diastolic blood pressure).**



Nutrition Reviews 2001;59:292

The following table summarizes the dietary composition of recommended dietary guidelines

TABLE OF DIETARY GUIDELINES	
Nutrient	Recommended Intake
Saturated fat*	< 7% of total calories
Polyunsaturated fat	Up to 10% of total calories
Monounsaturated fat	Up to 20% of total calories
Total fat	25%-35% of total calories
Carbohydrate**	50%-60% of total calories
Fiber	20-30 g/d
Protein	Approximately 15% of total calories
Cholesterol	< 200 mg/d
Total calories***	Balance energy intake and expenditure to maintain desirable body weight/prevent weight gain

\*Trans fatty acids are another LDL-raising fat that should be kept at a low intake.

\*\*Carbohydrates should be derived predominantly from foods rich in fiber/complex carbohydrates including grains, especially whole grains, vegetables, and fruits.

\*\*\*Daily energy expenditure should include at least moderate physical activity (contributing approximately 200kcal/d).

### Carbohydrate Regulation Dietary Approaches

#### Glycemic Index and Glycemic Load

There has been significant research over the last ten years or so to quantify effects of specific foods on blood sugar levels, and associated insulin levels and insulin function. Glycemic index compares the glucose curve for a given 50 gm portion of food (eg. brown rice) and compares it to a curve for a control food (eg. glucose or potato). For glycemic load, the glycemic index is then multiplied by the quantity of carbohydrate in a food serving (eg. for pasta vs. kidney beans). The composition of these tables and how to best apply this information is still being worked out.

#### Lower Carbohydrate Diets – Atkins, Southbeach, Zone, etc.

More recent research has suggested that lower carbohydrate diets may be effective and helpful, and should be considered for weight-loss maintenance and glycemic control. This approach tends to reduce amounts of dietary carbohydrate and replace it with protein (usually fish and lean meats) and healthy fat (mostly monounsaturated fat). Future research should help to determine what the optimal type and amount of protein, fat and carbohydrate is, and/or whether there may be different approaches required for different people (eg. based on genetic, metabolic or other factors).

#### Abnormal Glucose Tolerance/ Reactive Hypoglycemia

Because general dietary patterns can often be based on quick and easy or refined foods, and there may be some underlying susceptibilities, hypoglycemic-like symptoms can sometimes occur. A review of hypoglycemia suggested that the symptoms could be categorized as adrenergic (e.g. anxiety, sweating, irritability) or neuroglycopenic (e.g. headache, fatigue, dizziness), although both are nervous system effects (Field, 1989). A tendency toward hypoglycemia can be identified by developing one or more of these symptoms if a meal is delayed too long.

### Anti-Inflammatory Diet: Evidence Base

Recent research suggests that chronic inflammation is a characteristic feature of aging (Sarkar, 2004). Although this may result from several factors, we know that the prevalence of obesity and

type II diabetes (T2DM) is significantly increasing, which significantly increases the risk for cardiovascular disease (CVD), and we now also understand that CVD is an inflammatory process. In addition, obesity, atherosclerosis and inflammation are associated with neurodegenerative diseases (Napoli, 2005), and the development and progression of cancer (Schwartzburd, 2004).

An interesting study of gene expression and activity in young versus old mice suggests that most genes maintain normal levels of functioning with aging (Lee, 1999). However, less than 1% of genes had a greater than 2-fold increase in activity and less than 1% of genes had a greater than 2-fold decrease in activity. The decrease in activity corresponded to energy metabolism as shown by reduced glycolysis and mitochondrial dysfunction, and the increase in activity was associated with greater stress responses involved with DNA repair and antioxidant defenses. The research also showed that caloric restriction was able to reverse these changes that occurred with aging.

Insulin resistance is a primary mechanism that contributes to metabolic syndrome and CVD risk, and is considered an inflammatory disease (Garg, 2003). Its characteristics include weight gain (especially waist circumference), hypertension, diabetes, elevated triglycerides, low HDL, small/dense LDL and others. Although overweight and obesity are thought to be the most important causes of this syndrome, there may be other influences such as genetics and inflammation. A study has suggested that as many as 47 million Americans have metabolic syndrome (Ford, 2002).

Accumulating evidence is beginning to suggest that diet can have a significant anti-inflammatory effect. The following Table summarizes nutrient influences on inflammatory markers:

**TABLE 1. Nutrients' effect on inflammatory markers and potential modulation of the risk for cardiovascular disease and type 2 diabetes mellitus (Ann N Y Acad Sci. 2006;1083:214-38).**

Nutrient	Effect on inflammatory markers	CVD <sup>a</sup> risk	Type 2 DM <sup>b</sup> risk
Saturated fatty acids	↑ CRP, ↑ IL-6, ↑ E-selectin		
Trans fatty acids	↑ CRP, ↑ IL-6, ↑ E-selectin, ↑ VCAM-1, ↑ ICAM-1	↑	↑
Monounsaturated fatty acids	—	↓	
ω-3 fatty acids	↓ IL-1β, ↓ IL-6, ↓ IL-8, ↓ TNF-α, ↓ CRP, ↓ VCAM-1, ↓ ICAM-1, ↓ E-selectin	↓	
High glycemic index carbohydrates	↑ CRP	↑	↑
Fibers	↓ CRP		
Antioxidants	↓ CRP, ↓ TNF-α, ↓ VCAM-1, ↓ ICAM-1, ↓ E-selectin	↓	
Alcohol	Moderate intake: ↓ IL-6 No or excessive intake: ↑ IL-6, ↑ IL-8, ↑ IL-10, ↑ IL-12, ↑ IL-13, ↑ TNF-α		

<sup>a</sup> cardiovascular disease, <sup>b</sup> diabetes mellitus.

## Dietary Fats and Anti-Inflammatory Effects

### *Dietary Fats*

Currently Americans get approximately 34-40% of their total daily calories from fat. All naturally occurring fats are generally consumed as one of three types of fatty acids: saturated fatty acids, monounsaturated fatty acids, and polyunsaturated fatty acids.

Recently, clinical research has focused on the roles that fatty acids may play in the promotion of inflammation. Evidence from epidemiological and clinical secondary prevention trials have found that polyunsaturated fatty acids (PUFAs) have a significant influence on the prostaglandin pathways. Polyunsaturated fatty acids can be divided into two categories: the omega-3 and the omega-6 fatty acids. These polyunsaturated fatty acids are considered essential fatty acids since humans are unable to synthesize them and thus must obtain them from the diet.

### *Monounsaturated Fats*

Although not extensive, evidence to suggests that olive oil, high in monounsaturated fat, may also have anti-inflammatory effects. The research supporting this association includes epidemiological studies of rheumatoid arthritis from Greece (Linos, 1999) and olive oil supplement studies in subjects

with rheumatoid arthritis (Kremer, 1990). Foods high in monounsaturated fats in addition to olive oil include olives, nuts and seeds, and avocado. This is an important area for future research.

### Mechanism of Fat and Inflammation

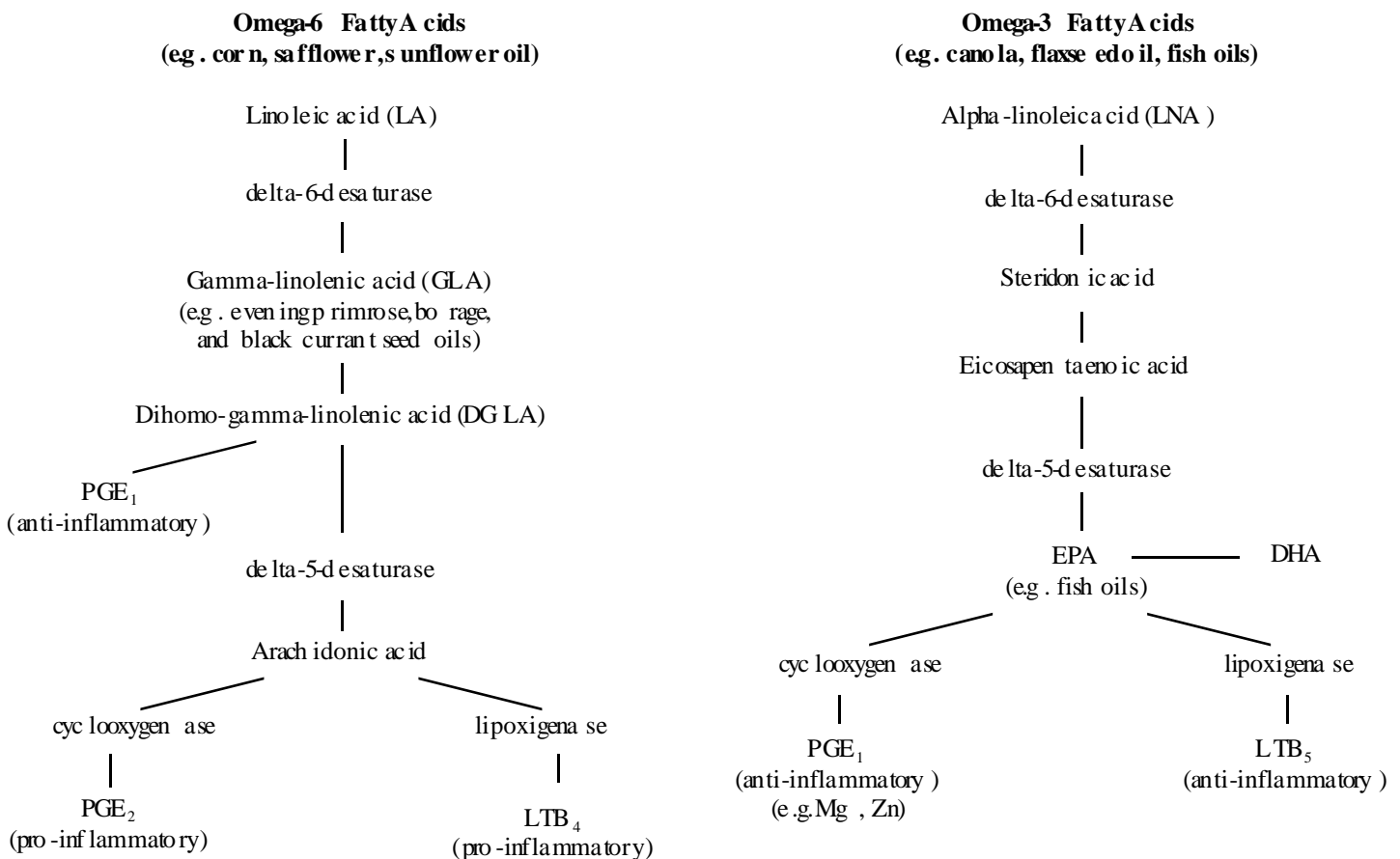
The strongest and best documented anti-inflammatory effect, as related to dietary intake, is the consumption of specific types of dietary fat. The omega-6 fatty acid linoleic acid and the omega-3 fatty acid linolenic acid are the predominant essential fatty acids in humans. Linoleic acid can be elongated and desaturated to arachidonic acid while linolenic acid (ALA) is elongated and desaturated into EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid). EPA and DHA can also be obtained from consumption of cold-water fish such as salmon, sardines, and albacore tuna.

Prostaglandins, leukotrienes, and thromboxanes are eicosanoids derived from essential fatty acids. Eicosanoids derived from arachidonic acid are generally proinflammatory and proaggregatory agonists, while omega-3 fatty acids tend to inhibit platelet aggregation, are less immunosuppressive and anti-inflammatory.

Additionally, omega-3 fatty acids offer further benefits such as:

- Increase of cell membrane omega-3 fatty acid phospholipid composition which will affect cell membrane fluidity and function
- Inhibition of cyclo-oxygenase and lipoxigenase enzymes
- Inhibition of the release of pro-inflammatory cytokines (e.g. IL-1, IL-6 and TNF $\alpha$ )

## Metabolic Pathways of Essential Fatty Acids



Factors thought to impair delta-6-desaturase activity include Mg, Zn, and B1 deficiency; aging, alcohol, trans fatty acids; and high cholesterol levels.

## The Mediterranean Diet

A Mediterranean Diet is similar to other balanced calorie weight loss diets and the DASH diet for hypertension. The important features are: (a) high intakes of vegetables, fruit, cereals and whole grain breads, beans, nuts and seeds; (b) significant amounts of monounsaturated fat (eg. olive oil); and (c) only low to moderate amounts of dairy products, fish and poultry, and little red meat.

Several studies have suggested that a Mediterranean Diet will have anti-inflammatory effects. Also, a well-known study, the Lyon Diet Heart Study, showed that a Mediterranean Diet was effective for secondary prevention – it could significantly reduce future heart disease risk in people who already had heart disease. After an average follow-up of four years, people who closely followed a Mediterranean Diet had a 50-70% lower risk for another heart attack, stroke, unstable chest pain, heart failure or hospitalization (de Lorgeril, 2006).

## Vegetarian Diets, Inflammation and Rheumatoid Arthritis (RA)

There is evidence that a vegan diet has anti-inflammatory effects (Jenkins, 2003). While most of this effect probably derives from the fatty acid composition, there is likely some influence from fiber and anti-oxidant nutrients.

A meta-analysis of fasting followed by a vegetarian diet in RA suggested a long-term statistically significant clinical benefit (Muller, 2001). The best study (still small at 27 subjects) had subjects fast for 7-10 days, followed by a gluten-free vegan diet for 3.5 months and then an individually designed lactovegetarian diet for 9 months (Kjeldsen-Kragh, 1999)

## Other Research

Several types of research are examining the influence of caloric restriction with interesting results. An excellent study compared different approaches such as 25% caloric restriction, 12.5% caloric restriction with exercise and a very low calorie diet (890 kcal/day) until 15% weight loss was achieved (Heilbronn, 2006). Another study examined alternate day caloric restriction influences on inflammation and oxidative stress in overweight adults with asthma (Johnson, 2006). These studies are beginning to generate data on different approaches and combinations of approaches as they relate to inflammation, oxidative stress, and other markers in a variety of disorders.

## **Elimination/Challenge and Rotation Diets – for GI disorders and other symptoms**

Food intolerance and food allergy can have significant beneficial effects for gastrointestinal disorders (IBS, constipation, diarrhea, etc.) and a range of other disorders. Unfortunately, there are not tests that are 100% effective to identify potentially problematic foods, so an empirical trial is another way to test for intolerances. By rotating foods such as dairy, wheat, and sugar (these are probably the most common offenders), people can often identify foods that may promote symptoms. Implementing this approach does take time and understanding but cases will be presented to illustrate benefits.

## **Healthy and Practical Dietary Guidelines (and Targeted Nutritional Supplementation)**

Since patients can have significant difficulties following healthy dietary guidelines (and implementing lifestyle changes), it can be helpful to develop an overall nutritional program that utilizes both dietary guidelines and nutritional supplementation, in which the specific goals (eg. anti-inflammatory effects or less stomach/intestinal symptoms) are individually designed.

## Specific Dietary Guidelines and Recommendations

- Proteins – beans and bean products, fish, poultry, and/or lean meats. Proteins are very important for building muscle and for enzyme function. Type and amount will influence fat intake.
- Complex Carbohydrates – more whole grains and less refined flour products and sugars. Whole grains provide important fiber and nutrients, causing a slower and healthier rise in blood sugar (**lower Glycemic Index/Load**).
- Vegetables and Fruit – 5 to 7 servings per day that includes at least 2-4 servings of green vegetables or low carbohydrate vegetables, and 1-3 servings of fruit.

- Healthy snacks – these usually need to be stocked at home and brought in to work so that good foods are available when needed. These include vegetable sticks, nuts or seeds, fruit, avocado, popcorn, cheese and others.
- Eat 3-6 times per day and balance meals – it is very important not to miss meals (and sometimes snacks) and to balance meals with regard to protein, salad or low carbohydrate vegetables and starches.
- Limit junk food, caffeine and alcohol – based on individual needs and preferences

### Nutritional Supplement Program

Nutritional supplements must also be individualized to produce optimal effects. There is, however, a foundation nutritional program that can serve as the basis of a nutritional supplement program including:

- Multivitamin and Mineral – to insure adequate amounts of all nutrients.
- Omega 3 Fatty Acids (Flax or Fish Oil) or a Healthy Oil Formula – important for regulating immune function, cardiovascular function, nervous system function and other effects.
- Calcium, Magnesium and Vitamin D, or an Osteoporosis Formula – important for prevention of osteoporosis but also helpful for heart functioning, nervous system functioning, prevention of some types of cancer and other effects.

### **Emerging Issues to Watch**

- Epigenetic influences of diet and dietary components – Nutrition Reviews special issue: Diet, Epigenetic Events and Cancer Prevention. 66:S1-S72, 2008.
- Food and diet, and its impact on the environment, energy resources and health – see The Omnivore's Dilemma, by Michael Pollan (Penguin Press, New York, 2006).

### Additional Resources

American College of Nutrition, 300 S. Duncan Ave. Ste. 225, Clearwater, FL 33755; Voice line: (727) 446-6086, Fax: (727) 446-6202; Web: <http://www.am-coll-nutr.org/>

National Heart Lung and Blood Institute, Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III report). Web: <http://www.nhlbi.nih.gov/guidelines/cholesterol/>

National Institute on Aging, Office of Nutrition, National Institutes of Health; Building 31, Room 5C27, 31 Center Drive, MSC 2292, Bethesda, MD 20892; Phone: 301-496-1752 Web: <http://www.nia.nih.gov/>

Institute for Functional Medicine, 4411 Pt. Fosdick Drive NW, Suite 305, P.O. Box 1697, Gig Harbor, WA 98335; Phone: 800-228-0622, Fax: 253-853-6766; <http://www.functionalmedicine.org/>

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