4. Obesity, Metabolic Syndrome and Diabetes

Overview and Summary of Key Points

Globalization of markets, with wider access to the market economy and lower cost processed foods, has a depressing downside. Humanity is getting fatter and fatter, and diabetes and other metabolic diseases of affluence are becoming epidemic. Even in parts of the world where malnutrition and undernutrition are problems, it is not unusual for a family to include both undernourished and overnourished individuals (Doak et al, 2005). Although many Americans believe that increasing rates of obesity are strictly a U.S. phenomenon, they are, in fact, occuring around the world. (Popkin, 2001; Popkin, 2008).

To reverse the increasing trends of global obesity and obesity-related diseases, an increased emphasis is needed on dietary patterns that promote human health, including increased consumption of fruits and vegetables and vegetable protein, and decreased consumption of meat (particularly red meat) and saturated fats. A Mediterranean-style diet fits this type of dietary pattern. In fact, mounting evidence shows that a Mediterranean style-diet may be useful in preventing and treating chronic diseases related to mild chronic inflammation such as visceral (abdominal) obesity, metabolic syndrome, and Type 2 diabetes (Guigliano and Esposito, 2008). Excess abdominal fat is believed to increase blood levels of fatty acids, which can inhibit insulin's regulation of glucose (Bergenstal et al, 2007). A new study by researchers in Spain also concluded that long-term adherence to a Mediterranean diet could contribute to the prevention of age-related changes in blood pressure (Nunez-Cordoba et al, 2009).

A Mediterranean-style diet is rich in fruits, vegetables, whole grains, and dairy products (Guigliano and Esposito, 2008). It is also high in dietary fiber and low in refined carbohydrates. Finally, a Mediterranean-style diet contains a moderate to high content of vegetable proteins and a moderate content of fats (mostly unsaturated fats) (Guigliano et al., 2008). Consuming an organic Mediterranean-style diet offers additional protective health benefits, including elimination of dietary exposure to toxic pesticides (such as organophosphate pesticides) and increased levels of polyphenolic compounds (antioxidants) that may play an important role in alleviating inflammation and insulin-resistance, which are associated with an increased risk of chronic disease (e.g., metabolic syndrome and Type 2 diabetes).

In the following sections, current trends in obesity, diabetes and metabolic syndrome are highlighted. A review of how consumption of energy dense diets may be associated with an increased risk of obesity, metabolic syndrome and Type 2 diabetes is also provided. In contrast, evidence is presented for why a Mediterranean-style diet offers a practical approach to avoiding adult-onset obesity, metabolic syndrome and diabetes. Finally, in order to ensure optimal health, the chapter ends with a list of specific suggestions on how to follow an organic Mediterranean-style diet.

A. Obesity, Diabetes, and Metabolic Syndrome

In the United States, about a third of adults 20 to 74 years of age are obese (BMI $\geq$ 30) and another third are overweight (BMI 25.0 to 29.9) (Ogden et al., 2006). According to new statistics released by the Centers for Disease Control and Prevention (CDC), the number of obese American adults (about 34 percent) now outnumber those who are overweight (about 33 percent) (Reuters Health, 2009).

Children and adolescents have also grown fatter over the last two decades. A child weight's status is determined based on an age- and gender-specific percentile for BMI rather than by the BMI categories used for adults. Classifications of overweight and obesity for children and adolescents are age- and gender-specific because their body composition varies as they age and varies between boys and girls. The BMI value is plotted on the U.S. CDC growth charts to determine the corresponding BMI-for-age percentile (see the box on this page for definitions of childhood overweight and obesity).

In 2005-2006, 15.5 percent of U.S. children and adolescents aged two through 19 years were at or above the 95th percentile for BMI for age (now referred to as "obese") and 14.6 percent were at or above the 85th percentile for BMI for age and less than the 95th percentile (now referred to as "overweight")." Thus, collectively, 30.1 percent of children and adolescents aged two through 19 years were overweight or obese. The prevalence of high BMI in both children and adolescents showed no significant increases between 2003-2004 and 2005-2006. However, data from 2007-2008 are needed to further examine these trends (Ogden et al, 2008).

Definitions of Childhood Overweight and Obesity	
Classification	Definition
Overweight	Body Mass Index (BMI)-for-age at or above the 85th percentile and lower than the 95th percentile
Obese	BMI-for-age at or above the 95th percentile
Source: CDC, 2009	

Most recently, it was estimated that if current obesity trends continue, by the year 2030, 86.3 percent of adults will be overweight or obese and 51.1 percent will be obese. Black women (96.9 percent) and Mexican-American men (91.1 percent) would be the most affected. These same researchers estimated that, if current trends continue, by the year 2048, all Americans would be overweight or obese. In children, the prevalence of obesity (~ 15 percent) (BMI-for-age at or above the 95th percentile) would nearly double by 2030. Total health care costs attributed to obesity/overweight would double every decade to $860.7-$956.0 billion U.S. dollars by 2030, accounting for 16-18 percent of total US health care costs (Wang et al., 2008).

Diabetes is a serious condition associated with overweight and obesity (Geiss et al., 2006). There are two types of diabetes. Type 1 diabetes is "insulin-dependent diabetes." Type 2 diabetes is "insulin-resistant diabetes." Type 2 diabetes is strongly associated with obesity and cardiovascular risk. According to data from the National Health and Nutrition Examination Survey (2005-2006), the crude prevalence of diagnosed diabetes in persons aged 20 years and older rose from 5.1 percent in 1988-

1994 to 7.7 percent in 2005-2006, even after accounting for differences in age and gender. Compared with non-Hispanic whites, age- and gender-standardized prevalence of diagnosed diabetes was approximately twice as high in non-Hispanic blacks and Mexican Americans (Cowie et al, 2009).

A recent report released by the Centers for Disease Control and Prevention (CDC) reported that the rate of new diabetes diagnoses has nearly doubled over the last decade. The average-age-adjusted incidence of diabetes rose from 4.8 new cases per 1,000 persons (between 1995 and 1997) to 9.1 new cases per 1,000 persons (between 2005 and 2007). In the 2005-07 survey, the incidence rate of diabetes was highest in West Virginia and lowest in Minnesota. The ten states with the highest quartile of age-adjusted diabetes incidence included nine of 16 states located in the southern region of the U.S. (Alabama, Florida, Georgia, Kentucky, Louisiana, South Carolina, Tennessee, Texas and West Virginia) (MMWR, 2008). Factors associated with an increased risk for diabetes include older age, lower educational attainment, physical inactivity, obesity, weight gain, and being categorized in a racial/ethnic minority population (Geiss et al., 2006).

Obesity is a risk factor for the development of insulin resistance, with pancreatic beta cells compensating for insulin resistance by augmenting insulin secretion. The failure of beta-cells is believed to cause pre-diabetes, a condition that can lead to diabetes. Because it can take up to 10 years or longer for obese individuals to develop Type 2 diabetes, the full impact of the childhood obesity epidemic on the rate of Type 2 diabetes in young adults has not yet been seen (Lee, 2008).

In the future, it is estimated that more young adults will develop Type 2 diabetes in their 20s and 30s instead of at a much older age, e.g., in their 50s or 60s. If confirmed, this trend will prove costly since the longer a person has Type 2 diabetes, the more likely it is that he or she will develop serious diabetes-related complications such as kidney failure. To better handle this challenge, the U.S. health care system needs to develop "new models of care that address long-term chronic disease risk originating in childhood and extending into adulthood" (Lee, 2008). Increasing public resources for dietary interventions that prevent childhood obesity and related chronic diseases, such as Type 2 diabetes, must be part of this change.

As noted previously, overweight and obesity are associated with significant increase in cardiovascular risk. Overweight and obese subjects are more likely to have hypertension and abnormally high levels of the blood lipids cholesterol and triglycerides than are normal-weight subjects (Janssen et al., 2004). A relatively new term – "the metabolic syndrome" – has been added to the medical lexicon with a World Health Organization definition (Reaven, 2006).

"The Metabolic Syndrome"

An individual has "the metabolic syndrome" if he or she satisfies the following criteria. First, he or she must have at least one of the following conditions: diabetes mellitus, abnormal glucose tolerance, abnormally high fasting blood glucose level, or insulin resistance. Second, he or she must have at least two of the following four conditions:

(a) a waist-to-hip ratio of 0.9 or greater for men and 0.85 or greater for women and a BMI greater than 30;
(b) an elevated serum triglyceride level or a low serum high-density lipoprotein ("HDL") level;
(c) elevated blood pressure (hypertension); and
(d) protein in the urine.

The reason for creating the diagnosis of the metabolic syndrome was to identity persons at risk for cardiovascular disease.

B. Energy Dense Diets and Obesity, Diabetes and Metabolic Syndrome

Dietary energy density is defined as the amount of energy able to be metabolized per unit weight or volume of food (Yao and Roberts, 2001). Assuming people do not change their level of activity and burn more calories, a high energy density of a given volume of food consumed will result in increased energy intake and weight gain. Lower energy density diets can be achieved through dietary patterns that are consistent with the Dietary Guidelines for Americans. Dietary energy density can be lowered by increasing fruit and vegetable intake while limiting intake of foods high in saturated and *trans* fats such as baked goods and fried vegetables (US DHHS and USDA, 2005; Savage et al., 2008).

In a prospective study of 50,000 women, researchers found that high dietary energy density was reflective of a dietary pattern higher in saturated and *trans* fat and refined carbohydrates. However, these researchers noted that it would be misleading to recommend foods solely based on their energy density values since some foods with higher energy density values, such as olive oil and nuts, were not associated with weight gain, while consumption of foods with low energy density values, such as soda, fruit punches and potatoes, were associated with weight gain (Bes-Rastrollo et al., 2008). Other recent research reported that non-Hispanic white women who consumed lower energy density diets ate fewer meals and snacks in front of the television and more dinners as a family at the table (Savage et al., 2008).

Dietary energy density was associated with body mass index and waist circumference but not other metabolic risk factors in a cross-sectional study of free-living, young Japanese women (Murakami et al, 2007). In another cross-sectional study, dietary energy density was associated with elevated fasting insulin and metabolic syndrome in a nationally representative sample of U.S. adults (Mendoza et al, 2007). Finally, in a longitudinal study, an energy-dense, low-fiber, high-fat diet was associated with higher fat mass and greater odds of excess adiposity in young children (Johnson et al., 2008).

In a large, population-based prospective study involving more than 21,000 men and women of European-Caucasian origin, researchers reported a positive association between dietary energy density and the risk of developing Type 2 diabetes, independent of baseline BMI, total energy intake, fat intake and lifestyle factors. Dietary energy density was calculated as the available dietary energy per unit weight of foods (Wang et al., 2008). The researchers found there was a 60 percent higher risk in the highest quintile of energy density compared to the lowest quintile, in the adjusted analysis. More specifically, the researchers found that, "[c]ompared with the highest DED (energy-dense) quintile, participants in the lowest DED (energy-diluted) group consumed significantly more fresh fruit, more vegetables, less meat, less processed meat, [fewer] soft drinks, more alcoholic drinks, more non-energy containing beverages, and a lower percentage of energy from fat." Additional research is needed to determine the mechanism by which dietary energy density may contribute to the development of Type 2 diabetes.

C. The Mediterranean Diet: A Practical Approach to Reducing the Risk of Adult-Onset Diabetes, Metabolic Syndrome and Obesity

A practical approach to improving general health and avoiding the affluent disease trio of metabolic syndrome, Type 2 diabetes, and obesity is adopting a Mediterranean dietary pattern. The Mediterranean Diet refers to the

diet historically consumed in Southern Europe and the Mediterranean Basin. This diet nourished the healthiest people in the world. However, a new report by the Food and Agriculture Organization has warned that in places like Greece, Italy, Spain, Portugal, and Cyprus, the traditional Mediterranean Diet is being abandoned for a more Western diet that has contains more calories from meat and saturated fat (Tufts University Health & Nutrition Letter, December 2008). Such a trend is likely to have major negative health (and economic) consequences, if it's not reversed.

Martinez-Gonzalez et al. (2008) found that high adherence to a traditional Mediterranean diet was associated with an 83 percent relative reduction in the risk of developing Type 2 diabetes. These authors assessed adherence to the Mediterranean diet by using a score created by Trichopoulou et al. (1995), where the Mediterranean diet has a high ratio of monounsaturated to saturated fatty acids, moderate intake of alcohol, high intake of legumes, high intake of grains, high intake of fruit and nuts, high intake of vegetables, low intake of meat and meat products, moderate intake of milk and dairy products, and high intake of fish. Previously, researchers reported an inverse association between adhering to the Mediterranean diet and metabolic syndrome (Tortosa et al., 2007).

Martinez-Gonzalez et al (2008) cautioned against extrapolating the results of their research to non-Mediterranean countries where the consumption of favorable foods (e.g., olive oil, plant-based foods such as fruits, vegetables and legumes) are much lower in the general population. However, researchers who carried out a recent prospective study in the United States (U.S.), involving over 214,000 men and over 166,000 women (the National Institutes of Health – AARP – formerly known as the American Association of Retired Persons – Diet and Health Study) found that there was "strong evidence for a beneficial effect of higher conformity with the Mediterranean dietary pattern on risk of death from all causes, including deaths due to CVD (cardiovascular disease) and cancer, in a US population" (Mitrou et al., 2007).

Furthermore, in a 2-year study titled, "Dietary Intervention Randomized Controlled Trial" (DIRECT), researchers reported that, in addition to weight loss, adherence to a Mediterranean diet resulted in beneficial metabolic effects (Shai et al., 2008). According to these authors, among participants with diabetes (n = 36), "changes in fasting plasma glucose and insulin levels were more favorable among those assigned to the Mediterranean diet than among those assigned to a low-fat diet ($p < 0.001$ for the interaction among diabetes and Mediterranean diet and time with respect to fasting glucose levels)" (Shai et al., 2008).

Key elements of the Mediterranean Diet are high intakes of cereals, whole grains, vegetables, dried beans, olive oil, garlic, fresh herbs, seafood, and fruit. Wine, usually red wine, is consumed with food and in moderation. Meat and poultry are also eaten in moderation; poultry is served much more frequently than red meat. Eggs are included, but butter, cream and lard are not part of the Mediterranean Diet. The Mediterranean Diet includes whole grains. Whole wheat provides insoluble fiber. Whole grain oats and whole grain barley are rich sources of soluble fiber in the form of "beta-glucan". The Mediterranean Diet comprises more "unrefined" foods than most Western diets. Modern Western diets comprise many energy-dense foods with added sugars and added fats. Unrefined foods such as whole grains, fruits, and vegetables have a greater nutrient density than energy-dense refined foods (Drewnowski, 2005).

The amount of fat in authentic Mediterranean diets may vary from less than 30 percent of the calories in the traditional diet of Southern Italy to about 40 percent in the island of Crete (Contaldo et al., 2003). The main contributor is olive oil, which is rich in monounsaturated fatty acids. Scientists in Spain reported that subjects consuming a breakfast high in saturated fat (butter) had a higher expression of the pro-inflammatory cytokine, tumor necrosis factor–alpha, than subjects consuming either a breakfast with monounsaturated fat (olive oil) or a polyunsaturated omega-3 rich fat (walnuts) (Jimenez-Gomez et al., 2009). In addition, Mediterranean diets supplemented with either virgin olive oil or nuts down-regulated cellular and circulating inflammatory biomarkers related to atherogenesis in persons at high risk of cardiovascular disease (Mena et al., 2009).

Other sources of fat in the Mediterranean Diet are fatty fish (rich in omega-3 fatty acids) and eggs. Eggs of hens fed in the traditional Mediterranean manner contain higher levels of omega-3 fatty acids than the eggs of hens fed conventional layer diets (Simopoulos and Salem, 1992). The Mediterranean Diet is also rich in antioxidant phytochemicals . A recent study reported that moderate wine consumption was associated with higher omega-3 fatty acid levels (EPA and DHA) in a person's blood, even when fish consumption was taken into account. The authors concluded that components in the wine other than alcohol - antioxidants called polyphenols - may have exerted these effects, and that part of the cardio-protection of alcohol may be mediated through increased omega 3 fatty acids (EPA and DHA) (di Giuseppe et al., 2009). Rich sources of antioxidant phytochemicals in the Mediterranean Diet are

red wine (Dugo et al., 2003), fresh fruits and vegetables (Benbrook 2005; Rembialkowska, 2007; Benbrook et al., 2008); fresh herbs (e.g., rosemary and sage) (Fortes, 2005), and olive oil (Selvaggini et al., 2006).

There are various mechanisms that may explain the protective effect of the Mediterranean diet (as reviewed in Schroder, 2007 and Perez-Martinez et al., 2007). First, results from two research trials found that virgin olive oil protects against insulin resistance and metabolic syndrome (Estruch et al., 2006). A diet including olive oil, which is rich in monounsaturated fatty acids, may improve insulin sensitivity and result in better lipid profiles than diets rich in carbohydrate (Garg, 1998; Ros, 2003; Perez-Jimenez et al., 2002).

Second, adherence to an overall Mediterranean type dietary pattern is related to lower plasma concentrations of inflammatory markers and markers of endothelial dysfunction (Fung et al., 2005; Lopez-Garcia et al., 2004) – biomarkers which predict future occurrence of diabetes (Meigs et al., 2004). Third, increased adherence to the Mediterranean diet rich in whole grains, olive oil, and fruits and vegetables was associated with higher adiponectin levels (Mantzoros et al., 2006), which are associated with a reduced risk of diabetes (Martinez-Gonzalez, 2008). Finally, scientists are exploring the mechanisms by which resveratrol, the major antioxidant found in the skins of grapes (which is consumed as part of the Mediterranean Diet) may exert positive effects.

D. Resveratrol: a Role in Obesity and Diabetes?

Different phytochemicals may help ameliorate the effects of obesity and diabetes through multiple mechanisms of action. The major antioxidant found in red wine, resveratrol, has been studied the most extensively (King et al., 2006). As noted earlier, resveratrol is a natural polyphenolic stilbene derivative found in high concentrations in the skins of grapes. It is also found in commercial products of cranberries and grapes (Wang et al., 2002), and in other food items, such as berries and peanuts (Udenigwe et al., 2008).
Research suggests that the numerous potential benefits of resveratrol (e.g., vaso-protective, anti-inflammatory, anti-aging) may be due, at least in part, to its antioxidant properties (Manna et al., 2000; Olas et al., 2002; Liu et al., 2003; Udenigwe et al., 2008). Additional proposed mechanisms of action for resveratrol involve inhibition of cyclooxygenase (COX) activity, inhibition of certain activated immune cells and pro-flammatory mediators, and inhibition of transcriptional factors such as nuclear factor-kB (NF-kB) and activator protein (Udenigwe et al., 2008).

Resveratrol has been shown to activate a key gene called the "Silent Information Regulation 2 homolog 1" (SIRT1). When this gene "kicks in," it triggers a series of biochemical interactions that have been shown to extend lifespan, improve metabolic function, or combat metabolic disease in animal models (Ahn et al., 2008). For example, resveratrol was found to prolong the lifespan of mice fed a high calorie diet (Barger et al., 2008). In a randomized clinical trial, the effects of resveratrol on appetite and satiety are also being investigated (Clinical Trials Identifier NCT00654667, February 17th 2009),

Other examples of resveratrol's possible protective effects are reviewed below.

Hyperglycemia – elevated blood sugar – is the hallmark symptom of diabetes. The elevated sugar content makes blood "hypertonic", also called "hyperosmotic." Cells in the

lining of blood vessels and white blood cells, which are directly involved in immune system function, can undergo apoptosis (cell death) in response to this hyperosmotic state. Apoptotic biochemical changes during hyperosmotic shock-induced cell death are blocked by pretreatment with antioxidants. Resveratrol decreases hyperglycemia-induced apoptotic changes in human leukemia cells (Chan, 2005).

The rat made diabetic by streptozotocin has elevated blood sugar and blood lipid levels, just as humans with diabetes do. Resveratrol reduced the plasma glucose concentration by 25 percent and the triglyceride concentration by 50 percent in streptozotocin-induced diabetic rats (Su et al., 2006). Resveratrol may reverse the insulin resistance syndrome and facilitate control of human Type 2 diabetes (McCarty, 2005). The body has an "insulin signaling pathway", which is the biochemical pathway that controls how much insulin is manufactured. Resveratrol inhibits the insulin signaling pathway (Zhang, 2006).

More recently, long-term administration of resveratrol was found to reduce high plasma concentrations of triglycerides, total cholesterol, free fatty acids, insulin and leptin in obese Zucker rats. The resveratrol treatment also improved inflammatory status in the rats by increasing the concentration of adiponectin and lowering tumor necrosis factor-alpha production in visceral adipose tissue. Finally, the elevated systolic blood pressure in these obese rats was significantly improved by the resveratrol treatment (Rivera et al., 2008).

Diabetes is also associated with elevated blood levels of low-density lipoproteins. Low-density lipoproteins are carriers of "bad" cholesterol. Resveratrol inhibits copper-mediated low-density lipoprotein oxidation (Belguendouz et al., 1997). Resveratrol protects low-density lipoproteins against oxidative degradation in two ways, by binding pro-oxidant metals like copper and by scavenging free radicals. Currently, a randomized trial is being conducted to investigate the effects of resveratrol on cholesterol metabolism and insulin sensitivity in older adults (over the age of 50) with insulin resistance (Clinical Trials Identifier NCT00654667, February 17th 2009),

Other research has found that resveratrol inhibits ethanol-induced steatohepatitis in rats, due to its antioxidant properties (Kasdallah-Grissa et al., 2006; Kashdallah-Grissa et al., 2007). Steatohepatitis is a liver disease characterized by inflammation with concurrent fat accumulation. Two of the negative health complications associated with the current obesity epidemic are development of hepatic steatosis ("fatty liver") and non-alcoholic fatty liver disease (NAFLD) (Ahn et al., 2008). Data from numerous studies provide support that NAFLD is the hepatic (liver) manifestation of metabolic syndrome (Marchesini et al., 2003). The prevalence of NAFLD and non-alcoholic steatohepatitis (NASH) in obese patients has been reported to range from 69-100 percent and 25-30 percent of cases, respectively (Clark, 2006; Dixon et al., 2001; Ratziu et al., 2000). Thus, NAFLD and NASH are

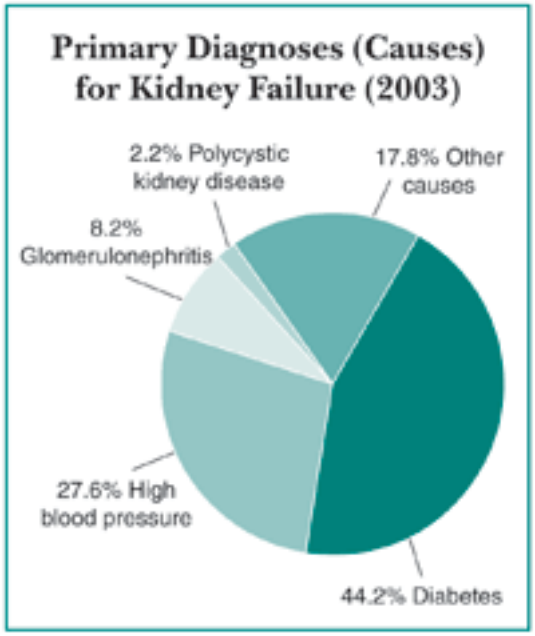
Other sources of resveratrol include peanuts and mulberries

important therapeutic targets for ameliorating symptoms resulting from metabolic syndrome.

With this information in mind, Korean researchers investigated the possible beneficial effects of resveratrol on hepatic gene expression, lipid content, lipid profiles, and non-alcoholic steatohepatitis (NASH) on mice fed an atherogenic (Ath) diet (Ahn et al., 2008). These researchers found that mice fed the Ath diet had significantly higher plasma total cholesterol (TC) and fasting cholesterol (FC) levels relative to the control group. The mice fed the Ath diet also had an increase in hepatic levels of total lipid, triglycerides, and TC compared with the control diet. The addition of resveratrol reduced the increase in the plasma levels of TC and FC caused by the Ath induced diet. Histological grading of the liver sections confirmed that resveratrol significantly ameliorated both hepatic steatosis and inflammation.

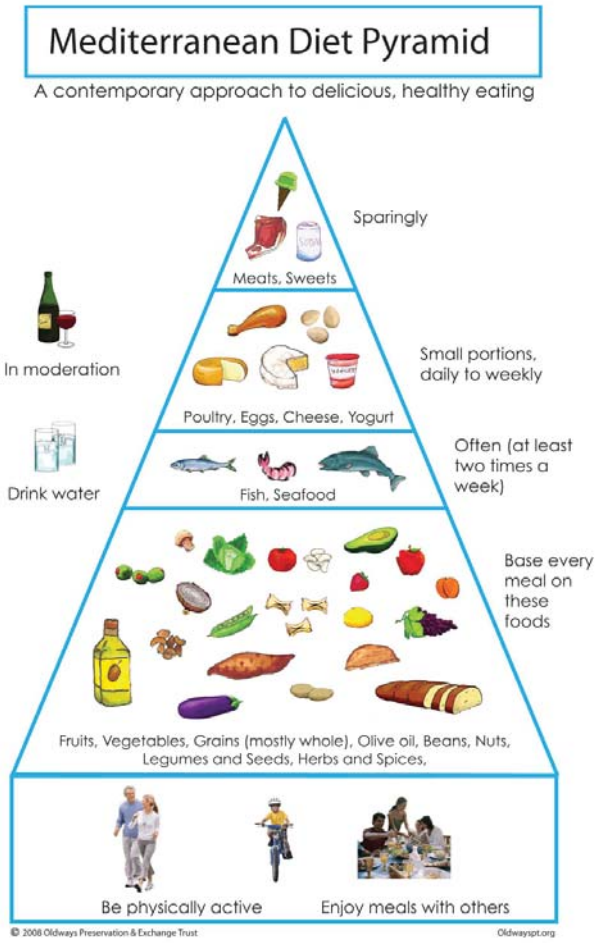
These researchers also found that the Ath diet up-regulated the mRNA expression of various genes involved in lipogenesis (the processes of fatty acid synthesis and subsequent triglyceride synthesis), and the addition of resveratrol to the diet reduced their expression. In contrast, the expression of factors involved in fatty acid beta-oxidation (lipolysis), were up-regulated by resveratrol treatment. Finally, hepatic expression of SIRT1 was increased by the resveratrol treatment. Based on these results, the researchers concluded that that resveratrol has beneficial effects on the prevention and treatment of NASH associated with obesity (Ahn et al., 2008).

One of the most serious complications of diabetes is kidney damage, called "diabetic nephropathy." This kidney damage first manifests itself as the loss of protein in the urine. The final stage of kidney damage is renal failure, where dialysis or a kidney transplant is required for survival. Hypertension – high blood pressure – is common in diabetes. Hypertension increases the risk of diabetic nephropathy. Resveratrol may have a positive effect on the elevated blood pressure of diabetes. The fructose-fed rat is an experimental model used in research on diabetes and the metabolic syndrome. Chronic treatment with resveratrol prevents the increase in systolic blood pressure and cardiac hypertrophy normally seen in the fructose-fed rat (Miatello et al., 2005).



Increased oxidative stress is a major reason why diabetic nephropathy develops. Resveratrol reduces oxidative stress in a widely used laboratory model for diabetes, the rat made diabetic by the administration of the chemical streptozotocin. Six weeks after they were given streptozotocin, rats developed excessive protein in the urine and a marked increase in oxidative stress. Treatment with resveratrol significantly reduced renal dysfunction and oxidative stress (Sharma et al., 2006).

Given the many positive effects of resveratrol on experimental models of diabetes and the metabolic syndrome, ensuring a generous intake of this substance is a prudent dietary measure. Resveratrol has not been found to produce adverse effects, even when consumed at high concentrations. However, the question remains as to how much resveratrol should be consumed on a daily basis in order to derive the most benefits from its protective effects (Udenigwe et al., 2008).



E. An Organic Mediterranean-Style Diet: The Best Bet for Optimal Health

Consuming a Mediterranean Diet has been shown to offer numerous potential public health benefits. Examples of these important public health benefits include: reducing a woman's risk of having a baby with spina bifida (Vujkovic et al., 2009); reducing the risk of chronic diseases related to chronic inflammation (e.g., metabolic syndrome, and Type 2 diabetes) (Guigliano and Esposito, 2008); and preventing age-related changes in blood pressure (Nunez-Cordoba et al., 2009).

Consuming an organic Mediterranean-style diet offers additional important public health benefits including reducing farmers,' agricultural workers' and consumers' exposures to toxic pesticides as well as increasing the dietary intake of polyphenolic compounds (antioxidants) that may play an important role in alleviating inflammation and insulin-resistance, both of which are associated with an increased risk of chronic disease (e.g., metabolic syndrome and Type 2 diabetes).

Below are specific steps for adhering to an organic Mediterranean-style dietary pattern.

1. Enjoy meals with others. Persons who share meals with family and friends often consume a more healthful diet than persons who eat in front of the television or "on the run." Taking time to enjoy meals with others also slows the pace at which food is consumed, giving the brain more time to signal that the stomach is "full".

2. Get regular physical activity every day - at a level that promotes a healthy weight, fitness and general well-being.

3. Consume an abundance of organic foods from plant sources including fruits and vegetables, whole grains and breads, lentils and other dried beans, seeds, and nuts (e.g., walnuts, almonds, pecans). Because nuts are high in calories, eat no more than a handful a day.

4. Emphasize a variety of minimally-processed and, wherever possible, seasonally fresh and locally grown organic foods.

5. Use olive oil as the principal fat, along with other plant-based oils high in monounsaturated fat such as canola oil. Choose these plant-based oils carefully. Whenever you can, purchase extra virgin and canola oils that are cold-pressed. When buying other oils, look for organic brands that use cold press technology as well. Organic oils are not extracted with hexane, a chemical that may pose health risks. By reducing the pressure and heat when oil is extracted from canola, soybeans or corn, organic oil processing typically produces oils higher in vitamins and antioxidants.

6. Use organic herbs and spices in cooking. Fresh aromatic herbs (and spices) are high in antioxidants and add taste to meals. You can grow fresh, organic herbs in a kitchen garden.

7. Eat fish on a regular basis (twice a week or more). Consume fish high in omega-3 fatty acids such as salmon, sardines, mackerel (N. Atlantic, Chub) and anchovies as well as lean finfish and shellfish.

8. Consume small portions daily to weekly of foods such as organic yogurt, poultry, cheese, and eggs. For individuals two years of age and older, limit high fat dairy options such as whole or two percent milk and limit high fat cheeses (instead use lower to medium fat cheeses such as feta, goat, and mozzarella). Choose low-fat poultry options. Eggs are limited to less than four per week (including those used in cooking and baking).

9. Use red meat and sweets only "sparingly." Substitute fish or poultry for red meat. Consume fresh fruit for dessert.

10. If acceptable to your primary care physician, consume wine with meals - in moderation (moderation is the equivalent of one 5 ounce glass of wine per day for women and two glasses of wine a day for men). If you drink alcohol, consume red wine made with organic grapes. Red wines made from organic grapes generally contain substantially more resveratrol than similar varietal red wines, based on reports from several countries (Levite et al., 2000; Miceli et al., 2003; Dani et al., 2007). Consumption of alcohol should be avoided during pregnancy and whenever it puts an individual at risk for a medical problem. Drinking organic purple grape juice can be a healthful alternative to drinking red wine.

Conclusions and Summary

Globalization of markets, with wider access to the market economy and lower cost processed foods, has led individuals to adopt more "energy dense" Western diets, which is believe to be at least a partial contributor to increasing rates of obesity worldwide. In contrast, mounting scientific evidence is illustrating that adoption of a Mediterranean-style diet may prevent or reduce the risk of numerous public health problems including spina bifida, adult-onset obesity, metabolic syndrome, Type 2 diabetes, and age-related changes in blood pressure.

Consuming an organic Mediterranean-style diet offers additional protective health benefits, including elimination of dietary exposure to toxic pesticides (such as OP pesticides) and increased levels of polyphenolic compounds (antioxidants) that may play an important role in alleviating inflammation and insulin-resistance.

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Appendix Table 1: Pesticides and Metabolites with CAS Numbers That Have Been Reported to be Endocrine Disruptors, Based on Studies Compiled by TEDX (The Endocrine Disruptor Exchange)		
www.endocrinedisrupton.org		
PESTICIDE	PESTICIDE TYPE	CAS #
aldicarb	acaricide	116-06-3
carbaryl	acaricide	63-25-2
carbofuran	acaricide	1563-66-2
chlordimeform	acaricide	6164-98-3
clofentezine	acaricide	74115-24-5
alpha-cypermethrin	acaricide	67375-30-8
dicofol [kelthane]	acaricide	115-32-2
tetrasul	acaricide	2227-13-6
toxaphene [camphechlor]	acaricide	8001-35-2
benomyl	fungicide	17804-35-2
biteranol	fungicide	55179-31-2
carbendazim	fungicide	10605-21-7
chlozolinate	fungicide	84332-86-5
cycloheximide	fungicide	66-81-9
cyproconazole	fungicide	94361-06-5
dichlorophen [2,2’-methylenebis(4-chlorophenol)]	fungicide	97-23-4
difenoconazole	fungicide	119446-68-3
diflubenzuron	fungicide	35367-38-5
dinocap	fungicide	39300-45-3
DNOC [4,6-dinitro-o-cresol]	fungicide	534-52-1
epoxiconazole	fungicide	133855-98-8 (formerly 106325-08-0)
etridiazole	fungicide	93-15-9
fenarimol	fungicide	60168-88-9
fenbuconazole	fungicide	114369-43-6
ferbam	fungicide	14484-64-1
flutriafol	fungicide	76674-21-0
hexachlorobenzene [HCB]	fungicide	118-74-1
hexachlorobutadiene [HCBD]	fungicide	87-68-3
hexaconazole	fungicide	79983-71-4
imazalil	fungicide	35554-44-0

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PESTICIDE	PESTICIDE TYPE	CAS #
iprodione	fungicide	36734-19-7
mancozeb	fungicide	8018-01-7
maneb	fungicide	12427-38-2
metiram	fungicide	9006-42-2
myclobutanil	fungicide	88671-89-0
nabam	fungicide	142-59-6
penconazole	fungicide	66246-88-6
pentachloronitrobenzene	fungicide	82-68-8
prochloraz	fungicide	67747-09-5
procymidone	fungicide	32809-16-8
propiconazole	fungicide	60207-90-1
pyrimethanil	fungicide	53112-28-0
quintozene [PCNB]	fungicide	82-68-8
tebuconazole	fungicide	107534-96-3
thiophanate [thiophanate-ethyl]	fungicide	23564-06-9
thiram [diethyldithiocarbamic acid]	fungicide	137-26-8
triadimefon	fungicide	43121-43-3
triadimenol	fungicide	55219-65-3
tributyltin	fungicide	
tridemorph	fungicide	81412-43-3
triphenylin hydroxide	fungicide	76-87-9
vinclozolin	fungicide	50471-44-8
zineb	fungicide	12122-67-7
ziram	fungicide	137-30-4
2,4,5-T [2,4,5-trichlorophenoxyacetic acid]	herbicide	93-76-5
2,4-D [dichlorophenoxyacetic acid]	herbicide	94-75-7
2,4-dichlorophenoxybutyric acid	herbicide	94-82-6
acetochlor	herbicide	34256-82-1
alachlor	herbicide	15972-60-8
amitrole [aminotriazole]	herbicide	61-82-5
asulam	herbicide	3337-71-1
atrazine	herbicide	1912-24-9

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www.endocrinedisrupton.org		
PESTICIDE	PESTICIDE TYPE	CAS #
borax [disodium tetraborate]	herbicide	1303-96-4
bromacil	herbicide	314-40-9
bromacil lithium	herbicide	53404-19-6
bromoxynil	herbicide	1689-84-5
chlorthal [dacthal]	herbicide	
cyanazine	herbicide	21725-46-2
DCPA (USA) [chlorthal-dimethyl]	herbicide	1861-32-1
dinoseb	herbicide	88-85-7
diquat dibromide	herbicide	85-00-7
diuron	herbicide	330-54-1
fluazifop-butyl	herbicide	69806-50-4
glufosinate	herbicide	51276-47-2
glufosinate-ammonium	herbicide	77182-82-2
glyphosate	herbicide	1071-83-6
ioxynil	herbicide	1689-83-4
linuron	herbicide	330-55-2
metolachlor	herbicide	51218-45-2
metribuzin	herbicide	21087-64-9
molinate	herbicide	2212-67-1
N-(4-fluorophenyl)-N-(1-methylethyl)-2-[[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]oxyacetamide/thiafluthamide (FOE 5043)	herbicide	142459-58-3
nitrofen	herbicide	1836-75-5
norflurazon	herbicide	27314-13-2
oryzalin	herbicide	19044-88-3
paraquat	herbicide	4685-14-7
pendimethalin	herbicide	40487-42-1
picloram	herbicide	1918-02-1
prodiamine	herbicide	29091-21-2
prometryn	herbicide	7287-19-6

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www.endocrinedisrupton.org		
PESTICIDE	PESTICIDE TYPE	CAS #
propanil	herbicide	709-98-8
quizalofop-ethyl	herbicide	76578-12-6
simazine	herbicide	122-34-9
terbutryn	herbicide	886-50-0
thiazopyr	herbicide	117718-60-2
tri-allate	herbicide	2303-17-5
trichlorobenzene	herbicide	
trifluralin	herbicide	1582-09-8
1,2-dichloropropane	insecticide	78-87-5
abamectin [avermectin B1]	insecticide	71751-41-2
acephate	insecticide	30560-19-1
aldrin	insecticide	309-00-2
amitraz	insecticide	33089-61-1
azadirachtin	insecticide	11141-17-6
bifenthrin	insecticide	82657-04-3
S-bioallethrin	insecticide	28434-00-6
bioallethrin [d-trans allethrin]	insecticide	584-79-2
bioresmethrin	insecticide	28434-01-7
carbon disulfide	insecticide	75-15-0
carbon tetrachloride	insecticide	56-23-5
chlordane	insecticide	57-74-9
cis-chlordane	insecticide	5103-71-9
chlordecone [kepone]	insecticide	143-50-0
chlorfenvinphos	insecticide	470-90-6
chloroform	insecticide	67-66-3
chlorpyrifos	insecticide	2921-88-2
cyfluthrin	insecticide	68359-37-5
lambda-cyhalothrin	insecticide	91465-08-6
cypermethrin	insecticide	52315-07-8
DDT	insecticide	3563-45-9
deltamethrin	insecticide	52918-63-5
demephion-O	insecticide	682-80-4
demeton-S-methyl	insecticide	919-86-8

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www.endocrinedisrupton.org		
PESTICIDE	PESTICIDE TYPE	CAS #
diazinon	insecticide	333-41-5
dichlorvos	insecticide	62-73-7
dieldrin	insecticide	60-57-1
dimethoate	insecticide	60-51-5
dinitrophenols	insecticide	25550-58-7
alpha-endosulfan	insecticide	959-98-8
beta-endosulfan	insecticide	33213-65-9
endosulfan (alpha and beta)	insecticide	115-29-7
endrin [hexadrin]	insecticide	72-20-8
esfenvalerate	insecticide	66230-04-4
ethylene dibromide [1,2-dibromoethane; EDB]	insecticide	106-93-4
etofenprox [ethofenprox]	insecticide	80844-07-1
fenitrothrion	insecticide	122-14-5
fenoxycarb	insecticide	79127-80-3
fenthion	insecticide	55-38-9
fenvalerate	insecticide	51630-58-1
fipronil	insecticide	120068-37-3
fluvalinate	insecticide	69409-94-5
tau-fluvalinate	insecticide	102851-06-9
formothion	insecticide	2540-82-1
heptachlor	insecticide	76-44-8
beta-hexachlorocyclohexane [beta-HCH, beta-BHC]	insecticide	319-85-7
delta-hexachlorocyclohexane [beta-HCH, beta-BHC]	insecticide	319-86-8
hexachlorocyclohexane [HCH; benzenehexachloride BHC; mixed isomers]	insecticide	608-73-1
lindane [gamma-HCH; gamma BHC; 99%+]	insecticide	58-89-9
malathion [cythion]	insecticide	121-75-5
methomyl	insecticide	16752-77-5
methoprene	insecticide	40596-69-8

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www.endocrinedisrupton.org		
PESTICIDE	PESTICIDE TYPE	CAS #
methoxychlor	insecticide	72-43-5
mevinphos	insecticide	786-34-7
mirex	insecticide	2385-85-5
monocrotophos	insecticide	6923-22-4
omethoate	insecticide	1113-02-6
oxydemeton-methyl	insecticide	301-12-2
parathion [parathion-ethyl]	insecticide	56-38-2
parathion-methyl	insecticide	298-00-0
pentachlorobenzene	insecticide	608-93-5
permethrin	insecticide	52645-53-1
penthrin	insecticide	26002-80-2
phenthoate	insecticide	2597-03-7
phosphamidon	insecticide	13171-21-6
precocene I	insecticide	17598-02-6
pyrethrins	insecticide	121-29-9
pyriproxyfen	insecticide	95737-68-1
quinalphos	insecticide	13593-03-8
resmethrin	insecticide	10453-86-8
ronnel [fenchlorphos]	insecticide	299-84-3
TDE [p,p'-DDD,4,4'-DDD]	insecticide	72-54-8
tebufenozide	insecticide	112410-23-8
tefluthrin	insecticide	79538-32-2
temephos	insecticide	3383-96-8
tetrachlorvinphos	insecticide	22248-79-9
tetramethrin	insecticide	7696-12-0
trichlorfon	insecticide	52-68-6
chlorpyrifos metabolite	metabolite	6515-38-4
DDT metabolite	metabolite	14835-94-0
DDT metabolite	metabolite	34113-46-7
DDT metabolite	metabolite	65148-76-7
DDT metabolite	metabolite	65148-77-8
DDT metabolite		

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www.endocrinedisrupton.org		
PESTICIDE	PESTICIDE TYPE	CAS #
DDT metabolite	metabolite	65148-83-6
DDT metabolite	metabolite	53-19-0
DDT metabolite	metabolite	65148-75-6
DDT metabolite	metabolite	4329-12-8
DDT metabolite	metabolite	65148-80-3
DDT metabolite	metabolite	65148-81-4
DDT metabolite	metabolite	65148-82-5
DDT metabolite	metabolite	43216-70-2
DDT metabolite	metabolite	65148-72-3
DDT metabolite	metabolite	65148-73-4
DDT metabolite	metabolite	65148-74-5
diuron metabolite	metabolite	3567-62-2
methoxychlor metabolite	metabolite	2971-36-0
methoxychlor metabolite	metabolite	2132-70-9
pentachlorophenol	molluscicide	87-86-5
metam sodium	nematicide	137-42-8
DBCP [dibromochloropropane]	nematicide	96-12-8
methyl bromide	nematicide	74-83-9
3-trifluoromethyl-4-nitrophenol [TFM]	piscicide	88-30-2
chormequat chloride	plant growth regulator	999-81-5
chlorocholine chloride	plant growth regulator	99-81-5
n-2-fluorenylacetamide	rodenticide	53-96-3
pyrinuron [pyriminil]	rodenticide	53558-25-1
piperonyl butoxide	synergist	51-03-6
ethiozin [ebuzin/tycor]		64529-56-2

About the Co-authors

Dr. McCullum-Gómez is a food and nutrition consultant whose areas of expertise include: community food security and sustainable food systems, nutrition during pregnancy, obesity prevention, and public health nutrition. Previously, she held positions as assistant professor, clinical dietitian, nutrition educator, and dietetic program director at Mansfield University. She received a Ph.D. in Nutritional Sciences from Cornell University and obtained her B.S. and M.S. degrees in Nutrition from The Pennsylvania State University. Dr. McCullum-Gómez is a column editor for the *Journal of Hunger and Environmental Nutrition* and serves as an ad hoc reviewer for numerous scientific peer-reviewed journals including *Journal of the American Dietetic Association* and *Journal of Nutrition Education and Behavior*. She is a member of the American Dietetic Association and Society for Nutrition Education. She is also the mother of twins, Emilio and Isabella.

Dr. Charles Benbrook is the Chief Scientist of the Organic Center. He has served in that position for four years, and has been a consultant to the Center since 2004. He has carried out analysis of pesticide exposures and risk for many years, beginning in the early 1980s while serving as staff director of a Congressional subcommittee. Benbrook has a PhD in agricultural economics from the University of Wisconsin-Madison, and a BS degree from Harvard University.

Dr. Richard Theuer was a member of the inaugural National Organic Standards Board from 1992 to 1995 and Chair of its Processing, Handling, and Labeling Committee. Subsequently he was a Technical Advisory Panel reviewer for many of the materials included on the National List. He currently is a member of the Board of Directors of OMRI, the Organic Materials Review Institute, and served as Chair in 2005 and 2006. He has been a member of the American Society of Nutrition since 1971 and is a professional member of the Institute of Food Technologists. He is Adjunct Professor in Food Science at North Carolina State University in Raleigh and Adjunct Professor in Nutrition in the School of Public Health at the University of North Carolina at Chapel Hill. Dr. Theuer was the Vice President of Research & Development for the Beech-Nut baby food company from 1983 to 1999 and served as President and Chief Executive Officer from 1986 to 1989. He currently reviews materials as ingredients for processed organic foods and consults for industry in the areas of product improvement, regulatory compliance, claim substantiation, and presentations and submissions to regulatory agencies. He authored the December 2006 Organic Center's State of the Science Report "Do Organic Fruits and Vegetables Taste Better than Conventional Fruits and Vegetables?" Rich can be contacted at rtheuer@bellsouth.net