Brought to you by an educational grant from
Xanodyne Pharmaceuticals, Inc.

ask the experts
A Series on Women and Nutrition

Ob/Gyn alliance

Module 5: Metabolic Syndrome

The Ob/Gyn Alliance *Ask the Experts* series is supported by an unrestricted educational grant from Xanodyne Pharmaceuticals.

BACKGROUND

Metabolic syndrome is a major public health challenge affecting nearly 25% of the US population. (1) This translates to 47 million adults in the US. Critical to management of this issue is a search for the cause which includes a combination of current Western practices and sedentary lifestyles which have contributed to the epidemic levels of obesity and overweight adults in this country. Because of the progressive nature of metabolic syndrome, early diagnosis and intervention are critical to preventing and/or reversing this disease trend.

WHAT PHYSICIANS NEED TO KNOW

Defining the Syndrome:

There is currently disagreement over the precise definition of metabolic syndrome among leading health organizations such as the World Health Organization (WHO), the European Group for Study of Insulin Resistance (EGIR), the National Cholesterol Education Program Adult Treatment Panel III (NCEP APT III), the American Association of Clinical Endocrinologists (AACE), the International Diabetes Federation (IDF), and the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI), as summarized in table below from Albertis et al (Lancet, 2006). (2)(3)(13) The debate and history of these definitions is beyond the scope of this series; this document will highlight the fundamental components of the disorder that are widely accepted.

As summarized by the NHLBI (http://www.nhlbi.nih.gov/health/dci/Diseases/ms/ms_whatis.html), in general, metabolic syndrome is characterized by a group of risk factors that are linked to an individual who is overweight or obese that increase his/her chance for heart disease, diabetes, and stroke. The term 'metabolic' refers to biochemical processes in the body's normal function. The five metabolic risk factors are as follows:

1) A large waistline or abdominal obesity
2) High blood pressure or hypertension
3) Higher than normal triglyceride level in the blood (or use of medication to treat high triglycerides)
4) Lower than normal level of HDL cholesterol in the blood (or use of medication to treat low HDL)
5) Higher than normal fasting blood sugar (or use of medication to treat high blood sugar)

These risk factors increase an individual's chance of getting heart disease, diabetes and stroke.

Definitions of the metabolic syndrome:

Risk factors	WHO (1998)[2]	EGIR (1999)[3]	ATP III (2001)[4]	AACE (2003)[5]	IDF (2005)*	AHA/NHLBI (2005)[6]
Obesity	W/H: men, 0.9; women, >0.85 BMI >30 kg/m^2	WC: men, ≥94 cm (37 in); women, ≥80 cm (31.5 in)	WC: men, >102 cm (40 in); women, >88 cm (34.6 in)	BMI ≥ 25 kg/m^2	Ethnic-specific WC	WC: men, >102 cm (40 in); women, >88 cm (34.6 in)
Triglycerides (mg/dL)	150	150	150	150	150+	50+
HDL-C (mg/dL)	Men: ≤35 Women: ≤39	Men: ≤39 Women: ≤39	Men: ≤40 Women: ≤50	Men: ≤40 Women: ≤50	Men: ≤40+ Women: ≤50+	Men: ≤40+ Women: ≤50+
BP (mm Hg)	≥140/90	≥140/90	≥130/85	≥130/85	≥130/≥85+	≥130/≥85+
Plasma glucose	IFG (>110 mg/dL), IGT (2h>140 mg/dL), or T2DM	IFG (>110 mg/dL), IGT (2h>140 mg/dL)	IFG (>110 mg/dL) or T2DM	IFG (>110 mg/dL), IGT (2h>140 mg/dL)	IFG (>110 mg/dL) or T2DM	IFG (>110 mg/dL) or T2DM
Other	Low insulin sensitivity Microalbuminuria	Hyperinsulinemia (used only in nondiabetics)		Hyperinsulinemia (used only in nondiabetics)		
Required for diagnosis	Low insulin sensitivity or IFG/IGT or T2DM plus ≥2 of the above risk factors	Hyperinsulinemia plus ≥2 of the above risk factors	≥3 of the above risk factors	Based on clinical judgment irrespective of numbers of risk factors present	Central obesity plus ≥2 of the above risk factors	≥3 of the above risk factors

Key: +, or under treatment; 2h, 2-h postglucose load of 75 g; AACE, American Association of Clinical Endocrinologists; AHA/NHLBI, American Heart Association/National Heart, Lung, and Blood Institute; ATP III, National Cholesterol Education Program Adult Treatment Panel III; BMI, body mass index; EGIR, European Group for Study of Insulin Resistance; HDL-C, high-density li poprotein cholesterol; IDF, International Diabetes Federation; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; T2DM, type 2 diabetes mellitus; WC, waist circumference; W/H, waist-hip ratio; WHO, World Health Organization.

*Alberti KG, Zimmet P, Shaw L; IDF Epidemiology Task Force Consensus Group. The metabolic syndrome—a new worldwide definition. *Lancet*. 2005; 366: 1059-1062

Prospective population studies have indicated that the diagnosis of metabolic syndrome carries a two-fold increase in relative risk of cardiovascular disease and a three to five-fold increase in risk of developing diabetes. (3) The diagnosis increases with age, and is highest in Mexican Americans (31.7%), followed by Caucasians (23.8%), African Americans (21.6%), and other ethnic groups (20.3%) (5). Women over the age of 75 are the most rapidly growing segment of our population and those between the ages of 65 and 75 are most likely to be diagnosed with metabolic syndrome.

Etiology:

Controversy exists as to the medical diagnosis of metabolic syndrome, largely because of the cluster of abnormalities that exists without a defining disease process. To date, there is disagreement regarding precise values for diagnosis as well as the single underlying cause of metabolic syndrome. *Abdominal obesity* (specifically visceral fat) and *insulin resistance* are proposed as two causative factors in the development of metabolic syndrome. Visceral fat stores are particularly problematic because of their association to multiple risk factors. Their effect on adiponectin, leptin, inflammatory cytokines, plasminogen activator inhibitor-1, resistin and angiotensinogen has been linked to insulin resistance. (6) (7) Waist circumference provides the best indirect measure of visceral fat.

Screening Practices:

Along with the current guidelines that offer straightforward values, the inclusion of waist circumference and a fasting lipid profile with the routine vital measurements should provide sufficient information to make a clinical diagnosis. These are normally requested for patients over the age of 35 however, patients who have family histories of hypertension, diabetes, CVD and obesity would benefit from screenings at an earlier age.

Clinical Management of Treatment and Prevention Strategies:

Lifestyle Modification

The primary strategy for treatment of the metabolic syndrome is lifestyle modification, with the goal of reducing risk factors for cardiovascular disease and diabetes. (8) Even in those patients with established diabetes, intensive management of metabolic syndrome will reduce the higher risk of CHD. Therapy goals should address associated major risk factors including: lowering LDL cholesterol, decreasing blood pressure, and normalizing blood sugars. Most individuals affected by metabolic syndrome are overweight,therefore a change in diet and increased physical activity should be emphasized. For example, a 7-10% reduction in abdominal obesity achieved by nutrition intervention during the first year was adequately induced clinically significant effects of the individual components of the syndrome and a decrease in the development of diabetes. (9)(10)

Exercising for at least 30-60 minutes on most days of the week is also critically important to successful management of risk factors. Alone or in combination with weight loss, exercise favorably affects HDL cholesterol levels, triglycerides, blood sugars. (9)(10) Further, both emphasize that reduction and smoking cessation are important lifestyle modifications to consider as part of a comprehensive treatment approach.

The National Diabetes Education Program has developed a six step action plan that health care professionals can follow for prediabetes treatment. (11) The six steps are as follows:

(1) Identifying and testing high-risk patients
(2) Discussing treatment options
(3) Setting realistic weight-loss goals
(4) Setting attainable diet and exercise goals
(5) Initiating lifestyle modifications
(6) Referring patients for weight-loss support and follow up

In summary, proactive lifestyle management plays a significant role in managing metabolic syndrome effectively. However, given the progressive nature of the condition and lack of resources (notably time) needed to support patient efforts, many patients fail to achieve their goals. For these patients and those found to have a high ten year risk for CVD, the NCEP ATPIII guidelines state that drug therapy of both major and metabolic risk factors can help lower risk. (11)

Pharmacological and Combined Approaches to Metabolic Syndrome

Many pharmaceutical agents are available that are effective in managing individual risk factors (insulin resistance, hypertension and dyslipidemia) for metabolic syndrome. A complete summary of the medications for each risk factors is beyond the scope of this summary; some of these medications are metformin and insulin; thiazide diurectics, angiotensin-converting enzyme inhibitors and receptor blockers, antiobesity drugs, as well as statins.

One study reported in the *New England Journal of Medicine* utilized a combination of medication and lifestyle modifications that resulted in greater weight loss than either therapy alone. (12) Thus, physicians must combine therapies to optimize successful treatment. Ideally, strategies for weight management include the fundamental need for preventive programs in individuals who are high risk for developing metabolic syndrome.

WHAT PATIENTS NEED TO KNOW

As summarized by the NHLBI (http://www.nhlbi.nih.gov/health/dci/Disease/ms/ms_whatis.html), in general, metabolic syndrome is characterized by a group of risk factors that are linked to an individual who is overweight or obese that increases his/her chance for heart disease, diabetes, and stroke. The term 'metabolic' refers to biochemical processes in the body's normal function. The five metabolic risk factors are as follows:

1) A large waistline or abdominal obesity
2) High blood pressure or hypertension
3) Higher than normal triglyceride level in the blood (or use of medication to treat high triglycerides)
4) Lower than normal level of HDL cholesterol in the blood (or use of medication to treat low HDL)
5) Higher than normal fasting blood sugar (or use of medication to treat high blood sugar)

These risk factors increase your chance of getting heart disease, as well as diabetes and stroke. It is very important to address each potential risk factor for minimizing your risk.

Specific steps you can do to improve the conditions associated with metabolic syndrome include the following:

- Decrease total fat in your diet--especially saturated fats found in high fat animal products, and hydrogenated and trans fats found in processed and refined foods. Avoid processed and refined food and replace them with healthy monounsaturated fats found in Extra Virgin Olive Oil, nuts, nut butters, seeds and canola oil.

- Increase intake of omega 3 fatty acids found in cold water fish (2-3 servings per week of sockeye and Chinook salmon; sardines, herring) and plant sources such as walnuts, flaxseed, pumpkin seeds, etc. Or take a high-grade fish oil supplement.

- Increase intake of dietary fiber from whole grains. These include wheat and non-wheat sources such as oats, millet, amaranth, quinoa, barley, wheat berries, legumes, fruits and vegetables.

- Moderate sodium intake. Read labels to be aware of the sodium content of the foods you purchase. Try to achieve an intake of 2300 mg or less sodium per day. Minimize intake of highly processed and canned foods that are high in salt and hidden forms of sodium. Limit the use of table salt.

- Consume small, frequent meals rather than large, less frequent ones. This practice helps maintain stable energy and insulin levels.

- Limit alcohol consumption to no more than 1 drink per day for women and 2 drinks per day for men.

- Exercise! You have to get moving--even small amounts help. Ideally, try to exercise for 60 minutes most days of the week and begin to incorporate strength training into your routine 2-3 times per week.

To ask a question related to program module, please email our experts at info@obgynalliance.com.

References:

1. Ford ES, Giles, WH, Dietz. Prevalence of the metabolic syndrome among US adults: Findings from the third National Health and Nutrition Examination Survey. JAMA. 2002; 287:356-359.
2. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome: a new world-wide definition: a consensus statement from the International Diabetes Federation. Diabetic Medicine. 23(5):469-80, 2006 May.
3. Executive summary of the Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA.2001;285:2486-2497. Med. 2006;23:469-480.
4. Isomaa B, Almgren P, Tuomi T, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care.* 2001;24:683-689.
5. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA.* 2002;287:356-359.
6. Scherer PE, Adipose tissue: from lipid storage compartment to endocrine organ. Diabetes. 2006;55:1537-1545.
7. Greenstone, CL. The Metabolic Syndrome: A Lifestyle Medicine Foe Worthy of a Seek and Destroy Mission. American Journal of Lifestyle Medicine 2008; 2; 109- 112.
8. Orchard TJ, Temprosa M, Goldgerg R, et al. The effect of metformin and intensive lifestyle intervention on the metabolic syndrome: the Diabetes Prevention Program randomized trial. Ann Intern Med 2005; 142:611-619.
9. Carr DB, Utzschneider KM, Hull RL, et al. Intra-abdominal fat is a major determinant of the national cholesterol education Program Adult Treatment Panel III criteria for the metabolic syndrome. Diabetes. 2004;53(8):2087-2094.
10. Clinical Guidelines on the identification, evaluation and treatment of overweight and obesity in adults: The evidence report. National Institutes of Health. Obes Res. 1998;6(suppl2):51S-209S.
11. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002:106(25):3143-3421.
12. Wadden TA. Combining lifestyle modifications and diet pills may help weight loss. N Engl J Med. 2005;105(suppl1):S63-S66.
13. Alberti KB, Zimmet P, Shaw L: IDF Epidemiology Task Force Consensus Group. The metabolic syndrome – a new worldwide definition. *Lancet*. 2005; 366:1059-1062.

Author Information:

B. Reardon and A. Lukes both serve on the Council for Nutrition created in 2006 and supported by Xanodyne Pharmaceuticals, Inc. Both are dedicated to education regarding nutrition, particularly as it relates to women's health and pregnancy.

Beth Reardon, MS, RD, LDN is the Director of Integrative Nutrition at the Carolina Women's Research and Wellness Center in Durham, NC. She is also an Integrative Nutritionist through Duke Integrative Medicine. She has published numerous articles relating to nutrition including ways to achieve optimal pregnancy outcomes through nutritional intervention.

Andrea Lukes, MD, MHSc, FACOG is the Founder and Chair of the Ob/Gyn Alliance. She has partnered with Beth Reardon to help create an educational channel for both providers and patients (TV segment in 2008 on Oxygen and ABC, formation of a Healthy Lifestyle Changes program through her private practice and research center – the Carolina Women's Research and Wellness Center).