

# New Insights on Metabolic Syndrome: A “Silent” But Visible Epidemic

*Philip E. Donahue, MD, FACS*

As surgeons, we evaluate varied problems, depending on our background and experience, but rarely make formal recommendations regarding the abnormalities observed in the metabolic syndrome (MS). The article by Ryan et al, from St. James Hospital/Trinity College Dublin which appears in this issue of *Annals of Surgery*, linking proinflammatory changes with the extent of squamous intestinal metaplasia in a cohort of patients with Barrett epithelium focuses attention on a common problem that should be more widely addressed by the medical community.<sup>1</sup> As a surgeon, I readily admit a focus on the “presenting problem” and not on broader questions of health maintenance; this article forced me to recognize that I should be more involved in finding ways to deal with MS, which affects 25% to 45% of the population, depending on ethnicity and sex, and has such a variety of consequences, associated risks, including cardiovascular disease, and an ever widening list of cancers.

Metabolic syndrome qualifies as a public health epidemic, but its cluster of abnormalities does not command the kind of attention directed towards more visible problems such as the preventable diseases of childhood or chronic lead poisoning, with more easily defined and recognizable consequences; this is probably not the correct approach.<sup>2-4</sup> Because many of the component physiologic abnormalities of MS are improvable (if not preventable) and directly affected by personal choices regarding lifestyle, diet, and exercise, greater emphasis should be placed on this condition. Obesity and hyperinsulinemia have been correlated with disease conditions for more than 20 years and defined more specifically of late as the metabolic syndrome. Specific details are defined by the World Health Organization, National Cholesterol Education Program, and the National Diabetes Federation (Table 1) who periodically update their definitions of these abnormalities. The weight parameter, readily apparent when viewing an American population, and lipid levels are more amenable to modification in some populations compared with others.

In the rodent, a low fat, low starch diet is effective in reversing abnormalities of MS resulting from a high fat and high refined sugar diet. Eating habits in human subjects are more difficult to control, but a low fat/starch diet combined with daily exercise program can be effective, as shown most effectively in patients after bariatric surgery. As epidemiologic studies reveal additional risks of MS (increased incidence rate for cardiovascular disease, cancers, and other conditions), it becomes apparent modifiable risks deserve more attention.<sup>5-7</sup> The present study on Barrett esophagus from Dublin shows an independent association between MS and the severity of Barrett esophagus (as defined by the extent of abnormal epithelium); the association of MS and immunoinflammatory changes with the extent of SIM is intriguing in light of our understanding of esophageal inflammation.

That obesity and esophageal diseases are related is known, with published studies including an epidemiologic report from the Trinity group showing greatly increased numbers of esophageal adenocarcinoma in obese compared with nonobese individuals. Furthermore, gastroesophageal reflux disease (GERD) and erosive esophagitis are more common in the obese, and the most likely explanation for these findings is the likely effect of obesity in promoting GER, followed initially by inflammation and esophagitis, and later

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From the Division of General Surgery, John H. Stroger, Jr. Hospital and University of Illinois at Chicago, Chicago, Illinois.

Reprints: Phil E. Donahue, MD, Cook County Hospital, Division of General Surgery, 1835 W. Harrison Street, Chicago, IL 60612. E-mail: phil@eolas.com.

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**TABLE 1.** Definitions of the Metabolic Syndrome: Minor Variations Among the Same Variables

	Abdominal Obesity (Waist Measurement)	Serum Triglycerides (TG)	HDL Cholesterol	Blood Pressure (BP)	Fasting Blood Glucose
2001 Cholesterol Treatment Trial	>40" men >35" women	>150 mg/dl	<40 mg/dl men <40 mg/dl men <50 mg/dl women	>130/85	>110 mg/dl
World Health Organization	High insulin levels, blood sugar, or postprandial glucose and at least 2 of: waist:hip ratio >0.9, BMI >30, or waist >37"	>150 mg/dl	35 mg/dl	>140/90 (or on Rx for high BP)	
International Diabetes Federation	>37" European men >31.5" women	Raised TG >1.7 mmol/l (males or 1.29 mmol/l females)		>130 systolic or >85 diastolic (or previous Rx for high BP)	Fasting glucose >5.6 Mmol/l or previous Dx Type II diabetes
National Cholesterol Education Program	Waist >40" in men or >35" women	Raised TG >150 mg/dl	<40 mg/dl men or <50 mg/dl in women	Elevated BP >130/85	Fasting glucose >100 mg/dl

by the appearance of Barrett epithelium. Because the transformation of Barrett epithelium to adenocarcinoma has been thought to be related in some way to chronic inflammation, which somehow facilitates the appearance of dysplasia in metaplastic epithelium, the current study linking a prothrombotic or proinflammatory state (as shown by elevations in fibrinogen, plasminogen activator inhibitor, or C-reactive protein identification) and immunoinflammatory changes in patients with MS is highly interesting.

When I recently began to query surgical residents or fellow attending surgeons about MS, many were aware that obesity and insulin resistance are components of the MS symptom cluster, but few knew specific details. They thought, as I had, that the primary risks of MS relate to cardiovascular disease and consequences of atherogenic plaque in the wrong places.<sup>8</sup> After considering the work presented by Ryan et al, I understand that additional dimensions of obesity in GERD should be considered. In addition, in an ideal world (don't we all practice in one?) there should be a more systematic identification of MS and a more organized approach to dealing with it because control of part of the complex will lead to improvements in others. Unfortunately, in my world and that of many colleagues, we are preoccupied with getting through the daily problem list, and we neglect systemic issues like excess weight, even when dealing with GERD. After all, we're the surgeons, right? When we counsel patients with severe obesity and GERD that weight control has a higher priority than reflux control per se, we are on the right track because failure rates of fundoplication alone in obese patients are excessively high. On balance, however, we should probably do more about the MS, since its implications are far-ranging.<sup>9-12</sup> I would encourage the readers to "Google" the metabolic syndrome (on their next web visit) or review materials from the American Heart Association web page (accessed February 2008, [www.americanheart.org/presenter.jhtml?identifier=4756](http://www.americanheart.org/presenter.jhtml?identifier=4756)) to learn more about the dimensions of MS.

This study will undoubtedly be followed by others that will add information to the association of the inflammatory

conditions to neoplasia, and we must be grateful to the authors for bringing forward a rigorous analysis of clinical data that will expand our view of GERD and the extent/severity of Barrett esophagus. The authors deserve further congratulations for their tenacity in addressing a soft target in a rigorous way, allowing many to expand our view of MS and the risks faced by persons with MS. These risks are daunting and deserve consideration by all practitioners, whether by reviewing the published medical data (including the references data in Professor Reynold's work), the web site ([www.metabolicsyndrome.org](http://www.metabolicsyndrome.org)), or comparable information readily available in the popular press or medical journals.

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