Evaluating metabolic syndrome in a medical physiology laboratory

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The metabolic syndrome, a condition characterized by central obesity, hypertension, insulin resistance, and atherogenic dyslipidemia (4, 9, 14), is a major and increasingly prevalent disorder in the developed world. For medical students, understanding the physiological and nutritional aspects of the metabolic syndrome is of fundamental importance for their future medical practice (4). This condition is suitable for study in a first-year medical and graduate student learning component of the first-year medical and graduate student physiology laboratory since the five variables used for diagnosis [fasting blood triglyceride, high-density lipoprotein cholesterol, and glucose levels, blood pressure, and abdominal obesity (14)] are readily determined.

The two primary risk factors for development of the metabolic syndrome apart from genetic factors are overweight/obesity and physical inactivity. We designed a laboratory that also addressed each of the latter two factors by including assessment of physical activity and body fatness, together with a lunch that required complete nutritional analysis.

We incorporated nutritional analysis in part because >50% of graduating medical students in the United States describe their medical education coverage of nutrition as inadequate (7). Improved nutritional training results in physicians more secure in their nutritional knowledge (9). The design of this laboratory allows new nutritional information to be readily integrated into existing curricula (13, 15).

Finally, this laboratory is well suited to a teaching strategy designed to directly involve students. All measurements, including blood draws, physical activity estimates, meal selection and analysis, and determinations of body fatness, are made by students on each other. This design creates personal as well as professional ties to the material, goals that enhance student interest and motivation (16).

METHODS

Informed consent. Thirty-five students signed informed consent forms to allow their data, as obtained in a class laboratory exercise in medical physiology, to be included in this publication. The class consisted of first-year medical students and graduate students. Participants agreed to allow their data to be included in published mean group data, with no individual data or identifiers to be used. Consent was obtained after the completion and assignment of grades in this course, and data analysis began only after obtaining consent. A third party eliminated the data from those individuals who did not consent, and then presented the investigators with the remaining data without identifiers. These procedures were reviewed and approved by the Bloomington campus Institutional Review Board of Indiana University.

Venous blood collection and analysis. The exercise takes place on one afternoon of a 14-week physiology laboratory and problem-based learning component of the first-year medical and graduate student curriculum. During week two of this block, student-measured blood pressure records are obtained and are later included in this laboratory. During weeks four and five, students learn to draw venous blood samples from each other, while under the supervision of a registered nurse and a trained phlebotomist (5). Fasting blood samples from weeks four and five are analyzed at Bloomington Hospital for a lipids panel (cholesterol, HDL cholesterol, low-density lipoprotein cholesterol, and triglycerides), and a basic metabolic panel [including blood urea nitrogen, creatinine, glucose, Na⁺, K⁺, Cl⁻, Ca²⁺, bicarbonate (measured as total CO₂), total protein, and albumin]. The data returned from Bloomington Hospital were given to students the next week (week six), which is the exercise described in this study.

Student-selected lunch. On the morning before this afternoon laboratory, students are given a standard equation for estimation of daily caloric expenditure (1). Their lunch caloric content is then restricted to a maximum of one-third of estimated daily caloric expenditure. One-third of the students are allowed any food choices whose total caloric content does not exceed the allowable lunch total.

In contrast to the ad libitum food choices given to this first group, meal composition is further constrained in the remainder of the class. A second one-third of the class is asked to follow a Step I diet of the National Cholesterol Education Program (NCEP). The Step I diet limits saturated fat to <10% of total calories and cholesterol to <200 mg/day (<70 mg for this meal). The diet should also contain >55% carbohydrate calories and >15% of dietary calories as protein (14).

The final one-third of the class must comply with the NCEP Step II diet, which limits saturated fat to <7% of total calories and cholesterol to <200 mg/day (<70 mg for this meal) (14). These basic
Teaching in the Laboratory

EVALUATING THE METABOLIC SYNDROME

Table 1. Blood lipid levels

<table>
<thead>
<tr>
<th>Variable</th>
<th>Recommended Level or Metabolic Syndrome Diagnostic Criterion (14)</th>
<th>Class Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglycerides, serum; mg/dl</td>
<td>Diagnostic criterion: &gt;150</td>
<td>99±52</td>
</tr>
<tr>
<td>Cholesterol, total; serum; mg/dl</td>
<td>Recommended: &lt;200</td>
<td>166±34</td>
</tr>
<tr>
<td>HDL cholesterol, serum; mg/dl</td>
<td>Diagnostic criteria: Males &lt;40; Females ≤50</td>
<td>48±12</td>
</tr>
<tr>
<td>LDL cholesterol, serum; mg/dl</td>
<td>Recommended &lt;130</td>
<td>99±33</td>
</tr>
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Values are means ± SD; n = 35 subjects. HDL, high-density lipoprotein; LDL, low-density lipoprotein.

recommendations persist in the updated NCEP version of the Step II diet, known as the TLC diet (14).

After lunch has been eaten in the laboratory, analysis of the selected lunch items is carried out using nutrition facts provided by the retailer. Because McDonald’s USA provides the most extensive nutritional information in the Bloomington, IN, area, they were chosen as vendor. Students used McDonald’s USA Nutrition Facts for Popular Menu Items as obtained on the internet (6) for calculation of lunch nutritional content. This list includes total calories and calories from fat, saturated fat (g), carbohydrate (g), and protein (g), cholesterol (mg), sodium (mg), dietary fiber (g), and vitamins A and C, calcium, and iron as the percentage of recommended daily value.

Body fatness and malnutrition estimates. During the afternoon exercise, central obesity, as estimated from abdominal circumference, was determined and the criteria for diagnosis of the metabolic syndrome were defined as >40 inches (102 cm) in males, and >35 inches (88 cm) in females (3). Four other simple, noninvasive estimates of body fatness or malnutrition were used. First, body mass index was calculated as \(\text{weight (kg)/[height (m)]}^2\) (2, 8). Second, triceps skinfold was compared with standards obtained from the combined National Health and Nutrition Examination Surveys of 1971–1974 and 1976–1980 (12). Third, body weight was compared with reference weights for various heights as derived from mortality experience data, and expressed as a percentage of the weight-for-height median values (12). Fourth, midarm muscle area, used to detect the presence of malnutrition, was determined from arm circumference and triceps skinfold and compared with data from National Health and Nutrition Examination Surveys (12).

RESULTS

The mean lipid levels in the class of 35, obtained from analysis of fasting venous blood samples, are shown in Table 1. Table 2 lists mean meal composition from the entire class. It also shows saturated fat and cholesterol contents of self-selected diets of persons assigned to the ad libitum, Step I, and Step II groups.

Mean results from the basic metabolic panel are listed in Table 3, and the class mean results from the five noninvasive indexes of body fatness and malnutrition are shown in Table 4.

DISCUSSION

The metabolic syndrome (or “syndrome X”) consists of a constellation of factors, including central obesity, atherogenic dyslipidemia, hypertension, and insulin resistance (4, 9, 14). These clustered factors contribute substantially to risk for both Type 2 diabetes and atherosclerotic cardiovascular disease (9). The metabolic syndrome is increasing in incidence in the US, and is said to afflict as many as 20–25% of the adults in this country (4, 14). The primary causes of and treatments for the metabolic syndrome include dietary and nutritional factors, making this issue an ideal site for a nutrition-physiology connection in medical education (13, 15).

Evaluating criteria for presence of metabolic syndrome. In 2002, the National Heart, Lung, and Blood Institute of the National Institutes of Health issued its Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (14). This report defines the metabolic syndrome as the presence of three or more of the following (14):

- Central obesity [waist circumference >40 inches (males), >35 inches (females)].
- Fasting blood triglycerides, ≥150 mg/dl.
- Blood HDL cholesterol ≤40 mg/dl (males), ≤50 mg/dl (females).
- Blood pressure ≥130/85 mmHg.
- Fasting glucose ≥110 mg/dl.

Because each of these criteria is readily evaluated, this laboratory allows a complete analysis and discussion of a condition that is epidemic across much of the developed world.

Diet composition. Evaluation of the features of the metabolic syndrome leads directly to consideration of the triglyceride- and cholesterol-lowering diets followed by the students. Our experience has been that students enjoy being randomized into the three diets and then searching the menu to meet the given dietary requirements. For many young adults this is their first exposure to a therapeutic diet. Discussion of diet composition, cholesterol transport and regulation, risk factors for insulin resistance, and potential medications used for treatment of hyperlipidemia, hypertension, or hyperglycemia make this area fertile soil indeed for conversation with medical students.

The National Heart, Lung, and Blood Institute has recently amended and expanded its definition of the former Step II diet. This diet is now known as the Therapeutic Lifestyle Changes
Table 3. Blood levels of electrolytes, glucose, protein, and protein breakdown products

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal Range</th>
<th>Class Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Na⁺] plasma, mEq/l</td>
<td>136–146</td>
<td>143.0±2.4</td>
</tr>
<tr>
<td>[Cl⁻] plasma, mEq/l</td>
<td>98–106</td>
<td>103.0±2.2</td>
</tr>
<tr>
<td>[Ca²⁺] total plasma, mg/dl</td>
<td>8.4–10.2</td>
<td>9.3±0.3</td>
</tr>
<tr>
<td>[K⁺] plasma, mEq/l</td>
<td>3.5–5.1</td>
<td>4.1±0.3</td>
</tr>
<tr>
<td>[HCO₃⁻] plasma, mEq/l</td>
<td>23–29</td>
<td>26.2±2.0</td>
</tr>
<tr>
<td>Glucose, blood, mg/dl</td>
<td>70–105</td>
<td>77±14</td>
</tr>
<tr>
<td>Protein, total, g/dl</td>
<td>6.4–8.3</td>
<td>8.0±0.5</td>
</tr>
<tr>
<td>Albumin, blood, g/dl</td>
<td>3.5–5.0</td>
<td>4.5±0.4</td>
</tr>
<tr>
<td>Creatinine, plasma, mg/dl</td>
<td>Males 0.7–1.3; Females 0.6–1.1</td>
<td>0.9±0.2</td>
</tr>
<tr>
<td>Urea nitrogen, plasma, mg/dl</td>
<td>7–18</td>
<td>14±3</td>
</tr>
</tbody>
</table>

Values are means ± SD; n = 35. [HCO₃⁻] is measured as total CO₂.

(TLC) diet (14). The TLC diet includes several additional lifestyle and dietary changes that can be mentioned and discussed during this portion of the laboratory. In addition to those issues directly commented on thus far (the need for adjustment of total caloric intake to maintain a desirable body weight, the maintenance of saturated fat intake <7% of dietary calories, and limiting cholesterol to <200 mg/day) several other recommendations can be considered.

One of these recommendations is that persons increase viscous (soluble) fiber intake to 10–25 g/day. This number far exceeds that contained in the lunches chosen by our students (Table 2). In addition, the nutritional information provided by McDonald’s USA lists only total fiber, and fails to distinguish soluble from insoluble fiber. To more directly address the issue of soluble fiber and its important role in the lowering of blood cholesterol, further information could be added from standard nutritional tables. Another alternative would be to prepare a lunch, designed to comply with all TLC diet guidelines, in a metabolic kitchen.

The recent dietary guidelines also suggest an intake of 2 g per day of plant stanols/sterols, recommend enough exercise each day to expend at least 200 kcal (14), and advocate replacement of animal proteins with soy protein in some situations. We have found that all of these dietary and lifestyle issues are made highly relevant and engaging in this laboratory.

Body fatness and malnutrition estimates. We chose to supplement measures of waist circumference with four other rapid, simple, noninvasive estimates of body fatness or malnutrition. Contrasting the results obtained from body mass index (2, 8), weight for height compared with the midpoint of an acceptable range (12), and triceps skinfold (12) helps students understand various methods for and problems with noninvasive determination of fatness. Our results show only the whole-class means, which include both males and females. A more meaningful analysis would separate data from males and females, and this is easily done during an actual class exercise.

This study of obesity and its origins and risks often begins with students remarking on the small size of the allowed lunch in kcal—the simple calculation of estimated daily caloric expenditure is often a first careful exploration into basic issues of energy balance for these students. The midarm muscle area (12) is used to estimate the possible presence of malnutrition, as may occur, for example, during anorexia nervosa. The physiological responses to malnutrition are readily expanded to include assessment of meal caloric content, protein content, and the levels of total protein, albumin, and urea nitrogen in the blood. Finally, although its full explication belongs in a laboratory devoted to renal function, the blood levels of urea nitrogen and creatinine can also properly be included in this overarching review of protein anabolism and catabolism during malnutrition.

Other possible points for emphasis. The low coefficient of variation (SD/mean) for plasma levels of Na⁺ and Cl⁻, as contrasted with the very wide range of individual levels of Na⁺ intake, is a useful starting point for a dialogue about extracellular fluid Na⁺ regulation and its complex relationship to Na⁺ intake. McDonald’s USA is not a preferred source for a wide range of foods low in Na⁺, and here a meal prepared in a metabolic kitchen could provide a broader array of foods low in Na⁺ content.

Although our chosen vendor does not provide potassium levels in the nutritional tables provided, these could be calculated and then contrasted with the numbers seen in the normal plasma range. Similarly, we chose not to emphasize Ca²⁺ intake and Ca²⁺ plasma regulation, but Ca²⁺ intake levels are directly available from the restaurant and easily could be included in class discussion. Most clinical laboratory panels also include bicarbonate and anion gap readings, and dialogue can readily be generated that helps integrate these readings into the broader understanding of extracellular fluid and acid-base regulation. We also chose to de-emphasize the vendor-provided nutritional information regarding vitamin A, vitamin C, and iron content, but these also represent possible areas for exploration. Many major restaurant chains provide this nutritional information.

Engaging student interest and personal ties to material. Stimulating student involvement, interest, and personal investment is essential to any successful teaching laboratory (16). We do this in part by simply using the students themselves as subjects. By having them estimate their daily caloric expenditure, by having them draw each other’s blood and then interpret their own results, by allowing them to choose their own lunch in full view of its nutritional content, and by randomizing them into clinically relevant therapeutic diets, we generate consid-

Table 4. Estimates of fatness and malnutrition

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal Range or Metabolic Syndrome Diagnostic Criterion (14)</th>
<th>Class Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist, inches</td>
<td>Diagnostic criteria: Males &gt;40; Females &gt;35</td>
<td>32±4</td>
</tr>
<tr>
<td>Body mass index, weight (kg)/(height (m))²</td>
<td>Overweight: 25–30; Obese: &gt;30</td>
<td>22.7±3.3</td>
</tr>
<tr>
<td>Triceps skinfold, %standard</td>
<td>Malnutrition: &lt;50; Obesity: &gt;150</td>
<td>78±23</td>
</tr>
<tr>
<td>Weight, %median</td>
<td>Normal range: 85–115</td>
<td>101±14</td>
</tr>
<tr>
<td>Mid-arm muscle area, %standard</td>
<td>Malnutrition: &lt;70</td>
<td>89±23</td>
</tr>
</tbody>
</table>

Values are means ± SD; n = 35 subjects.
erable personal stake in the results. In addition, during the course of the laboratory, we create a large table on the board in full view of all class members. On it we have students (who are randomly assigned a number) enter their blood results, and their analyses of nutritional content of the meals they chose. This table allows immediate visual inspection of all of the individual data, comparison of generated means, and some immediate feedback regarding intersubject variability.

In summary, the clustered diet- and activity-linked factors that confer risk for Type 2 diabetes and atherosclerosis constitute the metabolic syndrome. By evaluating all of the factors involved in this syndrome in a single setting, this laboratory helps medical students grasp the nature of the disorder, its relationship to dietary factors, and its link to physiological principles. The increasing importance of these measurements as obesity and its related disorders increase in prevalence makes this a laboratory exercise of enormous significance.

REFERENCES