Further Evolution and Challenges for *JABFP*

This issue of the *JABFP* marks the start of its 9th year of publication and is noteworthy on several counts. With the specialty now 26 years, or about one generation, old, this journal's readership now totals almost 55,000 Diplomates of the American Board of Family Practice and family practice residents. That number is projected to grow by at least 3000 each year as new residency-trained graduates become Board certified in this specialty.

It is also noteworthy that the *JABFP* enters a new year in good editorial health despite an increasingly fragile journal environment throughout medical publishing. The costs of publication have continued to escalate as a result of many factors, including frequent quantum jumps in the costs of paper and postage. Since pharmaceutical advertising simultaneously continues to change and to retrench in terms of medical journals, cost-cutting and downsizing of journals have become the norm in medical publishing, including the closure of some medical journals. The loss last year of the *Family Practice Research Journal* is the latest casualty of this trend in our field.

Although the *JABFP* has also undergone major budget cuts, we enter the new year with a streamlined editorial process, updated computer equipment, a new cover, and new publishing arrangements through MRA Publications. A new Health Policy feature is being inaugurated in this issue through the leadership of Dr. Howard Rabinowitz, who recently spent a year in Washington, DC, as a health policy fellow under the auspices of the Robert Wood Johnson Foundation. Another article in this issue, a "Formal Model of Family Medicine," describes the groundbreaking work of the American Board of Family Practice toward development of a computerized knowledge base and testing in family practice.

Preservation and ongoing development of this kind of forum for publication of original scholarly work are of vital importance to our specialty and its clinical discipline. This forum becomes progressively more important as other such journals in the field fall by the wayside. As we begin this new year in a challenging time, I am indebted to the continued dedication and involvement of the editorial staff, the associate editors, and editorial board, as well as the leadership of the American Board of Family Practice, which sponsors and supports this enterprise.

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Atherogenesis, Families, and Family Practice: Recognizing and Treating an Important Syndrome

A common and important syndrome that leads to premature atherosclerosis and end-organ damage has been described and needs to be recognized by family physicians. Individuals with this syndrome have multiple metabolic abnormalities, including insulin resistance, hyperinsulinemia, hypertension, central obesity, and abnormal low-density lipoprotein (LDL), high triglyceride, and low high-density lipoprotein (HDL) levels. The syndrome is estimated to occur in 2 percent of the general population and in the majority of persons with diabetes or atherosclerosis.[1,2] These risk factors can be expressed early in life, can be associated with the development of obesity, and are usually fully expressed by the third decade of life.[3] The syndrome is referred to by various names, including "familial dyslipidemic hypertension," "the atherogenic lipoprotein phenotype," "the deadly quartet," or "syndrome X."

In this issue of the Journal, Spangler and Ko-

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nen[4] describe additional deleterious effects of this syndrome, noting that the clustering of these risk factors in patients with noninsulin-dependent diabetes mellitus (NIDDM) leads to a markedly elevated risk of microalbuminuria. The development of renal damage and dysfunction should not be surprising given the extent of end-organ damage noted with diffuse atherosclerosis in diabetic patients, but these findings emphasize the importance of early recognition and treatment of this syndrome by patients and primary care physicians.

The paper by Spangler and Konen is an elegant example of the important contribution of primary care research to the medical literature. Conducted in primary care clinics, this study describes one sequela of the syndrome that develops prior to manifest disease; such a study might not be possible with patients seen in referral or tertiary care facilities. The study also describes the prevalence of an important condition in a primary care population and suggests that early recognition of this syndrome, which will progress without recognition and treatment, could lead to earlier treatment to reverse the damage done to the circulatory system and kidneys.

Current research suggests that this syndrome has a genetic cause characterized by insulin resistance and mediated by impaired fatty acid metabolism, which is fully expressed with the development of obesity.[2] The patients with this syndrome nearly all have central obesity, characterized by a large abdomen with small buttocks and thighs, which contributes further to the insulin resistance and makes for fairly simple clinical recognition. Abdominal fat deposition is associated with the male sex, high-fat diets, a lack of exercise, and cigarette smoking.[1] This genetic syndrome is therefore expressed as a result of, or altered by, lifestyle factors. Interestingly, a high frequency of glucose and lipoprotein abnormalities have been found in the spouses of persons with this syndrome, further suggesting that metabolic changes are also influenced by such nongenetic variables as culture, physical activity, diet, and smoking.[1] This reinforces the importance of family screening and interventions.

The changes in glucose and lipoprotein metabolism in this syndrome result in considerable risk for atherosclerosis. The LDL and very low-density lipoprotein (VLDL) in these patients have been found to be more dense, easily oxidizable, and very atherogenic compared with the LDL and VLDL of others in the population.[3,5] LDL that is oxidized is highly atherogenic and is recognized, not by the LDL receptor, but by the macrophages in the arterial wall.[1] Following meals, the patients with this syndrome have poor lipoprotein clearance, and the arteries will have prolonged exposure to these abnormal lipoproteins.[6] When triglycerides are elevated, ie, greater than 160 to 200 mg/dL, HDL production is impaired, and HDL levels are usually low. Glucose and insulin metabolism are also altered, and the high serum glucose levels lead to more VLDL production. Hyperinsulinemia is known to promote further obesity, raise blood pressure, stimulate the sympathetic nervous system, cause abnormal lipoprotein metabolism, and promote atherosclerotic plaque progression.[1]

It is essential that family physicians recognize how the presence of multiple risk factors greatly increases overall risk of premature death and disability from atherosclerosis. While having one to two risk factors increases risk of cardiovascular events during a 10-year period by a factor of 1.5 to 3, four or more risk factors, as with this syndrome, increase risk of premature events by tenfold or more.[7,8] The combination of high LDL and triglyceride levels with low HDL levels is particularly predictive of premature coronary disease.[6,8,9] In the study of microalbuminuria by Spangler and Konen, the clustering of risk factors was also highly synergistic rather than merely additive.[4]

Paradoxically, although this syndrome is easily recognized, it can be easily ignored until it is too late to prevent its consequences. The metabolic characteristics of this syndrome are moderately abnormal and therefore often missed or underestimated. A typical manifestation of this disease in primary care is premature atherosclerosis in a person who is modestly overweight and sedentary and who has a combined cholesterol disorder (total cholesterol 220 to 240 mg/dL, triglyceride 180 to 250 mg/dL, HDL 30 to 35 mg/dL, and LDL 130 to 160 mg/dL), moderately elevated fasting glucose levels or NIDDM, and borderline to mild (stage I) hypertension. These patients might have as many as four to six risk factors, but not one of them is quite high enough to merit immediate treatment with medication. Because each of the individual risks is not exceedingly high and physicians are often not

aware of the impaired metabolism and synergism of this syndrome, the condition is often unrecognized, and the patients are falsely reassured or lost to follow-up.

The metabolic abnormalities of this syndrome are highly modifiable by diet, exercise, weight loss, and certain pharmacologic agents.[1] Regular exercise improves insulin receptivity and lipolysis, down-regulates the sympathetic nervous system, and enhances endothelial function, resulting in a reversal of most metabolic and pathologic abnormalities of the syndromes. Patients followed angiographically in a recent trial of exercise and diet showed improvement in coronary lesions.[10] In primary and secondary prevention trials of cholesterol treatment, patients with combined hyperlipidemla were found to be at highest risk and to respond best to the treatment.[9-12] In these trials patients with combined hyperlipidemia in the treatment groups had 30 to 75 percent reductions in coronary events. Treatment of combined hyperlipidemias requires specific therapy and could require multiple medications.[13]

The tragedy of the multiple metabolic consequences of this syndrome is that, if the condition is not addressed early with vigorous lifestyle change, the patient could require multiple medications to deal with each of the sequelae, including the diabetes, hypertension, dyslipidemia, and atherosclerosis. The findings of renal effects related to this syndrome by Spangler and Konen[4] add another reason for family physicians to become knowledgeable about this syndrome and its treatment.

Family physicians must become aware of the importance of this syndrome, because we see many of these patients at a time when the syndrome can be prevented. Early recognition of this syndrome in individuals and families can lead to more comprehensive screening and could lead to treatment of this syndrome before it develops its devastating consequences. By recognizing how multiple risk factors can cluster and are synergistic, we can direct medical therapy to those at highest risk and encourage our affected patients to begin exercise programs and improve their nutritional habits.

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