Uric Acid, the Metabolic Syndrome, and Renal Disease

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Metabolic syndrome, characterized by truncal obesity, hypertriglyceridemia, elevated BP, and insulin resistance, is recognized increasingly as a major risk factor for kidney disease and also is a common feature of patients who are on dialysis. One feature that is common to patients with metabolic syndrome is an elevated uric acid. Although often considered to be secondary to hyperinsulinemia, recent evidence supports a primary role for uric acid in mediating this syndrome. Specifically, fructose, which rapidly can cause metabolic syndrome in rats, also raises uric acid, and lowering uric acid in fructose-fed rats prevents features of the metabolic syndrome. Uric acid also can accelerate renal disease in experimental animals and epidemiologically is associated with progressive renal disease in humans. It is proposed that fructose- and purine-rich foods that have in common the raising of uric acid may have a role in the epidemic of metabolic syndrome and renal disease that is occurring throughout the world.

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Uric Acid, Fructose Intake, and Metabolic Syndrome

In the past few years, there has been increasing evidence that hyperuricemia may be a true cardiovascular and renal risk factor (reviewed in reference [22]). Hyperuricemia predicts the development of hypertension (23), metabolic syndrome (23), diabetes (24), stroke (25), and cardiovascular events (25). Epidemiologic studies also have found that hyperuricemia is an independent risk factor for renal dysfunction in the normal population (26) and in patients with hypertension (27), diabetes (28), and CKD (29). Mild hyperuricemia in normal rats induces systemic hypertension, renal vasoconstriction, glomerular hypertension and hypertrophy, and tubulointerstitial injury inde-
In turn, fructose intake correlates well with the recent rise in metabolic syndrome, diabetes, hypertension, and kidney disease (40). Fructose constitutes 50% of table sugar and also is a major component in high-fructose corn syrup, which is used in the United States as a sweetener. Intake of fructose has increased markedly in the past few decades and correlates with the rising rates of metabolic syndrome. This leads to the hypothesis that fructose intake may be a novel mediator of the epidemic of renal disease. Future studies are planned to determine whether fructose intake may be increased in patients with progressive renal disease, particularly those with features of metabolic syndrome. The possibility that fructose may cause similar hemodynamic changes in the kidneys as uric acid also will be investigated, as well as studies to determine whether fructose can accelerate renal disease in experimental animals. A better understanding of the role of fructose and uric acid in the pathogenesis of the renal disease might make a major contribution to our understanding of the underlying mechanisms of the current epidemic.

### Acknowledgments

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### References


3. National Cholesterol Education Program: Third report of the National Cholesterol Education Program (NCEP) on Detection and Treatment of High Blood Cholesterol in

### Table 1. Definition of metabolic syndrome by WHO, NCEP ATP III, and IDF

<table>
<thead>
<tr>
<th>WHO Definition (2)</th>
<th>NCEP ATP III Definition (3)</th>
<th>IDF Definition (4)</th>
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</thead>
<tbody>
<tr>
<td>Insulin resistance identified by type 2 diabetes or impaired fasting glucose or impaired glucose tolerance or insulin resistance (by insulin clamp) plus two or more of the following:</td>
<td>Metabolic syndrome is defined by three or more of the following risk factors:</td>
<td>Central obesity (waist circumference, ethnicity specific) plus two or more of the following:</td>
</tr>
<tr>
<td>BMI &gt;30 kg/m² and/or waist:hip ratio &gt;0.9 (male) and &gt;0.85 (female)</td>
<td>Waist circumference &gt;88 cm (women) and &gt;102 cm (men)</td>
<td>Triglycerides ≥150 mg/dl or</td>
</tr>
<tr>
<td>Triglycerides ≥150 mg/dl</td>
<td>Triglycerides ≥150 mg/dl</td>
<td>treatment for this abnormality</td>
</tr>
<tr>
<td>BP ≥140/90 mmHg and/or antihypertensive drugs</td>
<td>HDL cholesterol &lt;40 (male) and &lt;50 (female)</td>
<td>HDL cholesterol &lt;40 (male)</td>
</tr>
<tr>
<td>HDL cholesterol &lt;35 (male) and &lt;39 (female)</td>
<td>BP ≥130/85 mmHg</td>
<td>and &lt;50 (female) or specific treatment</td>
</tr>
<tr>
<td>Microalbuminuria (albumin excretion rate ≥20 µg/min) or albumin:creatinine ratio ≥30 mg/g</td>
<td>Fasting glucose level ≥110 mg/dl</td>
<td>BP ≥130/85 mg/dl or</td>
</tr>
</tbody>
</table>

*IDF, International Diabetes Federation; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III; WHO, World Health Organization.*


35. Khosla UM, Zharikov S, Finch JL, Nakagawa T, Roncal C,


