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# Salt and the metabolic syndrome☆

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**Abstract** *Background and aims:* High blood pressure in subjects with the metabolic syndrome (MS) is largely related to dietary salt. We investigated in free-living men and women whether increase in dietary salt intake is associated with the presence and severity of the MS.
*Methods and results:* A total of 766 subjects (251M, 515F) of 44.9 ± 0.5 years/age and SBP/DBP of 120 ± 0.6/77 ± 0.4 mmHg were studied. Twenty-four hour urinary sodium ($UNa^+$) and potassium ($UK^+$) excretions were 143±2.5 mmol (median: 131.5) and 48 ± 0.9 mmol (median: 44). $UNa^+$ was higher in men than in women (median: 155.5 vs. 119.8 mmol/day; $P < 0.0001$). $UK^+$ ($r = 0.34$; $P < 0.0001$), measures of obesity ($r = 0.26$; $P < 0.0001$) and BP ($r = 0.15$; $P < 0.0001$) were significantly associated with $UNa^+$. The association with BP was lost after adjusting for weight.

Of the 766 subjects, 256 (33.4%) met the NCEP-ATPIII criteria for the MS. Median $UNa^+$ in men and women with no traits of the MS was 140 and 116.7 mmol/day, respectively ($P < 0.001$), increasing to 176 in men and 135 mmol/day in women with 4–5 components of the syndrome ($P < 0.001$). Weight, BMI and waist increased significantly across the quartiles of $UNa^+$ both in men and women; whereas, age, lipids and fasting glucose did not. SBP and DBP were associated with $UNa^+$ in men but not in women. $UK^+$ correlated with age in men and women ($r = 023$; $P < 0.0001$) and with obesity in women ($r = 0.14$; $P = 0.001$).
*Conclusions:* $UNa^+$ a measure of dietary sodium intake in free-living subjects was markedly increased in subjects with the MS. Higher $UNa^+$ was associated with obesity and higher BP, but not with age, dyslipidemia or fasting glucose.


## Introduction

Elevated BP is one of the most prevalent cardiovascular risk factors, and the single greatest contributor to cardiovascular disease worldwide [1,2]. High BP commonly clusters with other cardiovascular risk factors, such as in the

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metabolic syndrome [3–6]. The latter is a highly prevalent condition characterized by a cluster of risk factors, known to be associated with the development of type-2 diabetes and adverse cardiovascular events [3–6]. Central obesity, dyslipidemia, high BP, microalbuminuria, insulin resistance, and abnormal glucose metabolism are among the traits employed in defining the syndrome [3,7]. Although the mechanisms underlying the increase in BP associated with the metabolic syndrome are poorly understood, recent studies suggest that it may be related to dietary salt due the development of a salt sensitive phenotype [8,9] which can be reverted by weight loss [10,11].

There is unequivocal evidence to support the adverse effect of dietary salt on BP [12–16]. Obesity, a major component of the metabolic syndrome, is associated with increased food and sodium intakes [15]. However, no information is available on whether salt intake is increased in free-living subjects with the metabolic syndrome, and on whether the level of salt intake is related to the severity of the metabolic syndrome. In the present study, we examined the daily urinary excretion of sodium as a measure of the dietary intake in free-living men and women with and without the metabolic syndrome. The daily urinary sodium excretion was assessed in individuals with none, 1, 2, 3, 4 and 5 components (traits) of the metabolic syndrome. In addition to urinary sodium, measurements of urinary potassium were also assessed.

## Methods

### Study population

Voluntary subjects of 18–70 years of age, living in the city of Caracas, and attending the Center for the Detection and Treatment of Silent Risk Factors for Cardiovascular and Metabolic Diseases, from 2002 to 2006 were evaluated. Advertisement of Center activities and subject recruitment was achieved via radio and newspaper announcements, flyers, health fairs, and health screening programs. Our population consisted of otherwise healthy treatment-naive subjects. Only subjects with no history or presence of active coronary artery disease, heart failure, stroke, arteriosclerosis obliterans, advanced renal or hepatic dysfunction, active inflammatory disease states, greater than stage II hypertension, use of diuretics, steroids or laxatives, oral contraceptive use, and serum creatinine concentration $>2$ mg/dl or creatinine clearances of less than 50 ml/min, were evaluated. A complete history, physical examination and laboratory work-up, including hematology, chemistry, lipid panel, oral glucose tolerance test, liver function tests and urinalysis, were obtained. Antihypertensive and lipid-lowering medications were gradually discontinued over two weeks. Lipid-lowering medications were withheld for four weeks and antihypertensive drugs for eight weeks. In hypertensive subjects, BP was monitored on a weekly basis after antihypertensive drug withdrawal. Any hypertensive subject than during the washout period met criteria for stage II hypertension was withdrawn from the study and was restarted on medication. In addition, subjects were started on medication immediately after completion of the study. The research protocol was approved by the Central University Hospital of the city of Caracas, and by the Nova Southeastern University Review Boards. All participants gave written informed consent.

### Procedures

Diagnosis of metabolic syndrome was made following the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of the High Blood Cholesterol in Adults (ATP III) guidelines: waist circumference: men $>102$ cm ($>40$ in), women: $>88$ cm (35 in); triglycerides $\geq 150$ mg/dl ($\geq 1.7$ mmol/l), HDL-cholesterol: men $<40$ mg/dl ($<1.03$ mmol/l), women $<50$ mg/dl ($\geq 1.29$ mmol/l), BP $\geq 130/\geq 85$ mmHg, and fasting glucose $\geq 110$ mg/dl ($\geq 6.1$ mmol/l) [7]. Due to the young age of our study population subjects with 4 and 5 traits were combined as a group.

BP was measured with a standard mercury sphygmomanometer, and the cuff size was optimized for arm circumference. The same cuff and sphygmomanometer was used to measure the BP in a specific patient. BP was obtained after 30 min rest in the supine position. Because BP was the main variable of the study, resting BP was best attained with patients lying comfortably rather than sitting for 30 min. The average of three consecutive BP readings not greater than 4 mmHg apart from each other was employed. Heart rate was estimated from a 1-min pulse. Waist and hip circumferences were measured at the level of the umbilicus and at the broadest level of the trocanteric region, respectively. Body mass index (BMI) was calculated as body weight in kg/height in meters squared (kg/m$^2$). Plasma glucose was measured with an automated glucose analyzer (Beckman Instruments, Palo Alto, CA), employing a glucose oxidase technique. Plasma insulin was estimated by solid-phase radioimmunoassay (Diagnostic Products Corporation, Los Angeles, CA). Plasma lipids were measured by spectrophotometric techniques (Chiron Diagnostic Corp, East Walpole, MA).

Patient compliance is the best method to assure completeness of urine collection. In order to ensure compliance with study protocol and sample collection, frequent face-to-face investigator–patient contacts were scheduled throughout the study. Patients were repeatedly instructed about the importance of the complete collection and on how to obtain the 24-h urines. When non-compliant or uncertain about completeness of collection, urines were discarded and patients returned an additional 24-h collection. The collection period started immediately after discarding the first morning urine. In addition, the quality of the urine samples was also determined by constructing regression relations between 24-h creatinine and body weight, and 24-h urine volume and age in gender-specific groups. Based on the 95% confidence intervals for each group, a 24-h urine sample was considered acceptable if 24-h urine creatinine (mmoles) was between 5.8 and 38 for males, and between 3.9 and 32 for females. Two 24-h urine collections were obtained in a period of two weeks; the average of which was employed for the calculations.

### Statistical analyses

Twenty-four urinary sodium excretion and serum triglyceride were not normally distributed. Normal distribution of