### ARTICLE IN PRESS

#### *Journal of the American Society of Hypertension* **■**(**■**) (2017) 1–18

### Special Report

## Potassium homeostasis in health and disease: A scientific workshop cosponsored by the National Kidney Foundation and the American Society of Hypertension

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#### Abstract

While much emphasis, and some controversy, centers on recommendations for sodium intake, there has been considerably less interest in recommendations for dietary potassium intake, in both the general population and patients with medical conditions, particularly acute and chronic kidney disease. Physiology literature and cohort studies have noted that the relative balance in sodium and potassium intakes is an important determinant of many of the sodium-related outcomes. A noteworthy characteristic of potassium in clinical medicine is the extreme concern shared by many practitioners when confronted by a patient with hyper-kalemia. Fear of this often asymptomatic finding limits enthusiasm for recommending potassium intake and often limits the use of renin-angiotensin-aldosterone system blockers in patients with heart failure and chronic kidney diseases. New agents for managing hyperkalemia may alter the long-term management of heart failure and the hypertension, proteinuria, and further function loss in chronic kidney diseases. In this jointly sponsored effort between the American Society of Hypertension and the National Kidney Foundation, 3 panels of researchers and practitioners from various disciplines discussed and summarized current understanding of the role of potassium in health and disease, focusing on cardiovascular, nutritional, and kidney considerations associated with both hypo- and hyperkalemia. J Am Soc Hypertens 2017;  $\blacksquare$  ( $\blacksquare$ ):1–18. © 2017 National Kidney Foundation, Inc. and American Society of Hypertension. Published by Elsevier Inc. All rights reserved.

*Keywords:* Cardiovascular disease (CVD); chronic kidney disease (CKD); dietary intake; heart disease; hyperkalemia; hypokalemia; patiromer calcium (RLY5016); potassium; potassium homeostasis; potassium secretion; renal excretion; review; sodium-polystyrene sulfonate; sodium zirconium cyclosilicate (ZS-9).

This article is being published concurrently in the *Journal of the American Society of Hypertension and AJKD*. The articles are identical except for stylistic changes in keeping with each journal's style. Either of these versions may be used in citing this article.

In line with *AJKD*'s procedures for potential conflicts of interest for editors, described in the Information for Authors and Journal Policies, an Acting Editor-in-Chief (Associate Editor James S. Kaufman, MD) handled the peer-review and decision-making processes.

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2

#### **Aims of This Report**

To address the clinical importance of the emerging science related to potassium imbalance and management, the National Kidney Foundation (NKF) and the American Society of Hypertension (ASH) partnered to facilitate a scientific workshop, "Potassium Homeostasis in Disease and Health." The meeting was held on April 8, 2016, in Atlanta, GA, and attended by experts in nephrology, cardiology, nutrition, primary care, and pharmacology. The conference deliberations allowed the faculty attendees to exchange views on the current state of knowledge of potassium metabolism, in particular what is known regarding the common causes of potassium imbalance, the consequences of these imbalances, and dietary and pharmacologic approaches to the management of altered potassium homeostasis. This report summarizes the discussions at this meeting, highlights several controversies, and makes recommendations for epidemiologic and clinical research on potassium. Reflecting the synthesis of the deliberations of the 3 working groups (dietary consideration in potassium management, potassium homeostasis in nephrology, and potassium homeostasis in cardiology), this report includes both a narrative review and a list of recommended research questions.

#### Introduction

Potassium is the most abundant cation in the human body, with 98% being intracellular (140 mEq/L) and 2% being extracellular (3.8-5.0 mEq/L).<sup>1</sup> Maintaining normal potassium homeostasis and the appropriate balance of potassium across the cell membrane is essential for cell function: the large potassium gradient determines cell voltage, which is critical in excitable tissues such as nerve and muscle. Total-body potassium content and the distribution of potassium among the various body compartments depend on dietary and supplemental intake and on complex neurohumoral systems, acid-base balance, and, most importantly, kidney function.<sup>2</sup> Alterations in dietary potassium intake or in the various physiologic mechanisms responsible for maintaining normal potassium balance can result in abnormal potassium homeostasis (typically detected as abnormal extracellular potassium concentrations, ie, hypo- or hyperkalemia) and may cause adverse health consequences. We provide an overview of normal potassium physiology, including issues related to dietary potassium intake, and discuss causes and consequences of abnormal potassium homeostasis, as well as emerging treatments for hyperkalemia. We focus on the patient with non-dialysis-dependent chronic kidney disease (CKD) who has either acute or chronic cardiorenal disease (eg, chronic heart failure combined with CKD), a situation in which disease-modifying drugs that result in potassium concentration elevations may be used.<sup>3</sup>

#### **Dietary Intake of Potassium**

#### Measurement of Potassium Intake

Accurate estimation of potassium intake in free-living populations is challenging. The 2 main approaches are dietary surveys and urine collections. Dietary surveys encompass food diaries, 24-hour recalls, and food-frequency questionnaires. The usefulness of food diaries and 24-hour recalls to estimate usual potassium intake depends on the number of days assessed. Food-frequency questionnaires aim to capture usual intake by asking about eating habits over months or years, but their accuracy is limited by the number and relevance of food items included, the lack of specific product information, and recall bias.<sup>4</sup> In all diet surveys, error in estimating potassium intake can arise from inaccurate reporting by participants and reliance on determining the potassium content of foods by using food composition tables, which are often incomplete and infrequently updated.

Some investigators use urinary potassium excretion as a proxy for potassium intake. However, in contrast to dietary sodium, of which >90% is excreted in urine, the percentage of potassium intake that is excreted is much lower (typically <80%). The percent excreted also may depend on race (blacks excrete a lower percent of intake than whites) and diet.<sup>5</sup> Similar to dietary sodium intake, multiple collections are required due to substantial day-to-day variability in dietary potassium intake and other factors that influence potassium excretion (eg, gastrointestinal excretion and cellular distribution may vary day to day and between individuals, and single urine collections may not provide an accurate account of potassium homeostasis). Importantly, there are few data to support the use of spot urine collections to estimate usual dietary intake. Further, potassium excretion has a circadian pattern, with greater excretion in the afternoon and lower excretion at night and in the early morning.<sup>6</sup>

#### Usual Intake of Potassium

Based on National Health and Nutrition Examination Survey (NHANES) data from 2011 to 2012, mean daily potassium intake is higher in men than women (3,203 vs 2,403 mg/d; Table 1). However, when potassium is expressed per 1,000 kcal, women on average consume more potassium than men, and mean potassium intake increases with age, potentially because of improved diet. Potassium intake is significantly lower for blacks than for all other racial/ethnic groups, both overall and for women.<sup>7</sup>

#### **Health Effects of Dietary Potassium**

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