Physiology, Not Policy, Drives Sodium Intake

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In determining what constitutes "normal" sodium intake for humans, the disciplines of medicine and public health long ago fell prey to the "emperor's new clothes" syndrome; For decades a theoretical case has been built on assumptions that sodium intake has been increasing over time, is at levels far in excess of physiological needs, is a major cause of cardiovascular disease, and is modifiable by public policy.[1] Just as the emperor found out about his clothes, these suppositions do not reflect reality.

A frequent claim by the advocates of lower sodium intake is that the current average intake of 3,400 mg/d far exceeds the US guidelines.[1,2] That is true, as 2,300 mg/d is the current recommendation for healthy adults aged <50 years, and 1,500 mg/d is recommended for those at risk of cardiovascular disease and/or aged ≥50 years. The advocates' claim is only relevant, however, if i) the current guidelines are based on reproducible evidence of benefit in terms of health outcomes, ii) the current 3,400 mg/d average sodium intake is an aberration of physiology, and iii) it is physiologically possible for free-living individuals to achieve the recommended levels of dietary sodium on a consistent basis.

On each count the scientific evidence is unequivocal: the current guidelines are physiologically irrelevant. Thus, the mantra of the advocates that current sodium intakes are excessive is also irrelevant and, thus, misguided in its intent to frame public policy on sodium intake; at the core of the science that refutes the advocates' claim is 8 decades of neuroscience research that has defined the neural networks involved in regulating sodium intake in vertebrates.[3] These primal networks are interfaced with peripheral signals that inform the brain of the adequacy of organ perfusion (i.e., intravascular volume status). The renin angiotensin system and its generation of angiotensin II and aldosterone are the primary stimuli activating the neural networks that control sodium intake.[3] These well-established physiologic pathways provide the biological basis of the fact that actual human sodium intake is set by physiology and not public policy.

It is true, and obviously so, that when sodium intake is measured by the best techniques (24-hour urinary sodium excretion), there is a reproducible average intake with a "normal" distribution for the population.[4–6] That average—3,600 mg/d, with a range of 2,600–5,000 mg/d—is a mean intake that has been recorded consistently over 5 decades, across 45 countries, and in multiple ethnic groups.[6] It has also been verified by a number of National Institutes of Health–sponsored, controlled trials intended to decrease sodium intake and numerous governmental surveys monitoring sodium intake over time.[4–6] As with hemoglobin, fasting blood glucose, and many other physiologically set parameters, sodium intake as a critical determinant of intravascular volume regulation is set within a normal range in healthy individuals. This range of sodium intake appears fundamental to survival because intravascular volume is dependent on sodium and water. Although angiotensin II and other critical hormonal responses that modulate vasoconstriction can maintain organ perfusion as a rescue response to inadequate volume, there is little debate in terms of cardiovascular pathophysiology that dependence on vasoconstriction as opposed to volume maintenance for organ perfusion is associated with adverse health outcomes.

That reality was elegantly established, although not commented upon, in a 1972 *New England Journal of Medicine* report that documented 2 important physiologic principles.[7] First, as 24-hour urinary sodium excretion decreased, there was a logarithmic increase in plasma renin activity (PRA), and, second, in persons whose PRA was most increased, there was an increase in cardiovascular disease morbidity and mortality. What was not commented on, but recently noted by us,[6] was that the point at which the confidence interval of the PRA parabolic curve was intersected by the asymptote of the curve represented the lowest level of 24-hour urinary sodium excretion associated with maximal suppression of PRA (Figure 1). This observation demonstrates the physiologic coordination between sodium intake and the regulation of PRA and subsequent generation of angiotensin II. As noted above, the stimulation of angiotensin II and aldosterone release by low sodium intake is the proximate and most powerful input to the neural circuits to provoke an increase in dietary sodium appetite.[3]

Based on this physiologic regulatory loop between peripheral sensors of sodium adequacy and the regulation of sodium appetite, it follows that sodium intake in humans should be expressed by a classic normal distribution. That distribution, as with all essential nutrients, is characterized by a bell-shaped curve,[6,8] as we recently reported (Figure 2). The distribution is defined at both the lower and upper ends by a relatively strict cutoff. We observed that <1% of the free-living general population consumed <2,600 mg/d of dietary sodium or >5,000 mg/d, consistent with physiologic regulation within a defined and limited range. This scientifically

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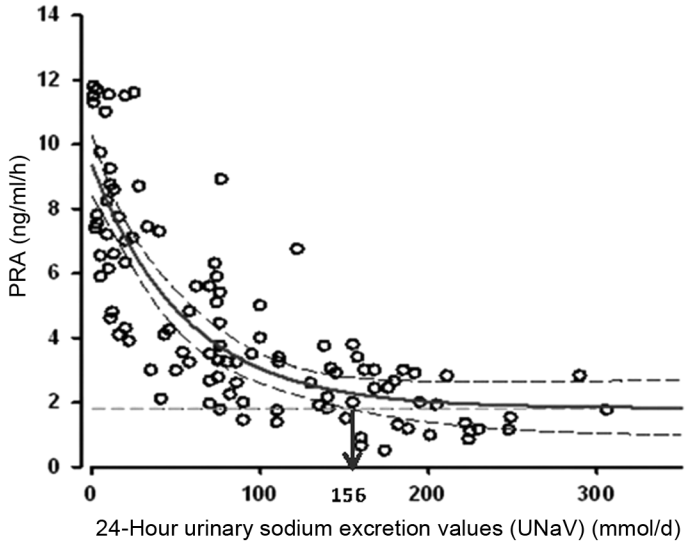

Figure 1. Physiologic relationship of 24-hour urinary sodium excretion to plasma renin activity (PRA) predicts mean sodium intake (based on Brunner *et al.*[7]).

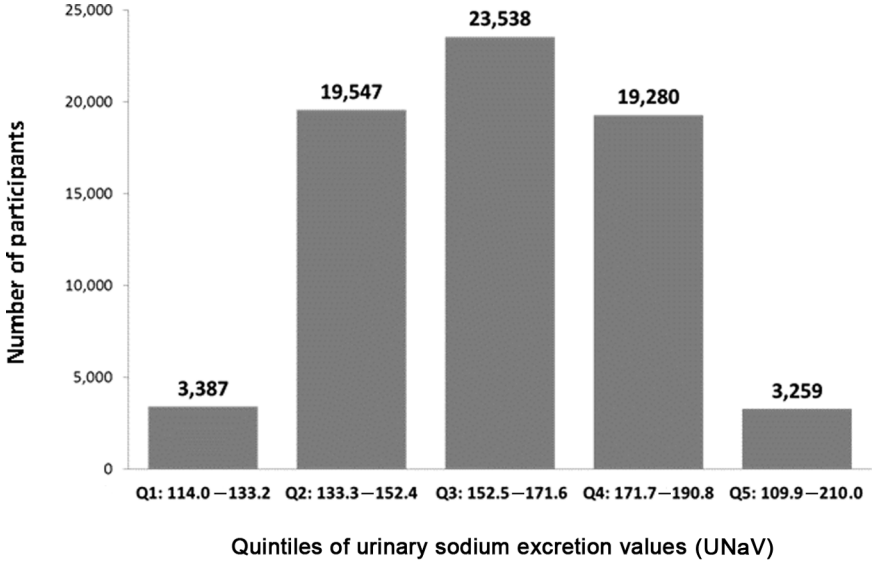

Figure 2. Population's normal distribution of sodium intake by quintiles of 24-hour urinary sodium excretion.

validated "normal" range of sodium intake indicates that a 3,400 mg/d sodium intake in the United States is not an aberration, but simply the expression of the norm for humans, and that it is not a normal physiologic state for healthy individuals to consume <2,600 mg/d, which explains the failure of decades of public policy efforts to lower sodium intake to ≤2,300 mg/d. From this evidence-based characterization of the normal range of dietary sodium intake, it is reasonable to conclude that sodium consumption outside the normal range should be associated with adverse health consequences; Indeed, the recently documented J-shape relationship between sodium intake and cardiovascular disease and all-cause mortality is consistent with pathologic consequences of either inadequate or excessive dietary sodium intake in humans.[9–11] Further, the nadir of the J-shaped mortality curve essentially overlaps the normal range of 24-hour urinary sodium excretion, which our work has described. This concordance of the normal range of sodium intake to optimal health outcomes offers compelling biological validation of the physiologic control of sodium intake.

The conclusions of the recent Institute of Medicine (IOM) report, *Sodium Intake in Populations*,[12] are in line with the evidence that science has provided regarding sodium intake in humans. The IOM report concluded that "excessive" intake was associated with an increase in cardiovascular disease risk, although the report was explicit in not defining what level of sodium intake constituted "excessive." It further noted that there was insufficient evidence

that an intake <2,300 mg/d was associated with either increased or decreased risk, but that intakes below 1,500 mg/d were associated with adverse outcomes. Those 2 conclusions of the report are entirely consistent with sodium intake in humans being regulated within a normal range. When sodium intake is less than the lower end of the normal range, there is no benefit and possible harm. Similarly, when sodium intake is in "excess" of this normal range, it would be anticipated that adverse outcomes would emerge. The delineation of a normal range for sodium intake does not preclude that other nutrients, disease conditions, or related physiologic determents may shift the range in a specific population or clinical setting.

Unfortunately, opinions expressed by the Director of the US Centers for Disease Control and Prevention (CDC), the president of the IOM, and several IOM committee members have attempted to characterize the key findings as "congruent" with current US sodium guidelines and those of major advocacy groups such as the American Heart Association (AHA).[13–15] Their widely disseminated opinions on the report's conclusions clearly misrepresent the facts as outlined in the report. Specifically their comments failed to acknowledge the clearly stated "Findings and Conclusions" of the IOM report. As noted above, the report was unequivocal in its acknowledging that current science does not support any benefit or harm of the current 2,300 mg/d US guidelines and was also unequivocal in its indicating that the <1,500 mg/d guideline was possibly harmful. As opposed to the comments of the director of the CDC and the president of the IOM, the IOM report's conclusions are not "congruent" with the current US policy or that of the AHA. In fact, the IOM report's conclusions, based upon current health outcomes evidence, invalidated all previous US sodium guidelines. In addition, these authors' suggestion that the media was responsible for the confusion is an unfounded and unfortunate placement of blame. Rather, these misleading public comments from the leadership of the CDC and IOM, as well as selected committee members, are in reality a source of confusion.

Current US policy and the unquestioning commitment by both the CDC and AHA[16] to continue on the same tack are not "congruent" with either the IOM report or the scientific evidence cited here, which was presented to the IOM committee.[17] It is incumbent upon the IOM to ensure an accurate interpretation of its report to all government agencies whose policies may be affected, including the 2015 Dietary Guidelines Committee. Further, the IOM should promptly convene a new committee to answer the 2 questions that the earlier committee was prevented from addressing based on the CDC limiting the scope of the final report.[18] Those questions are i) what defines "excessive" sodium intake and ii) what is the normal range of human sodium intake.

The current US sodium policy is a fallacy. Its execution is premised not on science but on the concept that if factual inaccuracies are repeated frequently enough, then they become reality. Fortunately, human physiology is not easily deluded. Whether our policy leaders can accept that reality or whether they choose to continue defending this fallacy, it is apparent that sodium intake in free-living individuals will not be modified by any attempt of the government. That has been the case for at least the past 50 years and will likely be well into the future.

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DISCLOSURE

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