Sodium[1]

Sodium is the major cation of extracellular fluid [ECF[2] (1 mmol, or molar equivalent, corresponding to 23 mg of sodium)]. The mean body content of sodium in the adult male is 92 g, half of which (46 g) is located in the ECF at a concentration of 135–145 mmol/L, ~11 g is found in the intracellular fluid at the concentration of ~10 mmol/L, and ~35 g is found in the skeleton. The concentration gradient between the ECF and intracellular fluid is maintained by the sodium–potassium pump activity, which transfers sodium and potassium, respectively, from inside to outside the cell and vice versa against the concentration gradient, using the energy supplied by ATP. In the polarized cells of the renal tubular epithelium or the intestinal wall, sodium enters the cell from the tubular lumen or from the gut through specific channels or other transport mechanisms and is then extruded from the cell into the adjacent capillaries attributable to the action of the pump, which is mainly distributed on the basolateral sides of the cell. In these cells, sodium transport is mostly associated with that of other substrates, e.g., phosphates, amino acids, glucose, and galactose.

Sodium absorption occurs almost quantitatively in the distal small bowel and the colon. Sodium balance in the body is closely linked to that of water and is finely maintained by the kidneys. Here, the sodium filtered by the glomeruli is reabsorbed in a proportion ranging from 0.5% to 10% according to the needs at the tubular level, in which angiotensin II, norepinephrine, aldosterone, and insulin stimulate reabsorption whereas dopamine, cAMP, the cardiac natriuretic peptides, and prostaglandins exert a natriuretic effect. Generally, small losses of sodium occur through feces and sweat; these losses increase with increasing sodium intake, although part of them are obligatory.

Sodium is an essential nutrient involved in the maintenance of normal cellular homeostasis and in the regulation of fluid and electrolyte balance and blood pressure (BP). Its role is crucial for maintaining ECF volume because of its important osmotic action and is equally important for the excitability of muscle and nerve cells and for the transport of nutrients and substrates through plasma membranes (1).

Deficiencies

Given the presence of added salt in a wide range of commonly used food products, a clinically relevant food deficit of sodium is extremely unlikely in healthy individuals. Indeed, a deficiency of sodium does not occur under normal conditions even with diets very low in sodium. In contrast, an excess of sodium in food is common to most populations worldwide, because of both the salt added to products during food processing and the widespread habit of adding additional amounts of salt in food preparation in the kitchen and at the table. This excess is a recognized causative factor of hypertension and cardiovascular diseases (CVDs) and also contributes to the development of chronic kidney disease, gastric cancer, calcium nephrolithiasis, and osteoporosis.

A condition of true sodium (and water) depletion can occur only in pathologic conditions, such as severe adrenal insufficiency, sodium-losing kidney disease, extensive burns, chronic diarrhea, uncontrollable vomiting, extreme and prolonged sweating, diabetic ketoacidosis, excessive intake of diuretics, or continuous gastric suction.

Toxicity

An acute toxicity from excess sodium intake with the possibility of fatal outcome has been reported in relation to the ingestion of huge amounts of sodium, such as 0.5–1 g of salt/kg body weight. In certain pathologic conditions (e.g., heart failure, decompensated liver cirrhosis, and renal failure), sodium intake to levels routinely present in our diet ($\geq$10 g/d) may lead to a dangerous increase in ECF volume.

However, even under normal conditions, the intake of high amounts of sodium tends to favor, especially in predisposed individuals, an increase of ECF volume and BP. The Intersalt study (2) showed that the higher the habitual consumption of sodium in a given population, the stronger the average BP increase with age and the prevalence of hypertension.

Food Sources

Dietary sodium intake is the sum of the generally small amounts of sodium present in natural foods, the higher amounts added during food preparation in the kitchen and at the table, and the even greater amounts added to many foods during their industrial processing (1 g of sodium corresponding to ~2.5 g of salt). Additional not negligible amounts of sodium may be acquired through oral or parenteral medications. The sources of sodium intake can otherwise be divided into "discretionary" (from the salt added to food in the kitchen or at the table) and "nondiscretionary" (the sodium naturally present in foods and that added during the industrial food transformation), the latter being mainly in the form of sodium chloride, with ~0.10 g being in the form of sodium glutamate, bicarbonate, etc.

The sodium content of foods is quite variable and depends on both the food source (e.g., animal foods naturally contain more sodium) and the level of transformation undergone by the food itself. Foods naturally low in sodium are fruit, vegetables, oils, and cereals, with their content ranging from traces to ~20 mg/100 g, with few exceptions. Meat and fishery products naturally contain from 40 to 120 mg/100 g, but some shellfish, such as mussels and oysters, contain up to 500 mg/100 g. Whole milk contains ~50 mg/100 g. The sodium content of processed foods obviously varies depending on the

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amount of salt added during their preparation. For example, bread may contain only traces to several hundred milligrams of sodium per 100 g (~1.5–2 g of salt). The sodium content of some traditional meats and cheeses is extremely high (up to 2500 mg/100 g), and so also is that of many frozen foods (up to 700 mg/100 g).

In most countries, cereals and cereal products, including bread, are the main source of nondiscretionary sodium, followed by the meat/eggs/fish aggregate and by milk and dairy products. The contributions to total sodium intake by fruit and vegetables are almost negligible (3).

Diet Recommendations

The recommendations for sodium intake issued by authoritative international sources are relatively homogeneous. Because of the lack of dose–response testing data, most national and international authorities have found it impossible to define a sodium average requirement or a recommended intake for the population. The available data suggest that the sodium minimum intakes that prevent deficiency signs or symptoms are very low, and there is no doubt that a balanced and varied diet, such to meet the need of other essential nutrients, contains an amount of sodium considerably higher than these levels. As a result, rather than setting reference intakes for covering the minimum physiologic needs, most authorities have found it convenient to set an adequate intake (AI) corresponding to a moderate intake of sodium, certainly compatible with a varied diet and a healthy lifestyle. Intakes at or above the AI have a low probability of inadequacy. An age-specific tolerable upper intake level (UL) or a standard dietary target have also been established by the same authorities to indicate the need to reduce the intake of sodium for the prevention of CVD and other chronic degenerative diseases. The goal for the population is that sodium intake should be at least lower than the UL or standard dietary target, although even lower levels of intake may be desirable (4).

In 2010, the Nutritional Guidelines for Americans, based on the analysis of the Institute of Medicine (IOM), set an AI of 1500 mg (or 3.75 g of salt) for all individuals aged 9–50 y and a correspondingly lower level for children and older people in relation to their lower calorie intake. This amount was considered suitable for both genders. For adolescents and adults of all ages (≥14 y), the IOM set the UL at 2300 mg/d because the UL is the highest daily nutrient intake level that is likely to pose no risk of adverse health effects to almost all individuals in the general population. The American Heart Association provided recommendations consistent with the IOM 2006 document. Recently, however, the new IOM Committee on the Consequences of Sodium Reduction in Populations has observed that the available evidence on the effects on direct health outcomes of reducing sodium intake to ≤1500 mg/d among individuals with diabetes, chronic kidney disease, or preexisting CVD does not support recommendations to treat them differently from the general U.S. population. As a result, this committee defined an AI of 2300 mg (or 5.75 g of salt) per day for all adult individuals. The recommendations by the U.K. Food Standard Agency and the Sodium Working Group of the Minister of Health for Canada are in line with those by the IOM.

The recent WHO guideline has set ≤2000 mg of sodium (5 g of salt) per day as a target for the population stating that this level is fully compatible with the prophylaxis of thyroid diseases caused by iodine deficiency, which can be prevented by more extensive use of iodized salt (5).

Recent Research

Recent experimental and clinical studies have highlighted major effects of sodium intake on endothelial function and potentially very important interactions between sodium intake and the immune system. Excess sodium intake also has been associated with, the latter greater risk of gastric cancer, nephrolithiasis, and osteoporosis because of increased urinary calcium losses favoring a negative calcium balance.

Recent meta-analyses of the randomized controlled trials on the effects of moderate sodium intake reduction documented significant BP reductions in adult hypertensive and normotensive individuals, as well as in children and adolescents (6).

Two meta-analyses of the prospective studies of the relation between habitual salt intake and CVD morbidity and mortality have shown that higher salt intake is significantly associated with a greater risk of stroke and other cardiovascular events (6,7). However, as noted by the 2013 IOM ad hoc committee, the evidence for the impact of excess sodium intake on these hard endpoints is still primarily based on observational studies, most of which are influenced by important methodologic limitations. Future studies should try to overcome these limitations, and ideally, a randomized controlled trial designed to describe the effects of different degrees of long-term sodium reduction on hard health outcomes should be implemented.

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[2]Abbreviations used: AI, adequate intake; BP, blood pressure; CVD, cardiovascular tolerable disease; ECF, extracellular fluid; IOM, Institute of Medicine; UL, upper intake level.

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