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SODIUM AND POTASSIUM

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PHYSIOLOGICAL SIGNIFICANCE OF SODIUM

Sodium chloride is the most abundant, naturally occurring sodium salt. It is found in large amounts in seawater, mineral springs, and underground deposits. The fact that mammals arose from a marine environment suggests

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how sodium may have become a major constituent of their extracellular fluid (64). Just as with seawater, it predominates over other mineral constituents of plasma such as potassium, calcium, magnesium, bicarbonate, and phosphate. Variation of the sodium and chloride concentrations of plasma may have direct and important effects on the osmotic pressure of the plasma, on plasma and interstitial fluid volume, on acid-base balance, on the maintenance of the electrical activity of body cells, and on the responsiveness of the cardiovascular system to circulating endogenous pressor agents (54). Thus, it follows that close regulation of the concentration and content of sodium within the body is a crucial physiological regulation required for health and efficiency of function in man and all higher animals. Disorders of sodium regulation are a central, or at least a contingent, feature of a variety of diseases of man (30, 49, 54, 69, 92).

ESTIMATES OF DAILY SODIUM INGESTION

Sodium chloride (NaCl) is a common ingredient in the food of man. It is present in processed foods where it is used as a flavor intensifier and a curing agent, as a formulating and processing aid, and as a conditioner of dough by the baking industry. In addition to the salt naturally present in food and to that added by the food processor, man customarily adds NaCl both during cooking and to the food presented at the table.

The total daily intake of NaCl in America and in other cultures has been the subject of a number of studies. Attempts have been made to arrive at estimates of both discretionary (consumer controlled) and non-discretionary (commercially controlled and/or naturally occurring) daily NaCl intake. Among these are the National Research Council (NRC) Survey of Industry (23, 88), the Food and Drug Administration's (FDA) Selected Minerals in Food Survey (43, 86), data on production and sale of salt (15, 36, 99), the Health and Nutrition Examination Survey (1), and data on daily urinary excretion of sodium (3, 21, 30, 71).

Estimates of Non-Discretionary Sodium Intake

NRC SURVEY OF INDUSTRY In 1970, a subcommittee of the NRC surveyed the food industry regarding the quantity of NaCl and other sodium salts added to food both to improve the taste of the food and to produce certain desired technical effects important in processing the food (88). This survey revealed that as much as 1 g of sodium accrued to the average total daily sodium intake as a result of the addition of sodium salts other than NaCl.

The amount of NaCl present in processed food in 1970 was estimated by NRC to be about 60% of the total quantity used by the food processing

industry. A portion of the NaCl used by industry does not appear in the final food product. It is used in various stages of processing but is discarded prior to packaging of the product, e.g. brines. Based on this estimate and on the tonnage of salt sold to the food processing industry in 1970, the estimated per capita NaCl consumption was calculated to be 18 g per day. A resurvey of the food processing industry carried out in 1975 revealed a non-discretionary daily intake of NaCl amounting to 8.4 g per day (23). This large difference in intakes estimated by the two studies could be related to a reduction in the amount of sodium used in food processing during the 5-year interval, but it is more likely to be related to errors of estimation by the 1970 survey. A similar discrepancy between the two surveys also exists with respect to the estimates of potassium chloride added to food, although it is opposite to that of NaCl.

FDA SELECTED MINERALS IN FOOD (MARKET BASKET) SURVEY A second attempt to assess daily intake of NaCl was made by the FDA. Food (consisting of 117 individual food items of 12 food composites) was purchased retail to make up a 3900-kcal daily diet such as might be consumed by a typical 15- to 20-year-old American male (43, 86). The food was purchased at markets in northeastern, southeastern, western, and central locations in the United States during 1976, 1977, and 1978. The foods were then prepared as they would be for home consumption but without the addition of NaCl during preparation. Table 1 lists the food composites and their sodium content for market basket collections in 1976, 1977, and 1978. A discretionary average intake of 1.9–2.0 g of sodium (4.8–5.1 g of NaCl)/day is included in Table 1 to account for the sodium normally used in home food preparation and seasoning at the table. The 1976, 1977, and 1978 analyses reveal that about 6.8 g of sodium (17.2 g of NaCl) were ingested daily with the 3900-kcal diet. Since the minimal daily requirement for vitamins and nutrients is now customarily expressed per 1000 kcal, Table 1 provides this information for the sodium content in the various food composites of the three separate market basket collections. The values for the 3 years are quite similar and average approximately 1740 mg of sodium/1000 kcal (4.39 g of NaCl/1000 kcal). The assumption used in this calculation is that the salt intake of adults who consume less than 3900 kcal per day is proportionately less.

ESTIMATION OF SODIUM INTAKE FROM PRODUCTION AND SALE OF SODIUM CHLORIDE Additional estimates of daily intake of NaCl have been made from the total amount of table salt purchased for the year 1968 (275,000 tons) (99). For a population estimated at 200 million, this amounts to 3.42 g per person per day. This was assumed to represent an estimate of

Table 1 Sodium content by food composite of 3900-kcal daily diet collected in FDA Selected Minerals in Food Survey

Food composite	1976[a] Sodium mg	1976[a] Sodium mg/1000 kcal	1977[b] Sodium mg	1977[b] Sodium mg/1000 kcal	1978[c] Sodium mg	1978[c] Sodium mg/1000 kcal
Non-Discretionary						
Dairy products	717	184	704	180	792	203
Meat, fish, poultry	1000	256	952	244	921	236
Grain and cereal products	2036	522	2005	514	2002	513
Potatoes	65	17	75	19	82	21
Leafy vegetables	18	5	22	6	22	6
Legume vegetables	224	57	243	62	258	62
Root vegetables	16	4	18	5	17	4
Garden fruits	264	68	285	73	284	73
Fruits	74	19	66	17	75	19
Oil and fats	380	97	387	99	406	104
Beverages	9	2	17	4	24	7
Total non-discretionary	4803	1232	4774	1224	4886	1252
Discretionary						
Sugar, salt, and adjuncts[d]	1970	505	1923	493	2042	524
Total intake	6773	1737	6697	1717	6928	1776

[a]Mean value of 20–25 market basket collections.
[b]Mean value of 25 market basket collections.
[c]Mean value of 8 market basket collections.
[d]Includes the salt normally used in home food preparation and for seasoning at the table.

the discretionary use of salt and was not adjusted for amounts not actually ingested.

Data from the Bureau of Mines for 1970–1973 on production and usage of NaCl in all aspects of food production and processing were used by Bowen et al (15) to calculate daily per capita NaCl consumption. The manufacture of NaCl for all purposes, of which food processing was one, averaged 23.6 g/person/day. Bowen et al (15) estimated that the total daily usage of NaCl for food processing and production was 8 g/person/day, with an additional 6.5 g/person/day used for discretionary purposes. This amounts to a total daily NaCl intake of 14.5 g/day. This figure was adjusted for an estimated amount of NaCl used in food processing but not present in the final product. The Salt Institute estimates that 4.1% of total salt sales is for food-grade NaCl (36). Their estimate of total daily per capita NaCl consumption calculated from the sale of food-grade NaCl to both food processors and consumers in 1977 is 8–10 g.

HANES I An estimate of non-discretionary daily sodium intake was also made in the first Health and Nutrition Examination Survey (HANES I) (1). This survey sampled 20,749 persons aged 1–74 years during 1971–1974. Information regarding food intake was obtained on the basis of the 24-h recall method for the day, midnight to midnight, preceding the interviews and included all regular meals as well as foods and snacks eaten between meals. Only weekdays were used. Foods were grouped into 18 separate categories, many of which do not overlap with the categories chosen by the FDA market basket survey (Table 1). The daily non-discretionary NaCl intake for males 1–74 years of age was 6.3 g, whereas that for females was 4.6 g (Table 2). The results of this study also showed that intake of NaCl varied with age; the maximum (7.5 g) was ingested by males in the age range of 18–44 years. In the case of females, the maximum (5.5 g) was ingested in the age range 6–11 years. These are the first data to suggest that intake of NaCl is a function of age and sex and that the maximal intake occurs at a considerably younger age for women than for men (Table 2).

Non-Discretionary Intakes of Sodium Not Included in the Above Studies

SODIUM IN DRINKING WATER Sodium ion occurring in drinking water must also be taken into account when estimating non-discretionary sodium

Table 2 Mean daily non-discretionary sodium chloride intake by sex and age: United States, 1971–1974[a]

Sex	Age (years)	Mean sodium chloride intake (g/day)
Male	1–5	4.7
	6–11	6.3
	12–17	7.4
	18–44	7.5
	45–64	6.3
	65–74	5.6
Female	1–5	4.3
	6–11	5.6
	12–17	5.0
	18–44	4.6
	45–64	4.2
	65–74	3.8
Mean: 1–74 years		4.6

[a] Adapted from HANES I data (1).

intake. Although sodium ion ingested with food is substantially greater than that ingested with drinking water, the latter may represent from 0.5 to 10% of the total daily intake of sodium ion by normal individuals (63). The concentration of sodium ion in drinking water varies considerably from state to state, within states, and even within a given city (13, 19, 24, 26, 39, 52, 63).

A study by White et al (96), which sampled water supplies from 2035 municipalities, revealed that 41.8% had a sodium ion concentration exceeding 20 mg/liter. This is the maximal concentration of sodium considered permissible for use with the 500-mg sodium-restricted diet developed by the American Heart Association (5). Corley (26) listed 53 communities in Nebraska where he found a sodium ion concentration greater than 50 mg/liter in the drinking water. Bills et al (13) surveyed 150 municipal water supplies that provide an estimated 28% of the population of the continental United States with their water. They reported sodium ion concentrations of 1–340 mg/liter. With a daily water intake of 2.5 liters for an adult, a water supply that contained sodium ion at a concentration of 200 mg/liter would provide 500 mg of sodium ion per day. This is approximately the daily requirement for sodium ion as suggested by Meneely & Battarbee (70). For those individuals with cardiac decompensation who conscientiously follow their low sodium ion diet, the sodium ion ingested with drinking water may represent a hidden danger (24, 39).

The amount of sodium ion ingested by individuals within a given community may also differ and depends on the sources of the water supplied to inhabitants. A recent study of the city of Houston, Texas, whose municipal water system is very complex and involves both surface and ground water sources, has shown a sodium ion concentration varying from 19 to 235 mg/liter in various portions of the city (85). The water was sampled from 50 different locations within the city limits. Those sections of the city supplied by deep wells had the highest sodium ion concentration in their drinking water. For patients on a 500-mg sodium-restricted diet, only the water containing the lowest sodium ion concentration could be used.

The long-term effect of ingestion of drinking water that contains high concentrations of sodium ion was studied by Tuthill & Calabrese (17, 94). High school sophomores (300) living in a community in which the drinking water contained a sodium ion concentration of 107 mg/liter had a blood pressure frequency distribution curve that was shifted upward for both systolic and diastolic blood pressures when compared with high school sophomores (300) from a nearby, appropriately matched community with drinking water that contained 8 mg of sodium/liter. Females from the community with the elevated sodium concentration in drinking water exhibited a blood pressure frequency distribution pattern characteristic of

females 10 years older, whereas males from this same community had a pattern characteristic for males 2 years older. These results are so striking as to suggest the need for additional studies in this area.

SODIUM FROM WATER SOFTENERS In those areas where home water softeners are used, additional sodium ion is added to the water (22). The generally used cation exchange process depends on the ability of an exchanger to give up its sodium for other cations in the water (usually calcium and magnesium ions). The higher the concentration of these cations, the higher the sodium ion concentration in the drinking water. Information is not readily available regarding either the concentration of sodium in drinking water within a given community or the use of water softening processes by municipal water authorities within that community.

SODIUM IN DRUGS Although few prescription drugs contain sodium, a number of nonprescription, over-the-counter drugs may contribute significantly to the daily sodium intake (11, 41). Sodium is present in many of these medications, both as an active ingredient and as an excipient. Some common sodium-containing excipients include sodium algenate, sodium bisulfate, sodium caprylate, sodium carboxymethyl cellulose, sodium chloride, sodium hexametaphosphate, and sodium saccharin.

It was noted recently that some over-the-counter antacids can supply a total daily sodium intake of at least 1200 mg (equivalent to 3 g of NaCl) (41). Of the pain relievers, only aspirin (sodium salicylate) may present a potential problem to patients on a restricted sodium diet. Approximately 49 mg of sodium (125 mg of NaCl) are contained in each dose. Certain antacids, e.g. Sal Hepatica (1000 mg/dose) and Brioshi (710 mg/dose), and sleep aids, e.g. Miles Nervine Effervescent (544 mg/dose), also contain significant amounts of sodium. Although it is difficult to estimate the amount of sodium ingested daily from drugs by the average American, it is clear that this source must be taken into consideration in the estimation of total sodium intake.

Estimates of Discretionary Intake

Mickelson et al (71) carried out a 28-day study on 10 healthy men fed "carefully controlled low-sodium" foods, but permitted to add table salt to their food. The basal diet provided 2500 kcal. Total intake of sodium ion by the men amounted to 5.55 ± 0.85 (SD)g/day (14.0 g of NaCl/day). Of this, the nondiscretionary intake was 3.71 ± 0.33 g (9.1 g of NaCl), whereas the discretionary intake was 2.18 ± 0.33 (5.5 g of NaCl). Others have estimated the discretionary intake of NaCl to be 3–6.5 g/day (85).

Estimates of Total Intake from Daily Urinary Sodium Excretion

Daily intake of sodium has also been estimated by the daily urinary excretion of this ion. Dahl & Love (30) studied employees at the Brookhaven National Laboratories. Twenty-four hour urine collections were made on 1124 males periodically over a 3-year period. Calculating from these urine analyses, they estimated daily intake of NaCl to be 10 g (range 4–24 g). The Handbook of Biological Data lists daily sodium excretion to be 60 mg/kg/day and urinary chloride excretion to be 100 mg/kg/day (3). This amounts to 3.6 g of sodium and 6 g of chloride excreted per day for a 60-kg adult. If all of the sodium ion excreted is the result of ingestion of sodium chloride, the total intake would amount to 9 g/day.

Coatney et al (21) studied the 24-h urinary sodium excretion of 16 healthy subjects of military age on two to eight occasions over a period of 5 months. They estimated the average daily NaCl intake at 11 g/day.

Table 3 summarizes the estimates of daily NaCl intakes as discussed above and attempts to separate the total intake into non-discretionary and discretionary intakes. As can be seen, the total NaCl intakes estimated in the variety of ways discussed above are roughly comparable, varying from 10 to 14.5 g/day. The discrepant value of 17.1 g/day estimated by the 1976–1978 FDA Selected Minerals in Food Survey is based on a total dietary intake of 3900 kcal, which accounts, in part at least, for this high value. No estimate has been made in Table 3 of the amount of sodium ion ingested by way of drugs.

The weighted means of the levels of NaCl added to foods are shown in Table 4 by category of the processed food. The values listed do not mean that all manufacturers who process food of a given category have the same level of NaCl in their product. By using these weighted mean values and data on the mean portion or amount of each of these categories consumed daily per person, as determined by the U.S. Department of Agriculture, an estimate of the daily NaCl intake was made. The NRC Subcommittee cautioned that this method overstates the average intake of NaCl.

The figures given in Table 4, representing responses from more than 20 food processors, suggest a possible non-discretionary daily intake of 6.9 g of NaCl for humans 2 years and older in 1970. These data suggest that the baked goods, breakfast cereals, and grain products categories account for 32% of the total daily non-discretionary NaCl intake. The HANES I data indicate that the grain products category (including bread, rolls, biscuits, muffins, cornbread, crackers, and unsalted pretzels) contributes 20–27% of the daily non-discretionary NaCl intake in all age and sex subgroups. This is a somewhat lower estimate than that of the FDA market basket survey,

Table 3 Sources of dietary sodium and estimates of total sodium intake[a]

Determinatives	Sodium intake [NaCl (g/day)]	Comments	Ref.
Non-discretionary sources of sodium			
Naturally occurring sodium in foods	2.5–4.5	Estimated food composition	15
	3.0	Chemical analysis (institutional diet)	21
Sodium added by industrial processing			
Salt	6.9	1970 NRC estimate (3200-kcal diet)	85
	8	1966–70 Bureau of Mines data	15
	8.4	Total 1975 usage by food industry	85
Other sodium-containing ingredients	1.0	Calculated from 1970 NRC survey	85
Total non-discretionary sodium	12–12.5	Calculated from 1976, 1977, and 1978 FDA Selected Minerals in Food Survey (3900-kcal diet)	43, 86
	4.6–6.3	HANES I Survey (1971–1974)	1
Discretionary addition of salt to foods by the consumer	3.4	1968 retail sales	85
	4.4–6	1965 USDA survey	85
	6.5	1966–70 Bureau of Mines data	15
Total salt usage	8–10	1977 sales of food-grade salt	36
Total sodium intake	10	Urinary excretion	30
	11	Urinary excretion	3, 21
	14.5	1966–70 Bureau of Mines data	15
	12	Estimated from review of literature in 1976	70
	17.1	1976–1978 FDA Selected Minerals in Food Survey (3900-kcal diet)	43, 86

[a] These values are not necessarily additive (see text for discussion). These data are adapted from a report of Select Committee on GRAS substances (85).

but the HANES data do not include in the grain products category the NaCl ingested with cereal products. The meat, fish, and poultry category contributed 20.8% to the total non-discretionary intake in the FDA survey, whereas the mixed protein dishes and meat categories contributed 21 and 18% of the non-discretionary intake of males and females, respectively, in the HANES report. The milk and milk products category was the third major source of non-discretionary NaCl intake, contributing 14.9 and

Table 4 Calculation of a possible average daily intake based on level of addition of sodium chloride to food by food category[a]

Food category	Level of addition to processed food (mean %)	Possible average daily intake (g) (2–65 + yrs)
Baked goods, baking mixes	1.31	1.8
Breakfast cereals	1.09	0.2
Grain products such as pastas or rice dishes	0.74	0.2
Fats and oils	1.43	0.2
Milk products	0.45	0.2
Cheese	1.00	0.1
Frozen dairy desserts, mixes	0.04	—[b]
Processed fruits, juices, and drinks	0.48	0.6
Meat products	2.49	1.9
Poultry products	0.83	0.1
Egg products	0.64	—
Fish products	0.96	0.1
Processed vegetables, juices	0.68	0.6
Condiments, relishes, and salt substitutes	3.18	0.3
Soft candy	0.42	—
Sugar, confections	0.51	—
Sweet sauces, toppings, syrups	0.47	—
Gelatins, puddings, fillings	0.41	0.1
Soups, soup mixes	1.02	0.3
Snack foods	2.08	—
Beverages, nonalcoholic	0.04	—
Beverages, alcoholic	0.02	—
Nuts, nut products	1.12	0.1
Reconstituted vegetable proteins	7.27	—
Gravies, sauces	1.17	0.1
Dairy products analogues	0.64	—
Hard candy	0.41	—
Seasonings and flavorings	50.53	—
Calculated possible average daily intake of added sodium chloride for the age group, 2 to 65 + years		6.9

[a] These data are adapted from a report of Select Committee on GRAS Substances (85).
[b] Less than 0.05 g.

14.0% to the total for the FDA and HANES surveys, respectively. These data suggest that two categories, grain and cereal products and meat products, account for about 50% of the total daily non-discretionary NaCl intake. Thus, these two food categories, as well as milk and milk products, should be given special consideration in attempts to reduce sodium intake. It must be cautioned, however, that individuals vary considerably in the quantities of food ingested from each of the categories listed in Table 4. It

is for this reason that labeling of sodium content of processed food should be undertaken. This has also been recommended by the Salt Institute (81) and is under consideration by the FDA (86). The consumer interested in reducing sodium intake could then make rational choices both between the same processed food products of different food processors and among the various food composites listed in Table 4.

ABSORPTION OF SODIUM

Water and electrolytes are readily absorbed by the intestinal tract. The transport of sodium across intestinal epithelium appears to be dependent upon a system of pumps and passive leaks located in the limiting membranes of the cells. In the duodenum and jejunum, NaCl moves from the blood into the intestine when hypotonic solutions enter, whereas in the ileum, a net absorption of NaCl occurs from hypotonic solutions. The total daily load of NaCl presented to the intestines for absorption amounts to about 44 g for an adult (46). This large amount of NaCl results both from dietary NaCl as well as from the NaCl contained in gastrointestinal secretions.

Kramer & Ingelfinger (62) showed that the absorption of sodium from the intestines of humans with an ileostomy was related directly to the sodium content of the food. No threshold of absorption was reached even at the highest sodium intake (261 mEq/day or 15.1 g of NaCl/day). However, a relatively constant amount of sodium (about 40–50 mEq/day) escaped absorption at all intakes of sodium tested. Thus, varying levels of dietary sodium were reported to have little effect on the amount of sodium delivered to the colon (46).

These results suggest that the small intestine has a large capacity to absorb dietary sodium. The greater the sodium intake, the greater the sodium absorption. Thus, the responsibility for handling the ingested sodium is passed to the kidneys by the small intestines.

It has also been shown that glucose in luminal fluid enhances the rate of absorption of sodium in the jejunum (46). This observation is of particular interest since it may relate to the commonly observed association between obesity and hypertension (20). However, data to support such an association are lacking.

CONTROL OF SODIUM LOSS AND SODIUM INTAKE

Regulation of the sodium concentration and/or the sodium content of the body involves two main processes: the control of sodium loss from the body, as well as the control of sodium intake. The concentration of sodium in

extracellular fluid is maintained relatively constant by an elaborate mechanism that involves glomerular filtration rate, the cells of the juxtaglomerular apparatus of the kidneys, the renin-angiotensin-aldosterone system, sympathetic nervous activity, the concentration of catecholamines in circulating blood, and blood pressure (31, 50). A critical analysis of the mechanisms that affect extracellular fluid volume and the regulation of sodium concentration in extracellular fluid is beyond the scope of this review, but it has been reviewed by others (31, 49, 50).

Our understanding of the mechanisms that affect physiological control of sodium loss from the body appears to be more secure and advanced than that for the physiological control of sodium intake. Evidence from studies of two species (sheep and rabbit) shows that sodium intake may be as closely controlled as output (34, 35). Additional evidence exists that the rat may control its sodium intake, but only if the sodium is in solution (48, 91). This interesting observation suggests that dietary sodium intake may not be controlled in this species, or at least controlled secondarily to dietary caloric intake. Some evidence has been put forward that this may also be the case for man (9, 76). There is a clear need for additional studies of the physiological mechanisms that control NaCl intake.

ACUTE TOXICITY OF SODIUM CHLORIDE

Lethal levels of NaCl are not encountered in processed foods, but fatalities have occurred in several hospital nurseries where NaCl was accidentally used in place of sugar in preparing infant feeding formulas (14, 40, 51). Deaths have also resulted from its use as an emetic where vomiting did not occur and in some instances where children have surreptitiously consumed lethal amounts of table salt over a short period of time (33, 80, 95). The use of hypertonic saline injections to induce abortion has also resulted in the death of some women (18, 83). Toxic effects sometimes occur after intraspinal injections of saline for intractable pain (56, 89). In addition, an excessively high concentration of sodium ions resulting from sodium bicarbonate therapy for salicylate poisoning or for excessive diarrhea and vomiting in infants has produced permanent brain damage and other pathologic effects (8).

The major pathologic findings in deaths resulting from NaCl toxicity were subarachnoid hemorrhages and multiple small intracerebral hemorrhages, shrinkage of the convoluted tubular cells from the basement membrane of the kidneys, and diffuse reddening of the mucosa of the stomach and small intestine (51). In most cases, vomiting, diarrhea, peripheral circulatory failure, and respiratory depression preceded death.

In most cases of NaCl toxicity, the actual amount ingested is not known with certainty. Gauthier et al (51) estimated that the infants who received

NaCl instead of sugar in their formula ingested sodium at a concentration of 2000–2500 mEq/liter (116–146 g of NaCl/liter). However, the volume ingested by each infant is unknown. Arena (6) pointed out that a level tablespoonful of NaCl contains more sodium and chloride ions (about 350 mEq) than a 5-kg human infant and that ingestion of this amount by a newborn is equivalent to ingestion of about a pound by an adult. Schatz (82) reported severe toxic symptoms in a 17-year-old female weighing 102 lbs who drank four glasses of salt water at 20-min intervals, with each glass containing two heaping dessertspoonsful of NaCl. The total amount of NaCl ingested was estimated to be 150 g (3261 mg/kg [body wt]). The author stated that 3 g/kg is regarded as lethal and that smaller amounts have been known to kill. Gosselin et al (53) reported that the probable lethal dose for adult humans ranges from 0.5 to 5.0 g/kg. Battarbee & Meneely (10) state that visible edema occurs in the healthy adult man with 35–40 g of NaCl per day when consuming an ordinary diet that contains 3.7–7.6 g of KCl per day. These authors have emphasized that the tolerance to NaCl is interrelated with the dietary potassium intake (10, 69, 70).

CHRONIC TOXICITY OF SODIUM CHLORIDE

The long-term effects on the American population of ingestion of NaCl at levels of 10–14.5 g/day, or greater, are not known with certainty. This subject has been reviewed by a number of investigators, committees, and task forces (10, 20, 30, 38, 49, 54, 69, 70, 81, 85, 92, 93). It is clear, however, that the levels of NaCl ingested by Americans are 10–20 times the minimal level compatible with health in man (27, 70). Although hypertension develops in certain species of animals fed high levels of dietary NaCl chronically (25, 28, 67, 68), the level of intake that induces hypertension in man has not been established.

Battarbee & Meneely (10) pointed out that the relationship between dietary intake of NaCl and blood pressure is clearer when different populations are compared than when comparison is within a single population. Thus, Dahl (28) reported a positive correlation between dietary intake of NaCl and the percentage of the population that is hypertensive in a series of different populations. The highest intakes were found in northern Japan (28 g/day), where about 38% of the population is hypertensive. In contrast, Alaskan natives rarely add salt to food (4 g/day) and rarely have hypertension. Isaacson et al (57) reported hypertension in 22 of 100 healthy Bantu males whose mean daily NaCl intake was estimated to be 18.6 g/day from their mean 24-h urinary sodium output. These data fit well on Dahl's line, which illustrates the relationship between mean daily NaCl intake and percentage of the sample population that is hypertensive (140/90 mm Hg).

Dahl & Love (30) studied 1346 adults. They categorized salt intakes of

these individuals as low, average, and high and found differences in the prevalence of hypertension in the three groups, i.e. 0.8 per 100 persons in the low salt group, 6.8 per 100 in the average, and 10.5 per 100 in the high. In an earlier study, Dahl & Love (29) reported that the 24-h urinary excretion of sodium was significantly greater in hypertensive than in normotensive individuals. Others have been unable to verify a relationship between level of dietary NaCl intake and hypertension (10, 32, 84). Battarbee & Meneely (10) have concluded that attempts to correlate the incidence or degree of hypertension with sodium consumption in subsets of a given population "are almost futile," since the dynamic range of sodium consumption is not likely to be large enough to bring out a clear correlation. An additional factor that must be taken into account is the simultaneous dietary potassium intake (10, 69, 70). A number of studies have shown that potassium can ameliorate some of the toxic effects of ingestion of sodium in excess (10, 69, 70).

In spite of the difficulty in assigning NaCl a role in the development of hypertension, a number of investigators, clinicians, committees, and task forces feel that it is appropriate to recommend reduced NaCl consumption for the U.S. population (10, 27, 49, 93). However, others argue that a reduction in NaCl intake is neither appropriate nor necessary for those who do not have an elevated blood pressure (81).

Recently, Senator McGovern stated that the 5 g of NaCl per day recommended by his Dietary Goals Committee was intended to represent salt added to the diet by individuals or processors and did not include salt that occurs naturally in food (4, 65). This would increase the daily total recommended salt level from 5 g to a level of 8 g. The Food and Nutrition Board of the National Academy of Sciences favors even greater restriction of intake to 3 g/day (93). The controversy is not likely to end between those who believe that present evidence is sufficient to recommend limitations of salt intake for the general population and those who believe that such limitations should be recommended only by an individual's physician. The Surgeon General suggests "that a prudent approach, given present knowledge, would be to limit salt consumption by cooking with only small amounts, refraining from adding salt to food at the table, and avoiding salty prepared foods" (74).

TERATOGENICITY AND MUTAGENICITY OF EXCESSIVE SODIUM INTAKE

No significant teratogenic effect was observed in mice given NaCl orally at 480 mg/kg on days 6 through 15 of gestation (44). There was also no adverse effect on nidation or on maternal or fetal survival. The data were

also negative in rats receiving oral doses of 368 mg/kg on days 6 through 15 of gestation and in rabbits at approximately the same exposure on days 6 through 18 (45).

In another study, both teratogenic and embryocidal effects of NaCl were observed in Japanese dd-strain mice injected once subcutaneously with either 1900 or 2500 mg/kg on either days 10 or 22 of gestation and sacrificed 1 week later (73). Abnormalities of the toes and feet as well as clubfoot were the most prevalent malformations.

No studies have reported a mutagenic property of NaCl.

SODIUM SUBSTITUTES AND MATCHING THE TASTE OF NaCl

Potassium salts appear to be the most likely substitutes for the taste of sodium salts. However, when potassium chloride (KCl) is substituted completely for NaCl, it imparts an unpleasant, rather bitter taste. Combinations of KCl with citric acid or other acids, monopotassium glutamate, choline, ammonium chloride, fructose, and spices are often used to mask the taste of KCl and have been used in certain processed foods.

It is commonly held that the taste of NaCl is unique. The only salt (lithium chloride) with a taste that closely resembles that of NaCl is toxic to man. It is interesting that a recent report suggests that an organic molecule, glycinamide hydrochloride, holds promise as a substitute for the taste of NaCl in the seasoning of food (87). These investigators reported that a 15:85 (wt/wt) solution of monosodium glutamate and glycinamide HCl gave the most acceptable flavor as assessed by a group of food panelists.

A few studies have also been carried out to test the feasibility of substituting KCl for NaCl on a 1:1 basis (47, 61, 71). Frank & Mickelson (47) reported that such a mixture was palatable to 72 test panelists and was judged by them to be equal in saltiness to an equal weight of NaCl. This has essentially been confirmed by others (61). Mickelson et al (71) reported in a later study that a group of 10 healthy young men placed on a low sodium diet and provided with a 1:1 mixture of NaCl and KCl used the same amount of the mixture to season their food as did a control group provided with undiluted NaCl. In the group provided with the mixture of the two salts, the sodium intake associated with seasoning at the table was reduced to 44% of the control group. Further, the subjects given the salt mixture did not compensate during the 28-day test period by ingesting large amounts of the mixture. The group consuming the salt mixture was also given bread and butter made with a 1:1 mixture of NaCl and KCl. The responses to a questionnaire completed by each subject at the end of the study indicated that no one detected any unusual flavor in either the bread

or the butter prepared with the 1:1 mixture. It seems clear from this and other studies (47, 55, 61) that the substitution of a 1:1 mixture of NaCl and KCl in many processed foods is feasible from the standpoint of consumer acceptance. This alone could reduce non-discretionary sodium intake to a maximum 50% below present levels. Many food processors will be reluctant to make this substitution until it is adequately substantiated that the salt mixture will not affect the acceptability of their product by consumers. A large-scale, non-proprietary study should be undertaken to evaluate acceptability, efficacy, and safety of a 1:1 or other appropriate mixture of NaCl and KCl in processed foods, especially meat products, baked products, and dairy products.

KCl has also been shown to substitute completely for NaCl in certain technical aspects important in the processing of food, e.g. curing of meat and meat products (75), curing of fish (79), commercial peeling of potatoes (where potassium hydroxide can be substituted for sodium hydroxide) (72), and chemical curing of black olives prior to canning (78).

There is also growing evidence, discussed later, that potassium can ameliorate some of the toxic effects of ingestion of sodium in excess (2, 16, 28, 66–68, 90, 100). Thus, substitution of KCl for NaCl, either partially or completely, would not only reduce intake of NaCl, but would provide additional protection against its toxic effects.

PHYSIOLOGICAL SIGNIFICANCE OF POTASSIUM

Potassium is the lightest element that contains a naturally radioactive isotope. In fact, in the entire lower third of the periodic table, potassium (atomic number 19), is the only substance that is radioactive in nature, having six known isotopes. Three of these (^{38}K, ^{42}K, and ^{43}K) are artificial, unstable, and shortlived. The natural element is made up of the isotopes ^{39}K, ^{40}K, and ^{41}K. Of these, ^{39}K and ^{41}K are stable and account for nearly 93.4 and 6.6% respectively, of all natural potassium. The natural radioactive isotope is ^{40}K, which has a half-life of 1.3 billion years. ^{40}K, which is now in the last stages of its radioactive decay, survives today as only 0.012% of natural potassium, and its significance is dwindling away to nothing. It was undoubtedly of great importance, however, in the early history of the earth's crust. If one makes reasonable assumptions about its rate of decay and early abundance, as well as about the energy given off by its radioactive disintegrations, it can be calculated that the heat produced would have been enough to keep the earth in a molten state (42). It appears highly probable that the decline of ^{40}K through radioactive decay was an important factor in the hardening of the earth's crust. There is another interesting fact about potassium. It is much less abundant than sodium in ocean water, but more

abundant than sodium in sedimentary rocks. Certain evidence suggests that living cells are at least partly responsible for the extensive removal of potassium from the oceans. Marine organisms may have produced this result by absorbing potassium into their cells in preference to sodium. When they died, they sank to the sediment at the bottom, taking potassium with them.

An adequate explanation as to why potassium becomes concentrated in the interior of living cells is not available. However, it is a fact that of the approximately 175 g of potassium in the human body, only 3 g are found outside the cells. On the other hand, the sodium of the body is located almost entirely outside the cells in the extracellular spaces, i.e. in the blood plasma and interstitial fluid.

The uptake and storage of potassium by cells may be regarded as a protective device to avoid the toxic effects that occur when the potassium concentration in blood rises unduly. If potassium concentration in blood rises more than three or four times normal, the beating of the heart will cease. With a little further increase, nerves cease to conduct the electrical impulses and muscles fail to contract. If as little as 6% of the cells' potassium were allowed to escape quickly into the extracellular space, the organism would promptly die. Fortunately, the cells of our bodies never release their potassium as long as they are alive, except slowly and in very small amounts.

Potassium moves about in the body by diffusion, absorption, and secretion. Potassium probably enters the blood from the intestine largely by diffusion, but an absorptive process may also be involved. It reaches cells by diffusion through capillary walls. Potassium must enter cells against a concentration gradient and thus requires an active metabolic process. It is excreted into urine by both filtration and secretion (12). A small amount is excreted in feces.

There are few bodily processes not influenced in some way by changes in the concentration of potassium in plasma. For example, it is the principal base in tissues and blood cells and plays an important part in the regulation of acid-base balance. It is also important in the transmission of nerve impulses to muscle fibers and to the contractility of the muscle itself.

ESTIMATION OF DAILY NON-DISCRETIONARY POTASSIUM INTAKE

The total daily non-discretionary intake of potassium by Americans has also been the subject of a number of studies. Among these are the NRC Survey of Industry (23, 88) and the FDA Selected Minerals in Food Survey (43,

86). Other estimates include that of Mickelson et al (71), who measured the potassium intake of 10 men during a 28-day period.

NRC Survey of Industry

NRC estimated that 361,000 kg of KCl were added to foods in 1970 by food processors (88). Sixty percent of the latter responded. When corrected to 100% and expressed on a daily per capita basis, about 8 mg of KCl/person/day was estimated to be ingested as a result of KCl added to processed food.

A resurvey in 1975 indicated a 2.5-fold increase in usage of KCl by food processors (23). At that time, the daily per capita addition of KCl to foods was estimated to be 12–20 mg. Reasons for the increase are not known with certainty. However, there is no evidence that the level of addition of KCl to any food product has changed since 1975.

FDA Selected Minerals in Food Survey

The same market basket surveys used to estimate sodium intake were also used to estimate potassium intake (43, 86). Table 5 shows that for the collections made in 1976, 1977, and 1978, the mean potassium intake was 4681, 4549, and 4735 mg or 8.8, 8.6, and 8.9 g of KCl, respectively. These

Table 5 Potassium content by food composite of 3900-kcal daily diet collected in FDA Selected Minerals in Food Survey

	1976[a] Potassium		1977[b] Potassium		1978[c] Potassium	
Food composite	mg	mg/1000 kcal	mg	mg/1000 kcal	mg	mg/1000 kcal
Dairy products	1311	336	1236	317	1254	332
Meat, fish, poultry	716	184	698	179	694	178
Grain and cereal products	519	132	535	137	565	145
Potatoes	910	233	836	214	874	224
Leafy vegetables	108	28	106	27	109	28
Legume vegetables	154	40	151	39	161	41
Root vegetables	59	15	57	15	60	15
Miscellaneous vegetables and vegetable products	127	33	150	39	165	42
Fruits	350	90	333	85	364	93
Oils, fats, and shortening	73	19	80	21	82	21
Sugar and adjuncts	64	16	63	16	59	15
Beverages including water	290	74	304	78	348	89
Total intake	4681	1200	4549	1167	4735	1213

[a] Mean value of 20–25 market basket collections.
[b] Mean value of 25 market basket collections.
[c] Mean value of 8 market basket collections.

data are representative of a 3900-kcal diet. The potassium intake expressed as mg/1000 kcal is also given in the table and is 1200, 1167, and 1213 for 1976, 1977, and 1978, respectively.

Other Estimates of Potassium Intake

Meneely & Battarbee (70) estimated that the average American diet provided a daily potassium intake of 50–100 mEq or 3.7–7.5 g of KCl. Wilde (97) estimated an intake of 50–150 mEq of potassium daily or 3.7–11.0 g of KCl.

Mickelson et al (71) measured potassium intake of 10 young men during a 28-day period. These individuals were allowed discretionary use of NaCl and were maintained on a 2500-kcal basal low sodium diet supplemented with low sodium snacks and soft drinks. The average daily intake of potassium by individuals in this group was 4141 ± 100 mg (7.8 g of KCl). A second group of 10 subjects was fed the same diet, except that a 1 : 1 mixture of NaCl and KCl was substituted for the NaCl of the first group and the salt mixture replaced NaCl in bread and butter. The daily potassium intake of individuals in this group averaged 6038 ± 100 mg (11.4 g of KCl), of which 4745 mg (9.0 g of KCl) was ingested with the food.

TOXICITY OF POTASSIUM CHLORIDE

It would not be difficult to ingest enough potassium in food to be lethal if the cells of the body did not sense an increase in blood concentration of potassium as food is absorbed from the intestines. The excess potassium is stored in large amounts (as much as 30 g) safely inside the cells. The kidneys are also important. They eventually excrete in the urine nearly all the potassium ingested with food except for small amounts needed for growth.

An additional protective mechanism in humans is vomiting, which occurs if the stomach is offered too much potassium. No fatalities have been reported following oral ingestion of KCl in aqueous solutions. Winkler et al (98) have pointed out that it is difficult for healthy individuals to ingest orally amounts of KCl too great to permit regulation of potassium ion by storage and excretory processes (increased potassium clearance) without causing nausea and vomiting. However, in individuals with diseases of the kidney, heart, and liver, a possibility for an elevation of blood potassium level exists.

It is difficult to poison the body with potassium when it enters the blood stream slowly, as it must from the intestines. If, however, potassium is injected quickly into the bloodstream, it is extremely toxic. It is much more toxic when injected into a vein than into an artery. From the vein it goes directly to the heart, which may stop beating. From the artery it goes to

less sensitive capillary beds in the skin and muscles, where it diffuses through the porous capillary walls and is taken up by the tissue cells.

Keith et al (58) reported that 9.5 g of KCl (about 160 mg of potassium/kg) i.v. over 90 min or a single dose of 12.5 g of KCl (about 200 mg of potassium/kg) orally were tolerated without evidence of toxic effects in two healthy subjects.

Ulcers and stenosis of the intestine have been observed in patients receiving enteric-coated tablets that contain KCl, usually incorporated into one of the thiazide drugs (7). It is estimated that 1 in 35,000 patients receiving this therapy for hypertension showed evidence of lesions. This should be kept in mind in the substitution of KCl for NaCl in food.

PROTECTIVE EFFECT OF POTASSIUM

Students of biology have long observed the reciprocal functions of sodium and potassium on the tissues of animals in vitro. This reciprocity may also play an important role in the development and maintenance of hypertension. In 1928, Addison (2) reported that administration of potassium to hypertensive patients resulted in a decline of blood pressure, whereas administration of sodium salts produced a rise. He postulated that the prevalence of hypertension in North America was the result of diets low in potassium and high in sodium. Priddle made somewhat similar observations in 1931 (77). McQuarrie and his colleagues (66, 90) confirmed the reciprocal effects of sodium and potassium on the blood pressure of some diabetic children. Although it is not often recognized, the reciprocity is also illustrated in the decline of blood pressure in those hypertensive patients treated by the Kempner rice-fruit diet, which is low in sodium and high in potassium (37, 59, 60). In spite of this impressive array of data, a reduction in the blood pressure of hypertensive patients has not been found uniformly by investigators who manipulated the daily sodium and potassium intakes (55).

The experimental studies of Meneely et al (67, 68) in rats support the thesis of a reciprocity between sodium and potassium in the development of hypertension induced by dietary sodium overloading. They observed an ameliorating effect of potassium added to the diet on blood pressure only when high levels of NaCl were ingested (8.4 and 9.8% NaCl in diet). High potassium also induced a striking improvement in survival of the rats. Dahl et al (28), using the salt-sensitive strain of rats developed in his laboratory and a wider range of ratios of sodium to potassium in the diet, reported that dietary sodium was hypertensinogenic whereas potassium was antihypertensinogenic. The results were somewhat more complicated than those reported by Meneely et al (67, 68). The ratio of sodium to potassium in the

diet, although important, was not the primary factor in influencing the development of hypertension. The absolute concentrations of sodium and potassium were also important. Thus, on diets with different absolute concentrations of NaCl and KCl, but the same sodium-to-potassium molar ratios, rats given the higher absolute NaCl level had the higher blood pressures (28).

The studies of Young et al (100) on the chronic effects of potassium loading on sodium balance of normotensive dogs may provide clues regarding the protective effect of potassium. They showed that an increase in daily potassium intake from 30 to 200 mEq/day produced an increase in plasma potassium concentration of 0.47 mEq/liter accompanied by a 56% increase in sodium excretion in spite of a 58% increase in plasma aldosterone concentration. After 6 days of potassium loading, the cumulative negative sodium balance was 44 mEq and was accompanied by a 6.7% decrease in extracellular fluid volume (^{22}Na space). Blood pressure did not change in these animals. Similar studies in adrenalectomized dogs maintained on fixed doses of aldosterone and hydrocortisone showed a fall in mean blood pressure of 14 mm of Hg after 5 days of potassium loading. These studies point up both the importance of the adrenal cortex to maintenance of a stable blood pressure under these conditions and the importance of plasma potassium concentration on sodium balance.

The intriguing reciprocal relationship between sodium and potassium on physiological responses and their interaction in the development of hypertension has been reviewed by others (10, 67, 70). An understanding of this relationship remains fundamental to our understanding of the factors involved in hypertension.

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