Maximum Sodium Chloride Intake and Thirst in Domesticated and Wild Norway Rats

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The following studies are concerned with the questions of a) how much salt can be put in a rat’s food before it stops eating; b) how much salt a rat can ingest before toxic symptoms set in; and c) the extent to which salt toxicity depends on the amounts of water that a rat drinks in relation to the salt content of its diet.

These studies were originally undertaken because of observations made during an investigation of the effects of domestication on the Norway rat (1). In the course of that investigation comparisons between recently trapped wild Norway rats and domesticated Norway rats from our colony showed: a) that the adrenals are definitely smaller and less active in the domesticated rat; b) that 2 or 4% salt added to the diet resulted in a greater increase of water intake in wild than in domesticated rats; and c) that about 30% of wild rats trapped from the streets have an abnormally high water intake in relation to body weight. These observations indicated that wild and domesticated rats may differ in their salt and water metabolism, perhaps as a direct or indirect consequence of differences in the size and activity of their adrenals.

Further experiments have now been undertaken to determine just what differences in salt and water metabolism actually exist between these two strains. The results, which are presented in this report, show that marked differences do exist between the two, but more importantly, they indicate principles that may be involved in the ingestion and metabolism of very large amounts of salt and water by animals in general.

Received for publication September 4, 1953.

1 This work was carried out under a contract between the Office of Naval Research and the Johns Hopkins University.


METHOD

The 36 adult domesticated Norway rats (27 males, 9 females) used for these experiments came from our colony, which was started 30 years ago with albino rats from the Wistar Institute. A few piebald and hooded rats from the colony of Dr. E. V. McCollum were added 28 years ago. Since then no new strains have been added. Their weights ranged from 155-366 gm. The 36 adult wild Norway rats (18 males, 18 females) were all recently trapped in the radius of six residential blocks in Baltimore. The traps have been described elsewhere (2). Their weights ranged from 178-563 gm. Only healthy appearing rats were used in these experiments.

The domesticated rats were kept in individual regular stock metal cages, 8 x 12 x 10 inches, each equipped with a screen bottom, a nonspillable food cup, and 1-3 inverted graduated 100-cc water bottles. The wild rats were kept in specially designed metal cages, also equipped with a screen bottom, a removable tray with a nonspillable food cup, one or more inverted graduated 100-cc water bottles, and a sliding door through which the rats could safely be transferred to the weighing cage or to the device used for holding wild rats (3). The food cup and guard fit into a recess built into the corner of the tray. A small hole in the screen floor over this cup provides access to the food. The tray can be slipped out for cleaning or for removing the food cup, without giving the rat an opportunity to escape.

All food cups were removed, weighed, and refilled daily between 9 and 11 A.M. At the same time the level of fluid in the water bottles was read and then each was refilled. The bottles were removed and cleaned every other day. All rats were weighed weekly.

External conditions were maintained as nearly constant as possible. The room housing the rats was kept at a temperature near 75°F, and it was illuminated with electric lights during the day and was kept dark at night. Daily procedures such as cleaning and record-taking, with their constant noises, were carried out as uniformly as possible.

The domesticated rats received our stock diet continuously from the time of weaning to 15-30 days before the start of the experimental diets, at which time they were given a low-salt diet. The stock diet contained graham flour 72.5%, skim milk powder 10.0%, casein 10.0%, butter 5.0%, calcium carbonate 1.5% and sodium chloride 1.0%; the same ingredients were used for the low-salt diet except for the omission of the salt and the use of saltless butter in place of the regular salted butter. In most instances the wild rats were
started on the low-salt diet within 1-2 days after capture, but were not changed to the several experimental diets until their water intakes had reached fairly constant levels, which usually required 30-50 days.

Twelve groups of rats (3 per group) of each strain received the low-salt diet plus 0, 2, 4, 6, 8, 10, 15, 20, 25, 35, 50 and 70% respectively, of added salt (as percentage of diet). Unless they died earlier, or were killed in a moribund condition, all of the animals were kept under observation for 72-92 days. At the termination of this experimental period the rats were sacrificed by crushing the cervical cord; at autopsy the adrenals, thymus, pituitary, spleen and kidneys were weighed and preserved for histological and histochemical studies. The results of studies of adrenals from these animals will be reported in detail in another paper.

RESULTS

Survival Times. Table 1 summarizes the results. It shows that on concentrations of salt from 0-25% inclusive, all domesticated rats were alive and in good health at the end of the 89-92 day period, with the exception of one rat on 4% salt diet that was killed at 24 days because of hematuria. On these concentrations all of the wild rats with the exception of two, also were alive and in good health at the end of the 72-92 day experimental period. On the 35% concentrations, two domesticated and one wild rat died; the other three were killed after 41-42 days in a moribund condition. All 12 rats on the 50 and 70% concentrations died early. It is noteworthy, however, that a domesticated rat survived 17 days on the 70% concentration.

Acceptance of Salt Diet and Food Intake. Almost all rats started at once to eat the salt diets, at least in small amounts; some ate them as freely as the low-salt diet. With the exception of the rats on the 50 and 70% salt diets, all the others gradually increased their intake until, after 5-15 days, they were eating as much or more than they had previously eaten of the low-salt diets. The rats on the 2 and 4% concentrations ate these salt diets as freely as the low-salt diet; the rat on the 6% concentration reduced its intake for only 1 day; the rat on the 8% concentration ate almost normal amounts at once; the rat on the 10% concentration reduced its intake for 3 days and then ate even larger amounts than before; and the rats on concentrations from 15 to 50% showed that with increasing salt concentrations there is a progressively greater reduction in food intake on the first day and a progressively longer time interval before return to the intake levels on the low-salt diet. Of special interest however is the fact that the rat on the 70% diet ate 5 gm on the first day and continued to eat much the same amounts throughout the first 10-day period.

There were no definite differences between wild and domesticated rats with respect to their acceptance of the high salt diets during the first 10-day period.

Figure 2 summarizes the results for the entire experimental period. The ordinates show average daily food intake in gm/kg body weight for the three rats on each of the salt diets, and for a control group on the low-salt diet; abscissas give time in days. The intake averages are given for the last 10 days on the low-salt diet and for the subsequent 70-90 day experimental period in 10 day intervals. Records are shown for domesticated (A) and wild (B) rats. These curves show that with the exception of the rats on the 35, 50 and 70% concentrations, both wild and domesticated rats continued to eat the high-salt diets in large amounts throughout the 70-90 days of the experiment; and that there were no differences in intake between the wild and domesticated rats.

The curves show that in almost all instances
during the second 10-day interval, food-intake increased well above its level on the low-salt diet and that in the succeeding 10-day periods it tended to decrease at a slow rate. They show further that with only two exceptions the salt diets were eaten in larger amounts (as much as 25% more) than the control low-salt diet.

A few wild rats on salt diets of 15% and above learned to spill their food. This was very unusual since we have found through many years of experience with our food-cups that none of the domesticated rats succeeded in spilling food. These wild rats may not have been adjusted to the high-salt diets as well as the other rats and so continued to search for plain unsalted food. Their records have been omitted from the averages in figure 2.

**Body Weight.** Figure 3A shows the average body weight curves for the 3 domesticated rats on each concentration of salt for the last 10 days on the low-salt diet and for 7-9 subsequent 10-day periods on the experimental diets. On all concentrations up to and including 25%, the domesticated rats either maintained their weights during the experimental period, or gained at about the same rate as the controls. On the three highest concentrations all of the rats rapidly lost weight.

Figure 3B shows the body weight records for the wild rats. The records are quite similar to those of the domesticated rats except that during the last two 10-day periods the rats on the 4, 10 and 15% concentrations showed small losses.

**Sodium Chloride Intake.** Figure 4 shows the average daily amounts of salt in gm/kg body weight that the domesticated (A) and wild (B) rats on the various salt diets ingested with their food. For the domesticated rats the salt intake varied roughly in proportion to the percentage of salt in the diet on all concentrations up to and including 35%; on the 50-70% concentrations the salt intake in gm/kg body weight decreased promptly. Furthermore, in the lower concentrations the intake of sodium chloride at each concentration remained extraordinarily constant throughout the experimental period. The intake levels ranged from slightly over 1 gm/kg body weight at the 2% level to 23 gm/kg body weight on the 35% concentrations.

The wild rats had essentially similar records except for the smaller amounts ingested by the wild rats on the 20 and 35% concentrations during the first 10-day period.

**Thirst.** Figures 5A and 5B summarize the observations on the domesticated and wild rats respectively. The ordinates show the average daily water intake for the three rats in each experimental group in cc/m² body surface. Earlier experiments had shown that water intake is a function of body surface, averaging 800 cc/m² for the rats from this colony on our stock diet containing 1% added salt (4). The intakes for the 12 groups of domesticated rats for the last 10-day period

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**Fig. 1.** Daily food intake for individual domesticated rats, one for each of the diets with the various concentrations of salt for the last 10 days on the low-salt diets, and for the first 10 days on the salt diet. Ordinates show food intake in grams; abscissas time in days.
on the low-salt diets ranged from 450–820 cc/m², most of them falling below the normal average for rats on the full stock diet. The controls that remained on the low-salt diet throughout the experiment drank constant and very small amounts of water, averaging 620 cc/m². The rats on the 2 and 4% diets increased their water intake only a small amount, approximately to the average level for rats on the full stock diet containing 1% salt. On the 6 and 8% concentrations, the rats showed an immediate and significant increase in water intake, which was then maintained at almost constant levels for each group. On the higher concentrations the water increased still more abruptly and at each concentration after the short initial adjustment period, was maintained at a nearly constant level throughout the experimental period. The rats on the 25% sodium chloride concentration drank the largest amounts of water—5,500 cc/m² body surface which is about 9 times as much as the average for the controls.

Figure 5B summarizes the observations on the daily voluntary water intake of wild rats. When first brought into the laboratory about one-third of the wild rats drank very large amounts of water. In most instances water intake decreased at a steady rate during the 20–50 days on the low-salt diets, reaching fairly constant levels between 800 and 2,150 cc/m² body surface by the end of the first 30 days. With one or two exceptions these levels were well above those for the domesticated rats. The intake for the control wild rats averaged 1,700 cc/m². These 3 rats happened to have a much higher water intake than any of the rats in the experimental groups.

On all concentrations with the exception of 25%, the wild rats increased their water intake to levels that were not only higher in absolute amounts than those of the domesticated rats, but higher in relation to their own pre-experimental levels.

The voluntary water-intake levels for the two strains of rats may also be expressed in
terms of the amounts of water ingested per gram of salt. Figure 6 summarizes the results. The ordinates give the water intake in cc/gm of salt; the abscissas the various concentrations of salt in the diets.

Figure 6A shows that at salt concentrations of 4, 6, 8, and 10%, the domesticated rats drank about the same amounts of water per gram of salt, approximately 60 cc. It is noteworthy that at these concentrations the rats gained weight. Even at 25% the intake still averaged 51 cc/gm of salt. A sharp drop occurred at the 35, 50 and 70% concentrations on which the rats lost weight rapidly and died.

Figure 6B shows that the water intake of the wild rats per gram of ingested salt was definitely higher than that of the domesticated rats at concentrations up to and including 15%; and that at the higher concentrations the differences were smaller. The intake at the different concentrations from 4-15% decreased progressively as the concentrations of salt increased rather than leveling off at 50-60 cc as it did in the domesticated rats.

Physiological Effects. No edema, ascites or diarrhea was noticed at any time, even in the rats receiving the very high salt diets. NaCl content of blood serum was determined in 12 additional domesticated rats, 2 on the low-salt diet and 2 on each of the diets with the following concentrations of salt: 2, 4, 6, 8, and 10%. Blood was taken from the abdominal vena cava while the rats were under ether 20 days after the start of the diets. Table 2 gives the results. Values were only slightly higher for the rats on the high-salt diets than for those on the control diets, as was to be expected from the relative constancy of the water intake per gram of salt ingested with these concentrations.

Anatomical Effects. The adrenal weights of the domesticated rats remained fairly constant at all concentrations of salt; for the wild rats they tended to decrease as the concentrations of salt increased, and also showed a wider range of variation.

The kidneys of both strains increased in weight as the salt concentrations increased. Histological studies of the kidneys failed to reveal any pathological changes. The domesticated rats showed some distention of the tubules. The results of the histological and histochemical studies of the adrenals and other
organs will be reported in detail in a later paper.

**DISCUSSION**

The results of these experiments have demonstrated that Norway rats are able to handle very large amounts of salt and over long periods of time apparently without ill effects. That rats have this ability was demonstrated by Gamble *et al.* (5). In their experiments each rat was tested with a diet containing progressively higher amounts of salt each week; the concentrations of salt were increased in six steps over a 6-week period from 2.9–17.4%. Apparently the rats thrived on this regimen. On the highest concentrations they received an average of 7.5 gm/kg body weight of salt/day. The present experiments showed that the rats can consume even larger amounts and over longer periods without ill effects. Some of our rats survived the ingestion of as much as 30 gm/kg body weight of salt in 1 day. 

Viewed by itself this observation that rats are able to thrive on such high amounts of salt would indicate that salt in any amount is not toxic to rats. When viewed, however, in relation to other observations, it becomes clear that salt may be ingested to the point of toxicity, depending on the amount of water with which it is accompanied.

To obtain information on the toxicity of salt without water, a few observations were made on the effects of giving salt by stomach tube in single doses, to rats without access to water. It was found that under these circumstances a dose of 3–4 gm/kg body weight regularly kills domesticated rats from our colony in just a few hours. This agrees well with the values determined by Mitchell *et al.* for chickens (6). (Salt given by injection into the tail vein (25% solution) killed our domesticated rats almost instantaneously in doses as low as 0.6 gm/kg.) It is clear that salt is toxic to our rats when thus administered.

Since in the present experiments, in which water was accessible at all times, the rats got along well after ingesting very high amounts of salt over long periods of time, it must be concluded that salt, when given with adequate amounts of water, is not toxic to rats.

The rats continued to gain weight at their

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*Fowl are also able to ingest very large amounts of salt (6–8).*
normal rate when they drank from 50–60 cc of water/gm of salt. They were able to get this amount of water on diets containing salt in concentrations up to 15–25%. On higher concentrations of salt they apparently did not thrive because of their inability to get adequate calories from the high salt diets and their inability to get adequate amounts of water to take care of the salt. For instance, a rat weighing 250 gm and requiring 15 gm of stock diet/day for maintenance, would have to eat 30 gm/day of a 50% salt diet. In order to properly excrete the excess salt it would have to drink 50–60 cc of water/day for each gram of ingested salt, or 750–900 cc of water every day, which is approximately 3–4 times the animal’s body weight. This may represent an almost impossible task for the rat. In these present experiments only a few rats drank amounts of water equivalent to, but not exceeding, their own body weights.

Our finding that 50–60 cc of water are needed to handle each gram of salt confirms the findings of Gamble et al. (5) and Adolph (9, 10). From the point of view of studies on the rat’s ability to self-regulate its own dietary requirements the present studies are in need of some comment (11). As a background for these comments it must be kept in mind that when given free choice of distilled water and solutions of various concentrations of salt, rats show preference for concentrations of 0.8–0.9% which closely approximate the salt content of normal blood. They drink about 60 cc of these concentrations on the average, that is, they ingest about 0.5 gm of salt/day, or 2.0–2.5 gm/kg body weight. This is a considerably smaller amount of salt than was re-

**FIG. 5.** Average daily voluntary water intake for the 3 rats on each of the various salt diets and for a control group of 3 rats on a low-salt diet (10-day averages). Ordinates give water intake in cc per square meter body surface; abscissas time in days.
Fig. 6. Average daily voluntary water intake in cc/gm of ingested salt (for 3 rats on each of the various salt diets) for last 20 days of experimental period.

The importance of the supply of water has further been brought out by the observation that the rats will immediately stop eating salt food when the supply of water is removed.

Of further interest here is the fact that the rats closely regulated their water intake to the amounts of ingested salt, that is, up to the point at which the salt content of the diets became too high to permit adequate amounts of water to be ingested.

One other aspect of the part played by salt may also be worthy of comment: that is that the amount of this all-important substance remains pegged at such a constant level in the blood despite the wide range and difference in the amounts that are ingested. On the one hand, it is difficult to reduce the salt content of a diet low enough to produce visible signs of nutritional deficiency. Osborne and Mendel (13) found that young rats grew normally on diets containing only 0.035% of salt, making a daily intake of only 20 mg/kg. On the other hand, the present experiments have shown that rats may thrive on diets containing 15-25% salt or daily intakes of 15-20 gm/kg, a thousand-fold difference.

Since these experiments originally were undertaken as part of the study of the effects produced by domestication in the Norway rat, we should like to comment also on this aspect of the results. It was found that the wild rats apparently have a greater need for water when they ingest excess salt than do the domesticated rats. Through the range of lower concentrations of salt in the diet they consistently drank more water; also their water

received from several of the diets in the present experiments. It is higher, however, than the amounts of salt present in the stock diet from which rats receive approximately 0.6 gm/kg body weight of salt/day.

In the present experiments in order to satisfy their caloric needs, the rats were forced to eat diets containing high amounts of salt. That they did not regard the salt as a poison in any sense is shown by the fact that they ate these diets in large amounts with very little hesitation. This behavior contrasts sharply with their reactions to foods containing only minute amounts of poison such as strychnine or morphine which they refuse altogether and so literally starve themselves to death (12).
intake was more erratic. In explanation of the higher water intake of the wild rats we may consider results of experiments on the effects of treating normal rats with desoxycorticosterone (14). In such animals thirst is a function of both the amount of injected DCA and the amount of ingested salt. It is possible then that the wild rats with their larger and more active adrenals may secrete more DCA or similar compounds in order to conserve what salt is available to them, and as a result show a corresponding increase in thirst. This same mechanism may explain at least part of the high water intake found in so many of the wild rats when they are brought into the laboratory and placed on the regular stock diet. In the wild state rats live largely on grain and seeds and probably have only a very low salt intake. Rats that have survived under these conditions may have inherited a highly efficient salt conserving mechanism. When they are brought into the laboratory and placed on a diet containing 1-2% salt, they may need more water, just as the domesticated rats do when they are treated with higher amounts of DCA.

On the basis of these observations on rats, we should now like to make a few remarks about the use of salt in man. Man, like the rat, is able to adjust to widely varying intakes of salt. In some parts of the world he receives little or no added salt, in other parts very large amounts. Since in European countries salt is used in such large amounts, a high salt intake may be considered to be a characteristic of civilization. Mahatma Gandhi in his Monograph on Common Salt has given an excellent statement of the part played by salt in a modern civilization (15). It has been estimated that the average European takes from 12-20 gm of salt/day. Many individuals eat much larger amounts. Based on results of the rat experiments it would seem likely that man also is able to ingest many times his usual intake of salt, providing he takes sufficient amounts of water. His failure to do this probably gets him into difficulty. Owing to cultural ideas about the use of water for quenching thirst, he may not get adequate amounts of water in relation to salt intake. This would certainly be true in countries where thirst is quenched only with wine or beer. In some instances when the salt intake is very high, it would not be possible to take adequate amounts of fluid without becoming intoxicated.

It is likely that when individuals with diseased kidneys or adrenals are forced to take much salt they may readily develop toxic manifestations indirectly attributable to the salt, e.g. hypertension, edema and adrenal dysfunction, even when otherwise normal amounts of water are ingested.

**SUMMARY**

Rats are able to handle very large amounts of salt, 15-20 gm/kg body weight/day, providing they are permitted to ingest sufficiently large amounts of water. Domesticated rats need from 50-60 cc of water/gm of salt ingested to maintain health. No such statement can be made for wild rats since other functions apparently influence their water intake. The ingestion of large amounts of salt over 2-3 months time did not produce any visible dietary deficiencies, nor did it produce any detectable pathological changes in the kidneys. When given access to water, rats will freely eat diets containing as much as 35% salt; they will eat fair amounts of a diet containing 50-70% salt. Salt does not produce as much thirst in domesticated Norway rats as in their wild ancestors. A greater secretion of a salt-conserving hormone from the larger and more active adrenals of the latter may account for this difference. On the basis of the results of these experiments it was suggested that difficulties encountered by man in using salt may result from his failure, for cultural and social reasons, to drink adequate amounts of water for excreting the excess of salt ingested.

**REFERENCES**