

PHYSIOLOGICAL ASPECTS OF THE REQUIREMENT FOR SODIUM IN MAMMALS

A. R. MICHELL

Department of Veterinary Medicine & Animal Husbandry, Royal Veterinary College (University of London), Hawkshead Lane, North Mymms, Hatfield, Herts AL9 7TA

CONTENTS

INTRODUCTION	149
CALCULATION OF REQUIREMENT	150
PHYSIOLOGICAL PITFALLS RELATING TO SODIUM REQUIREMENT	151
CRITERIA OF ADEQUACY	152
SODIUM BALANCE: CURRENT ACCOUNT AND RESERVES	153
SODIUM REQUIREMENT IN SELECTED MAMMALS	154
SHEEP	154
CATTLE AND GOATS	154
PIGS	155
RATS	155
CATS AND DOGS	155
HUMANS	155
SALT AND HYPERTENSION	156
HOW MUCH SODIUM IS EXCESSIVE?	157
CONCLUSION	157
REFERENCES	158

INTRODUCTION

There is, without doubt, a requirement for dietary sodium in mammals. The purpose of the present article is to review, not the exact requirements of various species, but their order of magnitude and their physiological basis. In particular, it questions the cavalier assumption that since Na is beneficial, adequate provision can be safely equated with a generous excess, and argues that Na intake is frequently an uncontrolled factor in experiments. Above all, even where it is taken into account, published requirements for Na tend to be substantial overestimates. It is widely assumed that animals kept on a generous and often unstated excess of dietary Na can be regarded as having a 'normal' intake.

Many animals, especially herbivores, actively seek salt and consume it freely. This 'Na appetite' is the most extensively studied example of a 'specific appetite', i.e. an appetite for a specific dietary component which varies in intensity according to physiological need. Numerous experiments in a variety of species, mainly rats, rabbits and sheep, show that salt appetite increases with increasing Na deficit (Denton, 1982; Bell *et al.* 1985). The fact remains, however, that Na appetite also exists in the absence of Na deficiency, and sometimes fails to respond to an increased demand for Na, e.g. during pregnancy in sheep (Michell & Moss, 1988). Michell (1974, 1978) suggested that salt appetite was a reflection

of potassium balance, as well as Na balance, and based on a mechanism which monitored the rate of active transport of these ions by Na^+/K^+ -transporting ATPase (EC 3.6.1.37); there is evidence to support this hypothesis (Michell, 1979; Vivas & Chiaraviglio, 1987).

Spontaneous Na intake is not, therefore, a guide to Na requirement, and much of the work on salt appetite, interesting though it is, relates to hyperacute and massive deficits (Michell, 1975, 1976*a*). As Thureau (1979) remarked, it is important to study 'natural examples of a particular regulatory task rather than subjecting animals to extremes which they never experience in nature'. Although physiologists and psychologists have sought to relate salt appetite to the defence against Na deficiency, this condition is clinically unusual in herbivores in the absence of endocrine or enteric disorders. Indeed the paradox is that despite this preoccupation with deficit, it has become increasingly recognized in recent years that the main clinical problem with human salt intake is that consumption is excessive, probably harmful, and that the psychological and cultural pressures maintaining a high intake are intense (Michell, 1978, 1984; Hunt, 1983; Houston, 1986).

CALCULATION OF REQUIREMENT

There are two traditional approaches to calculation of nutritional requirement.

(1) Empirical; the demonstration that a certain intake is required to avoid specific adverse effects.

(2) Factorial; calculation of the required intake to meet specified demands, e.g. for growth, pregnancy or lactation, and unavoidable ('obligatory') losses.

Apart from technical difficulties both approaches have inherent problems. With the empirical approach there may be a subjective component in defining adverse effects. For example, maximum growth rates are not necessarily optimal. In the case of Na, low aldosterone levels are not necessarily a sign of optimal Na intake; they may equally indicate excess. With factorial experiments, quite apart from the difficulty of measuring all forms of loss, the definition of 'obligatory' loss is often extrapolated from higher levels of intake. Na, however, tends to be excreted in quantities reflecting intake until the latter becomes extremely low, whereupon excretion may become virtually zero. Again, there is a tendency to relate obligatory loss to body-weight, but this assumes that the ability of both the kidney and the colon to respond to the Na-conserving effects of aldosterone depends on size or body-weight. Except in newborn animals this assumption is extremely dubious.

Any statement of requirement strictly relates to the environment, husbandry and diet of the animals involved. For example, the availability of dietary components may vary with the type of diet. Obligatory losses may vary with temperature, humidity and activity. Above all, individuals may vary in their requirement, and their requirements may alter with stresses, e.g. a chronic, low grade diarrhoea. Requirements are, thus, uncertain estimates and are often increased to allow a margin of safety. If this margin of safety extends to include outlying individuals in the population curve, the intake of most individuals will actually be substantially above requirement. Recently it has been suggested that requirements should be stated as a range of intakes, each achieving a defined probability of covering a known percentage of the population (Beaton, 1988).

Basically a requirement represents the intake which will maintain normal health, including growth where appropriate, and the health and growth of dependent progeny. Higher levels of intake may be desirable to sustain maximum growth rates or increase palatability, but these are commercial rather than physiological criteria and mark the difference between a nutritional requirement and a feeding recommendation.

PHYSIOLOGICAL PITFALLS RELATING TO SODIUM REQUIREMENT

There are at least three pitfalls which contribute to the general tendency to pitch Na requirement well above its probable true level. Each is a reflection, in differing degrees, of the underlying assumption that Na is safe and beneficial and that a liberal intake is therefore desirable.

(1) The assumption that signs of adaptation to a low Na intake, e.g. elevated aldosterone secretion and the resulting decrease in the Na:K ratio of urine, faeces, sweat or saliva, indicate a state of Na 'deficiency'. If the underlying assumptions were different, namely that excess Na intake was harmful, then signs of aldosterone suppression, i.e. high Na:K ratios, would be viewed as danger signals rather than evidence of normality. Thus Morris & Peterson (1975) showed that the levels of Na intake required to maintain 'normal' salivary Na during lactation were over four times those needed to sustain normal health, both in ewes and their lambs.

(2) Low-Na urine indicates inadequate Na intake: it may. However, it depends whether there is any evidence that, for the majority of individuals, chronic adaptation to 'low' Na intake has demonstrable adverse effects. It also depends whether urine is actually the predominant route of Na excretion; in many herbivores, provided they are on moderate rather than exorbitant Na intakes, faecal Na excretion predominates (Michell, 1986; Michell & Moss, 1987). Thus recent findings of Grim & Scoggins (1986) showed sheep on intakes of 25 mmol/d excreting only 6 mmol/d in urine. This might suggest the onset of intense renal Na conservation at this level of intake but, more likely, it simply indicates that these individuals were excreting about 75% of their Na in faeces (Michell & Moss, 1987).

(3) That 'inappropriate' losses of Na in urine are obligatory losses. Two examples suffice: the first is a classic experiment in humans published over 30 years ago. Strauss *et al.* (1958) studied the pattern of Na excretion following abrupt reduction of Na intake. Although the kidney can swiftly produce a virtually Na-free urine it responds differently when a generous Na intake is suddenly curtailed. There is then an exponential fall in excretion resulting in a net negative balance equivalent to about 1 d surplus intake, over a range of intakes. In essence, surplus Na is excreted cautiously over a number of days. This excretion of excess is readily confused with an accumulating deficit, i.e. obligatory loss. Thus Devlin & Roberts (1963) observed substantial urinary loss of Na in lambs suddenly deprived of 4 mmol Na/kg per d. These losses account for the very high Na requirement attributed to sheep (Agricultural Research Council (ARC), 1980), but it is likely that they are a reflection of delayed excretion of surplus Na following these very high baseline intakes (Michell, 1985a). The estimate is further increased by measured excretion of Na originating from unmeasured intake in tap-water.

The second example is recent (Michell *et al.* 1988). When sheep were kept on Na intakes close to 'requirement' throughout pregnancy (about 70 mmol/d), urinary excretion of Na increased sharply during the last third of pregnancy. This is clearly 'inappropriate' since it marks the time of maximum Na accumulation within the conceptus and the approach to the even greater demands of early lactation. The obvious conclusion would be that the Na requirement for pregnancy needed to be increased, at least during the later stages. But this conclusion would be mistaken. In parallel experiments on only 10% or less of these Na intakes, urinary and faecal Na conservation was sustained to the very end of pregnancy, probably because aldosterone secretion had not been suppressed by excess salt intake.

CRITERIA OF ADEQUACY

The ambiguity of aldosterone-dependent criteria has already been discussed. Other indicators offer similar problems for different reasons. A reduced Na intake leads to a fall in extracellular volume and plasma volume. The difficulty is to define normality; excess Na intake expands the extracellular fluid (ECF), in fact there is a different steady state for varying levels of Na intake (Walser, 1985; Michell, 1989*a*). Similarly, glomerular filtration rate (GFR) is affected by Na intake and ECF volume (Roos *et al.* 1985). Since GFR is the basis of renal function and many aspects of tubular re-absorption are influenced by Na re-absorption, experiments on unstated Na intakes are essentially unrepeatable. Worse, experiments on exorbitant salt intake are experiments on animals in a state of chronic ECF expansion, not normal animals. Thus 10 g salt/kg diet is often regarded as 'normal' for laboratory rats, but, as a dose rate, it is approximately equivalent to 700 mmol/d in humans (Michell, 1984). This is about 41 g salt/d, nearly 60% above the exceptionally high intakes associated with a 40% incidence of hypertension in Northern Japan (Dahl, 1960).

One highly unconventional criterion might serve to indicate Na intakes which are dangerously above requirement. Although the link between salt and hypertension remains highly controversial (see p. 156), there is little doubt that the age-related rise in blood pressure, which is accepted as normal in most cultures, does not occur on low Na intake. Granted that essential hypertension may be a multifactorial problem, that the distinction between normotensive and hypertensive may be along a continuum rather than across a sharp boundary and that Na intake probably contributes to hypertension in a substantial number of individuals, an upper limit of safe Na intake might be defined by the level which avoids this age-related increment in arterial pressure.

Failure to distinguish between adequate and liberal provision of Na has tended to conceal the fact that many animals are accustomed to a routine excess of dietary Na (Michell, 1978). Nevertheless it is significant that during the last 20 years, and especially in the 1980s, the whole emphasis of research on the physiology of Na excretion has switched from the defence against depletion to the mechanisms dealing with surplus salt, notably natriuretic hormones (Michell, 1989*b*). The key question is, since renal, enteric and adrenal mechanisms can secure an extremely low level of obligatory loss, is any greater intake of Na actually necessary (Michell, 1978)?

There seems to be little risk in being routinely adapted to a low Na rather than a high Na turnover either in animals or people (Michell, 1984), with the exception of individuals with particular medical problems. Moreover, there is no experimental support for the idea that the chronic expansion of ECF volume associated with liberal salt intake actually confers significant protection against deficits of the magnitude associated, for example, with diarrhoea or haemorrhage.

In herbivores, the possible adverse effects of chronic adaptation to low salt might include: (1) poorer ability to excrete the large dietary load of K, especially if water were restricted; (2) poorer ability to sequester excess K in rumen fluid or draw on it as a reserve of Na; (3) a less favourable environment for the microflora in ruminants as a result of the altered salivary Na:K ratio; (4) effects of the latter on the absorption of other minerals (e.g. Na intake below 0.3 mmol/kg may impede magnesium absorption in sheep; Martens *et al.* (1987)), or (5) in any species, an increased energy expenditure resulting from stimulation of Na⁺/K⁺-transporting ATPase by enhanced mineralocorticoid secretion provoked by low Na intake (Michell, 1984, 1987; Milligan & McBride, 1985).

These are all interesting possibilities but there is insufficient evidence as yet to assess their actual importance. Relationships between Na⁺, K⁺ intake and Mg status, for example,

deserve further attention. Thus, while a low Na^+ intake, by promoting aldosterone secretion and increasing salivary K^+ , may impede Mg absorption (Care, 1988), excess Na (or indeed excess aldosterone) by causing expansion of ECF volume increases urinary loss of Mg during the resulting natriuresis (Dirks, 1983).

SODIUM BALANCE: CURRENT ACCOUNT AND RESERVES

The problem of defining the hinterland between surfeit and deficit of Na was addressed by Hollenberg (1980, 1982), who focused attention on an intermediate level of Na or 'set-point' above which excess Na was excreted like a drug but below which body Na was defended. Essentially this was a development of the concept of Strauss *et al.* (1958) and the quantitative implications are supported by findings from experimental dogs (Daniels *et al.* 1985). The specificity of a set-point, rather than a series of steady states varying with intake, led to a controversy with Bonventre & Leaf (1982).

As Simpson (1988) emphasises, however, there is something very distinctive about one of these steady states, whether or not it is a set-point in the engineering sense: below a certain level of intake, Na virtually vanishes from urine. This does not mean that the animal or person is Na depleted. Using a full reservoir as an analogy, if the inflow were small, just sufficient to balance any leaks in the dam (obligatory losses), the situation would be stable. It would remain so over a considerable range of water levels. We would expect emergency measures to be activated before the water level fell dangerously low, but not every time it was slightly below the top, i.e. not just because water ceased to overflow.

Such a concept can only apply where there is an actual reservoir. In the case of Na there are potentially several. As already indicated, ECF volume can vary within individuals over a range: the extremes will be associated with circulatory shock (contraction) or oedema (expansion). In between there may well be an optimum, but we know little about it. The factors influencing this optimum might include diffusion distances in interstitial fluid, or the relationship between plasma volume, arterial pressure and cardiac work. Gut fluids provide an additional reservoir of Na which is large in herbivores, especially ruminants (Michell, 1985*a*). Above all, bone provides potentially the largest reservoir of all, though the least understood and perhaps the least responsive; it may in fact be more important as an 'overflow' for excess Na (Michell, 1976*b*).

The whole purpose of a reservoir is to *buffer* supply of water against everyday fluctuation in rainfall. Provided the two balance out over a season, without the reservoir falling too low, there are no problems. No-one expects the reservoir to be full every day, let alone overflowing, still less that *daily* rainfall must exceed daily consumption. Averaged over the season, however, rainfall must match leakage (obligatory loss) plus consumption (growth, pregnancy, lactation).

Recent evidence from sheep (Michell *et al.* 1988) implies that even over the 'season' of pregnancy and lactation, there is no need for Na intake to match *current* demand. Even on Na intakes which are well below published requirement, and probably below the actual demands of late pregnancy and early lactation, ewes and their dependent lambs actually manage very well. The lambs are indistinguishable from controls. The ewes are healthy enough to sustain two consecutive pregnancies and lactations, although their exchangeable Na inevitably is reduced; their reservoirs are depleted (Sansom *et al.* 1983; Vincent *et al.* 1987). Granted that obligatory losses are low, the reservoirs can be repleted in the period preceding the next pregnancy, and even during the early stages. For example, if obligatory losses were 3 mmol/d (and they could be less), 150 d at 10 mmol/d intake could allow the accumulation of over 1000 mmol Na^+ . Assuming dry matter intake of 1 kg daily, this

would be met by a diet with as little as 0.016% Na⁺ in the dry matter. At least in animals adapted to marginal environments, 'requirement' may need to be viewed over a season and perhaps to combine a daily average with a higher daily minimum to cover periods of peak demand such as pregnancy and lactation. These considerations are not restricted to herbivores; similar seasonality in Na balance must apply to Yanomamo Indians (Oliver *et al.* 1981) if they manage on such exceptionally low intakes.

Within species, daily requirement for mature non-pregnant, non-lactating individuals, i.e. maintenance requirement, probably does not relate closely to body-weight since obligatory loss can be very low in all individuals. The exception, perhaps, is the dog, where the huge range of mature sizes of different breeds would imply that even if a 2 kg toy dog and an 80 kg St Bernard both reduced their urinary Na concentration to 0.1 mmol/l, their actual losses would differ as a result of differing urine volume. For similar reasons, when it comes to comparing species as disparate in size as rats, humans and cattle, requirement is best related to body-weight (or perhaps to metabolic mass). Since duration of pregnancy and lactation, and numbers and net growth rates of offspring, differ so widely between species, the only easily validated comparisons are for maintenance requirement, i.e. the amount to cover obligatory loss in urine, faeces, hair, skin (including sweat) or salivary secretion. The assumption is that ingested Na is virtually 100% available, and this seems reasonable since even in sheep excreting Na predominantly in faeces, this Na is not 'trapped' but is readily water-soluble (Michell & Moss, 1987); moreover, trapping of cations by plant fibres and cell walls affects heavy metals rather than Na (Van Soest, 1982).

It is instructive, therefore, to examine the published evidence concerning maintenance requirement in a number of species and see, quite simply, whether it suggests that mammalian Na requirement, expressed as mmol/kg per d, is generally of the order of 0.1, 1.0 or more. The claim that maintenance requirement is higher in a particular species implies that its obligatory losses are greater.

SODIUM REQUIREMENT IN SELECTED MAMMALS

The main constraint on selection of species for comparison is the dearth of reliable information, even in animals of major economic concern; again this is a reflection of the fact that since Na can be safely consumed in large amounts, provided that water is available, there is actually little incentive to investigate Na requirement (Michell, 1985*b*). This discussion concentrates on rats, sheep, cattle, pigs, dogs, cats and humans. The situation in horses is complicated by the fact that they lose substantial quantities of Na on exertion because their sweat is hypertonic (Snow & Harris, 1989).

SHEEP

The maintenance requirement for sheep suggested by the ARC (1980) is put at just over 1 mmol/kg per d. It is, however, suspect because the faecal losses are estimated from cattle and the urinary losses from lambs which have been suddenly removed from very high Na intakes (Michell, 1985*a*). Recent findings from sheep (Michell *et al.* 1988) suggest that obligatory losses are no more than 0.05 mmol/kg per d and that 0.1 mmol/kg per d can provide for pregnancy, let alone maintenance.

CATTLE AND GOATS

The ARC's (1980) suggested requirement for maintenance in cattle (0.3 mmol/kg per d) is more reasonable and is supported by recent findings in steers from McSweeney & Cross

(1989), while their findings in goats suggest that maintenance plus growth can be sustained by 0.3–0.7 mmol/kg per d.

PIGS

For pigs (ARC, 1981), it is suggested that up to 40 mmol Na/kg diet is needed (about 2 g salt/kg), but it seems likely that the obligatory loss is less than assumed, probably about 0.6 mmol/kg per d (Michell, 1985*b*).

RATS

The situation in laboratory rats is somewhat different from most other species since they are growing throughout the period when they are mainly used (Mohring & Mohring, 1972). Brensilver *et al.* (1985) found that if Na intake fell below 250 $\mu\text{mol/d}$, weight gain slowed though growth and positive Na balance continued. Grunert *et al.* (1950), Toal & Leenen (1983) and Louis *et al.* (1971) all provide essentially similar estimates, corresponding to about 0.05% Na⁺ in the diet. Indeed the findings of Ganguli *et al.* (1970) and National Research Council (1978) suggest that even pregnancy and lactation can be accommodated at these levels, though more recent findings (Bursey & Watson, 1983) suggest that slightly more is needed (about 0.17% Na⁺). Prepubescent rats also need slightly more Na (300 $\mu\text{mol/d}$) to sustain growth (Fine *et al.* 1987). Nevertheless, growing rats (0.4 kg) can manage on about 250 $\mu\text{mol/d}$ provided they are not pregnant, and thus, the actual maintenance requirement would be 0.6 mmol/kg per d or less. Interestingly, Na requirement is only slightly above the intake at which Na vanishes from the urine in rats (Brensilver *et al.* 1985).

CATS AND DOGS

The maintenance requirements of cats are essentially unknown (Michell, 1989*a*) and it even turns out that some estimates have been derived from 50-year-old values in poultry! With dogs, however, it is likely that despite earlier, high estimates obligatory losses are of the order of 0.05 mmol/kg per d, comparable with sheep (Michell, 1989*a*). Empirical findings indicate that maintenance requirement probably lies in the range 0.2–0.7 mmol/kg per d, with the latest National Research Council (1985) estimate at 0.4–0.5 mmol/kg per d (Michell, 1989*a*).

HUMANS

All in all, it seems unlikely that Na requirement in mature mammals exceeds 0.6 mmol/kg per d, unless they are pregnant, lactating, or have unusually high obligatory losses; the actual requirement could conceivably be considerably lower. Applied to humans, this would suggest that for a 70 kg adult Na requirement is below 40 mmol/d, well in the range that many clinicians would regard as unsustainably low. Indeed, conventional manufacturing and labelling would certainly make it hard to obtain such a low Na intake, largely because we are accustomed, addicted, to salted food (Michell, 1984). Findings from humans confirm that 10 mmol/d (0.14 mmol/kg per d) can be enough to sustain even the demands of pregnancy, growth or sweating; indeed, in the case of the Yanomamo Indians, 1 mmol/d (0.01 mmol/kg per d) seems adequate for all their needs (Oliver *et al.* 1981; Frohlich & Messerli, 1982; Hunt, 1983; Houston, 1986; Anon, 1989). Granted that for some minerals and vitamins the requirement : toxicity ratio is about 1 : 10 (Michell, 1984) and the daily human maintenance requirement is probably well below 40 mmol, the burden of proof should really move to those who continue to accept Na intakes in the range 100–300 mmol/d as normal and harmless, not least because the incidence of essential hypertension is very high and the likelihood is that at least a substantial proportion of cases have been

precipitated or exacerbated by a lifetime of excess salt consumption (Weinberger, 1987). In fact, the probabilities suggest that far more people are at risk from the salt on their eggs than the salmonellae inside them!

The continuing controversy over salt and hypertension would require a review in itself, and even then the verdict on the putative link would remain 'not proven' (Michell, 1984, 1989*a*; Anon, 1986; MacDonald, 1986; Singh *et al.* 1987; Swales, 1987). Nevertheless the grounds for suspicion are extremely strong, and with as many as 60 million Americans affected by hypertension, the 1988 Report of the Surgeon General identified reduced salt intake as one of five important objectives for the general population (McGinnis & Nestle, 1989). No discussion of Na requirement could be complete without considering the most important clinical problem associated with our uncertainties over adequate or excessive salt intake.

SALT AND HYPERTENSION

There appears to be no exception to the rule that hypertension is rare and that blood pressure remains stable despite advancing age in low salt cultures (Anon, 1988; Michell, 1989*a*). There are a few instances of really high salt cultures which apparently escape hypertension but most of these are dubious (Michell, 1989*a*). Ancestral Na intake was probably little more than 30 mmol/d (Eaton & Konnor, 1985), well below the level likely to cause hypertension (Houston, 1986; Anon, 1988). It is likely that high Na intake in infants may be decisive in its long-term effects (Dahl, 1972; Hofman *et al.* 1983). It is also likely that any hypertensive effect of Na is potentiated by stress (Anderson, 1984; Henry, 1988). Prenatal salt loading exacerbates the hypertension of spontaneously hypertensive rats (Di Nicolantonio *et al.* 1987). The adverse effect of salt may not be entirely due to Na; there may be a separate, additive effect of chloride (Weinberger, 1987). Thus preliminary studies by Kurtz *et al.* (1987) showed that equimolar doses of Na raised blood pressure (and volume) when accompanied by chloride but not by citrate. Apart from its putative role in causing hypertension, excess dietary salt also exacerbates the associated cardiac changes (Schmieder *et al.* 1988).

Evidence on salt and hypertension falls into three main categories.

- (1) Cross-cultural studies.
- (2) Salt loading studies.
- (3) Salt reduction in hypertensives.

The main criticism of the former is that differences between cultures are often gross, but not always, e.g. where subgroups of isolated cultures have merely adopted different dietary customs. Salt loading studies are of dubious value since they are necessarily short-term. Salt restriction does seem beneficial in many hypertensives, though often this is grudgingly conceded, even when it appears as effective as 'mainstream' therapy, e.g. with diuretics (Michell, 1984). Hypertension in diabetics is particularly salt-sensitive (Dodson *et al.* 1989). Generally, however, the effects in mild hypertension are definite but modest (Grobbee & Hofman, 1986; Anon, 1989). A therapeutic effect of Na restriction on established hypertension is, however, a separate issue from excess Na contributing to its aetiology, though they may be related. A recent study (McCarron *et al.* 1984) which appears to show that 'higher intakes of Na were associated with lower mean systolic blood pressure and lower absolute risk of hypertension' needs to be interpreted with more than a grain of salt. The differences in Na intake were small (12%), intakes (which were estimated rather than measured) were high in both groups (> 1 mmol/kg per d) and, above all, the study compared normals with established hypertensives. As Kurtzman (1985) remarked, really to grapple with the link between salt and hypertension 'you would have to show that a low-

salt diet prevented the development of hypertension in predisposed individuals if instituted early enough'. So far, the nearest we can approach this is in low-salt cultures with their remarkably low incidence of hypertension; it is not that they are inherently resistant because when they move to 'Western' diets and environments they become susceptible.

HOW MUCH SODIUM IS EXCESSIVE ?

Clearly this question cannot be satisfactorily answered until Na requirement has been more carefully defined for a range of species. Moreover, it is probable that the magnitude of excess, as with the dose-response relationship of a drug, needs to be viewed on a logarithmic scale (Hollenberg, 1980; Scribner, 1983; Michell, 1984). Thus, if the Yanomamo Indians can even manage on 0.2 mmol/d according to the most recent estimates (Anon, 1988), we need to examine the effects of 1, 10, 100 or 1000 mmol/d rather than attempting to discriminate between the effects of 150–300 mmol/d.

Failure to grasp this can lead to a bizarre consensus in the interpretation of results. The outstanding example is the recent 'Intersalt' study of 10000 people in fifty-two populations (Anon, 1988). In forty-eight centres, there was no relationship between the prevalence of high blood pressure and the amount of Na excreted (ingested). But the rate of rise of arterial pressure with age did correlate. In four centres, low Na intake correlated with a low incidence of hypertension and the absence of an age-related increase in pressure. 'It seems at least possible that salt intakes as low as these may have an important influence on blood pressure, although they are clearly not feasible and possibly hazardous in most cultures' (Swales, 1988).

Some of the purported hazards are bizarre indeed (Michell, 1980, 1989*a*), but what of the low intakes? There actually was a significant, positive correlation between Na excretion and systolic pressure across the fifty-two centres until the four lowest centres were excluded because their intakes were regarded as abnormally low! Yet these four were *all* the centres except one (96 mmol/d) with median intakes below 100 mmol/d. And within these five centres the two with median intakes of 50–100 mmol/d had a prevalence of hypertension of 5–26%; the three on 0.2–27 mmol/d had a prevalence of 0–1%. In centres with intakes averaging above 100 mmol Na⁺/d the prevalence of hypertension was 18%; in those below 0.8 mmol/kg per d the prevalence was 5% or less. The association between salt and hypertension stares the impartial interpreter in the face, but it is discarded by arbitrarily ignoring the all-important dose range. Instead the analysis concentrated futilely on intakes averaging 100–250 mmol/d. This type of error flows directly from the widespread failure to grasp just how high these intakes are, compared with likely estimates of requirement.

CONCLUSION

The object of the present review has not been to analyse, species by species, the precise requirement for Na associated with various stages of growth or reproductive life. Such a review would be exceedingly long because despite the general scarcity of relevant information, that available is subject to a variety of technical and theoretical shortcomings and inconsistencies.

Instead, the aim has been to focus on maintenance requirement, the most suitable basis for comparison between species, and search for convergence in the evidence regarding its likely order of magnitude. There is little reason to suppose that mature mammals, free of reproductive demands, require more than 0.6 mmol/kg per d and plenty of reason to suspect that they can manage on very much less. For those who claim, for example in

humans, that intakes in the range 2–4 mmol/kg per d are necessary and healthy, the onus of proof is to demonstrate either commensurately high obligatory losses or measurable adverse effects in a significant proportion of a population accustomed to more moderate intake.

Above all, the aim has been to challenge the notion that enough is known about Na requirement, and the assumption that provided Na intake is generous, the actual amount scarcely matters. The result of these misconceptions has been that insufficient attention has been paid to exploring the lower limits of Na requirement, that clinicians do not really understand what they mean by 'low' or 'excessive' Na intake and that physiologists accept as normal experimental animals adapted to chronic salt-loading. Our view of dietary Na needs to become more sceptical and less benign.

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