The Differential Diagnosis of Hypernatraemia in Children, with Particular Reference to Salt Poisoning

An evidence-based guideline

September 2009

Royal College of Paediatrics
and Child Health

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Responsibility for appropriate practice lies solely with the individual health professional.

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All members of the guideline development group and reviewers made declarations of interest and further details of these are available on request from the College's Science and Research Department.

Stakeholder organisations

The following organisations were consulted on the draft guideline:

British Association for Community and Child Health
British Association for Paediatric Nephrology
British Inherited Metabolic Disease Group
British Paediatric Mental Health Group
British Society for Paediatric Endocrinology and Diabetes
Child Protection Special Interest Group
Child Public Health Special Interest Group
Community and Child Health College Specialty Advisory Committee
Contact a Family
Mental Health College Specialty Advisory Committee
Nephrology College Specialty Advisory Committee

Summary of guidance

Descriptions of deliberate poisoning in children leading to hypernatraemia

There are credible case reports of children deliberately and abusively administered salt [Grade C]. These are described from different countries and by different authors. The ages of the children ranged from 6 weeks to 6 years.

There is a single, credible case report of deliberate and forcible administration of sodium bicarbonate by a babysitter causing the death of the child [Grade C].

Although there are credible case reports of significant hypernatraemia in children secondary to water deprivation, at least some of these children are likely to have been administered salt as well [Grade C].

Prior probability of deliberate salt poisoning

Taking a Bayesian approach to the diagnosis of deliberate salt poisoning, it is important if possible to establish the proportion of children presenting with hypernatraemia in whom deliberate salt poisoning is the cause. This provides the prior probability before any consideration of the individual child's circumstances. As for any other clinical situation, this needs to be taken into consideration together with the child's individual presentation and findings in estimating the likelihood of salt poisoning.

The prior probability would be ideally established by reference to good quality UK studies of children presenting with hypernatraemia in whom the proportion with deliberate salt poisoning (the prior probability) had been established. In the absence of such studies, the prior probability has to be estimated from establishing separately the incidence of hypernatraemia in children presenting to hospital and the incidence of deliberate salt poisoning.

Incidence of hypernatraemia in children in the UK

Hypernatraemia is rare in children presenting to secondary care [Grade C]. There is no accurate estimate of the incidence in the UK. A Texas study suggests an annual incidence of approximately 2 per 100,000 children.

In exclusively breast fed infants, estimates of the rate of hypernatraemic dehydration range between 1 in 200 to 1 in 1,400 babies [Grade B].

The incidence of hypernatraemia secondary to child abuse

Non-accidental salt poisoning is a very rare event. Most UK paediatricians will never be responsible for a case [Grade C].

The probability of a child presenting with hypernatraemia being the subject of non-accidental salt poisoning

Taking the estimate of annual incidence using the Texas series together with the BPSU study, approximately 1 in 200 admissions with hypernatraemia could be expected to be secondary to salt poisoning. However, the error on this estimate is likely to be very large.

Non-accidental salt poisoning is a rare cause of hospital admission with hypernatraemia [Grade C].

Other described mechanisms causing hypernatraemia through excessive sodium intake

Errors by professionals

- Accidental substitution of salt for sugar in making up feeds
- Errors in making up oral rehydration solutions
- Inadvertent administration of concentrated intravenous saline

Errors by parents or carers

- Accidental substitution of salt for sugar in making up feeds
- Errors resulting in the administration of excessively concentrated feeds
- Errors in making up oral rehydration solutions
- Erroneous administration of an overdose of sodium phosphate
- Inappropriate use of an adult sodium phosphate enema
- Accidental administration of baking soda

Side effects of medical treatments

- Intravenous 3% saline for treatment of intracranial hypertension
- Instillation of hypertonic saline into a body cavity as treatment for hydatid cysts
- Saline used as an emetic
- Softened water and salt water used for antegrade continence enemas
- Sodium bicarbonate administered during a cardiac arrest
- Sodium bicarbonate paste to burned skin
- Intrauterine saline used as an abortifacient

Side effect of parental practices

- Saline used as an emetic following accidental ingestion
- Excessive quantities of oral rehydration solution
- Application of salt to the skin in a healthy baby to promote health
- Application of salt crystals to burned skin
- Topical use of sodium bicarbonate for nappy rash
- Baking soda added to feeds to treat cold symptoms or wind

There are well described credible instances where errors by parents and professionals have led to significant, sometimes fatal, hypernatraemia secondary to salt, sodium bicarbonate or sodium phosphate administration [Grade C]. The judgements as to whether these episodes were accidental rather than abusive or neglectful are based on the context and circumstances, not the biochemical findings [Grade C].

In many of the case reports of infants and children being fed inappropriately concentrated feeds the true cause cannot be ascertained with any degree of confidence. There remains the alternative possibility of abuse or neglect [Grade C].

Some medical interventions involving the administration of additional sodium to children have on occasion resulted in fatal hypernatraemia [Grade C].

There are credible reports of well-intentioned actions by parents or carers that have resulted in hypernatraemia [Grade C]. Some parents have initially denied their actions, and although this should raise suspicions of possible non-accidental injury, this may also occur for other reasons [Grade C].

Accidental or voluntary ingestion by children

The existing evidence suggests that young but otherwise healthy children in the UK do not spontaneously and voluntarily ingest sufficient salt to cause significant hypernatraemia [Grade C].

The one existing case report involving two healthy young children does not provide credible evidence that otherwise healthy young children spontaneously and voluntarily ingest sufficient salt to cause significant hypernatraemia [Grade C].

Additional mechanisms involving excess sodium ingestion described in adults

- Deliberate self-harm using Soy sauce
- Accidental ingestion of salt by adults with learning difficulties or dementia
- Accidental ingestion of flavour intensifier containing sodium chloride and sodium glutamate by a young adult with learning difficulties
- Inadvertent ingestion of sea water in near drowning
- Deliberate administration of saline in exorcism ritual
- Substitution of Milton for Eusol used for postoperative wound irrigation

The diagnosis of salt poisoning

Clinical findings in salt poisoning

The following symptoms and signs are reported in accidentally poisoned infants and children:

1. Vomiting
2. Convulsions or muscular twitching
3. Fluttering of eyelids or facial muscles
4. Refusing feeds
5. Avid thirst
6. Respiratory distress
7. Fever
8. Diarrhoea
9. Peripheral circulatory failure
10. Drowsiness and coma

The onset of coma can be rapid following salt ingestion [Grade C].

The common symptoms and signs of deliberate salt poisoning include vomiting, diarrhoea, drowsiness or coma, irritability, seizures, and thirst [Grade C].

Symptoms do not differ from those seen in accidental poisoning [Grade C].

Some children poisoned with salt have a modestly raised blood glucose [Grade C].

When calculating the amount of sodium required to raise the serum sodium by a specified amount, the total body water (approximately 65% of the child's weight) should be used to determine the volume of distribution. [Grade D]

The amount of salt that could be fatal to an infant or child is likely to be in the range of 0.75 to 3 grams (approximately 13 to 51 mmol) per kilogram body weight [Grade C].

Post-mortem vitreous humour sodium and urea provide a useful guide to plasma sodium and urea concentrations before death [Grade C].

Associated findings

Some but not all children with hypernatraemia caused by deliberate poisoning have evidence of other forms of child abuse [Grade C].

Subdural haemorrhage occurs only in a small minority of cases of salt poisoning [Grade C].

Most reported cases of coexisting subdural haemorrhage and hypernatraemia are non-accidental, and in several children the evidence suggests that the subdural haemorrhage preceded deliberate salt poisoning [Grade C].

The finding of a subdural haemorrhage in association with hypernatraemia should raise the suspicion that the cause may be non-accidental injury [Grade C].

Recommended investigations in children presenting with hypernatraemia

A sample of gastric contents for analysis of sodium content should be obtained as soon as possible after admission in all children presenting with hypernatraemia [Grade D].

Careful measurement of weight at the time of admission coupled with a second weight after restoration of full hydration provides a reliable estimate of the degree of dehydration [Grade B]. This should be undertaken if possible in children presenting with hypernatraemia [Grade D].

A urine sample for calculation of fractional urinary sodium excretion (for which plasma and urine sodium and creatinine measurements taken at a similar time are required) in the presence of normal renal function should help to ascertain whether the hypernatraemia is secondary to excessive sodium ingestion [Grade D]. Regular urine samples for fractional urinary sodium excretion are recommended in children presenting with hypernatraemia [Grade D].

Measurement of bicarbonate, calcium and phosphate concentrations as well as sodium and chloride concentrations should assist in distinguishing the different sodium containing substances [Grade D].

In a child with hypernatraemia a urine osmolality can assist in excluding diabetes insipidus [Grade D]. It is best interpreted in conjunction with a simultaneous serum osmolality.

Differential diagnosis of salt poisoning

As well as the causes of excessive sodium intake there are a number of other causes of significant hypernatraemia, all due to water depletion. Although hypernatraemia may occur with mineralocorticoid excess, this is mild and it is rarely, if ever, severe enough to constitute a clinical problem.

Lack of water intake:

1. Inadequate breast milk resulting in inadequate water intake
2. Unconscious or mentally impaired (described in adults)
3. Essential hypernatraemia without structural abnormality of the hypothalamus
4. Adipsia secondary to structural abnormalities involving the hypothalamus
5. Deliberate water restriction
6. Lost in the desert or at sea with lack of available water combined with increased evaporative water loss.

Case reports of osmoreceptor dysfunction are all in association with other endocrine or structural brain abnormalities. There are no case reports of otherwise normal children presenting with isolated hypernatraemia being due to abnormal osmostats [Grade C].

Increased water loss

Increased renal loss

1. Central diabetes insipidus
2. Nephrogenic diabetes insipidus
3. Renal medullary damage

Increased gastrointestinal loss

Hypernatraemic dehydration secondary to diarrhoea

Increased evaporative loss

1. Skin conditions including Netherton syndrome
2. Endurance exercise in marathon runners
3. Lost in the desert or at sea, with increased transepidermal water loss

What key tests will help distinguish excess sodium intake from water depletion?

"The distinction between accidental and non-accidental salt poisoning cannot be made on clinical or physiological grounds, since the end result of both is the same. Only a meticulous evaluation of the history and the attendant circumstances of the case can resolve this… The two conditions that should be distinguishable on clinical and physiological grounds are hypernatraemic dehydration and salt overload (however induced)."[43]

Measurement of urinary sodium concentration does not reliably distinguish dehydration from excess sodium intake. [Grade C]

In the absence of renal failure, a raised calculated urinary fractional sodium excretion is indicative of increased sodium excretion by the kidneys. The urinary fractional sodium excretion rates reported in the 3 severely hypernatraemic individuals were all 9.5% or above, well above the upper reported limits in healthy children and in those presenting with gastroenteritis and dehydration. [Grade D]

24 hour urinary sodium excretion rates of up to 11 mmol per kilogram per day have been observed in infants with salt poisoning. In view of the small number of cases reported and the absence of published normal values, particularly in infants, a cut off point above which excessive sodium intake can be inferred cannot be given. [Grade D]

How well known among the public is the lethal dose of salt?

Most parents would be concerned about the serious risks of giving a dose of salt in the minimum **lethal** dose range. [Grade C].

Summary of recommended immediate investigations in children presenting with hypernatraemia in whom the differential diagnosis includes possible salt poisoning

- Accurate weight measurement at admission and following restoration of full hydration
- Simultaneous plasma and urine sodium and creatinine at admission and repeated regularly
- Plasma bicarbonate, calcium, chloride and phosphate
- Simultaneous serum and urinary osmolality
- Sodium concentration of gastric contents

1. Introduction

Salt is toxic in large enough quantities, and may result in serious illness or death. Excessive intake of salt, for whatever reason, results in hypernatraemia, the hallmark of sodium intoxication. Hypernatraemia resulting from deliberate, non-accidental salt poisoning can be difficult to diagnose.[1] A diagnosis of non-accidental salt poisoning needs to be made with the utmost care due to the medico-legal considerations involved, and the implications for the child and carers.[2, 3]

A small number of high profile cases involving the prosecution of parents for non-accidentally poisoning children have highlighted the importance of the medical evidence, and the need to establish professional guidance on the investigation and diagnosis of children with suspected non-accidental salt poisoning.

The reliability of the clinical process, including diagnostic tests, needs to be established to ensure, where possible, that suspected cases of salt poisoning are correctly and promptly identified, that salt poisoning is not over-diagnosed, and that all possible explanations for hypernatraemia are considered.

The use of the term “poisoning” in the title does not imply that the administration or intake of salt or other agent leading to hypernatraemia was necessarily deliberate.

Clinical need for the guideline

There are currently no evidence-based guidelines relating to the differential diagnosis of hypernatraemia in children or guidance on the assessment leading to a diagnosis of hypernatraemia due to sodium poisoning and its causes.

Following the inquiry into the death of Victoria Climbié (2003), safeguarding and promoting the welfare of children and young people has become a national priority within child health[4, 5]. The National Service Framework for Children, Young People and Maternity Services highlights the high cost of abuse and neglect to both individuals and to society and the duty on staff to be proactive in safeguarding children by “being alert to the signs and symptoms of abuse or neglect”.[6]

There is a risk of death or disability from salt poisoning. The limited evidence on mortality among children with hypernatraemia due to salt poisoning (intentional or not) is difficult to interpret.[3, 7, 8]

The evidence base for a diagnosis of salt poisoning has not been systematically reviewed, and if sparse this needs to be made explicit to paediatricians.
Where non-accidental salt poisoning occurs, there are major implications of incorrect diagnosis. There are also serious implications of over-diagnosing non-accidental poisoning. Other rare medical diagnoses need prompt recognition and management.

Individual paediatricians are not likely to encounter the problem frequently, and therefore are likely to benefit from readily obtainable guidance.

Guideline aims

The aims of the guideline are:

- To assist in the differential diagnosis of hypernatraemia in children, with particular reference to the recognition and diagnosis of excessive intake of sodium and its causes.
- To recommend the investigations that are useful in distinguishing the different causes in children.
- To be a resource that individual paediatricians can use to assist them in reaching a diagnosis when confronted by unexplained hypernatraemia.
- To highlight areas where further research would be helpful.

Audience

The intended audience for the guideline is paediatricians and other medical practitioners who may be involved in the investigation and management of children presenting to hospital with hypernatraemia (e.g. A&E consultants). It is also intended to be relevant to tertiary specialists and others providing information, e.g. chemical pathologists.

Scope

The guideline covers the clinical and biochemical diagnosis of hypernatraemia in children. It is focussed on the diagnosis of poisoning by agents including salt, the differential diagnoses and the possible causes of poisoning.

The guideline covers children aged up to 18 years presenting with hypernatraemia in all health settings. It is relevant to children in populations similar to those in the UK, but the guideline does not address the different child protection practices in other countries.

The guideline does not cover the investigation of preterm neonates developing hypernatraemia in hospital. However, the guideline should be a useful source of reference for the published reports of accidental salt poisoning in hospital. The scope also excludes the diagnostic features of pathological findings.

The guideline does not cover the child protection procedures when non-accidental injury is suspected. The guideline does not include the specific investigations required to diagnose all the other conditions that may present with hypernatraemia. The guideline does not cover the medical management of hypernatraemia.

2. Methodology

This section sets out in detail the methods used to develop the evidence for the guideline. The methods are in accordance with the RCPCH Quality of Practice Committee standards for guideline development[9].

Guideline Development Group (GDG)

A multidisciplinary guideline development group (GDG) was established. The group included health professionals in paediatrics, sodium handling and evidence-based medicine. Support was provided from the Royal College of Paediatrics and Child Health. Details of all the members are listed at the beginning of the document.

Development of the scope

The guideline development group agreed a scope for the guideline explicitly stating the need for the guideline, the population and topic/clinical areas to be included and not included in the final document.

Identifying the evidence

The aim of the literature review was to seek to identify all available published evidence relevant to the questions identified by the project group in relation to hypernatraemia in children. Where evidence was not available, this is stated and the need for future research specified. Where evidence in children is lacking but exists from studies in adults this was sought and incorporated into the guidance.

Literature searches were developed by an information specialist focusing on the two clinical questions: 'What are the possible causes of Hypernatraemia in children and their frequency in children?' and 'What key tests will help distinguish excess sodium intake from water depletion?'. Search strategies were initially developed on the Medline database and subsequently adapted for other databases. The search was run using the Ovid interface on the following databases; Medline (January 1966 to September 2005), PreMedline (March 2006), OldMedline (1950 to 1965), Embase (January 1980 to September 2005) and CINAHL (January 1982 to March 2006). No language restrictions were applied to the search. Modified filters were developed to exclude letters (unless they presented primary data), commentaries, editorials and newspaper articles. Additionally a filter was used on the searches to exclude animal studies. No systematic attempt was

made to search 'grey literature'. Details of all the search strategies are available from the College's Science and Research Department upon request.

Bibliographies of all identified reviews, reports and included papers were also hand searched to identify relevant literature. Papers identified as relevant by the GDG supplemented the literature search.

Study selection

For each topic area, the guideline lead and a member of the College Science and Research department independently reviewed abstracts from the literature searches to identify studies that met the following predefined inclusion and exclusion criteria:

Included:

Research papers with primary data reporting original findings relevant to the questions (including case series and case reports) as well as systematic reviews. No language restriction was applied to such papers.

Excluded:

- Studies on adults, unless the subject includes sodium intoxication or adds anything to the differential diagnosis of hypernatraemia.
- Studies involving inpatient pre-term infants.
- Hypernatraemia review articles in foreign languages.
- Studies on tests of renal clearance.
- Study reports of hyponatremia.
- Management or treatment studies unless there was likely to be a description of the cases.
- Studies where serum sodium concentrations are less than 150 mmol/l.
- Studies of children admitted to hospital settings with gastroenteritis or infectious diarrhoea.

The lists of abstracts identified for possible inclusion by the two reviewers were compared and any discrepancies were resolved by discussion, with the guideline lead making the final decision in cases of uncertainty. All papers identified at the abstract stage for possible inclusion were obtained and translated where appropriate. The guideline lead and a member of the research team then further assessed the full papers to exclude any study that did not meet the predefined inclusion criteria.

Eligible papers with a study design other than a case report were critically appraised for methodological quality using the standard SIGN checklists[10] where appropriate. The guideline lead agreed whether each paper was of a sufficient methodological quality to inform the evidence review for the section to which it had been allocated.

Publications other than case reports were critically appraised. Case reports of accidental and non-accidental poisoning of children were reviewed using the procedure described below.

Synthesising the evidence

The findings were summarised by the guideline lead into an evidence summary as a series of statements. The draft and final versions of the guideline were presented to GDG for comment.

Formulation and grading of recommendations

A spreadsheet containing extracted data for included studies was used to develop evidence statements and recommendations.

The researcher graded each evidence statement according to the level of evidence upon which it was based using an adaptation[3] of the Oxford Centre for Evidence-based Medicine hierarchy of evidence table[11] presented in the table that follows. The purpose of a hierarchy is to reflect the effectiveness of the study design to answer a particular research question. For example, questions relating to prognosis, the highest possible level of evidence is a cohort study (evidence level 1), which would equate to a grade A recommendation if relevant to the clinical question. The guideline lead independently assessed the accuracy of the grading. Disagreements were resolved through discussion.

[3] For the purposes of this guideline, case reports and case series that had been subjected to peer review were considered to be level 4 evidence

Level	Therapy/Prevention, Aetiology/Harm	Prognosis	Diagnosis	Differential diagnosis/ symptom prevalence study	Economic and decision analyses
1a	SR (with homogeneity*) of RCTs	SR (with homogeneity*) of inception cohort studies; CDR† validated in different populations	SR (with homogeneity*) of Level 1 diagnostic studies; CDR† with 1b studies from different clinical centres	SR (with homogeneity*) of prospective cohort studies	SR (with homogeneity*) of Level 1 economic studies
1b	Individual RCT (with narrow Confidence Interval‡)	Individual inception cohort study with ≥ 80% follow-up; CDR† validated in a single population	Validating** cohort study with good††† reference standards; or CDR† tested within one clinical centre	Prospective cohort study with good follow-up****	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multi-way sensitivity analyses
1c	All or none§	All or none case-series	Absolute SpPins and SnNouts††	All or none case-series	Absolute better-value or worse-value analyses ††††
2a	SR (with homogeneity*) of cohort studies	SR (with homogeneity*) of either retrospective cohort studies or untreated control groups in RCTs	SR (with homogeneity*) of Level >2 diagnostic studies	SR (with homogeneity*) of 2b and better studies	SR (with homogeneity*) of Level >2 economic studies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)	Retrospective cohort study or follow-up of untreated control patients in an RCT; Derivation of CDR† or validated on split-sample§§§ only	Exploratory** cohort study with good††† reference standards; CDR† after derivation, or validated only on split-sample§§§ or databases	Retrospective cohort study, or poor follow-up	Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multi-way sensitivity analyses
2c	"Outcomes" Research; Ecological studies	"Outcomes" Research		Ecological studies	Audit or outcomes research
3a	SR (with homogeneity*) of case-control studies		SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies
3b	Individual Case-Control Study		Non-consecutive study; or without consistently applied reference standards	Non-consecutive cohort study, or very limited population	Analysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations
4	Case-series (and poor quality cohort and case-control studies§§)	Case-series (and poor quality prognostic cohort studies***)	Case-control study, poor or non-independent reference standard	Case-series or superseded reference standards	Analysis with no sensitivity analysis
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"	Expert opinion without explicit critical appraisal, or based on economic theory or "first principles"

*	By homogeneity we mean a systematic review that is free of worrisome variations (heterogeneity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need be worrisome, and not all worrisome heterogeneity need be statistically significant. As noted above, studies displaying worrisome heterogeneity should be tagged with a "-" at the end of their designated level.
†	Clinical Decision Rule. (These are algorithms or scoring systems which lead to a prognostic estimation or a diagnostic category.)
‡	See note #2 for advice on how to understand, rate and use trials or other studies with wide confidence intervals.
§	Met when all patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but none now die on it.
§§	By poor quality cohort study we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both exposed and non-exposed individuals and/or failed to identify or appropriately control known confounders and/or failed to carry out a sufficiently long and complete follow-up of patients. By poor quality case-control study we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both cases and controls and/or failed to identify or appropriately control known confounders.
§§§	Split-sample validation is achieved by collecting all the information in a single tranche, then artificially dividing this into "derivation" and "validation" samples.
††	An "Absolute SpPin" is a diagnostic finding whose Specificity is so high that a Positive result rules-in the diagnosis. An "Absolute SnNout" is a diagnostic finding whose Sensitivity is so high that a Negative result rules-out the diagnosis.
‡‡	Good, better, bad and worse refer to the comparisons between treatments in terms of their clinical risks and benefits.
†††	Good reference standards are independent of the test, and applied blindly or objectively to applied to all patients. Poor reference standards are haphazardly applied, but still independent of the test. Use of a non-independent reference standard (where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference') implies a level 4 study.
††††	Better-value treatments are clearly as good but cheaper, or better at the same or reduced cost. Worse-value treatments are as good and more expensive, or worse and the equally or more expensive.
**	Validating studies test the quality of a specific diagnostic test, based on prior evidence. An exploratory study collects information and trawls the data (e.g. using a regression analysis) to find which factors are 'significant'.
***	By poor quality prognostic cohort study we mean one in which sampling was biased in favour of patients who already had the target outcome, or the measurement of outcomes was accomplished in <80% of study patients, or outcomes were determined in an unblinded, non-objective way, or there was no correction for confounding factors.
****	Good follow-up in a differential diagnosis study is >80%, with adequate time for alternative diagnoses to emerge (e.g. 1-6 months acute, 1 - 5 years chronic).

Grades of recommendation

A	Consistent level 1 studies
B	Consistent level 2 or 3 studies ***or*** extrapolations from level 1 studies
C	Level 4 studies ***or*** extrapolations from level 2 or 3 studies
D	Level 5 evidence ***or*** troublingly inconsistent or inconclusive studies of any level

Critical appraisal of case reports

There is currently no agreed method for critically appraising case reports. These can be important for identifying rare problems that would otherwise not be ascertained in large research studies. In particular they can help to identify rare complications or adverse events, and for demonstrating rare causes mimicking a more commonly presenting condition. They are limited by the fact that an individual case rarely provides convincing proof of a cause-effect relationship.

It is particularly difficult to undertake research into child abuse for several reasons. In many instances there is no good evidence as to whether an individual child was abused, and therefore a reference or 'gold' standard is unavailable. It is likely to be difficult to obtain parental consent for research. As a result, it is very likely that the best available evidence will continue to come from case reports. In the case of a report of child abuse, the strength of a conclusion may be determined not only by the medical findings, but also by evidence from other sources.

The Welsh Child Protection Systematic Review Group (http://www.coreinfo.cf.ac.uk) developed a hierarchy of confidence as to whether child abuse was likely.[12] In cases where bruising was not thought to be due to child abuse they also recorded whether factors that influence bruising were excluded, namely abuse, neurodisability and medical conditions predisposing to bruising. Their ranking categories for cases where the child was thought to have been abused are reproduced below:

Level	Criteria used to define abuse
1	Abuse confirmed at case conference or civil or criminal court proceedings or admitted by perpetrator.
2	Abuse confirmed by stated criteria including multidisciplinary assessment.
3	Abuse defined by stated criteria.
4	Abuse stated but no supporting detail or evidence given.
5	Suspected above.

These rankings (referred to as Cardiff rankings) potentially provide some hierarchy of strength of evidence, and permit this to be based on the whole circumstances rather than the purely medical contribution. However, where the conclusion is strongly based on the medical evidence, there is no independent source of verification, and results in a circular argument if the case is then used to provide evidence for the diagnostic accuracy of the clinical findings. There is also a considerable difference in the strength of evidence where a perpetrator admits causing injuries from the more common situation where abuse is agreed to have occurred at a case conference.

In the case of presentations with hypernatraemia, case reports are potentially important in identifying rare complications of medical conditions and drugs. They may also help to address the question as to whether young children have ever been reported to ingest voluntarily sufficient salt or other agents to cause hypernatraemia.

Accordingly, a method of peer reviewing individual case reports has been devised. It is possible that a published case might be seriously flawed in its interpretation, or in the light of subsequent advances in knowledge an alternative explanation seems more plausible. The critical appraisal process allows the peer reviewer to make judgements on three aspects of a case report.

For the purposes of the hypernatraemia guideline, the following three factors were included for peer review:

1. The putative causal agent for the outcome. This might be salt (sodium chloride), other sodium salt or water deprivation.
2. The context in which this occurred. For example, the deliberate administration of hypertonic saline in the treatment of a hydatid cyst.
3. The author's conclusions as to why this occurred. Categories include deliberate self-poisoning, complications of treatments given, etc.

If the peer reviewer disagrees with the original author(s) they are also asked to explain their reasons. This should provide a mechanism to establish to what extent current medical opinion concurs with the original conclusions of the case report, and why. Where all peer reviewers agree with the original conclusions 'beyond reasonable doubt', this case report can be considered to be robust. Alternatively, where peer reviewers disagree with the original conclusions and an alternative explanation seems more credible, the conclusions of the case report can be said to be seriously flawed.

The peer reviewers were asked for each of the 3 questions above to express their opinion as one of the following categories:

1. Agree with author(s) beyond reasonable doubt
2. Agree with author(s) on balance of probability
3. Cannot tell from publication whether author(s) correct
4. Disagree with author(s) on balance of probability
5. Disagree with author(s) beyond reasonable doubt

The degree of agreement between the two peer reviewers for the 60 cases where both had indicated their opinion as to cause is indicated below:

- Identical scores: 22
- One category different: 28
- More than one category different: 10

The authors' original conclusions as to why the hypernatraemia occurred were categorised as follows:

1. Accidental ingestion by patient
2. Child abuse
3. Deliberate self harm
4. Error by parent
5. Error by carer or other

6. Error by professional
7. Side effect of treatment initiated by patient
8. Side effect of treatment initiated by parent
9. Side effect of treatment initiated by other
10. Side effect of treatment initiated by professional
11. Side effect of treatment, unclear by whom initiated
12. Side effect of a medical condition

The peer reviewers were also given the option of specifying any other category not in this list.

Peer reviewers were identified as either having experience in salt handling, or in child protection, or both. Each case report was peer reviewed by at least two reviewers, one with expertise in salt handling and the other in child protection. The one case report of accidental ingestion of salt by two very young children was given to all peer reviewers, together with a case report of voluntary salt ingestion by an adult. Altogether 60 cases of either accidental or non-accidental salt poisoning in children where there was any information on the individual child were subjected to peer review. The largest case series[3] of 12 children with non-accidental salt poisoning had to be excluded from peer review, as it was not possible except in one case (which was also reported separately)[13] to identify information on each individual child.

Peer reviewers were permitted to seek the views of colleagues if they wished, but not to confer with the other peer reviewers of their cases.

Each peer reviewed case where the authors concluded the cause was child abuse was also ranked using the Cardiff group's rankings above. The comparisons are:
Cardiff ranking category 1 (8 cases):

- both peer reviewers agreed beyond reasonable doubt in 3 cases;
- both peer reviewers agreed, one on balance of probability & the other beyond reasonable doubt in 4 cases;
- one agreed beyond reasonable doubt, the other did not feel able to tell, in 1 case.

Cardiff ranking category 2 (5 cases):

- both peer reviewers agreed, one on balance of probability & the other beyond reasonable doubt in 1 case;
- both peer reviewers agreed on the balance of probability in 2 cases;
- one agreed on balance of probability, the other did not feel able to tell, in 2 cases.

The Cardiff ranking system could not be applied to the cases where child abuse was not considered by the authors to be the cause of the hypernatraemia.

The peer reviewed findings of each individual case are reported in sections 4.2 and 4.4. Where the peer reviewer's opinions differ, this is made clear in the text.

Consultation

A draft of the guideline was circulated to the organisations and individuals listed at the beginning of the document. Their responses were incorporated into the guideline where appropriate.

Updating

It is hoped that the document will be updated in approximately 2-3 years time from date of publication by the College's Science and Research Department. In the meantime, the College would welcome feedback from users of the guideline as to how useful it was. Comments can be submitted to clinical.effectiveness@rcpch.ac.uk.

3. Incidence of hypernatraemia due to nonaccidental salt-poisoning

3.1 Incidence of hypernatraemia in children in the UK

Several cross sectional studies were found that partly addressed this question. Nine publications since 1990 were found reporting young babies presenting with lactation failure, which included numbers of babies with hypernatraemic dehydration.

Oddie et al[14] (evidence level 2b) surveyed all hospital readmissions within the first month of life during 1998 from a population of 32,015 live births in the former Northern Region of the UK. They estimated the incidence of hypernatraemic dehydration secondary to breast feeding to be 7.1 per 10,000 (1 in 1,408) breast fed infants, with serum sodium varying between 150 and 175 mmol/L.

A similar study from South Denmark[15] (evidence level 2b) of readmissions of term infants over a period of 21 months from January 1999 identified 11 breast fed infants with serum sodium of 150mmol/L or above (maximum 159mmol/L). With an annual rate of approximately 3,000 births, the estimated incidence of hypernatraemia was just over 1 in 500 births.

A large study from Pittsburgh, USA[16] (evidence level 2b) reviewed all admissions to one hospital between January 1997 and December 2001 of infants with a serum sodium of 150 mEq/L or above in whom this was thought to be secondary to inadequate milk intake. They calculated an incidence of 2.1 per 1,000 live births, or 4.7 per 1,000 (1 in 213) breast fed newborn infants.

A Portuguese study[17] (evidence level 2b) surveyed all hospital readmissions between January 1998 and December 2001 of exclusively breast fed infants presenting with a serum sodium of 150mEq/L or greater. They estimated the frequency of hypernatraemia at 2.6 per 1,000 live births. The highest sodium was 162 mEq/L, and none had serious complications.

A Jamaican study[18] (evidence level 2b) found an increased incidence of hypernatraemia from 0.4 per 1,000 live births between 1993 and 1995 to 1.3 per 1,000 between 1996 and 2001 when the Baby Friendly Initiative was implemented.

A study from Vancouver[19] (evidence level 2b) surveyed all breast fed babies less than 28 days presenting to one hospital with a serum sodium exceeding 145mmol/L. They found 19 babies with hypernatraemic dehydration, the highest serum sodium being 207mmol/L. No denominator information was supplied, so the incidence cannot be calculated. Similarly, an Italian study[20] (evidence level 1b) of all referrals of healthy term breast fed infants to one unit over a 6 month period from October 1999 found hypernatraemia in 19 of 53 infants with postnatal weight loss of over 10%. No denominator information on the population from which these babies presented was given. A study from Cincinnati (a tertiary centre)[21] (evidence level 4) reported 5 breast fed infants with a serum sodium between 161 and 214 mmol/L over a 5 month period. These appear to be selected cases, and the authors did not attempt to estimate the incidence. However, in a retrospective review between 1990 and 1994, they found an increasing number of cases. A further case series from Israel[22] (evidence level 4) provided no estimate of incidence.

None of these reported any infants with suspicions of salt poisoning.

No studies were found of the incidence of hypernatraemia in children (excluding lactation failure) in the UK. One study from Houston, Texas[23] (evidence level 2b) reported 68 children of all ages admitted to hospital with hypernatraemia (>150mmol/L) over a 2-year period from January 1992. The hypernatraemia was hospital acquired in 41 (60%), and 60 children had an associated medical problem before developing hypernatraemia. Gastroenteritis was a contributing factor in only 14 children. There were no cases due to errors in infant feeds, pharmacy errors, salt poisoning or breastfeeding malnutrition. The authors did not attempt to estimate the annual incidence per head of population. The city of Houston had a total population of just under 2 million in 2000[24], with 594,000 children under the age of 20 years. This would indicate an approximate annual incidence of between 5 and 6 per 100,000 children with hypernatraemia, or 2 per 100,000 children with hypernatraemia on admission.

A similar study from Pittsburgh in adults in 1993[25] reached similar conclusions about the range of causes of hypernatraemia.

In summary, there is a paucity of evidence on the incidence of hypernatraemia outside the neonatal period, where the best estimate of hypernatraemic dehydration in breast fed infants is 7.1 per 10,000 live births. A very approximate figure of 2 per 100,000 children per year is suggested by the Texas study.

Evidence statement
Hypernatraemia is rare in children presenting to secondary care [Grade C]. There is no accurate estimate of the incidence in the UK, and further research is recommended. The Texas study suggests an annual incidence of approximately 2 per 100,000 children. In exclusively breast fed infants, estimates of the rate of hypernatraemic dehydration range between 1 in 200 to 1 in 1,400 babies [Grade B].

3.2 Incidence of hypernatraemia secondary to child abuse in the UK

In 1996 McClure et al[26] (evidence level 2b) reported a prospective study, under the auspices of the BPSU, which included all cases of non-accidental poisoning. During the 2 years from September 1992, they identified 3 cases of salt poisoning, giving an approximate annual incidence of 1 per 10,000,000 children aged under 16 years. This study found large regional differences in reporting rates of all non-accidental poisonings and suffocations, and therefore there may have been an overall under-reporting of cases. Therefore, in a hypothetical district of one million inhabitants of all ages there would be approximately 1 case of salt poisoning in children every 40 to 50 years.

Evidence statement
Non-accidental salt poisoning is a very rare event. Most UK paediatricians will never be responsible for a case [Grade C].

3.3 Probability of a child presenting with hypernatraemia being the subject of non-accidental salt poisoning

Taking the estimate of annual incidence using the Texas series together with the BPSU study, approximately 1 in 200 admissions with hypernatraemia could be expected to be secondary to salt poisoning. However, the error on this estimate is likely to be very large.

Evidence statement
Non-accidental salt poisoning is a rare cause of hospital admission with hypernatraemia [Grade C].

4. Causes of hypernatraemia

4.1 Causes of hypernatraemia in children (and adults) other than excessive sodium intake

Clinical question

What are the possible causes of hypernatraemia other than excessive sodium intake reported in children (and adults)?

Reports of causes of hypernatraemia other than excessive sodium intake have been identified via a literature search. These have been categorised under the headings suggested by Haycock.[27] Causes of excessive sodium intake are covered in the next sections.

4.1.1 Water depletion

4.1.1.1 Lack of water intake

Inadequate breast milk

As well as the case series already described (see section 3.1 on the incidence of hypernatraemia), there are many individual case reports[28-62] from different parts of the world, including some with fatal consequences[56]. One case report was of a baby with glucose-galactose malabsorption[63], where the hypernatraemia was probably secondary to watery diarrhoea.

Several of these publications[33, 36, 37, 39, 40, 43, 58] suggest that high concentrations of sodium in breast milk are at least partly responsible for the hypernatraemia. This is almost certainly wrong[64]. The concentrations described (e.g. 47 mmol/L in the paper by Peters[33]) are less than the concentration of sodium that would be used to correct hypernatraemic dehydration: the usual recommendation for initial correction is isotonic saline (sodium concentration 154 mmol/L).

The true cause of breast-feeding associated hypernatraemia is inadequate water intake, insufficient to replace the high insensible water losses that are typical of the newborn infant.

Unconscious or mentally impaired

A number of case reports describe adults with psychiatric conditions[65-70] severe learning difficulties[71], dementia[72], or who are unconscious[73] in whom hypernatraemia is secondary to inadequate water intake. There is one case report of a 17 year old with schizophrenia who developed severe hypernatraemia associated with thirst deficiency during a period of psychosis.[74] Otherwise there were no case reports relating to children.

Adipsia and essential hypernatraemia

The distinction between adipsia (lack of thirst perception), essential hypernatraemia and inadequate water intake in the unconscious and mentally impaired (above), is not always clear.

Louis Welt originally coined the term essential hypernatraemia in an editorial[75], to be applied to cases of upward resetting of the hypothalamic osmostat, along with essential hyponatraemia for the downward resetting of the osmostat. When others described cases of chronic hypernatraemia associated with hypothalamic dysfunction,[76, 77] they used it to include cases where there was loss of osmoregulation of both thirst and antidiuretic hormone (ADH) release but with preservation of baroreceptor mediated ADH release. These abnormalities are almost certainly due to destruction of the osmoreceptors, rather than a resetting of their threshold.

There are a small number of case reports describing essential hypernatraemia without an associated structural lesion of the hypothalamus.[78-88] The syndrome is characterized by features including: adipsia-hypodipsia, recurrent hypernatraemia, obesity, inability to excrete a water load, lack of growth hormone release in response to provocative stimuli, blunted thyrotropin releasing hormone responses, hypothyroidism, autonomic dysregulation, alveolar hypoventilation and hyperlipidaemia associated with hypernatraemic crisis.

There are also case reports of adipsia with resulting hypernatraemia in children with structural CNS abnormalities, including aqueduct stenosis[89], abnormalities of midline structures including absent septum pellucidum and/or agenesis of the corpus callosum[90-96] hypothalamic tumour[97-102], holoprosencephaly[103-107] and hydranencephaly[108].

Case reports of osmoreceptor dysfunction are therefore all in association with other endocrine or structural brain abnormalities. They present with hypernatraemia and adipsia. It is very important to distinguish such cases from hypernatraemia due to salt poisoning, and specialist referral should be considered where this may be a possibility.

Evidence statement
There are no case reports of otherwise normal children presenting with isolated hypernatraemia being due to abnormal osmostats [Grade C].

Deliberate water restriction

As well as the abusive withholding of water already described, there are other circumstances in which this may occur.

One adult case report describes a 24-year-old Italian man with nephrotic syndrome due to amyloid disease who decided to restrict his fluid intake severely in order to combat his hypoalbuminaemic oedema.[109] He was admitted to hospital with a sodium of 193 mmol/L. He made a full recovery without significant neurological complications after slow restoration of his fluid deficit.

There is also the potential for iatrogenic hypernatraemia from over-enthusiastic restriction of fluids in intensive care settings.

4.1.1.2 Increased water loss

Increased renal loss

Central diabetes insipidus

Central diabetes insipidus is due to lack of vasopressin (antidiuretic hormone) release from the pituitary gland. In diabetes insipidus sodium homeostasis is maintained without hypernatraemia as long as the child has access to water. However, this is a well-recognised cause of hypernatraemia both in children and adults.

Diabetes insipidus is a rare condition in children, with an estimated frequency from all causes (including nephrogenic) of 5 per million children per year in Caucasian populations.[110, 111] Causes include:

- Craniopharyngioma is the most common space occupying cause, with or other tumours such as optic glioma[112] being seen less frequently. Germinoma is an important cause in older children. It is seen in a significant proportion of children with Langerhans' cell histiocytosis. Other rare infiltrative causes include Hodgkins disease, leukaemias and sarcoidosis.
- Idiopathic diabetes insipidus without recognisable CNS malformation[113] is a common cause, where autoimmune factors may be important.
- Associated with CNS malformations especially septo-optic dysplasia[114] and holoprosencephaly, hydranencephaly or arhinencephaly[115-121].
- Following severe brain injury[122] hypoxic damage[123] intracranial haemorrhage[124], and carbon monoxide poisoning[125].
- It can be familial, presenting at different ages.
- It can be associated with hypothyroidism and learning difficulties in the Schinzel-Giedion syndrome[126].

In a child with hypernatraemia a urine osmolality can assist in excluding diabetes insipidus (grade D). This is best interpreted in conjunction with a simultaneous serum osmolality: children with long-standing hypernatraemia in association with diabetes insipidus (cranial or nephrogenic) can generate relatively high urine osmolalities because of volume contraction and reduced glomerular filtration rate.

Evidence statement
In a child with hypernatraemia a urine osmolality can assist in excluding diabetes insipidus (grade D).

The water deprivation test has a suboptimal sensitivity and specificity, and should be interpreted alongside the history, baseline biochemistry and general context. The diagnosis can be made following an assessment that may include the water deprivation test, with a response to the administration of DDAVP.

The survey of hypernatraemia in children from Texas[23] found that 9 of 68 (13%) of children with hypernatraemia (in the majority of whom it was hospital acquired) had central diabetes insipidus and this was the main cause of excessive urinary water loss.

Nephrogenic diabetes insipidus

The group of conditions called nephrogenic diabetes insipidus (NDI) have in common polyuria and polydipsia secondary to renal resistance to the action of vasopressin, in contrast to central diabetes insipidus where there is lack of vasopressin release.

Some people use the term NDI to mean only the genetically determined forms of the disease (due to mutations in the gene for the V_2 vasopressin receptor[127], the X-linked variety[128], and to mutations in the gene for the water channel aquaporin 2, the autosomal recessive variety[129, 130]), whereas others use it more broadly to include impairment of urinary concentrating ability due to diseases of the renal medulla such as nephronophthisis, sickle cell disease, reflux nephropathy and analgesic nephropathy.

The distinction from central diabetes insipidus is the lack of response to DDAVP.

The survey of hypernatraemia in children from Texas[23] found that 3 of 68 (4%) of children with hypernatraemia had nephrogenic diabetes insipidus.

Renal medullary damage

Conditions or drugs affecting renal medullary function may result in excessive renal water loss. These include:

- Renal disease (renal dysplasia, medullary cystic disease, reflux nephropathy, polycystic disease)
- Systemic disease with renal involvement (sickle cell disease, sarcoidosis, amyloidosis, methylmalonic acidaemia)
- Drugs (amphotericin, phenytoin, aminoglycosides, methoxyflurane, and possibly high doses of Ticarcillin and carbenicillin)

Strictly speaking, these should all be considered as examples of acquired vasopressin resistant, nephrogenic diabetes insipidus. Although there is a report of children with hypernatraemia secondary to urinary tract infection[131], it is likely that the cause was increased water loss due to fever and reduced intake due to malaise with or without vomiting.

Investigation is as for diabetes insipidus.

Increased gastrointestinal loss

Hypernatraemic dehydration secondary to diarrhoea

Gastroenteritis was historically the major cause of hypernatraemia in children.[132] There are numerous accounts of hypernatraemia associated with diarrhoeal illness in children. The most important mechanism is excessive intestinal water loss secondary to high osmolar feeds rather than excess sodium absorption from the gastrointestinal tract.[64, 133]

The frequency of hypernatraemia secondary to gastroenteritis has reduced over many years. [134-137]

The survey of hypernatraemia in children from Texas[23] found that only 14 of 68 (20%) children with hypernatraemia had gastroenteritis as a contributing factor. It predominantly affected full-term infants under 1 year of age and accounted for approaching 50% (13 of 27) of patients with hypernatraemia on admission to hospital.

Increased evaporative loss

Skin conditions

Excessive transepidermal water loss can be sufficient to result in hypernatraemia in infants with Netherton syndrome (characterized by ichthyosis, trichorrhexis invaginata, and atopic diathesis)[138-140] and in collodion babies[141].

Endurance exercise

There are well-documented cases of hypernatraemia and hyponatraemia in marathon runners. One study found hypernatraemia (sodium >146 mmol/L) in 25% of "collapsed" marathon runners, and 9% in marathon runners who had not experienced collapse.[142] The same study found the incidence of hyponatraemia (sodium <135 mmol/L) to be 6% and 5% respectively. The mechanism of hypernatraemia includes excessive transepidermal water loss.

A second study showed a 30% to 40% rate of hypernatraemia after a 100 metre swim over 1 minute in well-trained athletes. In this instance the mechanism could

not have been evaporative water loss, nor is it an endurance event. The authors speculated that this could be due to a shift of hypotonic fluid from the extracellular to the intracellular compartment.[143]

Both studies were in adults. However, with quite young children competing in endurance events hypernatraemia is a risk if adequate water replacement is not taken.

Lost in the desert or at sea

The combination of inadequate water intake and increased transepidermal water loss leads to hypernatraemia. At sea, drinking seawater will also contribute to hypernatraemia.

4.1.2 Mineralocorticoid excess

A number of conditions with mineralocorticoid excess are encountered in paediatric practice. These include:

- Primary hyperaldosteronism
- Deoxycorticosterone-secreting adrenal tumours
- Congenital adrenal hyperplasia due to 11-hydroxylase deficiency

Although hypernatraemia may occur with mineralocorticoid excess, it is very mild and it is rarely, if ever, severe enough to constitute a clinical problem. In one large series (50 patients with primary hypoaldosteronism) from the MRC Blood Pressure Research Unit in Glasgow[144], the mean sodium concentration for the whole series was 141.8 mEq/L. For a subgroup of 30 women the average was 143.3 and the highest recorded mean value only 147.0 mEq/L, and for another sample of men the corresponding figures were 143.6 and 145.7 mEq/L respectively.

Another review of patients with primary hypoaldosteronism by Relman[145] states “the mean normal serum sodium concentration is approximately 140 mEq/L; 95 per cent of all normal values are between 136 and 145 mEq/L. In primary aldosteronism the serum sodium is usually in the range 140 to 147 mEq/L.”

In another study[146], Conn reported on the electrolyte values in a subgroup of 18 patients with primary hypoaldosteronism from a total population of 145 studied. Two patients had sodium concentrations of 151 mmol/L, two others 148 mmol/L and all the rest were 147 mmol/L or below.

The cause of this very mild hypernatraemia in patients with primary hypoaldosteronism appears to be a slight upward resetting of the osmostat.[147, 148] These two studies describe carefully investigated cases, whilst a third[149] is a review with a commentary.

Most patients with mineralocorticoid excess therefore have sodium concentrations in the normal range, with a few having mild hypernatraemia up to just above 150 mmol/L, in itself of little or no clinical significance. Dangerous, potentially lethal hypernatraemia is never seen in these conditions.

4.2 Mechanisms causing hypernatraemia through accidental excessive sodium intake

Clinical question

What other agents, mechanisms and circumstances are described in those children with hypernatraemia who were not considered to have been abused?

A number of scenarios have been reported in which a variety of agents administered to 119 children have caused hypernatraemia, sometimes fatal. None of these was considered by the authors to be due to child abuse.

4.2.1 Errors by professionals

4.2.1.1 Accidental substitution of salt for glucose in newborn infants

One of the earliest reports was of the accidental making up of babies' feeds with salt instead of sugar in Binghamton Hospital, USA, in 1962.[8,150] There are now two additional reports of similar occurrences from different countries. In Binghamton fourteen babies were affected, and six died. The problem was recognised when the sixth baby was found to be hypernatraemic (sodium 244mEq/L), the first five not having had serum sodium measured. A further eight babies with sodium concentrations of between 162 and 274mEq/L all survived. All eleven infants who were symptomatic had either seizures or muscular twitching. All but one vomited, and all displayed avid thirst until too ill to feed. Five infants had respiratory distress.

In 1967 there was a report from Sydney[151] of a similar occurrence in a neonatal nursery. Five babies, all but one premature, aged 1 to 4 weeks were affected, with three deaths. All but one vomited and two had diarrhoea.

More recently in 1984 was reported a series of five term newborn babies in Austria[152, 153] who all died following accidental intravenous infusion of 10% saline instead of 10% dextrose. They had serum sodium concentrations between 159 and 247mmol/L. They were reported to have 'cramps' and oedema.

In all three occurrences there had been an error in the pharmacy either in preparing the feeds, or in the third case in incorrect labelling of the infusion. These reports were not subjected to peer review.

4.2.1.2 Other errors by professionals in making up feeds or ORS

In 1983[154], a baby in Canada developed hypernatraemia (sodium 182 mmol/L) having received an excessive amount of salt in a chicken meat-based formula whilst in hospital. The authors did not discuss who made up the feed, apart from stating "care… must be exercised in formula preparation, even in a hospital setting." The two peer reviewers, whilst agreeing that this appeared to be the mechanism, therefore felt they were unable to determine who had caused the error or why.

A case report from Spain in 1989[155] reported a fatal outcome in an infant of 7 months in whom double strength oral rehydration solution was made up and initiated in clinic, with a resulting hypernatraemia of 189 mEq/L. It was not clear who made the error, and the two peer reviewers came to different conclusions though both considered beyond reasonable doubt that the hypertonic ORS was the cause.

A case report from Seattle in 1967[156] described an infant of 6 weeks whose mother had for some time made up double strength feeds, and who was admitted with a sodium of 174 mEq/L following the development of a mild diarrhoeal illness. The mother reported that the doctor had advised making up the feeds at this strength. The doctor had thought the infant was receiving a different formula. Both peer reviewers agreed (one beyond reasonable doubt, the other on the balance of probability) with the authors' conclusions that this was due to the doctor's mistaken instructions, noting the lack of detail in the report to substantiate the findings.

4.2.1.3 Inadvertent administration of concentrated intravenous saline

A 12 year old with type 1 diabetes was inadvertently given 500mls of 5% saline intravenously instead of 0.9% saline for treatment of diabetic ketoacidosis.[157] His serum sodium reached 172mEq/L. He complained of headache, vomited, developed seizures, then became comatose and died 4 days later.

4.2.2 Errors by parents or carers

There are a number of reports of different errors by parents or carers that resulted in hypernatraemia. These case reports were subjected to peer review.

4.2.2.1 Errors by parents or carers in making up feeds

A case report in 1976 from Toronto[158] describes a 2-month-old girl hospitalised with dehydration and a 2 day history of vomiting feeds but no diarrhoea, who had an admission sodium of 212 mEq/L. "Within 24 hours after admission the mother discovered that table salt instead of sugar had been used in the baby's recent feeds." The first peer reviewer agreed beyond reasonable doubt with the authors' conclusion that this was an error by the mother. The second reviewer was unsure, as there was no assessment made by the authors as to whether this was correct.

A report from Germany in 1976[159 (case 2)] briefly described the death of a 9-week-old infant from hypernatraemia following accidental use of salt rather than sugar in making up feeds by the mother. The admission sodium was 195 mmol/L. One peer reviewer agreed with the authors' conclusion that this was an error by the mother beyond reasonable doubt in view of the clear story; the other peer reviewer did not feel able to tell whether the authors' conclusions were correct, as the specific question about how the error occurred was not raised and the possibility of non-accidental administration was not discussed.

A report of two cases from Graz, Austria, in 1983[160] describes two separate incidents. The first case was a 21-day-old boy who received double strength infant formula from birth. His admission sodium was 181 mmol/L. He was the fifth child of a 22-year-old mother. No details of the reason for the error were reported. One peer reviewer agreed beyond reasonable doubt with the authors' conclusions as to cause. The other reviewer felt unable to tell whether the authors' conclusions as to cause were correct from the information supplied.

The second case was admitted at 30 days of age with a sodium of 196 mEq/L. She had received infant formula from birth at 5 times the correct strength. She was the third child of a 32-year-old mother. No details were given of the reason for the error. Neither peer reviewer felt able to tell whether the authors' conclusions as to cause were correct from the information supplied.

A case report from France in 1999[161] described a 5 week old baby, admitted with a sodium of 211 mmol/L following presentation with poor feeding and weight loss for 3 days. Suspecting salt poisoning, all the nutrients and medications used for the baby were analysed, and the boiled water used in the previous 72 hours was found to contain 23gms per litre of NaCl. The parents explained that a switch between two saucepans' contents, salted water for cooking and boiled water for the formula preparation was "highly probable". A social work survey revealed no previous problem, the history seemed plausible, and the boy made normal subsequent progress after returning home. Both peer reviewers agreed (one beyond reasonable doubt, the other on the balance of probability) with the authors' conclusions that this was due to unintentional salt poisoning.

Another case report from France in 1999[162] described a 5 day old girl admitted with a sodium of 186 mEq/L. Her mother had misunderstood the written feeding instructions ("6 x 70mls the first week… ") and had made up feeds with 6 scoops of milk powder to 70mls water rather than the correct mixture (presumably 1 scoop to 1 fluid oz water: this was not stated). Both peer reviewers agreed (one beyond reasonable doubt, the other on the balance of probability) with the authors' conclusions that this was due to unintentional administration of hypertonic feeds.

A case report from Guys Hospital, London in 1972[163] described a 9-month-old girl who was admitted with a sodium of 207 mEq/L following a 2 day history of vomiting without diarrhoea. She had been fed on full cream powdered milk, at the time of admission "receiving 227g three times a day, each containing 6 to 7 *very heaped* scoops of powder and a teaspoon of sugar to 198g water, supplemented with one or two tins of baby foods daily. There was no added salt." Both peer reviewers agreed (one beyond reasonable doubt, the other on the balance of probability) with the authors' conclusions that this was due to the mother's mistaken administration of hypertonic feeds.

A case series from Sheffield, also in 1972[164], described three children with hypernatraemic dehydration, two of whose mothers had made up feeds with heaped scoops resulting in hypertonic feeds. The first, a 2½-month-old boy, had two admissions, with sodium of 160 and 167 mEq/L, before the problem was identified. The second, a 6-day-old boy, had an admission sodium of 174 mEq/L. The peer reviewers agreed on the balance of probability (one reviewer beyond reasonable doubt in the first case) with the authors' conclusions that the hypertonic feeds had contributed to the hypernatraemia. In both cases, the reviewers pointed

out that it was not possible to tell the degree to which the hypertonic feeds had contributed. This report also demonstrated the marked variation in sodium content of milk feeds obtained from mothers attending their routine postnatal check-ups.

A case report[165] described 3 children from Chicago, USA, in 1985 with hypernatraemia, the common factor being that the children all had severe psychomotor retardation and had unintentionally been fed undiluted processed foods with extremely high sodium concentrations.

The first case was of a 2 year old in care with severe developmental delay and thoracic myelomeningocele. He was admitted with a sodium of 190 mEq/L and evidence of a urinary tract infection. “On careful investigation it was found that for the week prior to admission his foster parents had been feeding him unreconstituted condensed tomato soup with a sodium concentration of 290 mEq/L.” The possible reasons for this were not discussed. The two peer reviewers commented that without further information this could have been due to abuse or neglect.

The second case involved a 15 year old with tuberous sclerosis, admitted with a sodium of 169 mEq/L, and whose nursing home staff had been giving him mainly canned pureed foods, with recent mild fluid restriction to help curtail his vomiting. One of the two peer reviewers felt unable to tell from the publication whether this was the cause, noting that there had also been a 3 month history of vomiting and a 20lb weight loss.

The third case of an 18-month-old girl with severe perinatal hypoxic ischaemic encephalopathy, fed by gastrostomy, was admitted with a sodium of 153 mEq/L. “The family admitted to financial difficulties… and were feeding the patient almost exclusively undiluted canned Campbell’s Manhandler soup with a sodium concentration of 325 mEq/L.” Neither peer reviewer was able to tell from the publication whether this was correct. One noted that as there was also a history of diarrhoea and vomiting and of weight gain after rehydration, this might be a contributory factor rather than the cause. The other reviewer thought that without further information this could be considered abusive.

A very brief letter from Kentucky, USA, in 1991[166], reported an infant with ‘near fatal’ hypernatraemia when fed undiluted chicken soup. Neither peer reviewer felt that they could tell from the information given in the paper whether the author’s conclusion as to cause was correct.

Two case reports from Madrid, Spain, in 2000[167] described children whose parents' errors had resulted in hypernatraemia and the death of their child. The first case was of a 20 month old girl whose mother had inadvertently added 2 teaspoons of salt rather than sugar to each of two yoghurts (given despite the child's protests). This resulted in presentation with a seizure and loss of consciousness. Her admission sodium was 195 mmol/L. The mother only gave the information about the error when she was interrogated after the discovery of the hypernatraemia. Neither peer reviewer felt that they could tell from the information given in the paper whether the administration was truly accidental or abusive. The fractional sodium excretion at the time of admission (6 hours after the salt administration) could be calculated from their table 1 as 15% (i.e. markedly above the expected value of <1%. Based on UNa 240mmol/L; UCr 8mg/dL; PCr 0.99 mg/dL; PNa 195 mmol/L).

The second child[167] was 7 months of age and was given rehydration solution containing 40 mEq of sodium per litre together with a homemade solution of unknown quantity of sodium. This infant's admission sodium was 178 mmol/L. Both peer reviewers agreed (one beyond reasonable doubt, the other on the balance of probability) with the authors' conclusions that this was due to the accidental administration of overconcentrated saline in a homemade ORS. The calculated fractional sodium excretion 24 hours after admission was 21%, again well above the expected fractional excretion of <1% (based on UNa 107mmol/L; UCr 3mg/dL; PCr 1.0 mg/dL; PNa 170 mmol/L). Both these cases, therefore, provide good evidence of excretion of a large sodium load.

Two cases were reported from Saudi Arabia in 1988 where incorrect reconstitution of a commercial ORS by parents contributed to hypernatraemia[168]. In the first case a 4-month-old boy had been given a solution made up in 120 to 130mls water instead of 1 litre. His admission sodium was 168 mEq/L. The second case was a 7 day old whose mother was making up the solution with 60-70mls water, instead of 1 litre. His admission sodium was 200 mEq/L. The second infant died. Both peer reviewers agreed (one beyond reasonable doubt, the other on the balance of probability) with the authors' conclusions that these were both the result of errors by parents.

A case report from Baltimore, USA, in 1960[169] described a 4-month-old infant admitted with a serum sodium of 200 mEq/L. The mother had erroneously substituted salt for sugar in an oral rehydration solution prescribed by the family

physician, resulting in the baby consuming an estimated 25 to 30g (1 tablespoon) of sodium chloride in 2 pints of water over a 24 hour period. The baby became irritable, vomited, and refused feeds. The mother's error was not discovered until several hours later. Despite the baby being very ill at presentation, she subsequently made a full recovery after discharge home. Both peer reviewers agreed (one beyond reasonable doubt, the other on the balance of probability) with the authors' conclusions that this was due to an error by the mother.

A retrospective review of children with gastroenteritis from Minneapolis, USA, in 1958[170] included three children with hypernatraemia, aged 13 months, 3 weeks and 1 month, who had unintentionally received relatively large amounts of sodium. They had sodium concentrations of 167, >170 and 244 mEq/L. They had been given a home made salt solution in the first 2 cases and undiluted evaporated milk in the third respectively. The second infant died. The peer reviewers agreed (either beyond reasonable doubt or on the balance of probability) that the large sodium intakes had at least contributed to the hypernatraemia. However, given the lack of details in each case, it was not possible to ascertain the contribution of the diarrhoea.

A report from Spain in 1988[171] described a 16-month-old girl presenting with vomiting and diarrhoea, with an admission sodium of 176 mmol/L. She had been given a very large volume of a proprietary oral rehydration solution made up to double the recommended strength, in the context of a relatively mild illness. Both peer reviewers agreed with beyond reasonable doubt with the authors' conclusions as to the cause.

A second Spanish publication in 1992[172] described an 8-month-old breast fed infant who died with hypernatraemia having been administered by his relatives an oral rehydration solution made up at 5 times the recommended strength. The sodium on admission was 205 mEq/L. No further details are given of the reasons for this. Whilst both peer reviewers considered on the balance of probability that the hypernatraemia was secondary to the error, one considered that an investigation to exclude child abuse would be expected nowadays.

4.2.2.2 Errors by parents or carers in administering other medications

A paper from Spain in 2003[173] reported a 3 year old girl with pseudohypoaldosteronism type 1 who presented with seizures and a sodium of 203 mEq/L, this having been normal at 140 mEq/L the previous day. Although the mother contradicted her story on various occasions, the authors concluded that she may have given additional doses of prescribed medication as well as restricting food intake when her child had two small vomits. The child was prescribed sodium chloride and sodium bicarbonate. There was no further discussion about the mother's actions. One peer reviewer thought that on the balance of probability this was an error by the mother, but thought that the possibility of a non-accidental overdose should be considered. The other peer reviewer did not feel able to determine whether this was due to an error by the mother. Both noted the very high sodium concentration in a child whose condition involved excessive renal salt losses.

A case report from Washington, USA in 1973[174] described a 6-week-old boy who received a large oral dose of sodium phosphate. His admission sodium was 164 mEq/L, his calcium was 3.9 mg/dL [0/98 mmol/L] (normal 8.8 to 10.6 mg/dL [2.2 to 2.65 mmol/L]), and his phosphate 41.5 mg/dL [13.4 mmol/L] (normal 4.5 to 6.0 mg/dL [1.45 to 1.93 mmol/L]). "He had been receiving 15 drops of Fleet's Phospho-Soda orally twice a day… to acidify his urine as a treatment for ammoniacal diaper rash. A 9-year-old foster sister prepared the evening formula and, unable to find a medicine dropper, poured Phospho-Soda into the formula bottle. Later examination… suggested that 30ml (195 mmol of sodium and 157 mmol of phosphate) had been added to the formula." The two peer reviewers agreed (one beyond reasonable doubt, the other on the balance of probability) with the authors' conclusions that this was due to accidental administration. One felt that it could be deemed neglectful for a 9 year old to have the responsibility for the administration.

A report from Cincinnati, USA in 1989[175] described a 5-month-old girl who became hypernatraemic (sodium 159 mEq/L) together with other electrolyte disturbances following the inappropriate use of an adult sodium phosphate (Fleet) enema for mild constipation by her mother. The calcium (4.2 mg/dL [1.05 mmol/L]) and phosphate (44.3 mg/dL [14.3 mmol/L]) concentrations were severely disturbed. Both peer reviewers agreed beyond reasonable doubt with the authors' conclusions as to cause.

A case report from New York, USA, in 1990[1] reported the death of a child of 2 years following administration of a saline emetic by a babysitter after an accidental nortriptyline pill ingestion by the child. Admission sodium was 202 mEq/L. Fresh subdural and subarachnoid haemorrhages were found at postmortem. One peer reviewer agreed beyond reasonable doubt that this was an error by the babysitter. The other peer reviewer felt that without further information it was not possible to tell whether this was child abuse.

A case report from Seattle, USA in 1988[176] described a 3-month-old girl who had been administered baking soda in error by her parents. Her admission sodium was 176 mEq/L, and her bicarbonate 54 mEq/L. "Despite initial denials of giving… bicarbonate to their child by the parents, an analysis of the child's formula revealed the following electrolytes: Na^+ 242 mEq/L, K^+ 13 mEq/L, Cl^- 14 mEq/L. Moreover, baking soda was found stored in a can of powdered formula at home in the refrigerator, apparently having been placed there when the customary cardboard container had gotten wet." Both peer reviewers agreed (on the balance of probability) with the authors' implied conclusion that the cause was the accidental administration of baking soda. One commented that the possibility of non-accidental harm could not be excluded.

Evidence statement
There are well described credible instances where errors by parents and professionals have led to significant, sometimes fatal, hypernatraemia secondary to salt, sodium bicarbonate or sodium phosphate administration [Grade C].

The judgements as to whether these episodes were accidental rather than abusive or neglectful are based on the context and circumstances, not the biochemical findings [Grade C].

Evidence statement
Measurement of bicarbonate, calcium and phosphate concentrations in the blood as well as sodium and chloride concentrations should assist in distinguishing the different sodium containing substances [Grade D].

Evidence statement
In many of the case reports of infants and children being fed inappropriately concentrated feeds the true cause cannot be ascertained with any degree of confidence. There remains the alternative possibility of abuse or neglect [Grade C].

4.2.3 Side effects

4.2.3.1 Side effect of medical treatments

Ten children developed hypernatraemia following the deliberate administration of 3% saline as treatment for refractory intracranial hypertension due to head injury.[177] Serum sodium rose to between 157 and 187 mEq/L. One child died, but this was thought to be the result of the severity of the head injury. They concluded that this appeared to be both safe and effective, but considered that controlled trials were needed before widespread use.

There are a number of reports of hypernatraemia following the instillation of hypertonic saline into the body cavity during operative removal of hydatid cysts. Most reports are in adults. However, there are case reports in two children, aged 7 and 4 years from South Africa and Spain[178, 179]. Sodiums of 170 and 178 mmol/L resulted. The first child died.

Three children, one aged 20 months and the others aged 2 years, two from Australia and 1 from New Zealand[180, 181], are described receiving saline as an emetic to treat accidental poisoning. They had ingested warfarin, almond oil and pheniramine. Admission sodium concentrations of 176 and 204 mmol/L were recorded in 2 children. All three children died.

Sodium phosphate enemas are reported in association with hypernatraemia. Hypocalcaemic tetany is also a frequent occurrence.[182-193] There is one report of a child with hypernatraemia after receiving oral sodium phosphate for rickets.[194]

Two cases of hypernatraemia followed the use of antegrade continence enemas (ACE), one using salt water and the other with softened water (softening adds approximately 250 to 300 mg sodium per litre).[195,196] The child receiving salt water died.

One child aged 10 months had a sodium concentration of 183 mmol/L after receiving sodium bicarbonate during a cardiac arrest.[176]

A 7-month-old child had a sodium of 174 mmol/L after receiving sodium bicarbonate paste administered to 22% chemical burns due to crawling through sodium hypochlorite.[197] The boy died.

Several cases are described of hypernatraemia secondary to saline used as an abortifacient. One was in a 15-year-old girl, who survived with a sodium of 154 mmol/L.[198]

A 3 month old with truncus arteriosus and renal failure developed hypernatraemia with a serum sodium of 168 mmol/L secondary to excessive fluid loss with peritoneal dialysis.[199]

Evidence statement
Some medical interventions involving the administration of additional sodium to children have on occasion resulted in fatal hypernatraemia [Grade C].

4.2.3.2 Side effect of parental practices

Saline used as an emetic

There are several case reports of children with hypernatraemia secondary to saline used as an emetic following accidental ingestion. A case from Texas, USA, in 1973[200] described a 3-year-old boy with a sodium of 188 mEq/L at hospital admission who subsequently died. His mother had given him a mixture of salt and mustard in water after he had taken 36 aspirin tablets.

A 2-year-old boy from California found playing with a 'Darvon' bottle from which 4 capsules were thought to be missing was given salt water by his mother to induce emesis.[201] His admission sodium was 189 mEq/L and he subsequently died.

A 14 year old died after being given salt water ("at least 45 grams (5 tablespoons)") by his parents to induce vomiting, as he had returned from a party stating that he "may have" ingested a pill.[202] His admission sodium was 195 mmol/L.

A 2-year-old child was given approximately 100 grams of salt dissolved in water by the mother to induce vomiting because the child drank a small quantity of liquid detergent.[159 (case 1)] Despite an admission sodium of 184 mmol/L the child survived intact.

Another case report from Hamburg, Germany, in 2005[203] described 3 patients who died following the administration of salt used as an emetic. The third of these was a 4-year-old child, who was admitted moribund to hospital with a blood sodium of 245

mmol/L, and who died despite attempts at resuscitation. The description of the case was very brief: "A 4 year old girl ingested, according to her parents, some bathing foam when she was taking a bath. Her parents made her drink several glasses of saturated sodium chloride solution (exact amount unknown) to induce emesis, which was successful within minutes. The girl became very sleepy shortly afterwards, and her parents took her to bed. Two hours later, she was unresponsive and had seizures and her parents took her to hospital… Furthermore [at autopsy], signs of neglect were present, namely a very low body weight of 9.4kg [2.6 kg below 0.4th percentile] at a size of 99cm [25th percentile]." Both peer reviewers disagreed with the authors' conclusion that the salt administration was the result of an attempt at treating the bath foam ingestion, and on the balance of probability thought that this was more likely to be child abuse.

Excessive quantities of oral rehydration solution

A 6-month-old infant in Navarra, Spain, received very large quantities (5 litres in 18 hours) of oral rehydration solution made up correctly, with a sodium content of 90mmol/L, to treat mild diarrhoea and vomiting.[204] His admission sodium was 161 mmol/L. The calculated sodium intake prior to admission was 93 mmol/kg per day.

Application of salt or bicarbonate to the skin

A case report from Turkey in 1993[205] describes the death of an infant following a cultural practice of applying salt to the baby's skin. The infant had been irregularly salted since birth either by direct application to the skin or by adding the salt to the swaddling material. The infant presented at 30 days of age with a seizure, and was found to have a serum sodium of 190 mmol/L. The infant died despite fluid therapy. The salting of babies skin is reportedly an old custom in Turkish communities, with the probable purpose that healthy skin would result from the application and subsequent removal of the salt. Both peer reviewers agreed on the balance of probability with the authors' conclusion that the hypernatraemia resulted from this practice. However, this is a purely descriptive case report without the information that would help to corroborate the mechanism.

A report from Israel in 1986[206] describes a 3-year-old child whose parents covered the child's 25% burns with salt crystals in an attempt to cure the burn injury. The child's sodium at admission was 200 mmol/L, and the child subsequently died. The practice was apparently known to be used in the "primitive community". Both peer

reviewers agreed (one beyond reasonable doubt, the other on balance of probability) with the authors' conclusions that the hypernatraemia was due to the misconceived parental actions.

A case report from Dallas, USA in 1981[207] described mild hypernatraemia and metabolic alkalosis in a 4 month old associated with the topical use of baking soda by the parents to treat a severe nappy rash. The admission sodium was [apparently, extrapolated from the figure] 152 mEq/L, with serum bicarbonate above 35 mmol/L. The authors acknowledge that there is no direct evidence linking the biochemical findings with the parental actions. Both peer reviewers accepted beyond reasonable doubt the authors' conclusions as to cause, but commented that the mechanism was far from clear.

Sodium bicarbonate as a remedy

A case report from Arkansas, USA in 1981[208] described a 4 month old child whose grandmother had admitted adding one tablespoon of baking soda to an 8 oz feed as a home remedy for cold symptoms. The child's admission sodium was 164 mEq/L. Both peer reviewers agreed with the authors (one beyond reasonable doubt, the other on the balance of probability) that the hypernatraemia was due to the grandmother's administration of sodium bicarbonate (in the context that this was at the time a popular folk remedy, and therefore given in the mistaken belief of benefit).

A case report from Chicago, USA in 1987[209] described a 6 week old infant given water to which baking soda had been added as a treatment for 'gas', resulting in a serum sodium of 160 mEq/L, and a bicarbonate of 41 mEq/L. The mother had been adding 'two pinches' to each 6oz bottle of tap water for the previous 2 days, and the infant had consumed all 12 oz of this mixture. The peer reviewers agreed with the authors (one beyond reasonable doubt, the other on the balance of probability) that the hypernatraemia was due to the mother's administration of sodium bicarbonate in the mistaken belief of benefit.

A case report from Alabama, USA in 1995[210] described a 6 week old infant whose mother "periodically had been giving the baby 'a pinch of baking soda in water' for 2 days as recommended by the patient's grandmother to help the baby burp." At admission the serum sodium was 180 mEq/L, and with an anion gap of 49 mEq/L. The mother admitted giving the practice of giving baking soda after an initial denial of having done so. The child recovered and was then followed up for

4 years with no health problems. The peer reviewers both agreed, on the balance of probability, with the authors' conclusion that the hypernatraemia and metabolic alkalosis was due to well-intentioned administration of sodium bicarbonate, despite the mother's initial denial.

A 2 month old baby from Philadelphia, USA in 1988[211], who was given 4 teaspoonfuls of sodium bicarbonate by his mother over 24 hours to treat 'gas' developed hypernatraemia (167 mEq/L) and metabolic alkalosis (bicarbonate 39.6 mEq/L).

The mother of a 7 week old boy from Baltimore, USA in 1990[212], "added approximately one-half tablespoon of baking soda to his formula at the time that he felt warm, to 'help bring up his burps'… [and] two 'pinches' of baking soda to the mixture each time she prepares the formula, for the same reason." His sodium on admission was 155 mEq/L, with a bicarbonate of 29 mmol/L.

A case report, from Illinois, USA in 1983[213], described a 3 year old girl administered sodium bicarbonate as a remedy for mild abdominal pain whose admission sodium was 210 mmol/L. Her serum chloride concentration was very high at 185 mmol/L, and she had a mild metabolic acidosis with a base deficit of 14 mmol/L. She was noted to have "a large contusion over the right orbit and several minor facial lacerations". There was a delay in the foster parent's admission that they had been giving the baking soda, and "a formal investigation of the child's foster parents failed to reveal intentional abuse; evidently they thought sodium bicarbonate was a panacea for abdominal pain." The child was discharged to a new foster home. The peer reviewers noted that the high chloride concentration and metabolic acidosis were unexplained and both suggested that the girl had been administered salt rather than sodium bicarbonate. The girl's injuries at the time of admission were not explained. On this basis one of the two peer reviewers disagreed on the balance of probability and considered child abuse was more likely.

Evidence statement
There are credible reports of well-intentioned actions by parents or carers that have resulted in hypernatraemia [Grade C].

Some parents have initially denied their actions, and although this should raise suspicions of possible non-accidental injury, this may also occur for other reasons [Grade C].

4.2.4 Accidental or voluntary ingestion by children

Sodium, mainly in the form of salt, is a necessary component of children's diet. Sodium intakes by healthy children have been assessed in a number of studies, including two from the UK in 1986.

The first study from Southampton[214] used 24-hour urinary sodium excretion as a marker of intake in 28 children aged 3 to 5 years registered with a single general practice. Their sodium intake was also estimated by analysis of 3-day food diaries. The average daily excretion of sodium was 65 mmol, or 3.5 mmol/kg (range 28 to 105 mmol, or 1.6 to 6.2 mmol/kg). Analysis of the food diaries suggested a mean daily sodium intake of 69 mmol (range 32 to 98 mmol).

The second study from London[215] obtained two 24-hour urine samples from 34 children aged 4 to 6 years attending two primary schools. The mean urinary sodium excretion was 64 mmol (range 20.5 to 131 mmol). Neither study calculated fractional sodium excretion rates.

The specific question relevant to the differential diagnosis of hypernatraemia is whether an otherwise healthy child will spontaneously and voluntarily consume sufficient salt to cause them to become hypernatraemic. There are two sources of evidence to assist in answering this question. The first is a national database originally developed by the Department for Trade and Industry, subsequently transferred to the Royal Society for the Prevention of Accidents (RoSPA). The second is the identification of all relevant case reports.

The national database held by RoSPA is collected as part of the Home and Accident Surveillance System (HASS) and Leisure Accident Surveillance System (LASS).[216] The resulting database holds details of home and leisure accidents that caused a serious enough problem to warrant a visit to hospital. The data were collected by regular sampling from each of the same representative UK hospitals from 1978 to 2002 (18 centres before 2001 and 16 centres thereafter). DTI data collection stopped with the publication of the 24th Report in 2003[217] and the entire database was transferred to RoSPA who have made it available to users.

Over the 25-year period 1978-2002, 45,767 instances of suspected poisoning in children aged 0-4 years were sampled (about 8.5% of the estimated total national occurrences of poisoning for this age range over the same period). There were 8 recorded instances of accidental salt ingestion in children aged 0-4 years over this time.[218] Details of these cases are reproduced below:

Age	Ingestions: recorded mechanism	Outcome
<1 year	Baby accidentally given drink of water containing washing-up liquid & salt. Drank approx 20oz.	No treatment given. Discharged.
1 year	Dad saw patient eating some table salt.	Discharged. No treatment required.
1 year	Patient took drum of table salt off kitchen unit and ate a large mouthful.	Examined but no treatment given
1 year	Went to cupboard, got salt out, mum went to take it off her. Patient had lid in mouth and it came off and swallowed lots.	Examined but no treatment given.
2 years	Swallowed some salt and brown sauce.	Referred to GP.
3 years	Child unobserved in kitchen mum decorating dining room. When she went to check on patient he had the salt container to his mouth. Not sure how much swallowed.	Inpatient for less than one day.
3 years	Child ingested unknown quantity of table salt from plastic container in cupboard.	Referred to outpatient clinic.
3 years	Patient swallowed cooking salt. No more details.	Referred to outpatient clinic.

The HASS data above will not include any children with salt poisoning admitted directly to an inpatient facility and bypassing the A&E department, and children who died because of salt poisoning. Children in whom salt poisoning was not diagnosed initially and who were admitted subsequently for investigation will also not be included.

The information above suggests that voluntary salt ingestion sufficient to cause sufficient concern to result in an accident and emergency attendance is a very rare occurrence indeed, and those children attending following concerns about salt ingestion are not sufficiently ill to require hospital admission.

The only relevant case reports are described below.

A case report in 2004 from Oklahoma involved a 6 year old boy with a serum sodium of 234 mEq/L on admission.[219] He was also found to have bilateral chronic subdural haematomas, a burn on his left hand approximately 2 weeks old, and a past history of physical and sexual abuse. He was living with foster parents, who reported that he had pica, particularly of glass. The foster parents reported that he had complained of thirst, urinated frequently, and had vomited twice in two days. He had awoken his foster parents as he was thrashing in his sleep, and when he 'turned unresponsive' they initiated CPR and called the emergency services. The child subsequently alleged that his foster mother forced him to drink salt water. The foster parents denied any knowledge of salt ingestion. There was no evidence of iron deficiency. The two peer reviewers both strongly disagreed with the (non-paediatric)

authors' speculation that the child had ingested salt as a result of his pica, and considered that the child had been abused (one beyond reasonable doubt, the other on the balance of probability). This case therefore should not be used to provide evidence of voluntary salt ingestion by an otherwise normal child, and has been included in the list of case reports of non-accidental salt poisoning as a manifestation of child abuse.

There is a second case report in which the authors considered that two otherwise normal young children spontaneously and voluntarily ingested sufficient salt to cause significant hypernatraemia. This case from Ohio, USA[220] , published in 1964, relates to two 14-month-old twin girls who were considered by the authors to have ingested a considerable amount of rock salt, possibly aided and abetted by an older sibling. Their sodium concentrations on admission were 179 and 182 mEq/L.

It would be important to be aware that young, otherwise normal children have been reported voluntarily to ingest salt to this extent. This case was cited in a recent review of the evaluation of salt poisoning as a "well-described case of voluntary salt poisoning".[221]

Accordingly, this second case report was peer reviewed by the whole panel of 16 paediatricians. Eight disagreed with the authors on the balance of probability, one disagreed beyond reasonable doubt, and 5 said they could not tell from the publication whether the authors' conclusions were correct. Only two agreed with the authors on the balance of probability. The following points were made:

- This paper was published before the reality of child abuse was recognised, and child abuse was not discussed as a possible diagnosis
- The toddler who swallows bleach takes a swig and spills most of it. What they do not do is voluntarily go back for a second helping. It is unlikely that the ingestion response would be much different for salt
- The social history given in the case report is inadequate. However, there are some pointers to family stress:
    - 3rd pregnancy in a 19-year old mother
    - The mother did not visit for first 24 hours after admission
    - On a home visit a month after admission a large box of salt was again within easy grasp of the twins
- Both the twins were undernourished
- At their age, they would be unlikely to have the fine-motor control to ingest large quantities of salt, and could only have 'finger-fed' small quantities
- Neither child had reportedly eaten or drunk for almost 48hr, nor had they vomited; salt ingestion to cause this degree of hypernatraemia would generate thirst

- Even had an older sib attempted to feed them, this older sib couldn't have been much more than 5 years age, and would have struggled to force the twins to consume more than a teaspoon of salt
- The salt discovery was only revealed "upon further questioning"
- If twin 1 had ingested salt to cause the hypernatraemia of 182mmol/L (and given a normal upper limit of plasma Na of 140mmol/l) she would have needed to have absorbed 8.5 grams [(42*(0.6*body wt))/17.1]. This would amount to 1.75 standard (5 grams) teaspoons.

The case report is therefore not credible to a panel of expert paediatricians, and should not be used as evidence that young children will spontaneously and voluntarily ingest significant quantities of salt.

There is a report from Denver, USA, in 1985[222] of a 33 year old woman who compulsively ate salt 'by the shakerful' (estimated to be around 600mmol per day or ½ pound a week) following a gastric stapling procedure for obesity. Her serum sodium was only slightly elevated at 149 mEq/L. Her 24 hour sodium excretion was 452 mEq/24hrs, and a calculated fractional sodium excretion was 2%. She was found to have iron deficiency anaemia with a haemoglobin of 9.2 g/dl. Treatment with intramuscular iron resulted in rapid resolution of the salt cravings within 2 weeks. The authors concluded that the cause of her hypernatraemia was salt craving rather than an attempt at deliberate self-harm.

Although this case is an adult, it raises the possibility in children of compulsive salt ingestion as a rare form of pica. It should however be noted that her serum sodium was relatively low. It was therefore submitted to all the peer reviewers for appraisal. The breakdown of their opinions as to the cause was as follows:

- 7 agreed with the authors beyond reasonable doubt
- 5 agreed with the authors on the balance of probability
- 2 did not consider it was possible to tell from the information given
- 2 disagreed with the authors on the balance of probability

Those that did not agree considered that the woman may have had some secondary gain from her condition, pointing out her failure to respond to oral iron, the number of previous surgical procedures she had had, and the lack of psychological assessment.

Evidence statement
The existing evidence suggests that young but otherwise healthy children in the UK do not spontaneously and voluntarily ingest sufficient salt to cause significant hypernatraemia [Grade C].

Evidence statement
The one existing case report involving two healthy young children does not provide credible evidence that otherwise healthy young children spontaneously and voluntarily ingest sufficient salt to cause significant hypernatraemia [Grade C].

4.3 Characteristics of children with hypernatraemia in whom accident was the likely cause

Clinical question

What are the characteristics of children reported in the literature in whom an accident was the likely cause?

There are reports of 24 newborn infants less than 4 weeks of age who received excessive amounts of salt in their feeds, with 3 separate errors occurring in Binghamton, USA[8, 150]; Sydney, Australia[151]; and Graz, Austria[152, 153]. Five infants between 4 weeks and 7 months received either salt in their feeds or incorrect oral rehydration solutions.[151,159 (case 2), 161, 167, 169] Eleven children between 13 months and 14 years received salt, most commonly as an emetic.[1, 159 (case 1), 167, 181, 200-203,223] The three age groups' symptoms are reported separately.

The 14 term infants in Binghamton had the following symptoms and signs reported:

- Vomiting (13/14)
- Convulsions or muscular twitching (11/14)
- Fluttering of eyelids or facial muscles (7/14)
- Refusing feeds
- Avid thirst
- Respiratory distress
- Fever

None of the 4 low birth weight, 'premature' babies (gestations not specified, BW between 1.36 and 2.35 kilogram) in Sydney had convulsions, and one had muscular twitching. They had somewhat different symptoms:

- Vomiting and diarrhoea
- Peripheral circulatory failure
- Sunken eyes
- Respiratory depression
- GI and heel prick bleeding

Two of the 5 infants between 4 weeks and 7 months had refused feeds, one with accompanying weight loss of 10% of his body weight with clinical dehydration. One was reported as showing intense thirst. Two were drowsy and lethargic; three became comatose (one further was found dead). Two infants vomited. Three were seen to fit, have extensor spasms or be "on the verge of fitting".

The ten children in whom symptoms are described all became comatose, some very quickly (one within 15 minutes of receiving the saline emetic). Eight had seizures. Six had documented pyrexia. Three were documented as having vomited, one further child complained of feeling nauseated. Three had circulatory shock. Three had some degree of respiratory distress. One had bloody, fluid stools.

There are 10 case reports in the literature in which a patient has been documented to receive salt or saline, and a blood glucose on admission is available. Patients were excluded with pre-existing conditions such as diabetes or Cushing's disease, as well as those in whom additional glucose was also given (e.g. glucose in oral rehydration solutions).[158, 161, 167, 202, 223-229.]

The average blood glucose on admission was 9.4 mmol/L, with a standard deviation of 3.5 mmol/L. Seven of the 10 had a blood glucose above 8.0 mmol/L. The highest blood glucose was 17.3 mmol/L in a child whose mother had added salt instead of sugar to two yoghurts. The average sodium was 193 mmol/L, range 166 to 212 mmol/L.

Evidence statement
The onset of coma can be rapid following salt ingestion [Grade C].

Evidence statement
Some children poisoned with salt have a modestly raised blood glucose [Grade C].

4.4 Mechanisms causing hypernatraemia through non-accidental excessive sodium intake

Clinical question

What agents, mechanisms and circumstances are described in those children with hypernatraemia who were considered to have been abused?

The following cases are described.

4.4.1 Twenty children deliberately administered salt[3, 13, 219, 224, 230-235]

The largest reported series of salt poisoning cases was reported by Meadow, who had a specialist experience of non-accidental poisoning.[3] These cases had occurred over a number of years.
The criteria for making the diagnosis were:

- elevated serum and 'even higher' urinary sodium concentrations;
- other extensive investigations for natural disease normal/negative;
- cessation of hypernatraemia when separated from probable perpetrator; and
- circumstantial evidence indicating that either the child's mother or the father was poisoning the child.

In seven cases the mother confessed to the poisoning and explained how she had done it. Seven of the children had a combination of problems including failure to thrive/neglect in 4; recurrent apnoea/seizures in 3; other fabricated illness in 3; other drug ingestion in 2; and physical abuse in 2. Of the 5 cases where there was no parental confession, there was circumstantial evidence implicating the mother in 3, the father in 1 and implicating the parents without it being clear who was responsible in 1.

The mode of poisoning was available for 7 children, namely added to a milk drink in 4, to a fruit drink in 1 child, and administered via a nasogastric tube in 1 child (with a second child having 'exceedingly' high salt concentrations in their stomach). In another case 'it is probable that salt solution was introduced by tube into the rectum.' The normal sodium concentration of gastric aspirates was stated to be 50-60 mmol/L, with concentrations of over 200 mmol/L being highly suggestive of salt ingestion. A separate publication[234] found a gastric sodium of 660 mmol/L in a child whose mother subsequently confessed to administering salt.

The hypernatraemia was recurrent in 10 of the 12 children, usually for a period of about 3 months, although in one it recurred over a period of 45 months. Seven siblings also had a variety of relevant problems, with salt poisoning in 2, other fabricated illness in 3, failure to thrive and neglect in 4, physical abuse in 1 and sudden unexpected death at age 1 year in 1 child.

For 'at least' 9 of the children there was either definite or highly probable evidence that the parent poisoned the child whilst the child was in hospital as well as at home. There was evidence that one mother tampered with two samples of her breast milk. Two children yielded 'extraordinarily' high sweat concentrations of sodium and chloride (above 1,000 mmol/L) while in the care of their mothers, as did tests in two mothers. One mother subsequently admitted tampering with the test.

Eleven of the 12 cases did not have detailed descriptions that would allow a reader to form their own judgement about the certainty of the diagnosis in the individual cases, and did not permit them to be subjected to peer review. However, the descriptions of the pooled cases make it virtually certain that the diagnosis was correct in seven of the children, whose mothers confessed and explained the mechanism.

The doubly reported case[3, 13] was subjected to peer review. Both peer reviewers agreed with this being likely to be child abuse, one stating "highly likely", the other "beyond reasonable doubt". The lack of detailed biochemical results was noted.

In a case report from Virginia, USA, in 1992 of a fatal ingestion of salt[224], there was a radio-opaque mass in the stomach due to crystallized salt, which is radio-opaque when formed into a concretion. The 6-year-old child was originally reported by her adoptive mother to have voluntarily ingested a small amount of salt. The mother was later arrested and convicted for force-feeding table salt. No further details of the method of administration or the basis for the conviction were given. One of the two peer reviewers agreed with the authors beyond reasonable doubt. The other agreed on the balance of probability because the authors did not prove that the radioopaque concretion was salt and because although the mother was convicted after further investigation the evidence on which she was found guilty is not in the report.

A five year old child reported in 1983 from El Paso, Texas[230] was unusual in that he eventually admitted that his parents had made him eat salt 'by the spoonfuls' for enuresis. There was a background of previous concerns about child abuse, the boy had scars on his feet and ankles from burns, and he was subsequently placed in foster care. He had initially

been reluctant to speak about the presenting or previous episodes of abuse. Both peer reviewers agreed beyond reasonable doubt with the authors.

Two unrelated cases were reported from Seattle in 1979.[231,232] The first, a child of 2½ years, was reported by parents to have developed a voracious appetite and remarkable thirst. They had forcibly restricted water intake and increased his intake of salt 'with potato chips and salted French fries'. He was found to have 'numerous contusions and abrasions on his legs, nose and cheeks'. His behaviour in hospital improved and his appetite appeared entirely normal. He was placed in foster care prior to adoption. Both peer reviewers agreed strongly with the diagnosis of child abuse, though there was a lack of supporting evidence that deliberate water restriction was a factor in the hypernatraemia. In the second, 3 year old child, the explanation given for the hypernatraemia by the father's partner was that she had been awoken at approximately 11am by sounds of choking, and had found the girl 'in the midst of coughing with a cup of salt beside her crib'. In hospital there was evidence of other physical abuse, with 'multiple contusions and ecchymoses on her head and a healing laceration on her scalp', and evidence of 'sexual molestation'. Both peer reviewers strongly agreed with the diagnosis of non-accidental salt poisoning, but had strong reservations about the authors' suggestion of non-accidental water restriction as there was no evidence at all to support this.

A case reported from Great Ormond Street Hospital in 1976[233 (case 1)] involved a breast fed baby of a trained children's nurse who had first presented with hypernatraemia at the age of 2 months. This had recurred on a number of occasions despite changing the baby to low salt cows milk feed; a further episode of hypernatraemia had occurred whilst her mother was resident. Investigations pointed to an external source of sodium and it was concluded from calculations of the child's sodium balance that the mother had added about 6 grams salt to the child's feeds whilst in hospital. During interviews the 'mother was told that her baby had been receiving extra salt in her feeds but she did not volunteer that she had been responsible.' The child was transferred back to the referring hospital as an inpatient whilst mother attended a psychiatrist. Eventually the child was discharged home and returned moribund at the age of a year with severe hypernatraemia and died. Both peer reviewers agreed on the balance of probability with the authors' conclusion that this was child abuse. The reservations that prevented them from agreeing beyond reasonable doubt were:

1. The report presented several episodes, none of which had complete information. For example, there were no urinary biochemistry details from the fatal episode, though there were for the others (maybe because it was not available). This was otherwise the most convincing episode to suggest salt poisoning, with a sodium of 200, a chloride of 170, and a blood urea of only 7 mmol/L.

2. The episode where the plasma sodium rose from 135 to 144 mmol/L (both within the normal range) was not likely to be a significant rise. The fact that the authors made an issue over that, and calculated causative sodium balances for it, suggests that these authors may have decided that this child was poisoned, and could have lost a sense of clinical judgement in an attempt to confirm that view.
3. The authors described undertaking more sophisticated tests, including a water deprivation test, and reported that they were all normal. However, they did not give the data to show the evidence of normality, and some of these tests require experience and judgement to interpret.
4. There was quite limited discussion by the authors, particularly there was a lack of discussion on the post-mortem findings (Curling's ulcer in association with hypernatraemia).

A child reported from Newcastle in 1985[234] had first presented with recurrent hypernatraemia from the age of 10 weeks. The girl was found to have a markedly raised urinary sodium, and the diagnosis was eventually proved when a sample of vomit obtained shortly after admission was found to have an extremely high sodium content. Although the mother confessed to having caused the hypernatraemia, the mechanism was not described in the publication. The authors also stated that 'it was clear that father had no idea what had been going on'. The child demonstrated catch up weight gain and gross motor development after removal to foster care. Both peer reviewers agreed beyond reasonable doubt with the authors' conclusion that this was child abuse.

A case report from Cincinnati in 1980[235 (case 1)] described a 6-year-old hyperactive boy who died after being forced to eat 'Morton's Lite' salt as a punishment. This contains approximately equal proportions of sodium and potassium. His sodium concentration was 176 mEq/L, and his potassium concentration was 13.7 mEq/L. He had a contusion on his buttock at postmortem and it was considered likely that he had died from a cardiac arrhythmia secondary to potassium poisoning. His foster father was subsequently convicted of involuntary manslaughter. Both peer reviewers agreed beyond reasonable doubt with the authors' conclusions that this was child abuse.

A case report in 2004 from Oklahoma involved a 6 year old boy with a serum sodium of 234 mEq/L on admission.[219] He was also found to have bilateral chronic subdural haematomas, a burn on his left hand approximately 2 weeks old, and a past history of physical and sexual abuse. He was living with foster parents, who reported that he had pica, particularly of glass. The foster parents reported that he had complained of thirst, urinated frequently, and had vomited twice in two days. He had awoken his foster parents as he was

thrashing in his sleep, and when he 'turned unresponsive' they initiated CPR and called the emergency services. The child subsequently alleged that his foster mother forced him to drink salt water. The foster parents denied any knowledge of salt ingestion. There was no evidence of iron deficiency. The two peer reviewers both strongly disagreed with the authors' conclusion that the child had ingested salt as a result of his pica, and considered that the child had been abused (one beyond reasonable doubt, the other on the balance of probability). They made the following points:

1. There were bilateral subdural haematomas which were chronic and not explained by acute ingestion;
2. The child had a burn which was two weeks old;
3. The child reported foster mother made him drink salt;
4. There was a past history of physical and sexual abuse, presumably before he went into foster care.

This case is therefore very likely to represent child abuse rather than voluntary salt ingestion.

Evidence statement
There are credible case reports of children deliberately and abusively administered salt [Grade C]. These are described from different countries and by different authors. The ages of the children ranged from 6 weeks to 6 years.

Evidence statement
A sample of gastric contents for analysis of sodium content should be obtained as soon as possible after admission in all children presenting with hypernatraemia of uncertain cause [Grade D].

4.4.2 One child forced to eat sodium bicarbonate[236]

There is a single case report from Wisconsin in 1977 of a 6-year-old child who was forcibly administered sodium bicarbonate, together with vinegar, dishwashing liquid and possibly red pepper. His initial serum sodium was 183 mEq/L and pH was 7.07. He died some days after admission. The following story was recounted:

> "… the three siblings (ages 12, 11, and 10) began to relate a story. The live-in babysitter, who was in charge of the children while their long-distance truck-driving father was working, had found that the child had begged or stolen other children's lunches at school. She decided to make him vomit as a method of punishment; she

> gave him large glasses of sodium bicarbonate…. he was forced to drink it and was told he would be hit with a belt if he didn't…. in an attempt to induce vomiting the babysitter put her foot on the child's stomach."

The babysitter pleaded guilty to negligent contribution to the death of a minor. Both peer reviewers agreed beyond reasonable doubt with the authors' conclusions.

Evidence statement
There is a single, credible case report of deliberate and forcible administration of sodium bicarbonate by a babysitter causing the death of the child [Grade C].

4.4.3 Children prevented from drinking, "thirsting" [225, 237-239]

There have been several reports of hypernatraemia secondary to water deprivation involving 6 children, where there was not thought to be excessive salt administration. All three children in the first case series had good evidence of moderate to severe dehydration at the time of admission.

The first case report, from San Francisco, was of three children admitted with hypernatraemia in 1968.[237] The first child aged 2½ years had a serum sodium of 194.5 mEq/L on admission with a 3 day history of vomiting. He had been adopted at 5 months, had developmental delay and had lost weight 2 to 3 months before admission 'when his parents attempted to teach him to eat vegetables. Subsequently, he regained the weight on his usual diet. His father emphasised that his appetite and intake were usually enormous.' He had ecchymoses on his cheeks and knees. 'During his hospital course, it became apparent the patient had been periodically thirsted by his mother while his father was away from home.' He subsequently demonstrated catch up growth and development. Both peer reviewers agreed on the balance of probability with the authors' conclusions that this was due to the actions of a psychiatrically disturbed mother, with one pointing out that the additional administration of salt could not be excluded as a contributory cause.

The second child, a 3¾ year old, was admitted with a 3-day history of progressive loss of appetite, with increasing irritability and inability to walk or stand. He had had four loose bowel motions a week earlier and weight loss over 3 months. His initial sodium was 201 mEq/L. At the time of admission he had multiple bruises including 'a 2 x 2 cm bruise on the left cheek, a 3 x 4 cm bruise on the right buttock, and numerous smaller bruises over the lower extremities.' 'A baby sitter and the maternal grandfather each made unsolicited telephone calls to say that the patient's mother had instructed them on numerous occasions

in the past not to give the patient anything to drink when taking care of him. Apparently the mother disliked changing diapers and thirsted the child. The mother stated that the bruises occurred secondary to a fall, but their distribution did not seem consistent with the history. The grandfather claimed the child was beaten with a rubber hose.' One of the two peer reviewers agreed on the balance of probability with the authors' conclusions on cause. The lack of details of normal tests at follow up, and the lack of a formal child protection investigation led the second reviewer to state that they were unable to tell whether the authors' conclusions were correct.

The third child, a 7-year-old girl, was admitted with a history of vomiting and diarrhoea for 2 days starting 7 to 8 days before admission, then appearing to recover well. Two days prior to admission she became anorexic and had some degree of malaise. Her father returned home late at night and gave the girl a drink of water. The next morning she was too weak to walk, and was taken to a doctor, from where she was admitted to hospital severely dehydrated, extremely lethargic, nearly comatose and cyanotic. Her initial serum sodium was 183 mEq/L. She was found to have markedly desiccated skin and mucous membranes, a recent abrasion over the right forehead and two old resolving ecchymoses in the lumbar area. 'During hospitalization, a neighbour stated that the mother had exhibited bizarre behaviour and had been depriving the child of water. Sometimes the child stood on the front lawn and asked passersby for water. Apparently the motivation for the restriction was the patient's enuresis. The patient also has a peculiar craving for salt, eating the salt from a shaker at times.' Both peer reviewers considered that it was not possible to exclude salt administration as an additional cause, but otherwise agreed on the balance of probability with the authors' diagnosis of child abuse.

It has also been suggested by others that although there was clear evidence of water deprivation in these cases, the degree of hypernatraemia seen in the children was greater than could be accounted for by this mechanism alone, and that they may also have been given excess salt.[3] Urinary sodium was not measured in any of the three children. One of the peer reviewers calculated that the degree of dehydration in each case was enough to cause the reported degrees of hypernatraemia, assuming pure water loss.

A second publication, from France, in 1975[238] describes a 6-year-old girl who was admitted when she attended clinic with clinical signs of dehydration and a serum sodium of 189 mEq/L. Her grandmother then reported that she was detested and beaten by her mother who had also deprived her of water, tied her up and ensured she had no access to water; that the child had on occasion drunk her own urine and condensation from the windows; and that her brother had also been abused. She had previously been admitted with acute alcohol

poisoning, and had been noted to be small for her age when seen at the age of 3 months, but with subsequent loss to follow up. She was also found to have tight aortic stenosis associated with bicuspid aortic valve, which was treated surgically. She demonstrated a marked growth spurt following removal from her parents. The authors speculated that as well as water deprivation the child had been poisoned with salt, and there was no weight gain after rehydration suggesting that she was not dehydrated. Both peer reviewers agreed beyond reasonable doubt with the authors' conclusions that this child's hypernatraemia was caused by abuse.

The third publication, from Wisconsin, USA in 1981[239], describes a 21 month old girl who was admitted following a tonic-clonic seizure with a serum sodium on admission of 206 mEq/L, and with retinal haemorrhages (no cranial imaging was reported). The child had been initially brought up by her grandmother, then when she moved into a separate apartment with her mother at 7 months, her development ceased, she cried frequently, fed poorly, had temper tantrums, seemed irritable and rocked in her bed almost constantly. She was left almost exclusively in charge of a babysitter from the age of 10 months, and her reported behaviour included eating her pet rabbit's food and faeces, drinking from a toilet bowl and a bird bath, twiddling her fingers in the air above her face, and drooling almost constantly. Her weight increased after rehydration only by 2%, and subsequently she had a growth and development spurt when taken into foster care. The authors speculated that her hypernatraemia was the result of chronic water deprivation. Both peer reviewers agreed beyond reasonable doubt with the authors' conclusion that the hypernatraemia was due to child abuse. However, one commented on the causal agent "the extreme hypernatraemia with only a 150 grams weight gain following rehydration raises the distinct possibility of salt administration as an alternative or contributory cause for the hypernatraemia. The relatively modest rise in the blood urea concentration at presentation (BUN 40 mg/dl, equivalent to a urea of 14 mmol/l) seems to me to be less than would be predicted if the cause were water deprivation alone (which causes hypernatraemia by a reduction in body water, not by a change in total body sodium)."

A case report from Cincinnati in 1980[235 (case 2)] described a 2-year-old girl who was whipped by her mother's boyfriend and then tied up without food or water overnight. She was found dead the next day, and her postmortem vitreous humour sodium was 177 mEq/L. Her vitreous urea was 51 mg/dL. She was also found to have sickle cell trait. The authors concluded that the hypernatraemia was secondary to dehydration, with intravascular sickling being a contributory factor. The vitreous humour provides a reliable guide to the antemortem sodium and urea concentrations.[240, 241]

The last publication, from France in 1990[225], describes a 2 year 11 month old child with an initial sodium of 186 mmol/L, in whom there was suspicion of chronic water deprivation. The child was reported by her parents always to be demanding something to drink. She had been observed at preschool to be licking drops of water from windowpanes and from puddles. She improved after removal from her parents. Both peer reviewers agreed (one beyond reasonable doubt, one on the balance of probability) with the authors' conclusions that the child had been abused. However, they pointed out that the physiology was not well worked out, and considered that the authors had failed to distinguish between water deprivation and salt poisoning.

In the adult literature there is a case report of a prisoner who went on a "thirst strike"[242], with a resulting plasma sodium of 164 mmol/L, a fractional urinary excretion of sodium of 0.21% (suggesting a normal sodium intake and renal function[27]), and approaching a 20% increase in weight after restoration of hydration. The resulting sodium concentration was not nearly as high as in some of the children described above. It is therefore possible that the children reported as hypernatraemic secondary to water deprivation may also have been administered excessive salt.

Evidence statement
Although there are credible case reports of significant hypernatraemia in children secondary to water deprivation, at least some of these children may have been administered salt as well [Grade C].

Evidence statement
Careful measurement of weight at the time of admission and before restoration of full hydration provides a reliable estimate of the degree of dehydration [Grade B].

This should be undertaken if possible in children presenting with hypernatraemia of uncertain cause [Grade D].

Evidence statement
A urine sample for calculation of fractional urinary sodium excretion (for which plasma and urine sodium and creatinine measurements taken at a similar time are required) in the presence of normal renal function should help to ascertain whether the hypernatraemia is secondary to excessive sodium ingestion [Grade D].

Regular urine samples for fractional urinary sodium excretion are recommended in children presenting with hypernatraemia of uncertain cause [Grade D].

Evidence statement
Postmortem vitreous humour sodium and urea provide a useful guide to plasma sodium and urea concentrations before death [Grade C].

4.4.4 Associated findings

4.4.4.1 Other evidence of child abuse

A number of case reports describe other unexplained or manifestly abusive injuries. In others there is evidence of associated emotional abuse, with evidence of coercion relating to the forced ingestion and/or withholding of fluids.

Some case reports may have been published because of the strong evidence of associated abuse. This could mean that there is publication bias, and the actual rate of association with other evidence of child abuse is much lower. The specific association with subdural haemorrhage is dealt with separately below.

Evidence statement
Some but not all children with hypernatraemia caused by deliberate poisoning have evidence of other forms of child abuse [Grade C].

4.4.4.2 Psychosocial problems

Some case reports include evidence of psychopathology in the mother and of abuse at the hands of substitute carers. These are not surprising findings. For the same reasons as in those children where there was other evidence of abuse, it is not possible to draw conclusions from these.

4.4.4.3 Subdural haemorrhage

The common association between subdural haemorrhage in infants and child abuse means that it is crucial to know whether subdural haemorrhage can be a complication of severe hypernatraemia.

Laurence Finberg was a world leader in hypernatraemia in infants and produced a large body of work with colleagues in the mid 1950s-60s. In 1959 Luttrell and Finberg presented a series of 3 fatal cases of hypernatraemia in infants of 8 months

old or less, one of whom (case 3), "a neglected one-month-old", had intradural and subarachnoid haemorrhages with an initial serum sodium of 180 mEq/l.[243] One peer reviewer could not tell the cause of the hypernatraemia from the publication. The other peer reviewer agreed on the balance of probability with the authors' conclusion that this was secondary to hypernatraemic dehydration.

The same year the authors used clinical observation[244] and experimental studies[245] to add weight to the evidence that hypernatraemia may be a cause of subdural haemorrhage. The clinical paper included 7 cases of hypernatraemia with a subdural effusion, one of which was bloody and one xanthochromic. A major limitation of the clinical study is that most of the subdurals were chronic, and very little detail is given of all but one of the cases. Subdural tap may in itself cause bleeding, and in the one case where 5mls of grossly bloody fluid was obtained on subdural tap subsequent exploration showed no membrane or large haematoma.

The one case described in detail was of a 5-week-old infant with evidence of a chronic subdural hygroma, and acute presentation with salt poisoning, thought by the authors to be accidental. The mother made up the infant's formula while in the home of the child's grandmother, and "it was subsequently learned that sugar and salt were kept in identical canisters and that salt had inadvertently been substituted for sugar. The patient took between 360 and 600 ml of this mixture…" The timing of the poisoning and the chronicity of the subdural fluid collection excludes hypernatraemia as the cause. Both peer reviewers agreed, one on the balance of probability and the other beyond reasonable doubt, with the authors' conclusion in this case that this was due to an error making up the feed with salt instead of sugar.

These studies were also conducted before the widespread recognition of non-accidental injury in children, first highlighted in 1962 by the landmark article outlining the features of 'Battered-Child Syndrome'.[246] As stated by Kempe, "subdural haemorrhage with or without a skull fracture in our experience is an extremely frequent finding even in the absence of fracture of the long bones" and it was recommended that 'Battered-Child Syndrome' should be considered in any child with a subdural haemorrhage.

Therefore the lack of available neuroimaging techniques, coupled with the lack of appreciation of child abuse in the late 1950's makes it very difficult to interpret Finberg's findings.

Although Finberg predicted that subdural haemorrhages would occur in salt poisoning, when the Binghamton disaster then occurred (also reported by Finberg[8]) no child on whom a post mortem was conducted actually had a subdural haemorrhage.

If the only cases where both occurred had other evidence of child abuse (not simply evidence in the form of subdural haematomas), then one might reasonably conclude that the evidence suggests that subdural haematoma does not complicate hypernatraemia.

A more recent publication looking critically at the issue of subdural haemorrhage and its association with hypernatraemia[247] (evidence level 4) approached the topic from four different perspectives:

1. Chart review of hypernatraemic infants at autopsy (9 cases, multiple causes of death): none had a subdural haemorrhage.
2. Hospitalised children (aged <2 years) with hypernatraemia (134 cases): one case of confirmed fatal non-accidental injury had a subdural haemorrhage but this preceded the development of hypernatraemia.
3. Prospective collection of head injured hypernatraemic children (4 cases, < 2 years): three cases had a normal sodium at presentation and one was unavailable as the patient came from an outlying hospital.
4. Retrospective review of all cases of subdural haemorrhage (23 children <2 years), diagnosed by neuroimaging or autopsy over a three year period 1994-96: one case became hypernatraemic post head trauma but not at presentation.

There were a number of limitations to this study:

- the records of only 134 (66%) of the 203 identified hypernatraemic hospitalised patients were available for review;
- the retrospective review of subdurals was a hospital-based study, rather than population based;
- the study only sourced hospital records with no clear methodology of collection described;
- in the postmortem series vitreous fluid was not aspirated routinely in cases of intracranial haemorrhage so the authors could not be sure that all hypernatraemic cases were detected.

The authors found no children who presented with a subdural and hypernatraemia at presentation. They concluded that if hypernatraemia was present in association with a subdural haemorrhage it was most likely secondary to intracranial pathology, but did not describe a possible mechanism for this.

All children under 2 years with a subdural haemorrhage over a six-year period (1 January 1992 to 31 December 1998) in South Wales and Southwest England were reviewed retrospectively.[248, 249] There were 90 cases of subdural haemorrhage confirmed on computed tomography, magnetic resonance imaging, or post mortem examination.

Following the finding of cases with associated hypernatraemia, the association was formally reviewed.[250] As hypernatraemia during inpatient admission may occur for multiple medical reasons, only those hypernatraemic at presentation were included, with hypernatraemia defined as serum sodium above 150 mmol/l. The medical records of all potential cases were then reviewed again thoroughly, including all available biochemical and radiological investigations.

A total of 4 cases with subdural haemorrhage were identified as being hypernatraemic with the first recorded serum sodium. Two cases were excluded, one because following close review of the medical records the initial sodium at the referring hospital was actually normal. The second child was excluded as they were recovering from meningococcal meningitis, a well-documented infective cause of subdural fluid collections.[251]

The 2 cases that did have hypernatraemia at presentation and an associated subdural haemorrhage were both complicated, with other evidence of physical abuse and possible salt poisoning. One of the two cases was fatal.

The case series of salt poisoning assembled for this guideline was reviewed to ascertain the frequency of reported subdural haemorrhage. Forty-one children either had a postmortem in which the pathological findings in the brain were reported, a CT scan (10 children), or both (3 children). The causes of their hypernatraemia were as follows:

- Salt or saline, 36
- Concentrated feeds, 2
- Sodium bicarbonate, 1
- Water deprivation, 1
- Dehydration, 1[4]

Eight children were thought to have been abused, of whom two children[224, 235] were reported to have a subdural haemorrhage. In one child the subdural was thought to be chronic, in the other its age was not recorded. In one further child[1] of the 33 non-abused children the autopsy report stated "fresh blood was noted in the subdural space diffusely with marked subarachnoid haemorrhage and congestion of the dura and pial vessels. There were no bony abnormalities noted." This 2-year-old child died after reportedly being given a saline emetic by a babysitter after accidental pill ingestion.

A second child, born preterm at 33 weeks, presented aged 5 weeks with a sodium of 214 mEq/L associated with a 24 hours history of lethargy, fever, diarrhoea and vomiting.[252] A right tentorial subdural haematoma, cerebral oedema and intraventricular haemorrhage were found on cranial CT scan. A diagnosis of non-accidental injury was considered, but without other skeletal injuries or retinal haemorrhages the authors attributed the findings to hypernatraemic dehydration. Analysis of the premixed infant formula and the intravenous fluids used demonstrated appropriate sodium concentrations. Fractional urinary sodium excretion was not reported, but there appeared to be a high sodium excretion in the first 15 hours. The infant died 12 hours after admission; no postmortem findings were reported. Both peer reviewers agreed on the balance of probability with the authors' conclusion that the hypernatraemia was due to dehydration, with the infant being cared for in a hot room (an error by the parent).

Among the 25 adults with hypernatraemia with similar information about the presence of a subdural haemorrhage, there was one 35 year old woman[253] with the following description: "thin covering of blood over an area measuring 5 x 4 cm on the surface of the right temporal lobe". It is unclear whether this relates to a subdural haemorrhage. She had died within a few hours following the administration of a saline emetic as treatment of an overdose.

In the event, therefore, there are two cases[1, 252] where subdural haemorrhage and hypernatraemia co-exist and there is no other evidence of child abuse. This is not in itself good evidence that subdural haemorrhage can complicate hypernatraemia, but does not allow a causal connection to be ruled out.

[4] The authors' conclusions as to cause were subjected to peer review, see below.

Evidence statement
Subdural haemorrhage occurs only in a small minority of cases of salt poisoning [Grade C].

Evidence statement
Most reported cases of coexisting subdural haemorrhage and hypernatraemia are non-accidental, and in several children the evidence suggests that the subdural haemorrhage preceded deliberate salt poisoning [Grade C].

Evidence statement
The finding of a subdural haemorrhage in association with hypernatraemia should raise the suspicion that the cause may be non-accidental injury [Grade C].

4.5 Characteristics of children with hypernatraemia considered to have been abused

Clinical question

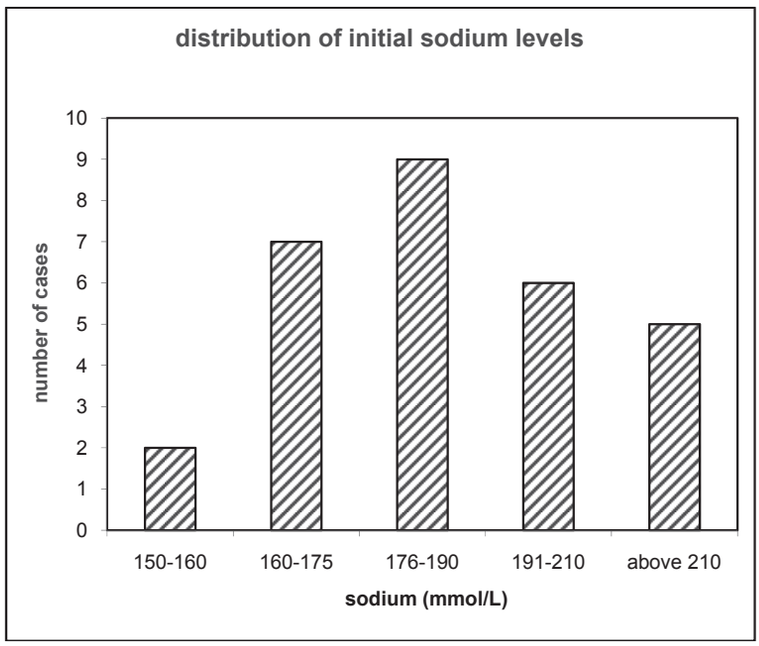
What are the clinical characteristics of children with hypernatraemia reported in the literature in whom child abuse was considered to be the cause?

The 29 children in whom the authors considered that child abuse was the cause[5] had the following clinical characteristics:

Age at first presentation: Mean 3 years 8 months (range 2 months to 7 years 2 months). All but one of the Meadow cases[3] were under 1 year at first presentation.

Sodium at presentation: Mean sodium 196 mmol/L (range 150 to 234 mmol/L). This excludes 5 of Meadow's cases, where the exact sodium was not reported. The distribution including all cases is shown below:

[5] Refs 219, 224, 225, 230-232, 233 (case1), 234-239



Other evidence of child abuse was reported in 11 of 17 children in whom this was ascertainable. This is likely to be subject to publication bias, and the overall proportion with other evidence of abuse is not known.

Meadow[3] described the following presenting symptoms:

- Vomiting (the predominant feature), also present in around half the other cases
- Diarrhoea, also present in 3 other cases
- Failure to thrive
- Drowsiness or coma, also present in 4 other cases
- Rigidity, hyper-reflexia
- Seizures, also present in 6 other cases
- Thirst, also present in 2 other cases

Other descriptions of symptoms include being too weak to stand or walk, irritability, headache, fever, and loss of appetite.

Evidence statement
The common symptoms and signs of deliberate salt poisoning include vomiting, diarrhoea, drowsiness or coma, irritability, seizures, and thirst [Grade C].

Evidence statement
Symptoms do not differ from those seen in accidental poisoning [Grade C].

4.6 Additional causes of hypernatraemia in adults

Clinical question

What additional agents and mechanisms causing hypernatraemia are described in adults?

There are a number of reported cases of deliberate self-harm in adults involving the taking of sodium. These include 2 reports of Soy sauce ingestion[254, 255] two of sodium hypochlorite (bleach), [256, 257] and one of salt.[258] One patient took an overdose of colchicine and induced a temporary diabetes insipidus.[259]

Three adults mistakenly took excessive amounts of salt. Two died as a result. Two had learning difficulties (one aged 41 with Down syndrome[226, 260] and a second aged 45 with Prader-Willi syndrome[261]); the third, aged 85, had dementia.[223]

A 26 year old with learning difficulties died after ingesting flavour intensifier containing sodium chloride and sodium glutamate, apparently in error. His peak sodium was 176 mmol/L.[262]

A 35-year-old fisherman was rescued after spending 11 hours in sea water in a hurricane. He had inadvertently swallowed sea water (with a sodium concentration of between 300 and 500 mmol/L). His initial sodium was 175 mmol/L.[228] He made a full recovery.

There are three case reports of hypernatraemia following exorcism rituals.[227, 263, 264] In each, as part of the ritual, the subject was required to drink large volumes of salt water. Sodium concentrations of 246, 255 and 153 mmol/L were recorded in women aged 36, 20 and 19 years respectively. All three women died (the third woman was said to have died of asphyxia, having been beaten as well).

A 53-year-old man developed hypernatraemia with a sodium of 168 mmol/L 12 days after his ischio-rectal abscess started being irrigated twice daily with Milton as a substitute for Eusol. The Milton contained 780 mmol/L of sodium, and his 24-hour urinary sodium excretion rose to a maximum of over 300 mmol/24 hrs.[265]

There are reports of adults developing hypernatraemia whilst on hyperosmolar feeds. The first[266], in a 59-year-old woman with psychosis who had refused to eat for 8 days, had a sodium of 164 mmol/L after one week of hyperosmolar feeds administered via a nasogastric tube. There was evidence of dehydration. The other reports from the 1950s and

1960s[267-269] described adults with hypernatraemia (sodiums between 160 and 192 mEq/L) following the introduction of high protein tube feeding. The patients had all been unable to swallow for various reasons, and all had evidence of some degree of dehydration.

There are 3 case reports in adults of hypernatraemia developing whilst taking lactulose as a treatment for hepatic encephalopathy.[270-272] Maximum serum sodium concentrations of 175, 169 and 173 mEq/L occurred. All patients had developed severe diarrhoea, and the authors concluded that the mechanism was excess gastrointestinal water loss. A similar mechanism was thought responsible in 3 cases treated for overdose with activated charcoal, in two cases in a 70% sorbitol solution, and in one with magnesium citrate.[273] They all developed diarrhoea and hypernatraemia (sodiums in the range of 160 to over 170 mEq/L).

Intravenous 20% mannitol given to promote a diuresis in a patient with severe liver disease was associated with a diuresis and a maximum serum sodium of 194 mEq/L.[274] The urinary sodium concentration was found to be very low, and the proposed mechanism was therefore excessive renal water loss.

A 70 year old developed hypernatraemia (sodium 167 mEq/L) after 8 days of intravenous 30% urea treatment given postoperatively following craniotomy for a pituitary chromophobe adenoma (partially resected).[275] The patient's recovery after rehydration suggested that the mechanism was an induced renal water diuresis rather than either diabetes insipidus or hypodipsia.

A case report in 2001 suggested that severe hypernatraemia was a side effect of olanzapine given to a 30 year old with schizophrenia.[276] He had been started on olanzapine 10 days before admission with neuroleptic malignant syndrome (NMS: fever, rigidity, confusion, autonomic dysfunction and rhabdomyolysis). His admission serum sodium was 190 mEq/L. He was clinically dehydrated, and the authors ascribed his hypernatraemia to a combination of reduced fluid intake, fever and excessive sweating, as well as a direct consequence of the neuroleptic malignant syndrome. Although there was good evidence of NMS, the inadequate water intake coupled with increased insensible losses could by itself have resulted in the hypernatraemia.

4.7 Excessive sodium administration without hypernatraemia

Clinical question

Can excessive sodium administration present without hypernatraemia?

There are two case reports of increased sodium intake in children without hypernatraemia.

The first was from Great Ormond Street Hospital in 1975.[277] A 3-month-old previously healthy bottle-fed girl developed diarrhoea. "After 3 days the parents sought medical help and were advised to give her clear fluid feeds prepared by adding 5 teaspoons of glucose and 1 saltspoon of salt to 600 ml (20 fl oz) water. Having no saltspoon in the house, they prepared each feed by adding 2 teaspoons of glucose and 5 pinches of salt to 240 ml (8 fl oz) water." The resulting solution contained 117 mEq/L of sodium. The baby took one litre a day of this solution and over 3 days developed swelling of the face, abdomen and legs. Her admission sodium was 144 mEq/L, and her blood pressure was 140/80 mm Hg. Her 24-hour urine sodium excretion was initially 20 mEq (4.5 mEq/kg per day). The peer reviewer with expertise in salt physiology agreed beyond reasonable doubt with the authors' conclusions as to the cause of the oedema and hypertension. The second peer reviewer did not feel able to tell whether they agreed with the authors' conclusions because of the complexity of the biochemical data.

The second case from Columbia, USA, in 1978,[278] concerned a one-month-old boy fed Karo syrup. He had been born at 35 weeks gestation, birth weight 2.3 kilogram. He was admitted with excessive weight gain and oedema over 2 weeks. His admission sodium was 142 mEq/L. The baby's fractional excretion of sodium was 1.5%. There was no mention of blood pressure. A paediatrician had prescribed Karo syrup (concentrated sweetened corn syrup) because of straining with bowel movements. Unfortunately, his parents had misinterpreted the instructions and as a result the infant had received a calculated 5 mEq/kg of sodium per day. One peer reviewer agreed beyond reasonable doubt that this was the cause of the infant's symptoms. The other disagreed beyond reasonable doubt, calculating that a healthy infant should have been able to excrete the relatively small sodium load.

The first case suggests that excessive sodium intake does not invariably cause hypernatraemia.

5. Lethal dose of salt

5.1 What is thought to be a lethal dose of salt?

A number of publications have estimated the likely lethal dose of salt, based on case reports of death following salt ingestion. Most, but not all, reports are of acute ingestion rather than chronic ingestion.

A case report in an adult who drank a known quantity of Shoyu sauce and subsequently died[254] estimated that the dose was 2.5 g/kg body weight. Other estimates in the literature suggest a lethal dose in the range of 0.75 to 3 grams per kilogram body weight.[150, 223, 279]

There are very small numbers of case reports in the literature in which the dose of salt and the child's size are accurately known from the publication. The smallest amount of salt associated with the death of an infant was reported in a German case in 1976[159 (case 2)]. 5 grams of salt were given in error to a 9-week-old baby (this would suggest a dose of around 1 g/kg body weight). A second case was reported from Australia in 1971[180], in which a 22 month infant weighing 12.3 kilogram died after administration of 1 pint of 5% saline as an emetic. The dose of salt was therefore 2.3 g/kg body weight. As some may have been vomited, the amount actually ingested may have been smaller. In the other cases where the dose and child's weight were both known, the quantities of salt were larger relative to their size.

Evidence statement
The minimum amount of salt that could be fatal to an infant or child is likely to be in the range of 0.75 to 3 g/kg (approximately 13 to 51 mmol) body weight [Grade C].

5.2 How is the dose of sodium required to raise the serum sodium by a specified amount calculated?

This question can be critically important in providing courts with information about the likely amount of sodium needed to raise the serum sodium by a specified amount.

Although sodium is principally distributed in the extracellular space, the free movement of water between the intracellular and extracellular spaces means that there is a very rapid shift of water out of the cells to re-establish the osmotic equilibrium. The original basis for this approach is to be found in a seminal paper by Edelman published in 1958.[280] Two

figures from the paper show clearly that there is no significant relationship between the plasma sodium concentration and the ratio of total body water to exchangeable sodium (found mainly in the extracellular fluid) (Fig 5), but a very good relationship between the plasma sodium concentration and the ratio of total body water to the sum of total exchangeable sodium (extracellular fluid) and potassium (intracellular fluid) (Fig 7):

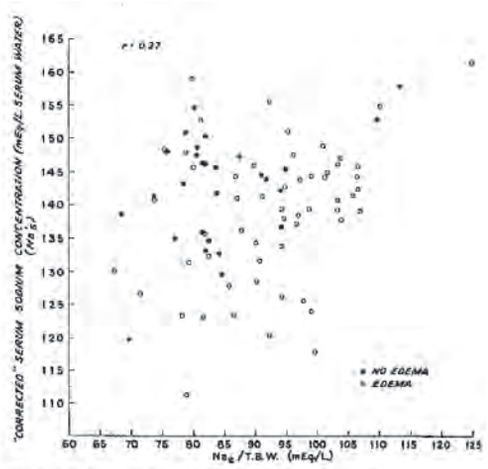


Fig. 5. The Relation Between "Corrected" Serum Sodium Concentration and the Ratio of Total Exchangeable Sodium to Total Body Water

The correlation is quite limited for both edematous and nonedematous patients and a regression equation is not justified.

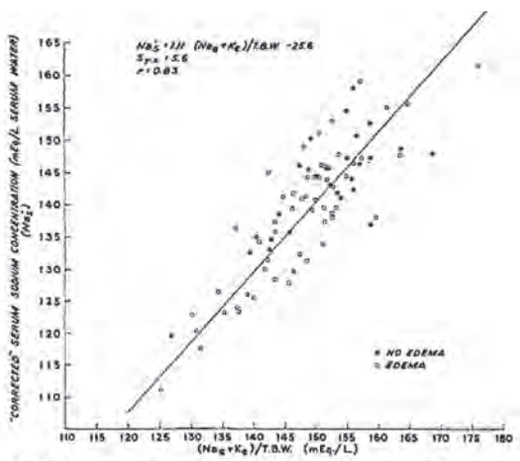


Fig. 7. The Relation Between Serum Sodium Concentration and the Ratio of $(Na_E + K_E)$/Total Body Water

The statistical data were calculated as described in the text. The regression is assumed to be linear. The presence or absence of edema does not appear to affect the regression relation.

Therefore, although administered sodium does not enter cells, any prediction of rise in serum sodium following excessive sodium administration should be calculated on the assumption that it is distributed throughout the total body water.[27]

One gram of salt contains 17 mmol each of sodium and chloride. Total body water amounts to approximately 65% of total body weight in children.[281] The extracellular space is approximately 25% of total body weight.

So taking an example, how much salt would raise the sodium from 140 to 180 mmol/l? Firstly, assume rapid assimilation (e.g. IV infusion) and with no correction for any of the administered sodium that might have been excreted by the time at which the elevated concentration was measured. This would require only 10 mmol sodium (equivalent to 0.59 grams of salt)/kilogram body weight [or 25% of 40 mmol/L] if the extracellular fluid space is taken as the volume of distribution. However, it would require 26 mmol sodium (equivalent to 1.53 grams of salt)/kilogram body weight [or 65% of 40 mmol/L], using total body water, the correct procedure. Roughly speaking this is the difference between 1 teaspoon and 3 teaspoons of salt for a 10 kilogram child.

In fact the amount needed will inevitably be more than this, firstly because some of the administered salt will already have been excreted by the time the initial abnormal measurement is made, and secondly because (if the salt was administered orally) it is almost certain that there will still be unabsorbed salt in the GI tract at the time of the initial measurement. The 1 and 3 teaspoon values actually assume (a) instant total absorption, and (b) no excretion of any of the administered salt at the time of measurement.

A method of calculating the excess salt load required to raise the serum sodium a given amount is as follows:

1. Concentration (mmol/l) = $\frac{\text{Amount (mmol)}}{\text{Volume (litres)}}$
2. The presumed pre-illness total body amount of Na^+ in the child's body is given by:

$$140 = \frac{\text{Amount of } Na^+ \text{ (pre-illness)}}{\text{Volume (0.65 x wt in kilogram)}}$$

$$\therefore \text{ total body } Na^+ \text{ (pre-illness)} = 140 \times (0.65 \times \text{wt})$$

3. The total amount of Na^+ in the child's body at presentation is similarly given by:

$$\text{total body } Na^+ \text{ (at presentation)} = \text{Pres } [Na^+] \times (0.65 \times \text{wt})$$

4. The excess total body Na^+ in mmol is given by

$$\text{Amount (at presentation)} - \text{Amount (pre-illness)}$$

This is divided by 17.1 to give the excess Na^+ in grams (17.1 mmol = 1 gram)

Example

A child presents with a serum $[Na^+]$ of 185mmol/l and a recent wt of 15 kilogram. The child now weighs 14.6 kilogram

1. Previous total body Na^+ = 140 x (0.65 x 15) = 1,365 mmol
2. Presenting total body Na^+ = 185 x (0.65 x 14.6) = 1,756 mmol
3. Excess Na^+ = 390mmol = 22.8 grams

Evidence statement
When calculating the amount of sodium required to raise the serum sodium by a specified amount, the total body water (approximately 65% of the child's weight) should be used to determine the volume of distribution. [Grade D]

5.3 How well known among the public is the lethal dose of salt?

There is no published information on this question. Accordingly, the RCPCH included a question about this in a survey of parents undertaken on behalf of the College by BMRB Omnibus.

BMRB Omnibus conducted face-to-face interviews with a nationally representative sample of 320 adults aged 16 years or over and who are the parent or guardian of a child aged 5 or under, across Great Britain. Their interview included the question:

> *"What do you think is the minimum number of level teaspoons of salt, consumed in one day, that could kill a one year old child?"*

They were given the options of ½, 2, 5, 10 or 20 teaspoons, and also could respond as 'don't know' or 'none of these'. Their answers were analysed by age, sex, social class and geographical region.

An average 1 year old weighs approximately 10 kilograms. From section 5.2, the minimum lethal dose of salt is thought to be between 0.75 and 3 grams of salt per kilogram. This suggests a minimum lethal dose of between 7.5 grams to 30 grams. A level 5mls te aspoon of salt weighs nearly 6grams. Therefore the correct answer is somewhere between 1¼ and 5 level teaspoons.

Responses obtained were as follows:
Half a teaspoon: 30%
2 teaspoons: 29%
5 teaspoons: 19%
10 teaspoons: 6%
20 teaspoons: 2%
don't know: 12%
none of these: 2%

Therefore nearly half (48%) of the respondents gave a correct answer (2 or 5 teaspoons).

Only 8% significantly over-estimated the minimum lethal dose, with a further 12% who responded that they did not know.

30% underestimated the minimum lethal dose (half a teaspoon equates to 0.3 grams per kilogram). This would be an underestimate even for an unusually small 1 year old of 7 kilograms (just under 0.5g/kg).

More women than men and more social grade AB (individuals in the UK aged 16-74 employed in higher and intermediate managerial, administrative and professional occupations) responded that they didn't know. There were no other major differences in responses.

Evidence statement
Most parents would be concerned about the serious risks of giving a dose of salt in the minimum lethal dose range. [Grade C]

6. Tests and investigations

6.1 What key tests will help distinguish excess sodium intake from water depletion?

"The distinction between accidental and non-accidental salt poisoning cannot be made on clinical or physiological grounds, since the end result of both is the same. Only a meticulous evaluation of the history and the attendant circumstances of the case can resolve this… The two conditions that should be distinguishable on clinical and physiological grounds are hypernatraemic dehydration and salt overload (however induced)."[27]

There are several recommendations in earlier sections relating to the initial investigations to be undertaken in children presenting with hypernatraemia where the cause is not certain. The section from which each is copied is included in brackets:

Evidence statement
A sample of gastric contents for analysis of sodium content should be obtained as soon as possible after admission in all children presenting with hypernatraemia of uncertain cause [Grade D]. (section 4.4)

Evidence statement
Careful measurement of weight at the time of admission and before restoration of full hydration provides a reliable estimate of the degree of dehydration [Grade B]. This should be undertaken if possible in children presenting with hypernatraemia of uncertain cause [Grade D]. (section 4.4)

Evidence statement
A urine sample for calculation of fractional urinary sodium excretion (for which plasma and urine sodium and creatinine measurements are required) in the presence of normal renal function should help to ascertain whether the hypernatraemia is secondary to excessive sodium ingestion [Grade D]. Regular urine samples for fractional urinary sodium excretion are recommended in children presenting with hypernatraemia of uncertain cause [Grade D]. (section 4.4)

Evidence statement
In a child with hypernatraemia a urine osmolality can assist in excluding diabetes insipidus [Grade D]. (section 4.1)

Evidence statement
Postmortem vitreous humour sodium and urea provide a useful guide to plasma sodium and urea concentrations before death [Grade C]. (section 4.4)

Evidence statement
Measurement of bicarbonate, calcium and phosphate concentrations in the blood as well as sodium and chloride concentrations should assist in distinguishing the different sodium containing substances [Grade D]. (section 4.2)

6.2 What level of certainty will such tests provide?

6.2.1 Urinary sodium concentration

The urinary sodium concentrations in children presenting with excessive salt intake, identified through the literature search for this guideline, are summarised as follows:

Urinary sodiums were reported in 9 [161, 167 (cases 1,2), 169 (case 1), 230, 231, 233, 234, 244] of 39 reported cases of salt poisoning (in one[234] this was stated to be above 300 mEq/L, and in another [167 (case 2)], the urinary sodium of 107 mEq/L was 24 hours later). The range of urinary sodiums was otherwise between 175 and 374 mEq/L. Meadow[3] reported a range of urinary sodiums in his 12 cases between 150 and 360 mmol/L, "usually… in the range 200-230 mmol/L."

There is a paucity of research evidence on urinary sodium concentrations in children with dehydration.[27] In a series of 10 infants with hypernatraemic dehydration[282] the authors reported a mean urine sodium of 98.5 mmol/L, with a range of 35 to 232 mmol/L. The volume depletion in hypernatraemic dehydration causes renal water conservation with the production of concentrated urine of small volume. The urinary sodium *concentration* is high whilst the urine sodium *excretion rate* is either not raised or low.

Although the urinary sodium concentrations in many of the children following salt poisoning were higher than in those with hypernatraemic dehydration, it is important to stress that a high urinary sodium concentration does not necessarily imply excess sodium intake.

Evidence statement
Measurement of urinary sodium concentration does not reliably distinguish dehydration from excess sodium intake. [Grade C]

6.2.2 Fractional urinary sodium excretion

The fractional urinary sodium excretion (FE Na) is calculated from simultaneous measurement of the blood and urinary sodium and creatinine concentrations[27], using the following formula:

$$\text{FE Na (\%)} = \frac{U_{Na} \times P_{Cr}}{U_{Cr} \times P_{Na}} \times 100$$

Where U_{Na} is urinary sodium, P_{Cr} is plasma creatinine, U_{Cr} is urinary creatinine and P_{Na} is plasma sodium. The units of measurement must be the same for the sodium concentrations (although the conversion factor for sodium between mmol/L and mEq/L is 1) and for the creatinine measurements (to convert from mg/dL to μmol/L, multiply by 88.4). Beware also of differences between laboratory reporting using micromol/L in plasma and mmol/L in urine, which are 1,000 times different: these have to be converted to the same units! The FE Na is a reasonable proxy for the sodium excretion rate.

6.2.2.1 Excessive sodium intake

There are only reports of 3 cases of excessive sodium intake where fractional sodium excretion was either calculated or could be calculated from the information given in the publication. Details of the three cases are given below:

FE Na = 15%[167 (case 1)], aged 20 months, serum sodium 195 mmol/L, salt added to yoghurt. The child received peritoneal dialysis, but details of this were not given.

FE Na = 21% [167 (case 2)], aged 7 months, serum sodium 178 mmol/L, rehydration fluid with excessive salt content. The child received a rehydration solution with 40 mmol/L of sodium.

FE Na = 9.5%[258], adult aged 26, deliberate self-harm, serum sodium 188 mmol/L, ingested salt solution. The patient received fluids containing 5% dextrose and 4 grams per litre of saline.

None of these patients received intravenous 0.9% saline.

6.2.2.2 Healthy children

A Medline literature search (available upon request from the College's Science and Research Department) was conducted to identify any studies of normal values for fractional sodium excretion rates in infants, children or adults; and also of studies reporting fractional sodium excretion rates in children with diarrhoea and dehydration.

There are a small number of case series reporting fractional urinary sodium excretions in normal healthy children, in healthy adults, as well as healthy term and preterm infants. Four studies report normal values in healthy children of different ages. These are summarised below:

	Age	**No.**	**Mean**	**SD**	**Mean + 2 SD**
Rossi [283]	1 to 14 years	50	0.67	0.37	1.41
Rossi [283]	1 to 12 months	8	0.48	0.18	0.85
Assadi [284]	6 to 12 months	8	0.4	0.1	0.6
Kalman [285]	1 to 13 years	21	1.2	0.3	1.8
Agras [286]	0 to 13 years	13	0.78*		1.1^{+}

* median, $^{+}$maximum

The normal ranges vary between the four studies, but numbers are small. In three of the four studies, a group of normal children was investigated for comparison with the subjects of the research.

Four publications report the FE Na in well term infants in the first 4 days after birth, and these are summarised below:

	Postnatal age	**No.**	**Mean**	**SD**	**Mean + 2 SD**
Awad H [287]	1 day	10	1.13	0.98	3.09
	3 days	10	1.48	1.38	4.24
Koo [288]	1st 4 days	6	0.3	0.24	0.78
Aggarwal [289]	2 days	25	1.0	0.7	2.4
	4 days	25	0.9	0.8	2.5
Andronikou [290]	<24 hours	10	0.6	0.3	1.2
	3rd day	10	0.4	0.3	1.0

It can be seen that somewhat higher normal ranges are reported in at least some of the studies. In none does the reported upper limit reach the levels reported in the three cases with excessive sodium intake.

One of the studies[287] was designed to assess the influence of gestational age and postnatal age on urinary sodium excretion, and demonstrated a statistically significant increase in FE Na with increasing prematurity. In preterm infants having serial measurements the FE Na decreased significantly with increasing postnatal age so that by 10 days postnatally the FE Na was less than 1%. A separate study [291] included 20 preterm infants of between 28 and 34 weeks gestation, followed until they reached term. They calculated FE Na values on the 14th day after birth, at 36 weeks corrected age and at term. The upper limits for FE Na (mean + 2 SD) were 1.01, 0.97 and 1.12 respectively.

Three case series in healthy adults demonstrated a normal range for FE Na that was consistent with the results seen in healthy children:

	Age	**No.**	**Mean**	**SD**	**Mean + 2 SD**
Bech [292]	Average 26 years	15	1.40	0.43	2.26
Berdeaux [293]	22-25 years	6	0.82	0.22	1.26
Al-Waili [294]	Average 35 years	7	0.87	0.6	2.07

6.2.2.3 Children with dehydration

A study from Turkey in 1983[295] studied 22 well-nourished infants aged 2 to 13 months presenting with acute diarrhoea, mainly of viral origin. Infants were randomised to receive an oral rehydration solution containing 40 or 90 mmol/L of sodium. From the investigations performed, the urinary fractional sodium excretion (FE Na) was calculated before treatment with the oral rehydration solution, then 18 and 36 hours later. One of the 22 infants had a serum sodium just above 150 mmol/L at presentation, and there were 3 infants with sodium concentrations of 150 mmol/L or above at 18 hours, all receiving the higher sodium rehydration solution. The FE Na results (%) were as follows:

	90 mmol/L ORS (n=12)		40 mmol/L ORS (n=10)	
	Mean +- SD	Mean + 2 SD	Mean +- SD	Mean + 2 SD
Admission	0.13 +- 0.45	1.03	0.04 +- 0.03	0.10
At 18 hours	1.22 +- 1.25	3.72	0.30 +- 0.44	1.18
At 36 hours	1.88 +- 1.07	4.02	0.98 +- 0.89	2.76

The relatively low initial FE Na implies a negative sodium balance before rehydration.

This study is important in the recognition of excessive sodium intake as it is children with hypernatraemic dehydration who are the most likely to be confused with them. However, none of these infants received intravenous 0.9% saline, and the effects of this treatment on the FE Na is unknown.

In conclusion, there are a small number of case series which report normal values for FE Na, and one study from which can be deduced the expected range of FE Na values in young children presenting with gastroenteritis and dehydration.

Evidence statement
In the absence of renal failure, a raised calculated urinary fractional sodium excretion is indicative of increased sodium excretion by the kidneys. The fractional sodium excretion values reported in the 3 severely hypernatraemic individuals were all 9.5% or above, well above the upper reported limits in healthy children and in those presenting with gastroenteritis and dehydration. [Grade D]

Further research into fractional excretion of sodium in normal infants and children and those with other causes of hypernatraemia including hypernatraemic dehydration is needed.

6.2.3 24 hour urinary sodium and chloride excretion

It is often not possible to obtain a 24-hour urine sample started at the time of the presentation with hypernatraemia, and this will be impossible in patients who die soon after admission. However, the following cases demonstrate that urine sample collection is of value even after several days.

One case in which there is information on the urinary volume as well as the urinary sodium concentration was of a 5 week old baby who had seizures and an admission sodium of 211 mmol/L[161]. No peritoneal dialysis was undertaken. His urinary sodium was measured on arrival and then 12 and 20 hours later and on the subsequent 3 days, together with urine outputs in mls/kg/hour at these times. Assuming that these values are representative of the whole 24 hour periods, the following 24 hour urinary sodium outputs were seen:

1st 24 hours: 11.3 mmol/kg
2nd 24 hours: 10.7 mmol/kg
3rd 24 hours: 10.1 mmol/kg

The infant had inadvertently been fed bottles for 72 hours containing 23 grams per litre of sodium chloride. He was said not to have finished his bottles, and it was not possible to calculate his sodium intake before admission.

In a second case, the mother had inadvertently substituted salt for sugar in making up an oral rehydration solution for diarrhoea[169]. The infant's sodium chloride intake was estimated to have been 25 to 30 grams in the 24-hour period up to 12 hours before admission. Treatment included peritoneal dialysis, which would have removed a significant amount of sodium and chloride. The 24-hour urinary sodium losses in the 2 days after admission were 45 and 19 mEq, or 6.3 and 2.7 mEq/kg respectively. The 24-hour urinary chloride losses were 34 and 28 mEq, or 4.7 and 3.9 mEq/L respectively. Serum sodiums were 200 and 160 mEq/L at the start of each of these two days.

A third infant aged 5 weeks in whom salt had inadvertently been substituted for sugar[244] had 24 hour urinary volumes and urinary sodium and chloride concentrations measured up to 8 days after admission. The excessive salt intake was estimated to have been 30 to 40 grams of sodium chloride. No peritoneal dialysis was undertaken. The 24-hour urinary sodiums and chlorides were as follows:

Day 1:	Na^+ 1.6 mEq/kg	Cl^- 1.3 mEq/kg	(serum Na^+ 193, Cl^- 157)
Day 2:	Na^+ 2.4 mEq/kg	Cl^- 2.1 mEq/kg	(serum Na^+ 161, Cl^- 135)
Day 3:	Na^+ 4.1 mEq/kg	Cl^- 3.3 mEq/kg	(serum Na^+ 161, Cl^- 127)
Day 5:	Na^+ 4.5 mEq/kg	Cl^- 3.0 mEq/kg	(serum Na^+ 154, Cl^- 115)
Day 8:	Na^+ 0.9 mEq/kg	Cl^- 0.7 mEq/kg	(serum Na^+ 142, Cl^- 105)

The urea was 48 mg/100ml at 24 hours and fell to 16 mg/100ml by day 8. This case demonstrated delayed urinary excretion of sodium and chloride, and particularly demonstrates the value of continuing to monitor 24-hour urinary output until the serum sodium and chloride normalise.

6.2.3.1 Normal 24 hour urinary sodium

The literature search was also designed to identify any studies of normal values for 24-hour urinary sodium excretion rates in infants, children or adults; and also of studies reporting 24-hour urinary sodium excretion rates in children with diarrhoea and dehydration. References were also searched in the appraised papers for other relevant studies.

A literature search found only a few studies measuring 24-hour urinary sodium in healthy infants and children. Most reported absolute output but not output expressed per body weight.

A study from Southampton[214] used 24-hour urinary sodium excretion as a marker of intake in 28 children aged 3 to 5 years registered with a single general practice. Their sodium intake was also estimated by analysis of 3-day food diaries. The average daily excretion of sodium was 65 mmol, or 3.5 mmol/kg (range 28 to 105 mmol, or 1.6 to 6.2 mmol/kg). Analysis of the food diaries suggested a mean daily sodium intake of 69 mmol (range 32 to 98 mmol).

A second study from London[215] obtained two 24-hour urine samples from 34 children aged 4 to 6 years attending two primary schools. The mean urinary sodium excretion was 64 mmol (range 20.5 to 131 mmol). Neither study calculated fractional sodium excretion rates.

A study from the Netherlands in 1980 investigated the relationship between blood pressure and the concentration of sodium in drinking water.[296] 348 healthy schoolchildren aged between 7 and 11 years of age were studied. Only 24-hour urine samples with a creatinine content of more than 0.16 mmol per kg body weight were analysed, and 14 children were excluded from analysis. 24 hour urinary sodiums were expressed as mmol/24 hours, i.e. not expressed per body weight; unfortunately, the results were expressed as means but it was not stated whether these were accompanied by standard deviations or standard errors. Sodium excretion was found to be slightly higher in children having a lower sodium content in their drinking water. Dividing the mean sodium excretion by the mean weights of the three groups suggested 24-hour urinary sodium excretions of 3.3, 2.8 and 3.1 mmol/kg per day (in the long term low, short term high and long term high drinking water sodium groups respectively).

A further study from the Netherlands[297] found a mean sodium excretion rate of 135.6 mmol/24 hours in 233 healthy children aged between 6 and 17 years. Dividing the mean sodium excretion by the mean weight of the children suggested a mean 24 hour urinary sodium excretion of 2.8 mmol/kg per day.

A cross sectional epidemiological study in Spanish schoolchildren aged 6 to 14 years investigated the relationship between 24 hour urinary excretion and blood pressure.[298] 553 children had a 24-hour urinary sodium measured. This was expressed as mEq/24 hours. Dividing the mean sodium excretion by the mean weight of the children suggested a 24-hour urinary sodium excretion of 3.3 mEq/kg per day.

A second cross sectional study from Spain investigated the relationship between 24 hour urinary excretion and blood pressure.[299] Results were expressed as means and standard deviations. Results were as follows:

Age	Sodium (mean +- SD)	Number	Sex
6-7 yrs	159 +- 30 mmol/day	52	Male
6-7 yrs	142 +- 30 mmol/day	55	Female
10 & 11 yrs	146 +- 34 mmol/day	103	Male
10 & 11 yrs	144 +- 26 mmol/day	90	Female
13-14 yrs	170 +- 40 mmol/day	67	Male
13-14 yrs	162 +- 30 mmol/day	74	Female

Although children were weighed, their sodium excretion rates were not expressed by weight.

A study from 19 centres across 14 European countries[300] on boys of 8 and 9 years of age reported the 24 hour urinary sodium output as means and standard errors of the mean, expressed as mmols per 24 hours. Mean 24 hour urinary sodium excretions from the different centres varied from 91 to 146 mmols. These were not expressed by body weight.

A separate study from Vienna[301] reported on 24 hour urinary sodium excretion rates in 43 boys and 29 girls of 8 and 9 years of age. They found mean 24 hour sodium excretions of 160 and 165 mmols per day respectively and standard deviations of 19 and 18 mmols. They also reported ranges of 65 to 288 mmols in boys and 62 to 291 mmols in girls, demonstrating an enormous variation between apparently healthy individual children.

A study from Chicago[302] included results of the 24 hour urinary sodiums obtained in healthy 11 to 14 year olds from 2 schools. Each individual collected their urine passed on each of 7 consecutive days, and the results presented as means and standard deviations both by day of the week and as overall mean values for the 7 days. The pooled mean 24 hour sodium was 133 mEq/L, with a standard deviation of 43.5 mEq/L. This would not serve as a good reference for normal ranges as it is a pooled result, each child having contributed 7 samples.

A study measuring the daily urinary electrolyte excretion in 74 children aged 5 to 12 years in Ghana presenting for surgery[303] reported a mean 24 hour urinary sodium excretion rate of 4.6 mmol per kilogram body weight/day. Unfortunately

only the mean daily loss was reported. Thirty-nine of these children were studied around 4 to 5 days postoperatively, having mostly had an appendicectomy.

An intervention study in Massachusetts[304] investigated the effects of supplementing the sodium intake of 191 9th to 12th grade girls in two schools (ages likely to be between 14 and 18 years) by 0.8 grams per day (2 grams of salt) for 8 weeks in a blinded randomised trial. Sodium excretion was only expressed as the change from baseline. A study investigating urinary calcium excretion in 89 healthy girls[305] also measured 24 hour urinary sodium. Urinary sodium was expressed as mg/day, but it was not possible to calculate excretion rate per body weight.

Evidence statement
24 hour urinary sodium excretion rates of up to 11 mmol per kilogram per day have been observed in infants with salt poisoning. In view of the small number of cases reported and the absence of published normal values, particularly in infants, a cut off point above which excessive sodium intake can be inferred cannot be given. [Grade D]

Evidence statement
Further research into sodium excretion rates in normal infants and children and those with other causes of hypernatraemia including hypernatraemic dehydration are recommended.

6.2.4 Use of weight change to assess dehydration

The use of weight change has been used as the 'gold standard' in studies assessing the effectiveness of various clinical criteria in determining the degree of dehydration in children with gastroenteritis. Weight after recovery correlates very well with pre-illness weight. Therefore accurate admission and post-recovery weights together provide a reliable method for determining the degree of dehydration in children.[27]

7. Recommendations for further research

Case reports

This guideline has confirmed that case reports are crucial to an appreciation of the range of causes for children presenting with hypernatraemia. As previously stated it is particularly difficult to undertake research into child abuse, and the best available evidence will continue to come from case reports.

When the diagnosis is of non-accidental injury, parental consent for publication is very unlikely to be obtained. A recently published letter[306] highlights the difficulties in getting case reports of factitious illness in children published in UK journals without parental consent. The guideline group recommends that a mechanism for publishing such case reports be established to avoid publication bias whilst maintaining patient confidentiality.

It is equally important to ensure publication of case reports concerning children in whom the diagnosis of salt poisoning was seriously considered but excluded. In particular publication is crucial where otherwise healthy young children were shown to have voluntarily ingested sufficient salt to render them hypernatraemic.

It is recommended that case reports should be prepared with sufficient detail to allow peer review as undertaken for this guideline.

Normal values for fractional excretion of sodium

Although some studies have already been undertaken from which normal values for the fractional excretion of sodium can be extrapolated in children of different ages, the numbers of subjects are still small, and further studies are recommended in normal children.

Further studies of fractional excretion of sodium in children presenting with other causes of hypernatraemia including hypernatraemic dehydration are recommended.

Studies of sodium excretion rates

Further research into sodium excretion rates in normal infants and children and those with other causes of hypernatraemia including hypernatraemic dehydration are recommended.

UK studies of hypernatraemia

It is recommended that studies of the prevalence of hypernatraemia in the UK are undertaken.

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