Hence, it cannot be ruled out that at least part of the analgesic effect was attributable to systemic absorption. However, based on previous studies with systemic administration, one would expect the analgesia obtained by less than 1 g of systemic magnesium to be limited. Therefore, it seems likely that at least a major portion of the action was because of NMDA receptor blockade. Other interactions may play a role.

But whatever the mechanism of the intra-articular effect, and whatever the contribution of a systemically absorbed fraction may be, the authors suggest a simple and practical approach to analgesia after a common, outpatient surgical procedure. In addition, they have added another piece of evidence to a growing body of literature showing that many of the receptors we always thought of as belonging to the CNS are just as active and effective mediators of analgesia in peripheral locations. Further research will be needed to determine the importance of their role as compared with central receptors. If this role is significant (and the present paper suggests it may well be), they may very well become targets for novel approaches to pain therapy.

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Editorial II

Four and a fifth and all that

This issue of the British Journal of Anaesthesia sees the publication of a survey.1 This, in itself, is fairly unusual, as few surveys of clinical practice reach publication. Way and colleagues relate how consultant anaesthetists prescribe perioperative fluids for children undergoing surgery. Whatever the limitations of surveys as scientific enquiry, as a snapshot of present practice, this paper is interesting. For one thing, it would seem to say that, at their own estimation, a quarter of consultants anaesthetizing children do so without having received any particular training for this purpose.

Nearly 50 yr ago, before the word acquired the niceties of present usage, Holliday and Segar came up with guidelines for maintenance fluids for children receiving i.v. therapy. Their figures for the volume of fluid required were derived from consideration of the child’s energy expenditure. The sodium content of the fluid was decided from work which had looked at urinary sodium output in a small number of children fed differing diets (glucose-water, cow’s or human milk).2 With minor modifications, these proposals have been generally accepted in the assonant form of ‘four-two-one of four and a fifth’, that is hourly maintenance requirements of 4 ml kg⁻¹ of fluid per kilogram for the first 10 kg of a child’s weight, 2 ml kg⁻¹ for the next 10 kg and 1 ml kg⁻¹ per kilogram thereafter; the fluid given consisting of 0.18% saline (one-fifth ‘normal’ saline 0.9%) in dextrose 4% solution.

This formula has the considerable merit of being memorable, and, in nearly 50 yr of service, overall it must be judged as having served the majority of children
well; but is it wrong? Or, at least, is it wrongly applied to the perioperative child? Can adherence to this formula produce iatrogenic disaster, death or permanent neurological injury from hyponatraemia?5

Hyponatraemia produces osmotic movement of water across cell membranes from the extracellular to the intracellular compartment. The most important site of the cellular swelling so produced is the brain. Children appear to be more susceptible than adults to the effects of hyponatraemia, and several hypotheses have been put forward to explain this. Young animals have a relatively large brain:intracranial volume ratio; thus, there is a greater increase in intracranial pressure for any given increase in brain volume. In the face of hyponatraemia, postpubertal animals show an adaptive mechanism whereby sodium is extruded from brain cells using a Na+-K+-ATPase mechanism. In prepubertal rats the activity of this enzyme system is much lower,4 so this adaptive mechanism is impaired. Clinically this brain swelling may present as a syndrome of headache, malaise, nausea and decreased level of consciousness, or it may present as seizures or sudden death from brain herniation. Hyponatraemia is formally defined as a serum sodium concentration of <130 mmol litre⁻¹; in children deaths have been reported with sodium concentrations of 128 mmol litre⁻¹.5

Taylor and Durward6 have previously assembled the arguments as to why the Holliday and Segar approach of relating water requirements to energy expenditure (and, via a simplification, to weight) produces a variable overestimate of the volume of water needed for maintenance. Most energy expenditure (80%) occurs in the major metabolic organs (heart, liver, kidney and brain), which account for only 7% of total body mass, so relating increased weight to increased energy expenditure will always produce an overestimate; insensible water losses are probably less than supposed; and relatively inactive and ill children in hospital require less water than their active healthy counterparts from whom figures were first derived.

Over and above these considerations, the most important physiological factor in the development of hyponatraemia in the perioperative child is antidiuretic hormone (ADH). ADH is crucial to the maintenance of osmotic homeostasis, but it is also crucial to the maintenance of blood volume and blood pressure. The litany of the accepted non-osmotic causes of ADH secretion (haemorrhage, relative hypovolaemia, pain, stress, nausea, sleep, morphine, non-steroidal anti-inflammatory drugs) forms a good description of the surgical patient.

The most important pharmacological factor in the development of hyponatraemia in the perioperative child is the formulation of the i.v. fluid that is given. While adults are generally prescribed isotonic solutions (saline 0.9% or Hartmann’s solution), children are prescribed iso-osmolar dextrose–saline, which (as the dextrose is metabolized in vivo) is effectively hypotonic.

Nobody set out to give children hypotonic maintenance fluid because it was hypotonic—it was given and, as this survey shows, continues to be given, because the predicted maintenance requirements of water and sodium are met by this solution. Adding sufficient dextrose to render the solution iso-osmolar allows the solution to be given painlessly into a peripheral vein.

Making a virtue of necessity, this protection against hypoglycaemia has been cited as another reason for using dextrose–saline as maintenance fluid in paediatrics.7 The notion was that, deprived of oral intake by preoperative fasting and lacking the glycogen stores of adults, children were at greater risk of hypoglycaemia. This is no longer thought to be a widespread problem. Neonates in the first 48 h of life, those in whom a glucose infusion has been interrupted,8 or children receiving preoperative total parenteral nutrition (TPN) may require glucose infusions to prevent hypoglycaemia (in which case a dextrose 5% infusion at 4 ml kg⁻¹ h⁻¹ may be insufficient). Such patients aside, children, like adults, generally show an increase in blood glucose levels in the morning, and a stress response to starvation and surgery, which includes hyperglycaemia even when no dextrose containing fluids are given.9 For normal children undergoing surgery, Welborn has suggested using dextrose 2.5% instead on the basis that using this solution produced a consistent increase in blood glucose but without the moderate to marked hyperglycaemia that can be seen when dextrose 5% is given at ‘standard maintenance’ rates.10 A saline 0.45% in dextrose 2.5% solution is commercially available in the UK.

So, ‘four and a fifth’ is more than a little removed from the ideal maintenance solution, yet it continues to be the most widely prescribed fluid in paediatric perioperative practice. What are the alternatives? There are two schools of thought. The first is that we should continue to prescribe dextrose–saline but less of it, while the second is that there should be a wholesale move to the prescription of isotonic maintenance fluids.

The argument for lower-volume but continued hypotonic replacement goes like this: The fluid requirements overall have been overestimated; fluid losses are made up of two components—an electrolyte-free insensible water loss and an electrolyte-containing urinary loss. Losses from both components have been overestimated but it is the renal loss that is affected by the action of ADH; thus, overall less replacement fluid is required but there is a need for some of this replacement to be ‘free water’—hence we should continue to use hypotonic replacement fluids but at volumes of about 60% of current values.11

The main argument against this approach for the paediatric surgical patient is that it presupposes that any hypovolaemia or other ongoing fluid losses are separately accounted for—using colloid or isotonic crystalloid for hypovolaemia and some matched solution as isovolaemic replacement for ongoing losses (e.g. drains or GI tract). This counsel of perfection may, of course, be the case, but if it is...
not then any degree of hypovolaemia is perpetuated. Indeed, the temptation to use one fluid for maintenance, surgical loss replacement and as volume therapy for anaesthetic drug induced hypotension almost certainly explains those reports of death when volumes of hypotonic fluid greatly in excess of the Holliday and Segar formula have been given.

What if children were to be given isotonic maintenance fluid? It is argued that if maintenance fluids were to be given as saline 0.9% at the current recommended volumes then this should remove the danger of hyponatraemia from most patients. It would mean that children would receive a large (5-fold) increase in sodium intake and potentially many more children would develop some degree of hyperchloremic acidosis. Using Hartmann’s solution rather than saline might ameliorate this.12 Either saline 0.9% or Hartmann’s solution could be presented with dextrose solutions in circumstances where hypoglycaemia was perceived to be a potential threat. The electrolyte load could be decreased by giving smaller volumes of isotonic maintenance fluid than currently recommended. The potential problems with such an approach are that it would expand the extracellular compartment in all cases. Applied across the board, this might be very disadvantageous to certain ill children. Also, it gives no free water.

This whole notion that giving isotonic fluids would provide a guarantee against postoperative hyponatraemia has been questioned. It has been demonstrated that women undergoing gynaecological surgery and receiving only near isotonic perioperative fluids show a decrease in their serum sodium concentration in the first 24–36 h after surgery. During this time these patients pass relatively large volumes of urine that is hypertonic to their serum, that is their kidneys generate free water. The explanation of this is thought to be that the expansion of the extracellular compartment by the near isotonic fluid that they receive induces natresis at a time when the raised ADH concentration associated with the perioperative period prevents the kidneys from excreting dilute urine—a process that has been labelled desalination.13

In this position of uncertainty, surely the solution is a trial? Possibly, but there are ethical considerations of monitoring plasma sodium concentrations for a sufficient period in large numbers of fit children, and several leading figures in this field consider that the point of equipoise has been passed.14 If no randomized controlled trial is available, then doctors are left in the familiar position of trying to take the best action in their everyday practice from a position of incomplete information.

More generally, this survey indirectly raises the issue of how anaesthetists continue in their professional education. As we embark on the era of re-accreditation how are developments to be translated into the workplace? This problem of hyponatraemia associated with routine maintenance fluids has been the subject of papers in the general medical and general paediatric journals for more than a decade. It was the ‘Lesson of the week’ in the British Medical Journal in 1999 and 2001.17 18 It has been the subject of an editorial piece in specialist anaesthetic journals19 and it has been raised in the correspondence section of the Bulletin of the Royal College of Anaesthetists.20 In 2002 a ‘newsflash’ on the subject was posted on the website of one Royal College (of Anaesthetists) at the request of another (Paediatrics and Child Health). The recommendations can still be found on the RCA website. If a ‘newsflash’ is only registered by less than half of its intended audience and only influences the actions of one-third of those who do register it then clearly it is ineffective as a means of mass communication. More radical suggestions, such as labelling of bags of dextrose 4%/saline 0.18% as a hypotonic solution, which may produce severe hyponatraemia,21 have not been implemented.

In 2000, a survey by Lobo and colleagues22 showed that, for nearly all adult patients, the prescription of i.v. fluid therapy was the exclusive preserve of the pre-registration house officer—and this was despite the fact that fewer than one in five newly appointed house officers could state how much sodium was present in a litre of ‘four and a fifth’. I.V. fluid therapy has been one of the great advances in medicine in the past century, yet its very ubiquity means that it receives less priority than it deserves. Prescription of type and volume of fluid should be done with the same care and thought as is afforded other drugs and should be given more prominence in medical education. Perhaps we should take heart from the fact that anaesthetic consultants bothered to reply to this present survey at all—the perioperative period may be the only time within a patient’s hospital stay when a senior doctor is involved in the prescription of i.v. fluids, so it is an obvious place for ‘on the job’ education to start.

Later this year, the National Patient Safety Agency will be issuing an alert on the subject of reducing the risk of harm when administering i.v. fluids to children. This will give the consensus view of experts based on the evidence as of December 2005, and so is likely to be very similar to the conclusions of many similar publications of recent years—will its impact be greater? It is difficult to be optimistic.

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