these circumstances results in the excretion of hypertonic urine, the retention of free water, and the development of hyponatraemia.\textsuperscript{1}

Despite clear and repeated warnings over the past few years,\textsuperscript{2,5,6} the routine administration of 4% dextrose/0.18% saline remains standard practice in many paediatric units. This practice is based on formulas developed for calculating maintenance fluid and electrolytes in healthy children over 40 years ago and there seems little understanding of the potential risks associated with their use during acute illness.

A global change of clinical practice is required to prevent these needless deaths. This is a challenge that the RCPCH should face up to, together with the Medicines Control Agency and the National Patient Safety Agency. A useful first step would be to label bags of 4% dextrose/0.18% saline with the warning that severe hyponatraemia may be associated with its use.

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References


Thyroid screening in Down’s syndrome: current patterns in the UK

Children and adults with Down’s syndrome are at increased risk of developing thyroid dysfunction, and screening for thyroid dysfunction is recommended as part of their health surveillance.\textsuperscript{1} Clinical history and examination are known to be unreliable indicators of thyroid dysfunction in Down’s syndrome. Venous blood for thyroid stimulating hormone (TSH) assay remains the gold standard. Capillary blood spot on filter paper

Table 1: Results of completed questionnaires (n=209)

<table>
<thead>
<tr>
<th>Age screening initiated (y)</th>
<th>No. (%)</th>
<th>Screening frequency</th>
<th>No. (%)</th>
<th>Screening method</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>167 (80%)</td>
<td>Yearly</td>
<td>35 (17%)</td>
<td>Venous TSH</td>
<td>174 (83%)</td>
</tr>
<tr>
<td>5–10</td>
<td>28 (13.5%)</td>
<td>Two yearly</td>
<td>113 (55%)</td>
<td>Capillary blood spot TSH</td>
<td>15 (7%)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>13 (6%)</td>
<td>Three yearly</td>
<td>20 (10%)</td>
<td>Both venous and capillary blood spot TSH</td>
<td>4 (2%)</td>
</tr>
<tr>
<td>No data</td>
<td>13 (6%)</td>
<td>Opportunistically</td>
<td>17 (8%)</td>
<td>Clinical history and examination only</td>
<td>3 (1.5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other</td>
<td>10 (4.5%)</td>
<td></td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No data</td>
<td>12 (5.5%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TSH, thyroid stimulating hormone.

Changes in serum sodium levels during treatment of hyperglycaemia

Carlotti et al.\textsuperscript{2,3} state that fluid and electrolyte management might contribute to the development of cerebral oedema in hyperglycaemia. There is a simple rule of thumb, formulated by Katz, which may help calculate water and electrolyte deficits and predict the changes in sodium levels which accompany changes in glucose levels,\textsuperscript{1} namely that a decrease of 0.29 mmol/l in serum sodium may be expected for every 1.0 mmol/l increment in serum glucose.

This may be explained as follows: hyperglycaemia causes an osmotic movement of water out of the cells, which leads to hyponatraemia by dilution. Thus, at presentation, the patient is usually dehydrated intracellularly. However, the serum sodium is lower than would be expected because of this dilution of the extracellular fluid. When the patient is treated with insulin, glucose enters the cells taking water with it, leading to a relative concentration of the extracellular fluid, and thereby a rise in serum sodium. This rise may be predicted and calculated using Katz’s formula.\textsuperscript{1}

Carlotti et al.\textsuperscript{2,3} also comment on the report of Glasier et al. that the chance of cerebral oedema during treatment is increased in children who present with high initial serum urea levels and when there is a lack of an increase in serum sodium levels during treatment.\textsuperscript{1} This increased risk may be explained by the fact that the urea level rises in proportion to the degree of dehydration. Urea contributes to serum osmolality and if the fall in urea is not taken into account the serum osmolality may be allowed to drop too rapidly, thereby increasing the risk of cerebral oedema. Carlotti et al.\textsuperscript{2,3} do not take this into account in their formula for calculation of osmolality. The calculation of serum osmolality as twice the sum of sodium and potassium plus the urea and glucose levels (all in mmol/l) corresponds better with the formally measured osmolality.\textsuperscript{1}

By treating hyperglycaemia using hypotonic solutions or glucose alone, the serum osmolality will fall rapidly and thereby increase the risk of cerebral oedema.

Serum osmolality must be monitored frequently, either by direct measurement or calculation from the sodium, potassium,
glucose, and urea levels. In this way, the effects of falling urea and glucose levels on the serum osmolality will be compensated to a large extent by the accompanying rise in sodium. Thus the osmolality falls slowly and in a controlled fashion at a rate of 1–2 mOsm/kg H2O thereby, reducing the risk of cerebral oedema.

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References

Author’s reply
We thank Dr Oudesluys-Murphy for her letter in response to our article. In essence, two points were made:

1. Can one estimate the deficits of Na+ and water if one applies the formula proposed by Katz? This calculation makes the presumption that one can predict the change in plasma sodium concentration (PNa) when water is drawn out of cells by hyperglycaemia. This assumption is not correct for a number of reasons:
   - Glucose must be added as a pure solute. Glucose will be retained in the ECF compartment (normal 10 L in a 50kg person with 30 L of total body water). With the net retention of 600 mmol of glucose without water in the ECF compartment, the PNa will rise by close to 57 mM if we assume that glucose distribution is only in the ECF compartment because water will shift from cells to the ECF. In more detail, the total number of osmoles in the body was 8550 milliosmoles (2850 × 30 L) before the addition of glucose and 9150 milliosmoles after the addition of glucose (8550 + 600). Therefore the new PNa will be 305 mOsm/kg H2O (9150/30 L). The new ECF volume is equal to the total ECF osmoles (2850 + 600) divided by the new osmolality of 305 mOsm/L or 11.3 L. Therefore 1.3 L of water will be drawn out of cells due to the high PNa. Bottom line: The new PNa is 57.5 mM, the new Pm is 124 mM, and the new ECFV is 11.3 L.
   - Addition of isosmotic glucose (285 mM) to raise the PNa by close to 50 mM with all the same assumptions: No water is drawn out of or enters cells because an iso-osmotic solution of glucose was added to the ECF compartment and all added glucose remains in the ECF compartment. When 2.3 L of this glucose solution is in the ECF compartment, the new PNa is 57 mM, the new Pm is 114 mM because water was retained in the ECF compartment without Na+, and the new ECF volume is 12.3 L. Bottom line: The new PNa is 57 mM, the new Pm is 114 mM, and the new ECFV is 12.3 L. Overall, because the ECF volume was expanded by different amounts in calculations A and B above yet the rise in the Pm was virtually identical, there is no consistent relationship between the PNa and the ECF volume. Moreover, there was no change in the total number of osmoles of Na+ in the ECF compartment in these two examples. In contrast, patients presenting with DKA have a contracted ECF volume and a deficit of Na+ when their PNa is 57 mM. Conclusion: If you do not know what the ECF volume is in quantitative terms, you cannot deduce the ECF Na+ content from the PNa. Accordingly, much as we would like to agree with the suggestion of Dr Oudesluys-Murphy, the facts do not support that view.
   - Potassium: Part of the deficit of K+ reflects the shift of K+ out of cells in a 1:1 relationship with a cation (Na+ or H+) of unpredictable amounts. The other major part of K+ loss from the ICF reflects the catabolic state (primarily a loss of K+ with organic phosphate (e.g. from RNA)). Since both of these components are not known with certainty, one cannot use the relationship described by Katz to help in this context.
   - Error in the assumption of Katz: The volume of distribution of glucose is larger than the ECF volume even if there is a lack of insulin action. Our reasoning is that, in cells that do not require insulin for glucose transport such as liver cells, cells of the proximal convoluted tubule, and red blood cells, the concentration of glucose is likely to be equal in their ICF and ECF compartments.

2. Urea should be included in calculations of effective osmolality. Urea is not an effective osmole across cell membranes when the change in the plasma urea concentration (Purea) is not abrupt. It is important to use the serotype specific assay to get true measure of adequacy of response (Balmer P et al. Measurement and interpretation of pneumococcal IgG levels for clinical management. Clin Exp Immun (submitted)). The study also suggests that there may be a group of children in whom an immune response to Pneumovax is detectable only by the serotype specific assay and who may be labelled as specific antibody deficient by the standard assay.

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References

Assessing immune responses to pneumococcal vaccines
The recent article and letter discussing recommendations for use of heptavalent pneumococcal conjugate vaccine (Prevenar) for at risk children is timely and interesting. We concur with the authors that further immunogenetics studies are necessary in various high risk groups to demonstrate the best protective schedule.

Children older than 2 years with recurrent infections and normal humoral immunity assessed by serum immunoglobulin levels and specific antibody responses to protein antigens, but repeated poor responses (less than 4-fold rise in antibody titers) to 25 valent pneumococcal polysaccharide vaccine (Pneumovax) using standard pneumovax based ELISA are labelled as ‘specific pneumococcal polysaccharide antibody deficiency.’

We looked at the immunogenetics of the heptavalent conjugate pneumococcal vaccine (Prevenar) in five children aged 4–12 years with specific polysaccharide antibody deficiency by the above definition. Blood was collected before and 4 weeks after immunisation with the heptavalent conjugate pneumococcal vaccine. Serum was analysed using the standard ELISA (using Pneumovax as the antigen) and by the newer serotype specific antibody assay.

Results are shown in table 1 and 2. The standard assay showed 4-fold response in only one child. However 5/5 children showed 5-fold responses to at least four of the serotypes using the serotype specific antibody assay.

Protection is assumed at a serotype specific antibody level of 0.2 ug/ml or greater. It is interesting to note that 4 out of 5 children had achieved such protective levels to four or more serotypes after immunisation with pneumovax as suggested by the serotype specific assay on the pre-proven serotypes.

Clinicians may be tempted to use the more easily available standard ELISA to assess responses to the conjugate vaccine in high risk children. These findings suggest that it is important to use the serotype specific assay to get true measure of adequacy of response (Balmer P et al. Measurement and interpretation of pneumococcal IgG levels for clinical management. Clin Exp Immun (submitted)). The study also suggests that there may be a group of children in whom an immune response to Pneumovax is detectable only by the serotype specific assay and who may be labelled as specific antibody deficient by the standard assay.

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Tables 1 and 2 can be viewed on the ADC website (www.archdischild.com/cgi/ eletters/archdischild;88/2/176R432)

References