Hypothermia following fever

A 15 month old child presented to A&E with a temperature of 39.2 °C. On examination she was fully conscious, tachycardic, and tachypnoeic. Examination revealed crepitations at the left base. A chest x-ray confirmed the presence of a left lower lobe pneumonia. She was commenced on intravenous cefuroxime; initial results revealed white cell count 19.1 x 10^9/l (neutrophilia) and C reactive protein 126 mg/l.

On arrival to the ward she was found to be hypothermic (33.6 °C). She had received paracetamol (15 mg/kg) and ibuprofen (5 mg/kg) in A&E. She had not been unduly exposed. This was her first presentation to hospital. In view of hypothermia with obvious sepsis a lumbar puncture was performed to rule out CNS involvement. This was entirely normal. Despite warming techniques she remained cool for the next 11 hours (fig 1).

Prolonged hypothermia provoked investigation of central causation. Thyroid function tests, cortisol, and computed tomography were normal. She recovered from her pneumonia and has been entirely well since.

In view of the temporal link between the antipyretics and the fall in temperature, it seems appropriate to consider causation. Both paracetamol and ibuprofen have previously been linked individually to hypothermia. Logically, giving both together may have a summative effect on decreasing temperature. Currently there seems to be a great hurry to “treat temperatures”, often using high doses of paracetamol combined with ibuprofen to reach the magic 37 °C. However the risks and benefits of fever should be weighed up. Fever induces host defence mechanisms preventing multiplication of organisms, but can also lead to febrile convulsions and increased cardiovascular demands.

Antipyretics are not without their problems and hypothermia may be one of these. Is hypothermia bad for you? Probably not in the short term, but generally we are not trying to induce it.

A recent case also describes hypothermia following a single dose of ibuprofen. This had a duration of four days.1 Ibuprofen has a half life of 2 hours and is unlikely to have such a prolonged effect. Hypothermic sepsis is uncommon in paediatrics but must also be considered in both cases.2 It is important to note that in neither case was a causal organism identified.

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Mosaic Down’s syndrome prevalence in a complete population study

From 1 January 1997 to 31 December 2001 we performed a retrospective observational study on the incidence, accuracy of clinical diagnosis, and prevalence estimation of Down’s syndrome in a well defined population of 1.7 million in Northern Ireland.1 A total of 208 postnatal cases of Down’s syndrome were diagnosed: 197 trisomy (94.7%), 4 translocation (1.4%), and 8 mosaic cases (3.85%) (expected ratios 94% trisomy, 5% translocation, 1% mosaic).1 In a population of 114 307 live births, a minimum prevalence of 167.9 per 100 000 (or in 395 births) was calculated.

The detection rate of mosaic variants is higher than quoted rates of 1–3%. This may be accounted for by inclusion of newly diagnosed adult cases in our study, but mosaic variants often do not have dysmorphic features and may not be identified in studies.

Ninety per cent of trisomy and 100% of translocation cases were diagnosed on clinical features alone, with karyotyping carried out for diagnostic confirmation. This figure fell to 37.5% for mosaic cases (p < 0.001), confirming the difficulties with the clinical diagnosis of mosaic Down’s syndrome, where few classical dysmorphic features are present.

The two mosaic cases diagnosed within seven days of life presented with simian creases, hypotonia, and characteristic facial features including epicanthic folds, upslanting palpebral fissures, and protruding tongue. One patient had a sandal gap.

Three mosaic children were diagnosed after day 7. One clinically felt to be Noonan syndrome was diagnosed at 6 months. Another (diagnosed at 19 months) presented with developmental delay, without dysmorphic features, and the third had a sample sent at 7.5 years, as a check sample and not time of first diagnosis.

Three mosaic patients were diagnosed as adults. One was an inpatient at a regional specialist assessment centre for learning disabilities, and was previously known to have Down’s syndrome. A second presented at 18 years of age and was educationally subnormal with no dysmorphic features. The
It is perhaps time to rethink whether there is any causal link between ASA and Reye syndrome. The relation between declining ASA use and increasing prevalence of allergies should also be more extensively evaluated. Paediatricians may want to consider ASA in place of paracetamol as their first choice antipyretic/analgesic in children, especially for those with a significant family and background history of atopy. If our prescribing habits change, we might yet see a decline in the prevalence of allergic diseases.

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Research, more hassle than it’s worth? A personal viewpoint

The scenario: You want to become an academic paediatrician. You undertake the necessary training and postgraduate examinations, and obtain a National Training Number (NTN). You then obtain a university-funded Clinical Lecturer post, at the end of your Specialist Registrar (SpR) “core training”. Interestingly, there has been a marked 25% reduction in Clinical Lecturer posts in the past five years. Despite the attached clinical commitments, this post would hopefully provide valuable laboratory based research, ultimately leading to a higher degree.

First problem: The post is in a different deanery and does not have an attached NTN. Over 15 months later, 69 extended letters (including multiple copies), and marked “external” pressure from both former and
current deaneries, you eventually manage to transfer to the NTN. The apparent lack of communication between the deaneries, the uncertainty over the NTN transfer, and personal "turmoil" over moving residence and starting in the vastly different world of laboratory science, cause intense personal anxiety. Despite the introduction "Calman" scheme in Paediatrics in 1996 and the potential for inter-deanery transfers, it appears easier to move for personal reasons, such as a partner moving, than for obvious academic reasons.

During the later stages of your research time, you start to fancy a career specialising in paediatric intensive care medicine (PICM). The recent introduction of "grid numbers" within paediatric specialties has enabled trainees to receive regional subspeciality training. This at the cost of alienating SpRs that joined the Calman scheme prior to its inception, who have already undertaken a substantial proportion of their paediatric training. During this "transition" phase, some SpRs wishing to subspecialise face an uncertain future.

Second problem: With the current deanery wishing to recognise "some" of the research time you earn your certificate of completion of specialist training (CCST), you do not have the minimum 24 months necessary to commit to a PICM grid post. You frantically write and speak to everyone involved with PICM training issues locally and nationally, including the Royal College of Paediatrics and Child Health (RCPCH), to resolve the matter. Countless e-mails later, you come to the realisation that you are very much alone in this "fight" to secure an academic subspecialty! The most frustrating aspect is that nobody, including the RCPCH, appears able to support you in your quest to obtain the necessary training, so that as a consultant you have all the necessary skills and experience. An additional problem may be that any clinical experience obtained in the hospital unit may not be recognised by the subspecialty committee to count as recognised training to secure your subspecialty. At the end of the day, the deanery and specifically the post-graduate dean alone, dictates the time available for your training. After approximately eight months of uncertainty, I still await anCCST date. Furthermore, at the prime of my research, I have really questioned the cumbersome bureaucracy that seems to stifle the enthusiasm and aspirations of those who are prepared to make major changes to their own and their family's lives to achieve their career goals.

Despite the Calman reconstruction of the middle grade staff training to "produce a shorter, more structured and organised training pathway", that independent clinical competence as a consultant can be achieved much earlier than in the past in many disciplines? SpR training has not been shortened. Indeed, the average time to complete a five year CCST programme is over six years, with 47% of trainees having their CCST date reviewed. Postgraduate deans are obviously under "pressure" to implement the UK national directive to increase consultant paediatric subspecialty roles substantially over the next 5–10 years, which will require the delivery of suitably trained doctors. The danger is that the system nudges along the less motivated trainees, without necessarily encouraging trainees wishing to "branch out" and pursue interests in their chosen field. One such group that Calman appears to have neglected is academic trainees. The rapid decline in academic trainees and suitable posts in the UK must be of major concern to everyone. Despite this apparent demise, there appears to be genuine interest in undertaking research among paediatric SpRs, even if they do not have the necessary skills, training, or opportunity to undertake this within their Calman training post.

What are the possible solutions? Above all, academic trainees need be encouraged and nurtured. Anyone involved in research will become disillusioned and frustrated at some point, but to face endless bureaucracy and timetraining during registrar training and CCST, is both unnecessary and pointless. In the end, all that will happen is that trainees with real academic promise will be discouraged even before they start. If deaneries are to continue to manage SpRs with subspecialty and/or academic interests, there needs to be closer links with the RCPCH and in particular the relevant College specialty advisory committees. In addition, at a local level, a "mentoring" system for future academic trainees needs to be established, primarily to encourage research ideas and methodology, but also to provide a support network. If training issues are not addressed, the future of subspecialty and academic paediatrics in this country appears bleak.

A closing note, although I know I am not unique in this situation, I really question whether I would have made the same choices, if I knew the obvious limitations of the current training scheme!

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Clinical improvement in cystic fibrosis following anti-tumourous chemotherapy

Clinical improvement in respiratory function in patients with cystic fibrosis (CF) has been reported following treatment with anti-tumourous chemotherapy. It has been suggested that long term upregulation of genes encoding proteins promoting multidrug resistance (MDR), including MDR P glycoprotein, may complement the function of the CFTR protein which is deficient in CF and may be the mechanism by which macrolides exert their effect in CF. Previous reports suggested an increase in MDR following chemotherapy in CF patients and called for more reporting of cases of CF patients undergoing chemotherapy.

We report a case of a male CF patient (homozygous ΔF508), aged 7 years, who underwent chemotherapy for acute myeloid leukaemia. He remained well during the six months of treatment, with no chest exacerbations. After cessation of treatment, nasal potential difference measurements showed a 6 mV response with a low chloride perfusion, unusual in CF, with typical CF baseline and A amiloride readings (~49 mV and 39 mV respectively). No increase in MDR P glycoprotein mRNA was detected from nasal brushings, compared to three other CF subjects. Nine months after chemotherapy, he remained clinically well, with good lung function (FEV1 (96%) and FVC (110%); pretreatment FEV1 and FVC both 60%).

Interpretation of these data is clearly limited by a lack of pre-chemotherapy testing. In order that the potential effect of these drugs can be understood, we suggest a formal protocol for collection of quantitative data from cases of CF patients presenting with malignancies, both before and after the initiation of chemotherapy. In addition to records of clinical status, as performed by previous groups, we recommend: (a) pre-and post-treatment sweat tests (chloride and sodium values); (b) collection of nasal or (opportunistically) bronchial brushings for quantification of MDR P glycoprotein mRNA, by real time RT-PCR; and (c) nasal potential difference measurements. If the role of MDR proteins in mediating this effect is further substantiated in future CF patients receiving chemotherapy, there may be a role for the development of novel drugs which modulate MDR proteins.

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doi: 10.1136/adc.2004.061275

Grant Support: Hazel Painter and Stephen Hyde are supported by the Cystic Fibrosis Trust

www.archdischild.com
Cyclical vomiting syndrome is a disorder of unknown aetiology, characterised by recurrent stereotypic episodes of nausea and vomiting, with full recovery between attacks. \(^1\) The onset may be within the first three years of life,\(^2\) although UK studies have found the average age of onset to be 5.3 years.\(^3\) Childhood co-morbidities include motion sickness, constipation, and abdominal migraine.\(^4\) Exacerbations can be triggered by physical factors (infection, tiredness, pain, exercise, foods) and psychological stresses, both positive and negative. The attacks usually subside in adolescence, at which stage many develop migraine headaches.\(^5\)

Our 7 year old patient first presented with vomiting and constipation at 2 years of age. Over time, he suffered repeated stereotypical episodes. Extensive blood investigations and radiological studies were negative. He was diagnosed with cyclical vomiting syndrome. Attempts to control the frequent attacks were made with anti-emetics, prokinetics, antidepressants, \(\beta\) blockers, \(5HT_1\) antagonists, and anticholinics. None were effective, although sedation with lorazepam during episodes. Extensive blood investigations and radiological studies were negative. He was diagnosed with cyclical vomiting syndrome. Attempts to control the frequent attacks were made with anti-emetics, prokinetics, antidepressants, \(\beta\) blockers, \(5HT_1\) antagonists, and anticholinics. None were effective, although sedation with lorazepam during exacerbations reduced the length of hospitalisation. Since diagnosis, he had been an inpatient on occasions. Notably, recent hospital admissions were of increasing frequency, with incomplete recovery between attacks. At age 6 years, he was empirically started on L-carnitine at 50 mg/kg daily. Pre- and post-treatment carnitine levels were within normal range. Eighteen months later, he had been an inpatient only once with a vomiting episode.

L-carnitine is a naturally synthesised amino acid derivative. It is a co-factor in transporting fatty acids across the mitochondrial cell membrane. Dietary supplementation is indicated in primary carnitine deficiency disorders, haemodialysis patients, and in inherited metabolic conditions with secondary carnitine deficiency such as organic acidemias and fatty acid oxidation defects.\(^6\) The success of L-carnitine prophylaxis in reducing the frequency of attacks in cyclical vomiting was first reported in 2002 by Calcar et al. in a series of six patients.\(^7\)

The trial of carnitine proved to be extremely effective in the management of this child’s condition. Although his blood levels were normal, carnitine dependence may be an important metabolic requirement in cyclical vomiting syndrome patients because of a high metabolic turnover. As far as we are aware, this is the most striking improvement by L-carnitine ever reported in the literature. L-carnitine responsive cyclical vomiting syndrome is a possible subgroup or phenotype in the diagnostic workup of children with this syndrome, and should be considered an early treatment option in children suffering from intractable cyclic vomiting.

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doi: 10.1136/adc.2003.047183

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**Table 1**

<table>
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<th>Number and duration of hospitalisations</th>
<th>1998</th>
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<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
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</thead>
<tbody>
<tr>
<td>No. of hospital admissions</td>
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<td>8</td>
<td>9</td>
<td>15</td>
<td>14</td>
<td>1</td>
<td>0</td>
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<tr>
<td>Average length of stay (days)</td>
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<td>2.75</td>
<td>5.78</td>
<td>4.20</td>
<td>4.28</td>
<td>2.00</td>
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</tbody>
</table>

**Table 2**

<table>
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<tr>
<th>Pre- and post-treatment serum carnitine levels</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total carnitine (normal range 23–60 (\mu)mol/l)</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Free carnitine (normal range 15–53 (\mu)mol/l)</td>
<td>6</td>
<td>39</td>
</tr>
</tbody>
</table>
importantly, the authors reflect on the lack of evidence there is for appropriate systems of care, education) to inform carers of the needs of this expanding population must now be addressed. This interesting report adds to the needs of this group of patients, optimise their care, and share responsibility for the needs of this patient group is also recognised.

One area of particular relevance not only to survivors of childhood cancer but also for other children with chronic diseases and indeed adults who have survived cancer, is the potential difficulties with future employment and life or health insurance. Although there may be differences between the United States and Europe relating to employment insurance, and disability programmes, nonetheless the principles of defending the rights of the patients and the provision of appropriate help and advice with insurance applications applies.

It is time to move forward and to consider the responsibilities of health care providers and others for the needs of cancer survivors. With an estimate of 1 in 810 individuals under 20 and 1 in 640 young adults (aged 20–39) having a history of cancer, the needs of this expanding population must now be addressed. This interesting report adds to that debate although inevitably cannot provide all the answers.

M E M Jenney

Advanced paediatric life support: the practical approach, 3rd edition


The majority of readers of Archives of Disease in Childhood will know this book very well. My task here is not to appraise the content of the eBook, which is the same as the (now famous) paperback, but to test how well it serves its purpose when used in the eBook format, and specifically on a personal digital assistant (PDA).

There are some books that you wish you could have with you at all times. The well known format of the APLS manual is an A4 size book with plenty of free space, large diagrams, and comfortable font size. There was clearly no intention to compromise any of these for the sake of portability; the manual does not aspire to be pocket size. The APLS manual in paper form is published by BMJ Books and luckily this forward thinking publisher has now brought out several of their publications in electronic format. Once you buy the PDA version of the APLS manual it can be used on your PDA as well as on your desktop PC. BMJ Books use Mobipocket Reader for their eBooks. This is a very good choice because Mobipocket is the only one (of the three common PDA friendly formats that support encrypted eBooks) that runs on Palm OS, Pocket PC, Psion, Nokia, and Sony Ericsson P800. The PDA world is still divided into those with palm and those with Windows operating systems and it is important that the book is available for both platforms.

Mobipocket Reader can be downloaded free so you do not need to pay anything more once you have your PDA and have purchased the book from the publisher’s website. As commonly happens with PDA software you are given a full version of Mobipocket for two weeks which afterwards converts into a basic version unless you purchase the full one. Just as the makers of Mobipocket hoped, I became so fond of the features available in the full version that I decided to pay. My reason was the ability to read in horizontal view, an option available on the full version (Mobipocket Pro) only.

As I mentioned earlier the content of the PDA book is the same as the paperback. The only difference I found was a somewhat shorter (but still satisfactory) index. The eBook also contains all the diagrams, tables, and graphs of the paper version. Unfortunately viewing them on the small PDA screen is not easy. You can either view the whole table or diagram on the screen (and it is so small that you cannot see the details) or you can enlarge it and then you will be able to see clearly but only part of it at a time. You can swap between the two views easily by tapping on the magnifying glass icon. To move to the other part of the graph you simply touch the screen and drag in the desired direction. All this works very well but, admittedly, it is not the same as simply viewing the whole picture, and this is perhaps the main inconvenience I experienced reading this book on a PDA.

Using Mobipocket Reader Pro I was able to rewrite the text; this is done using the “Modify” button. Parts of the text can be highlighted, copied, and pasted into other documents. For those who like colouring their books there is a “Highlight” option. In fact one can choose colours of the background, font, and highlights, a function of little practical use but entertaining. You can also add notes (“Annotate”) and create links whereupon a tap on a chosen word will take you automatically to the selected page. This last option is especially useful in the eBook situation where the pages are living beasts. Read horizontally this book has 1367 pages with the smallest font and 5808 with the biggest; in the vertical version these numbers are 1408 and 6099...

The links to the chapters or figures have been adjusted to the new format. This is where the new format is an advantage. To follow “For a more detailed description see chapter 5” one click is enough to open chapter 5. However, links using the paperback page number are redundant. In a chapter about shock, the sentence “A discussion of the relative merits of fluids can be found on page 114” is misleading; going to page 114 you will find a discussion about various types of laryngoscopes! The solution is to annotate. The request I would put forward to the publisher is to readjust these links to suit the digital format.

It is lovely to be able to have the book with me all the time. By nature of its content, it is the type of book that you would always like to remember in detail or have access to. I agree though that here is a comfort (psychological and physical) in opening a large and fully visible paperback when dealing with difficult clinical situations or learning about procedures. Pros and cons considered, if I could only have one I would go for the digital version. Luckily, there is no need to choose between them. I anticipate that both forms will happily coexist, the paperback among emergency treatment guidelines on the ward and the eBook in my pocket.

E Posner

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Aspirin, Reye syndrome, Kawasaki disease, and allergies; a reconsideration of the links

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Arch Dis Child 2004 89: 1178
doi: 10.1136/adc.2004.055681

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