Towards evidence based medicine for paediatricians

Edited by Bob Phillips

In order to give the best care to patients and families, paediatricians need to integrate the highest quality scientific evidence with clinical expertise and the opinions of the family.1 Archimedes seeks to assist practising clinicians by providing “evidence based” answers to common questions which are not at the forefront of research but are at the core of practice.

A word of warning. The topic summaries are not systematic reviews, though they are as exhaustive as a practising clinician can produce. They make no attempt to statistically aggregate the data, nor search the grey, unpublished literature. What Archimedes offers is practical, best evidence based answers to practical, clinical questions.

The format of Archimedes may be familiar. A description of the clinical setting is followed by a structured clinical question. (These aid in focusing the mind, assisting searching2 and gaining answers.) A brief report of the search used follows—this has been performed in a hierarchical way, to search for the best quality evidence to answer the question.3 A table provides a summary of the evidence and key points of the critical appraisal. For further information on critical appraisal, and the measures of effect (such as number needed to treat, NNT), books by Sackett et al and Moyer et al may help.4 To pull the information together, a commentary is provided. But to make it all much more accessible, the clinical bottom line is highlighted.

Readers wishing to submit their own questions—with best evidence answers—are encouraged to read the Instructions for Authors at http://www.archdischild.com

Critical appraisal note: evidence of equivalence versus no evidence of difference

When a randomised study compares two therapies and finds no difference in an important outcome between the two, does this provide evidence of equivalence or merely an absence of evidence of effectiveness? The practical answer requires integration of the study with clinical expertise.

If a dichotomous outcome is present (dead versus not, hospitalised versus sent home) then a variety of measures can be generated. Of these, those which give information of the risk reduction (relative, absolute, or its inverse; the number needed to treat) are useful. With continuous outcome measures, estimates of difference can also be produced, but may be more difficult to interpret. A confidence interval can be produced for each of these measures, within whose limits the true effect is likely to fall. This degree of uncertainty is the first element to be considered in the question. As a rule of thumb, if a study cannot exclude a 20% difference between the treatments, it is probably not evidence of equivalence.

The second element requires knowledge of the disease and outcome. If the outcome is fatal, disfiguring or had serious morbidity, perhaps a greater degree of certainty is required. There is also the rest of the clinical literature on the subject—does this result agree with the general tenor of evidence or does it stick out?

Combining these aspects—precision, importance, and congruence—allows an answer to the question of equivalence versus lack of difference.
Are routine chest x rays helpful in the management of febrile neutropenia?

**Scenario**
A friendly, coryzal 5 year old girl with acute lymphocytic leukemia attends with another episode of febrile neutropenia. According to departmental protocol, her admission includes a chest x ray. You wonder as to the value of this routine irradiation.

**Structured clinical question**
In a 5 year old girl with febrile neutropenia [patient] does routine chest radiography [intervention] assist in management decisions or diagnose occult pneumonia [outcome]?

**Search**
Secondary sources—nil.
SumSearch—“neutropenia” AND “radiography” AND filter “diagnosis”.
Search results—67 individual articles found, three relevant.

**Summary**
See table 1.

**Commentary**
There is no good quality study addressing the use of chest radiographs in uncomplicated febrile neutropenia. Two of these studies are consistent with clinical feeling—lack of abnormal signs or symptoms in children with febrile neutropenia rules out pneumonia. The methodological weaknesses would tend to favour this—with one study having clinical features as part of the reference standard, and the second tending to fail to perform chest radiography on children without symptoms. The third study only gives data on respiratory signs (ignoring symptoms) and has a subsequently reduced sensitivity and improved specificity.

<table>
<thead>
<tr>
<th>Citation</th>
<th>Study group</th>
<th>Study type (level of evidence)</th>
<th>Outcome</th>
<th>Key results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feusner et al (1988)</td>
<td>64 pediatric oncology patients with 134 episodes of febrile neutropenia</td>
<td>Prospective cohort (4)</td>
<td>Prevalence of “infectious” infiltrates</td>
<td>3.0% (95% CI 0.81% to 7.7%)</td>
<td>Diagnostic usefulness of “tachypnoea, chest pain or abnormal auscultation”</td>
</tr>
<tr>
<td>LR+ 82 (95% CI 11 to 575)</td>
<td>LR− 0.0 (95% CI 0.0 to 0.19)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Korones et al (1997)</td>
<td>54 pediatric oncology patients with 108 episodes of febrile neutropenia</td>
<td>Prospective cohort (4)</td>
<td>Prevalence of pneumonia</td>
<td>3.7% (95% CI 0.14% to 7.2%)</td>
<td>Diagnostic usefulness of “abnormal auscultatory findings, RR≥20 when afebrile or O2 sats &lt;95% twice in 4 hours”</td>
</tr>
<tr>
<td>LR+ 17.3 (95% CI 7.9 to 38)</td>
<td>LR− 0 (95% CI 0 to 0.79)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Katz et al (1998)</td>
<td>131 pediatric oncology patients with febrile neutropenia</td>
<td>Prospective cohort (4)</td>
<td>Prevalence of pneumonia</td>
<td>3.1% (95% CI 0.7% to 7.8%)</td>
<td>Diagnostic usefulness of presence of respiratory signs</td>
</tr>
<tr>
<td>LR+ infinite (lower 95% CI 0.00) LR− 0.5 (95% CI 0.25 to 1.0)</td>
<td>Only 128/131 patients received a chest radiograph</td>
<td></td>
<td></td>
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</tbody>
</table>

Does dexamethasone improve blood pressure in hypotensive ill neonates?

**Scenario**
A 25 week gestation baby, birth weight 695 g is ventilated for respiratory distress syndrome. Invasive blood pressure monitoring at 2 hours of age showed a mean of 23–25 mm Hg. The blood pressure did not improve over the next 24 hours, in spite of three intravenous boluses of 0.9% saline and concurrent infusions of dopamine and dobutamine at 15 µg/kg/min. A colleague suggests that dexamethasone might help to improve the baby’s blood pressure.

**Structured clinical question**
In hypotensive preterm infants [patient] does treatment with dexamethasone [intervention] increase blood pressure [outcome]?

**Search**
Secondary sources—nil.
Search strategy—“hypotension” AND “(dexamethasone OR steroid)” AND “newborn” AND “(clinical trial)”.
Search results—three articles found, two relevant.

**Summary**
See table 2.
**Commentary**

The study by Gassmaier and Weston was well constructed in terms of randomisation, blinding, and intention to treat analysis. Dexamethasone administration, after treatment with volume boluses, dopamine, and adrenaline infusion, improved BP such that adrenaline was discontinued in 63% babies (compared with 11% of placebo group).

The paper by Bourchier and Weston supports the idea that bolus steroids are a useful adjunct to conventional treatments for hypotension in sick, ventilated preterm infants. Dopamine and hydrocortisone both appeared to be effective ($p = 0.108$) in the treatment of hypotension refractory to treatment with fluid bolus. However, if five babies received hydrocortisone, one additional baby remained hypotensive, compared with similar babies who received dopamine. Confidence intervals for this NNT are wide (3, 45), suggesting a larger study would show statistical difference at the 5% level.

Dexamethasone appears to be a useful adjunct to the commonly used pathway for treating hypotension in neonates (fluid bolus ± dopamine ± dobutamine).

Although no adverse events related to steroid use are reported in either paper, no long term follow up is reported and caution is warranted as there is emerging evidence of increased risk of cerebral palsy, following postnatal dexamethasone use in babies at risk for chronic lung disease (Shinwell et al, *Arch Dis Child Fetal Neonatal Ed* 2000;83:F177–F181), without improvement in mortality (Halliday and Ehrenkranz. Early postnatal (<96 hours) corticosteroids for preventing chronic lung disease in preterm infants. *Cochrane Database of Systematic Reviews*, Issue 1, 2001).

**Clinical bottom line**

- Dexamethasone improved blood pressure in ill, ventilated neonates.

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**Table 2**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Study group</th>
<th>Study type (level of evidence)</th>
<th>Outcome</th>
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<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gassmaier and Weston</td>
<td>20 preterm babies (mean body wt 690 g), hypotensive in spite of volume support and inotropes</td>
<td>Randomised, double blind, placebo controlled trial (1b)</td>
<td>Discontinuation of adrenaline at 12 hours</td>
<td>Absolute risk reduction (ARR) for withdrawal of adrenaline was 52% and NNT = 2 (95% CI 1 to 8)</td>
<td>All blood pressure readings measured invasively</td>
</tr>
<tr>
<td>Bourchier and Weston</td>
<td>40 hypotensive preterm babies</td>
<td>Randomised, open trial of hydrocortisone v dopamine (1b)</td>
<td>Hypotension despite treatment: dopamine: 0/19; hydrocortisone: 4/21</td>
<td>Absolute risk increase (ARR) was 20% for hydrocortisone and NNH = 5 (95% CI 3 to 45)</td>
<td>Method of BP measurement not stated in this paper</td>
</tr>
</tbody>
</table>

**Does nebulised adrenaline reduce admission rate in bronchiolitis?**

**Scenario**

A 4 month old infant attends the emergency department in the late morning with bronchiolitis. It is the first episode of wheeze. Clinically, there is moderate indrawing and recession, tachypnoea (RR = 50), reasonable air movement on auscultation, and the oxygen saturation is 94% in air. You want to admit the infant, but the mother is breast feeding and keen to get home by 3 pm, when her other children get home from school. You have heard that in North America, nebulised adrenaline has been used in some cases and admission has been avoided.

**Structured clinical question**

In an infant with bronchiolitis [patient] does nebulised adrenaline (compared to other treatments) [intervention] reduce the need for admission [outcome]?  

**Search**

Secondary sources—Cochrane Library (2001): “bronchiolitis”, two systematic reviews (one irrelevant—anticholinergics and wheeze); PubMed clinical queries: “bronchiolitis” AND “epinephrine” [therapy, sensitive]—eight references (three irrelevant to question).
A systematic review that includes adrenaline as one of a number of bronchodilators fails to show significant differences in outcomes compared to placebo. However, adrenaline has an α adrenergic action which is thought to be important in bronchiolitis (as well as the β adrenergic bronchodilatory effects it has). The positive effect of adrenaline may therefore have been diluted in the systematic review by the inclusion of agents that have little or no effect.

The Menon et al study compared adrenaline with salbutamol, which is not routinely used in the UK in this condition. For this reason, data on studies comparing adrenaline to placebo in bronchiolitis are also presented. Studies comparing the two show a benefit of adrenaline over placebo as well as benefit over pure β adrenergic agonists.

It is thought that the α adrenergic properties of adrenaline are important in bronchiolitis, as the vasoconstriction of the pulmonary vessels reduces mucosal oedema and exudate, thereby reducing airway obstruction.

The regime used was 3 ml of 1/1000 adrenaline nebulised at arrival and 30 minutes later. The infants were then observed for at least two hours.

Currently, a multicentre trial in the UK comparing nebulised adrenaline with placebo is under discussion.

### Clinical bottom line
- Nebulised adrenaline probably reduced hospital admission in bronchiolitis
- Nebulised adrenaline appeared superior to salbutamol and placebo in relieving symptoms in bronchiolitis.

### Author
Maud Meates (Consultant Paediatrician, North Middlesex Hospital, London) [mmmeates@doctors.org.uk]

#### Table 3

<table>
<thead>
<tr>
<th>Citation</th>
<th>Study group</th>
<th>Study type (level of evidence)</th>
<th>Outcome</th>
<th>Key results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kellner et al (1996)</td>
<td>Wheeze &lt;24 months. Looking at a range of bronchodilators (incl adrenaline) compared to placebo</td>
<td>Systematic review—most studies double blind RCTs (level 1a)</td>
<td>Clinical score</td>
<td>Slight improvement in bronchodilator group; RR = 0.76 (95% CI 0.6 to 0.99)</td>
<td>May have seen a slight improvement because of inclusion of recurrent wheezers</td>
</tr>
<tr>
<td>Menon et al (1995)</td>
<td>42 first time wheezers less than 12 months. Nebulised adrenaline cf nebulised salbutamol</td>
<td>Double blind RCT (level 1b)</td>
<td>Hospital admission</td>
<td>No difference; RR = 0.85 (95% CI 0.47 to 1.53)</td>
<td>Small study</td>
</tr>
<tr>
<td>Reijonen et al (1995)</td>
<td>100 consecutive wheezers less than 24 months admitted. Compared adrenaline, salbutamol and placebo (N saline)</td>
<td>Double blind RCT (level 1b)</td>
<td>Oxygen saturation</td>
<td>Significantly higher in adrenaline group at 1 h (96% ± 94%)</td>
<td>Included some recurrent wheezers</td>
</tr>
<tr>
<td>Kristiansson et al (1993)</td>
<td>29 infants (&lt;18 months) with acute bronchiolitis. Adrenaline cf placebo</td>
<td>Double blind RCT (level 1b)</td>
<td>Mean symptom score change using the Respiratory Distress Assessment Instrument (RDAI)</td>
<td>Significant difference 33% cf 81% admitted; NNT = 2 (95% CI 1 to 3)</td>
<td>Both groups included recurrent wheezers</td>
</tr>
<tr>
<td>Sanchez et al (1993)</td>
<td>24 infants &lt;1 y, with first episode of bronchiolitis. Adrenaline cf salbutamol</td>
<td>Double blind crossover RCT (level 1b)</td>
<td>Significant improvement with adrenaline</td>
<td>Both groups included recurrent wheezers</td>
<td></td>
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</table>

Mean age 4.6 months (±0.5). Patients sedated with chloral hydrate.

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doi: 10.1136/adc.85.3.252

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These include:

Supplementary Material
Supplementary material can be found at:
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http://adc.bmj.com/content/suppl/2003/02/14/85.3.252.DC1

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**Acrodynia: a case report of two siblings**

Acrodynia, a rare disorder, is a form of chronic mercury poisoning.1 We report two siblings who developed the classic clinical picture of acrodynia.

A 4½ year old boy was admitted with dysuria, general weakness, and loss of appetite. He had hypertension (140/95 mm Hg) and tachycardia (141 beats/min). He was irritable and depressed, and had a diffuse itching papular rash with palmar erythema and superficial desquamation (fig 1). Initial evaluation revealed a normal complete blood count and a normal blood chemistry. Urine analysis and complement levels were normal. Vanillylmandelic acid in a 24 hour urine collection was 22.2 µmol/day. Duplex scan of the renal arteries, abdominal ultrasound, and computed tomography (CT) of the chest and abdomen, were all normal. Heart echocardiography showed mild hypertrophy of the myocardium. TSH was 5.53 mU/L, and free thyroxine 24.45 pmol/L. A brain CT scan revealed a point calcification at the right caudate nucleus and several bilateral areas of low density in the white matter. EEG was normal. A successive complete blood count revealed haemoglobin 165 g/l and haematocrit 48.1%.

After eight days, the patient’s 6 year old brother was admitted with general weakness, pain in his lower extremities, and a diffuse itching papular rash with palmar erythema and superficial desquamation. He was hypertensive (126/87 mm Hg) and tachycardic (140 beats/min).

Due to the fact that both siblings presented, at the same time, with more or less the same complaints and physical findings, it was suspected that their condition may have been the result of an environmental exposure. It was discovered that three months previously, the children had played with a broken sphygmomanometer for a few weeks.

Urinary mercury level for patient 1 was 158 µg/g creatinine and for patient 2, 113 µg/g creatinine. Urine mercury level for patient 1, after a dose of captopril (chelating agent), was 214 µg/g creatinine. Chelation was initiated with dinitrocaptopilliacid for a 19 day course. Two weeks later, symptoms had almost resolved and the rash disappeared. A month later, blood pressure and heart rate had returned to normal.

Torres and colleagues2 published a review of eight cases of acrodynia. In all these cases, and in ours, the physicians first thought of phaeochromocytoma. Mercury inactivates an enzyme that participates in the breakdown of catecholamines, and therefore their concentrations increase, stimulating a phaeochromocytoma like syndrome.

Torres and colleagues3 also reported that in two of the patients reviewed, haemochromatosis was observed, most probably due to intravascular and extracellular volume depletion. This was also found in our patients.

The brain CT findings of low density in the white matter, in patient 1, were not specific. Neurological examination was normal apart from mental changes that are common in acrodynia. To the best of our knowledge, this is the first time that abnormalities in brain CT have been described in acrodynia.

In summary, acrodynia, although rare, should be considered in every child presenting with hypertension, tachycardia, mental changes, and cutaneous manifestations. This case emphasises the fact that good history taking is an essential element in even the most puzzling clinical pictures.

Reference


therapy to be initiated in the early phase of lung hypertension in order to improve prognosis.

P Casano, M Pons Odeno, F J Cambram, J M Martin, A Palomque
Hospital Sant Joan de Déu, Unidad de Cuidados Intensivos Pediatrécicos, Passeig de Sant Joan de Déu, 2 08095, Esplugues de Llobregat, Barcelona, Spain; mponis@hsjcdcn.org

References


BOOK REVIEWS

www.bmjbookshop.com

Management for Child Health Services

Children’s services have increasing priority with the present government in the UK. If we are to use available resources wisely and provide the “seamless service” that children and their parents deserve, then we need good managers to oversee its delivery. Who are these people and where are they found? The editors of this book believe that “all involved in child health care, by definition, involved in its management”—so that none of us is excluded—and that “they should have the benefit of material drawn together specifically for this purpose”—material which they have sought to provide.

For me, much of this book was virgin territory, and I found it a good, readable introduction, and an information resource upon which I will draw in the future. Those with more experience would also find it useful. It is in no way a reference text book, but contributors from child health, legal, and management fields bring their experience together to cover the many different aspects involved in managing a service. Useful references are supplied at the end of each chapter for those who wish to delve further. The first chapter comprises a brief historical review of child health services during the twentieth century, and one realizes the degree of expansion from small and insipid beginnings. Later chapters are devoted to such topics as management skills, models of service quality, audit, finance, risk control, and management. Issues around the partnership of care with parents and carers are explored, and interagency working—never easy to carry out in practice—forms the basis of another chapter. It is particularly interesting and informative chapter was written as a case study of the establishment and running of an integrated secondary level child health service. Another chapter, which was perhaps a little easier reading, discussed legal and ethical principles relevant to child health using a hypothetical, if perhaps slightly artificial, family case history of a baby born with significant disability to a single mother who is also facing adolescent health issues in her teenage daughter. The final section is devoted to the services in the four countries comprising the UK, each with unique values and approaches, although built upon a common base.

As child health services and service plans continue to evolve, there is much we can learn from the experience of those who have been involved in establishing our present services—we must avoid their pitfalls and follow their successes. The book was written before the most recent service changes involving the establishment of Primary Care Trusts, and one can only speculate ultimately judged that a revised version will contain after “the next 10 years”. Will we, the present day paediatricians, leave a similar legacy for our successors?

R J Jefferson

Sudden infant death syndrome: problems, progress and possibilities

An internationally recognised disease classification, sudden infant death syndrome (SIDS) is unique in that the diagnosis is reached by exclusion, by failing to demonstrate an adequate cause of death. By definition it is imprecise, the diagnosis of SIDS depends on the thoroughness of the post-mortem examination, the extent of detail given in the clinical history and the meticulous nature with which the death scene investigation is carried out. Even if these conditions are satisfied to some chosen specification, this is not an endpoint but a rather a beginning, as we are still left with the question of “why did these babies die?”

The tragedy of SIDS is not a modern phenomenon. As child health services and service plans continue to evolve, there is much we can learn from the experience of those who have been involved in establishing our present services—we must avoid their pitfalls and follow their successes. The book was written before the most recent service changes involving the establishment of Primary Care Trusts, and one can only speculate ultimately judged that a revised version will contain after “the next 10 years”. Will we, the present day paediatricians, leave a similar legacy for our successors?

R J Jefferson


Coming back to the new edition of this book is like coming back to an old friend. Like many paediatricians, I have used the first edition as a valuable reference in child protection cases. The expertise and experience of all three authors are well recognised internationally and there is no doubt that this edition will continue to be a valuable aid to all clinicians working with children.

All aspects of abuse are covered and there are helpful summaries in each chapter. It is an easy book to read but also I find it easy to get information on individual issues in child protection. There is an interesting historical introduction: although I would have liked rather more before modern times.

The problem I find with this book is that it is not really evidence based in a modern sense. Papers are quoted with no real attempt to assess their quality. This is partially because there are so few quantitative studies in child protection but I think readers would have liked to have more descriptions on the quality of the methodology of the papers that are quoted. I would have liked the references tabulated in each area of abuse. There are also concerns regarding the section on epidemiology of child abuse. The histogram that is used as an illustration does not give incidence rates nor is it population based.

I particularly studied areas in the book that I know cause diagnostic difficulty and where there is controversy. One of these is subdural haemorrhage. I was disappointed that the section was quite short: only four pages. I was also disappointed at the number of references, only 14, in what is the most common cause of serious physical harm in physical child abuse.

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I find that neglect and emotional abuse are areas where it is difficult to put facts together for a clear diagnosis. The section on neglect has a helpful list of points to look for in the potentially neglected child and also ways of assessing the whole family. I found the section on emotional abuse less helpful.

Child protection is a very difficult area for clinicians and many shy away from committing themselves to clear diagnoses. This new edition will help give more confidence in dealing with these difficult cases. It is a pity that at nearly £70 it will not be accessible to young doctors outside libraries. Perhaps fewer photographs and being in paperback would make it less expensive and more accessible.

J R Sibert

Mosby’s atlas and text of pediatrics and child health


I enjoyed reviewing this book aimed at students and doctors in training, and I also learned from it. I must add that it is a good source of information for doctors who are preparing for examinations.

The book gives useful information, is highly illustrated and the format with text boxes and lists levels itself for easy reading and reference (revision for examinations).

The photographs are well placed with the text and with excellent explanations, which accompany the photographs, x rays, and scans. The quality of the photographs are superb too, thus the clinical phenotypes, which the authors want to illustrate are clearly visible. I found the book easy to read and understand.

I am sure that this book will prove very useful and will fill the gap in the market, as it will attract those adult learners who learn visually. It lends itself for scan reading for revision.

I teach examination preparation courses and I will bring this book to the attention of candidates sitting the DCH and MRCPCH exams. I would think that the GP tutors who come across this book would find it helpful in their teaching too. Many of the illustrations and slides will enhance anyone’s teaching methods.

More books like this are needed in paediatrics and child health as the pictures and illustrations that the doctors see will enhance their learning (and retention) skills. With problem orientated teaching (and learning) that we now practise, this type of book and presentations would be a most welcome addition. The market is not saturated, and I hope it will never be.

S Lingam

CORRECTION

Unfortunately the authors for the items in the Archimedes articles for September and November 2001 were not correctly coded and do not show up using searches on ADC Online or Medline. The authors for these articles should be cited as follows:

September


November

