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. 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. They are based on an original format from the Journal of Accident and Emergency Medicine.

A word of warning. These best evidence topic summaries (BETs) 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 They make no attempt to statistically aggregate the data, nor search the grey, unpublished literature.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 are practical, best evidence based answers to practical, clinical questions.

Each topic follows the same format. A description of the clinical setting is followed by a structured clinical question. (These aid in focusing the mind, assisting searching, 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. 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 and Moyer may help. A commentary is provided to pull the information together, and for accessibility, a box provides the clinical bottom lines.

Readers wishing to submit their own questions—with best evidence answers—are encouraged to read the Instructions for Authors at http://archdischild.com. Three topics are covered in this issue of the journal.

- Is silver nitrate the best agent for management of umbilical granulomas?
- Does adding ipratropium to salbutamol help children with asthma?
- Should tympanic temperature measurement be trusted?

Concealed, blinded, or masked?

In the anatomy of randomised controlled trials, the words blinding, masking, and concealment are commonly used. They are commonly misunderstood—and this has important consequences.

Blinding (or masking) is the process of obscuring to patient, observer, or both the treatment to which they are allocated. It relies on two therapies having no clearly discernible effects to “unmask” the allocation. Some of these may be thought about prior to the trial (such as the bradycardia of β blockers) but some are more surprising to investigators (during an early trial of HIV therapy, participants in the trial found half the capsules floated, half sank).

Concealment refers to the security of the randomisation list. Before a patient is offered a place on a trial, there should be no way of the investigator knowing which treatment the patient will receive. A trial may be well concealed, although impossible to blind, for example, Hi-Fi trial.

WHY BOTHER?

Schulz' looked at factors which appeared to affect the results of studies of therapy. Those trials which gave the most exaggerated effects had no allocation concealment. The factor of blinding had a less dramatic effect.

5 http://cebm.jr2.ox.ac.uk/docs/levels.htm
Is silver nitrate the best agent for management of umbilical granulomas?

Scenario
A mother brings her 2 week old baby to your clinic. The child has a small umbilical granuloma but is otherwise well. Should you use silver nitrate to cauterise the granuloma?

Structured clinical question
In a well, 2 week old neonate with an umbilical granuloma [patient], is silver nitrate cauterisation preferable to conservative treatment [intervention] in order to facilitate safe resolution of the granuloma [outcome]?

Search strategy and outcome
Secondary searches—Cochrane, Clinical evidence—none.
1. Silver nitrate.tw
2. Clinical trial limit, 1+2 found: 36 papers, of which none were relevant.
3. Umbilic$.tw , 1+3 found: 10 papers, 1 highlighting complications, 1 was a comment on this paper, 1 discussing the use of salt; 7 were irrelevant.

Summary
See table 1.

Commentary
The above papers suggest umbilical granulomas may be self limiting and resolve with conservative management such as the application of salt. They also suggest that application of silver nitrate is not without risk.

Anecdotal evidence suggests that cleaning with Steret alcoholic wipes may be as effective as salt. If they are used, they should be applied at each nappy change. It may also be beneficial to fold the front of the nappy to expose the umbilicus.

No randomised controlled trials have been performed to investigate whether conservative management is as effective as silver nitrate. A randomised controlled trial to investigate this is being planned.

Author
Justin Daniels (Paediatric Registrar, North Middlesex Hospital) [justin.daniels@virgin.net]

Clinical bottom line
- Silver nitrate may be dangerous—it can cause burns
- Conservative management involving salt may be just as successful


Table 1

<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>Kesaree et al (1983)</td>
<td>&gt;100 babies with umbilical granuloma, all treated with salt</td>
<td>Prospective cohort (level 2b)</td>
<td>Resolution of umbilical granuloma</td>
<td>100% clearance of granuloma (95% CI 96.38% to 100%)</td>
<td>Used salt crystals held in place with a swab for 5–10 minutes</td>
</tr>
<tr>
<td>Chamberlain et al</td>
<td>3 infants treated with silver nitrate for an umbilical granuloma</td>
<td>Case study (level 4)</td>
<td>Adverse effects</td>
<td>Silver nitrate caused chemical burns to periumbilical area, causing a visit to an emergency department</td>
<td>No denominator</td>
</tr>
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Does adding ipratropium to salbutamol (albuterol) help children with asthma?

Scenario
A 9 year old girl attended her general practitioner with a moderate to severe exacerbation of asthma. Initial treatment included nebulised salbutamol (albuterol) and oral steroids. She was admitted to hospital, and treated with salbutamol, ipratropium, and oxygen. In the morning, a consultant comments “Ipratropium? I’ve always found that doesn’t work.”

Structured clinical question
In a 9 year old child with moderate to severe exacerbation of asthma [patient], does ipratropium and salbutamol (albuterol) [intervention] compared with salbutamol alone [comparison] improve clinical outcomes (admission rates, relapse, etc) [outcome]?

Search strategy and outcome
Secondary sources—Cochrane review—1 relevant.

Search results—36 original articles, 1 relevant and not in Cochrane review.

Summary
See table 2.

Commentary
Pooling of studies in the systematic review has shown a significant reduction in hospitalisation rates for children with severe acute asthma treated with ipratropium added to β2 agonists in a protocol of multiple fixed doses. Insufficient data exists on the effects of ipratropium in more flexible multiple dose regimes, which may more closely resemble the actual treatment of children with acute asthma.

The recent study by Craven et al confirms this trend of shorter hospitalisation, but with insufficient numbers of severe asthma sufferers to show statistical significance. Importantly only 43% of eligible children entered this study, creating a possible selection bias.
In mild and moderate acute asthma, ipratropium has not been shown to significantly improve outcome in terms of hospitalisation rates or length of stay, or clinical care path progression rate.

Authors
Neil Patel (Senior House Officer in Paediatrics, Royal Hospital for Sick Children, Glasgow) [neil.patel50@hotmail.com]
Bob Phillips (Associate Fellow, Centre for Evidence-based Medicine, Oxford)

Table 2

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<tr>
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</tr>
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<tbody>
<tr>
<td>Plotnick and Ducharme (2000)</td>
<td>Systematic review of 13 randomised controlled trials of ipratropium added to β2 agonists in acute childhood asthma</td>
<td>Systematic review (level 1a)</td>
<td>Hospital admission for additional bronchodilators, lung function (% change in FEV1, from predicted or baseline)</td>
<td>All severities of asthma: 25% reduction, odds ratio 0.75 (95% CI: 0.62 to 0.89) NNT = 12 Severe asthma only: OR 0.71 (95% CI 0.58 to 0.89) NNT = 7 OR = 0.81 (95% CI: 0.66 to 0.99) 9.68% (95% CI: 5.70 to 13.68)</td>
<td>Reduction in hospital admission rate for children receiving multiple doses in fixed protocol. Significant reduction only seen for subgroup with “severe” asthma at presentation. Reduced need for additional bronchodilators significant only for children receiving ipratropium and β2 agonist in multiple dose protocols</td>
</tr>
<tr>
<td>Craven et al (2001)</td>
<td>210 children aged 1–18 years, with acute exacerbations of asthma (104 received ipratropium, 106 in control group)</td>
<td>Randomised controlled trial (level 1b)</td>
<td>Length of hospital stay (hours) Time taken to proceed through four stages of an asthma care plan</td>
<td>No significant difference between treatment and control groups (p = 0.46) No significant difference between treatment and control groups (p = 0.37)</td>
<td>In subgroup of 35 children over 6 years old there was a trend towards shorter hospital stay, but this was not significant</td>
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Table 3

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<tr>
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<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duce (1990)</td>
<td>20 relevant research studies</td>
<td>Systematic review (level 1a)</td>
<td>Evaluation of infrared tympanic thermometry with an 8mm probe</td>
<td>Tympanic thermometry was found to be an inaccurate, inconsistent, and insensitive method of core temperature measurement in neonates, infants, and children</td>
<td>Narrative review</td>
</tr>
<tr>
<td>Lanham et al (1999)</td>
<td>241 sets of temperature measurements from 178 paediatric patients (mean age 18.6 months)</td>
<td>Prospective cohort (level 4)</td>
<td>Rectal temperature of 38°C compared to tympanic temperature</td>
<td>Mean difference between rectal and tympanic measurements was −0.6°C Tympanic &gt;37.4°C Sens 80% Spec 85% LR+ 5.3 LR− 0.23 PPV 87% NPPV 85%</td>
<td>Age and presence of fever significantly affected the rectal-tympanic difference, which suggests that the tympanic method may not accurately measure temperature in younger, febrile children</td>
</tr>
<tr>
<td>Wilshaw et al (1999)</td>
<td>120 infants, 59 with and 61 without fever</td>
<td>Case-control (level 4)</td>
<td>Rectal temperature of 38°C compared to tympanic temperature</td>
<td>Mean difference between rectal and tympanic measurements was 0.05°C Tympanic &gt;38°C Sens 100% Spec 58% LR+ 2.4 LR− 0</td>
<td>Relation between tympanic and rectal measurements was affected by age and sex</td>
</tr>
</tbody>
</table>

Clinical bottom line
- In children with severe acute asthma, addition of ipratropium bromide to a multiple dosing regime of β2 agonists leads to a reduction in hospital admission rates (number needed to treat = 7, to prevent 1 admission), and a reduction in the need for additional doses of inhaled bronchodilator
- In children with mild or moderate acute asthma, no significant benefit of ipratropium bromide has been shown
- Single doses of ipratropium bromide do not significantly affect hospital admission rates, or the need for additional bronchodilators

Should tympanic temperature measurement be trusted?
Scenario
A 5 month old boy attends the emergency department with a history of fever given by his mother. His temperature as taken with a tympanic thermometer is 37.5°C. He says he is hot to the touch. He has no focus for his fever on examination. The departmental protocol recommends a full septic screen in this age group if the temperature is above 38°C. You would like to know how accurate temperatures taken by this method are, and whether you should check the temperature using another method.

Structured clinical question
In a 5 month old boy with a fever [patient], how accurate is tympanic thermometry [diagnosis] as a measure of core body temperature [outcome]?
Search strategy and outcome
Secondary sources—0.
Systematic reviews—1.
Original research—SumSearch “temperature measurement”, “child”, “fever” AND filter “diagnosis”—57 individual articles, 2 directly relevant.

Summary
See table 3.

Commentary
The systematic review reported 44 studies addressing the use of different methods of temperature measurement including, axillary, sublingual, tympanic, and rectal. Two further studies directly addressed the question of how representative tympanic measurements are of core temperature measurement. Both studies showed a correlation between tympanic and rectal methods of temperature measurement, although it was not strong enough to use as a basis to make decisions regarding clinical management.

A problem of information
A general practitioner in Scotland (John S Millar. British Journal of General Practice 2001;51:570) has told a story which will attract widespread sympathy and cries of “Well, you can’t win, can you?”

A man with a chest infection was given a prescription for erythromycin capsules. He pointed out that he had a history of allergy to aspirin and was told that the capsules were safe in that there was no cross-sensitivity between aspirin and erythromycin. Soon after taking the capsules, however, he developed tingling and swelling of his fingers and feet, the same symptoms he had had with aspirin. On reading the patient information leaflet included with the erythromycin capsules the patient’s wife discovered a warning to the effect that the capsules contained the colouring agent E110 which could cause allergic reactions, particularly in people allergic to aspirin. Despite the general practitioner’s attempts at mollification a formal complaint ensued.

The general practitioner points out that it is difficult for doctors to gain access to the information given in the patient information leaflet since standard sources such as the British National Formulary or the Pharmaceutical Data Sheet Compendium do not mention the problem of E110 in the erythromycin capsules and allergy to aspirin. The information provided about excipients in standard professional sources and patient information sheets is often incomplete. For instance, although the data sheet accompanying the erythromycin capsules warned about E110 it did not warn about another excipient, E104, which is known to cause urticaria in some people. There are nearly 200 licensed medicines containing E110 and, to date, the Committee on Safety of Medicines and the Medicines Control Agency have received some 20 reports of suspected adverse reactions to it. Where the information about cross-sensitivity with aspirin comes from is not stated.

It is clearly impossible for doctors to keep up with all this information in printed form; presumably the answer lies with the computer and in making sure that all relevant information is made available.

Authors
Anna Riddell (Research Registrar, Oxford Vaccine Group) [anna.riddell@paediatrics.ox.ac.uk]
Walter Eppich (Resident in Pediatrics, Duke University Medical Center)

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/L. A brain CT scan revealed a point calcification at the right caudate nucleus and a normal blood chemistry. The editors will decide, as before, whether to also publish it in a future paper issue.

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 an environmental exposure. It was discovered that three months previously, the children had played with a broken sphygmomanometer for a few weeks.

Urine 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 dimercaptosuccinic acid 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 reported that in two of the patients reviewed, haemocencentration was observed, most probably due to intravascular and extracellular volume depletion. This was also found in our patients.

The patient was admitted and treated with oxygen and erythromycin. After 12 hours she developed respiratory failure (respiratory rate 100 breaths/min, pH 7.16, pCO2 74 mm Hg, pO2 57 mm Hg, HCO3 26, base excess −5) and was transferred to the paediatric intensive care unit with intubation and pressure control (peak inspiratory pressure 22, peak end expiratory pressure 3, FiO2 0.35, respiratory rate 40). Twenty hours later, hypoxaemia necessitated increasing FiO2 to 1, and refractory hypotension required volume load and inotropes (TAM 38). Echocardiography diagnosed severe lung hypertension (pulmonary artery pressure 65 mm Hg), and decreased heart contractility. Nitric oxide 8 ppm and milrinone 0.37 µg/kg/min temporarily improved pO2, but this subsequently deteriorated (pO2 40 mm Hg). High frequency ventilation was initiated; nitric oxide up to 20 ppm was given, and inotropic support enhanced, but with no response. She suffered a fatal cardiac arrest 98 hours later. The family did not authorise necropsy.

Bordetella pertussis infection causing pulmonary hypertension

In Spain the incidence of whooping cough is less than five cases per 100 000 inhabitants.1 Mortality rate is 0.4% in the United States, heart failure being one of the most frequent causes.3 Although cases of death due to Bordetella pertussis infection as a consequence of lung hypertension have been described previously,4 this complication is not very well known. Here we report a recent case and review the literature.

A 23 day old girl, who had had a pertussis cough for several days, was admitted with breathing difficulty of 12 hours duration. On admission she had tachycardia (heart rate 180 beats/min), tachypnoea (70 breaths/min), pyrexia (38°C), and haemoglobin saturation 90% without oxygen. A chest x ray revealed right superior and half lobe infiltrates. Blood analysis showed 33 x 10⁹ leucocytes with left deviation and 33 mg/dl C reactive protein. Testing for respiratory syncitial virus was negative, direct immunofluorescence and culture for Bordetella pertussis were both positive.

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Fatal myocardial failure secondary to lung hypertension has been reported in four infants under 2 months with verified B pertussis infection.5 All presented with initial tachycardia (160—230 beats/min) refractory to treatment with volume load, and developed posterior persistent hypertension that did not respond to inotropic support.

Lung vasodilators such as nitric oxide, milrinone, or prostacycline may be useful in management of these patients, although they did not prove beneficial in our patient.

Because of the rapid deterioration of all these cases, we recommend early echocardiography diagnosis, enabling vasodilator

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

P Casano, M Pons Odena, F J Cambra, J M Martin, A Palomque
Hospital Sant Joan de Déu, Unidad de Cuidados Intensivos Pediátricos, Passeig de Sant Joan de Déu, 2 08015, Esplugues de Llobregat, Barcelona, Spain; mpions@hsjdcn.org

References


Sudden infant death syndrome: problems, progress and possibilities


As 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 but was only christened a syndrome 40 years ago and, after extensive research, the possibility of finding a collection of symptoms and signsmanifesting as a single cause appears extremely unlikely. Some experts suggest a triple risk causal mechanism for SIDS involving a vulnerable infant, a critical development period and an exogenous event that would not normally put a healthy child at risk. A particular, frustrated, with what they see as a definition of convenience, want to restrict the liberal use of such a diagnosis to exclude suspected cases of accidental suffocation and infanticide. Hypotheses continue to proliferate and, as the evidence for risk factors mount, the debate has widened from causation to the relative safety of accepted infant care practices.

In trying to understand how infants die, we have come to the realisation that we must first understand how infants survive. SIDS research has developed from basic epidemiological and pathological findings at death to a wider investigation of infant sleep structure, care practices, physiology, and genetics. This multidisciplinary approach is elegant illustrated in Byard and Krous's book. The eclectic choice of contributing experts gives a clear insight into current thinking and recent discoveries in different fields, while challenging the reader with a subtle consensus of disagreement. The book gives detailed background of each debate but is more than a reference manual for other researchers in the field. Given the rarity of SIDS, many medical professionals may not have had the experience of working with the sudden death of a child but will have to deal with mothers concerned about child safety, while some parents are reticent to accept advice unless they know how this has been derived, this book is also for them.

If there appears to be a lack of co-ordination in the approach among different research areas, a slightly over zealous interpretation of findings by some experts and perhaps more information than clarity in the overall picture. Then this book has given a true reflection of SIDS research as it currently stands. There is no ending to the story because infants still die suddenly and unexpectedly, but if SIDS research is to be ultimately judged on the number of young lives so far saved then the endeavours of those involved should be highly commended.

P S Blair


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 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.
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

