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. In doing this, we are adapting a format which has been successfully developed by Kevin Macaway-Jones and the group at the Emergency Medicine Journal—"BestBets".

A word of warning. The topic summaries are not systematic reviews, through 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 They make no attempt to statistically aggregate the data, nor search the grey, unpublished literature.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.

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 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. To pull the information together, a commentary is provided. But to make it all much more accessible, a box provides the clinical bottom lines.

Electronic-only topics that have been published on the BestBets site (www.bestbets.org) and may be of interest to paediatricians include:

- Is Heliox effective in the treatment of croup?
- Lorazepam or diazepam in paediatric status epilepticus?
- What is the sensitivity and specificity of transverse tibial fractures for non-accidental injury in children?

Readers wishing to submit their own questions—with best evidence answers—are encouraged to review those already proposed at www.bestbets.org. If your question still hasn’t been answered, feel free to submit your summary according to the Instructions for Authors at www.archdischild.com.

Three topics are covered in this issue of the journal:

- How useful is C-reactive protein in detecting occult bacterial infection in young children with fever without apparent focus?
- Does treatment with Echinacea purpurea effectively shorten the course of upper respiratory tract infections in children?
- In juvenile idiopathic arthritis is folate supplementation effective against methotrexate toxicity at the expense of methotrexate’s efficacy?

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How much regret are you prepared to take?

You’ll soon be faced—if you’re in general paediatrics in Europe—with a parent or adolescent asking for inhaled insulin. What will you do? There are, as we write, three randomised trials showing greater patient satisfaction and equivalent glycaemic control using inhaled instead of short acting subcutaneous insulin. The trials lasted 12 or 24 weeks. They were in adults. And there are many other non-injected insulins close to being released. What will you consider when making your decision? Most of us will think of safety, efficacy, and cost (within a publically funded health system). But should we also consider the potential problems if the preliminary evidence doesn’t turn out to be quite as impressive when studied further? When our evidence is less than 1A, should we ask ourselves: “How much regret am I prepared to take?”. When we make a decision, especially in the field of new interventions, we are often hoping that short term or proxy outcomes turn into tangible clinical benefits (e.g. that equivalence in 24 week sugar control is equally effective microvascular protection). We may consider potential long term effects (e.g. rates of lung damage from inhaled insulin). If we decide to prescribe, we should also think “What if these early markers were wrong? What would be the consequences?” and then estimate the potential harm we would have done. We should then take the opposite stance, and ask “But what if they were right, and we didn’t prescribe?” and estimate the potential failures. Knowing the strength of the evidence (e.g. randomised trials or case studies, adult data or paediatric studies, proxy or clinically important outcomes) will allow us to weight the scales, and, balancing these, we can make a more reasoned decision. In the end it can be summed up—when taking this course of action, how much regret am I prepared to take?

Acknowledgements


REFERENCES

4 http://cebmsjr2.ox.ac.uk/docs/levels.htm (accessed July 2002).
How useful is C-reactive protein in detecting occult bacterial infection in young children with fever without apparent focus?

Report by
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You are a specialist registrar in a paediatric day assessment unit and often see young children with high fever but no obvious focus of infection on physical examination. You wonder if a screening test can be done in such patients to identify those with occult bacterial infection. You know that in some units C-reactive protein (CRP) is measured routinely in all children with high fever. However, you are not sure if CRP measurement is a good screening test to detect occult bacterial infection in a young child with fever without apparent focus. You decide to find out more.

Structured clinical question
In young children with fever without apparent focus on physical examination and history [subject], is measurement of C-reactive protein a good screening test [intervention] to detect occult bacterial infection or bacteraemia [outcome]?

Search strategy and outcome
See table 1.

Primary sources
Medline (1951–2004) via Dialog DATA star: “C-reactive protein or acute phase reactant$ or acute phase protein$ or CRP AND fever without focus or fever of unknown origin or occult bacteraemia$”.

Outcome: A total of 58 articles were found. This was limited to 23 articles by selecting those in the English language and human studies related to children (up to 18 years of age). Each abstract was read and six relevant studies were found. One of these studies (Berger et al6) was relevant but was designed to look at the use of CRP in differentiating bacterial and viral infection, and children with identifiable focus of infection were included in the study. Therefore this was excluded from the analysis. Five more relevant articles were obtained from the references of the above studies.7–11 However, designs of these studies were similar to those of Berger et al, and all included children with identifiable focus of infection in their analysis. Subsequently none of them were included in the analysis here.

Pubmed and Embase: No further relevant articles were found.

Secondary sources
Cochrane library and Bestbets website: No further relevant article was found.

Commentary
The management of febrile young children without apparent source of infection remains controversial, because there has been no test available with adequate sensitivity and specificity required to distinguish children with occult bacterial infection from non-bacterial illness. Blood culture is the gold standard to detect occult bacteraemia; however, results are not quickly available.

Five studies evaluating the use of various acute phase reactants in this clinical situation are appraised here. The diagnostic nature of the question determines that the best possible research studies would be validating prospective cohort studies, but four of them were exploratory cohort studies and one was a retrospective analysis, and all of them had methodological flaws in them. Three prospective studies1 2 5 showed that CRP has better predictive value than other acute phase reactants, while one study4 found ANC to have better predictive value. Interestingly, in all of them mean CRP was significantly higher in children with serious bacterial infections compared with children with benign infections, and when taken in conjunction with other acute phase reactants, gave good probability of serious bacterial infection.

One may imagine that trend in CRP over time may be more important than a single CRP value, and a single very high CRP may have very high specificity and sensitivity to detect serious bacterial infections. However, none of these studies gave enough data to answer these two questions, and no other studies are available looking at the serial measurements of other CRP to detect occult bacterial infection in paediatric population.

The incidence of serious bacterial infections was high in all the studies, ranging from 11.3% to 29%. The prevalence of occult bacteraemia in non-toxic appearing children between 3 and 36 months of age with temperatures higher than 39°C has declined to about 2% following the introduction of conjugate vaccine against Haemophilus influenzae type b.12 13 Recently, conjugate pneumococcal vaccine has been introduced in a few countries such as the USA, and has been shown to substantially reduce the rate of invasive pneumococcal disease in immunised children,14 so a screening test to detect occult bacterial infections in children attending emergency departments in these countries may be of little value, as the pre-test probability is much lower.

On the basis of published evidence, it can be concluded that high CRP can only suggest the presence of serious bacterial infection. Nevertheless, taken in conjunction with other acute phase reactants, it can contribute towards decision making.

CLINICAL BOTTOM LINE

- Children with serious bacterial infections and occult bacteraemia are more likely to have high CRP than children with benign infections. (Grade B)
- A single CRP value gives a probability but never a certainty of presence or absence of serious bacterial infection. (Grade B)
- The use of CRP alone or with other factors may enhance clinicians’ abilities in the early recognition of clinically undetectable serious bacterial infection, allowing for a more selective strategy for determining which children need additional diagnostic studies and antibiotic therapy.

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REFERENCES