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, 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 They make no attempt to statistically aggregate the data, nor search the grey, unpublished literature.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.

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 Sackett1 and Moyer2 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.

The electronic edition of this journal contains extra information to each of the published Archimedes topics. The papers summarised in tables are linked, by an interactive table, to more detailed appraisals of the studies. Updates to previously published topics will be available soon from the same site, with links to the original article.

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.

• Are routine chest x ray and ECG examinations helpful in the evaluation of asymptomatic heart murmurs?
• Does intravenous mannitol improve outcome in cerebral malaria?
• Do antipyretics prevent febrile convulsions?

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**References**


Additional Information on each of the topics is available on the ADC website (www.archdischild.com)

**Are routine chest x ray and ECG examinations helpful in the evaluation of asymptomatic heart murmurs?**

Report by Susan Gardiner, Bradford Royal Infirmary, UK

A 6 month old infant is referred by the GP to the general paediatric clinic with an asymptomatic heart murmur.

A careful history does not reveal any symptoms of heart disease. On examination there is a soft systolic heart murmur,
but the infant is otherwise normal. You suspect that the child has an innocent heart murmur but are not 100% sure. In this case will a chest x ray and/or ECG examination add to your clinical evaluation?

**Structured clinical question**

In children with an asymptomatic heart murmur [patient] does a chest x ray and/or ECG examination [intervention] assist in the diagnosis or exclusion of congenital heart disease [outcome]?  

**Search strategy and outcome**

Secondary sources: none.  

Primary sources: Medline 1966 to October week 2, 2001: (heart murmurs OR (heart murmur$ OR cardiac murmur$).tw.) AND (electrocardiography OR ECG.mp) AND
A blood slide shows asexual forms of *Plasmodium falciparum*, his blood sugar has been checked to be normal, and he has been loaded with intravenous quinine. Antibiotics have been given until meningitis can be excluded by a normal lumbar puncture. Local experience suggests intravenous mannitol is of benefit in unconscious patients with cerebral malaria; its use however, is not recommended by the World Health Organisation.¹

### Structured clinical question

In a child with cerebral malaria [patient] will intravenous mannitol [intervention] improve mortality or neurological morbidity [outcome]?  

### Search strategy and outcome

Medline 1966 to January 2003 using the PubMed interface (mannitol AND malaria); no limits applied. There was a yield of just 15 articles, none being a relevant controlled trial. Further searches of related articles quoted in references found no controlled trial of mannitol use in cerebral malaria.

### Commentary

Only one article was found which was relevant to the clinical question. This study described the use of mannitol in 14 children with cerebral malaria (see table 2). Intracranial pressure was lowered in all cases and outcome was good or reasonable in all except the four with severe intracranial hypertension. However, there was no control group with which to compare the benefit of mannitol on case fatality or neurological outcome.

### Does intravenous mannitol improve outcome in cerebral malaria?

**Report by**

Richard J Tomlinson, Oshakati State Hospital, Namibia  

John Morrice, Mzuzu Central Hospital, Malawi

You are working in an African hospital during the malaria season. A 10 year old boy is admitted in coma with a fever after having had a convulsion at home.

A blood slide shows asexual forms of *Plasmodium falciparum*, his blood sugar has been checked to be normal, and he has been loaded with intravenous quinine. Antibiotics have been given until meningitis can be excluded by a normal lumbar puncture. Local experience suggests intravenous mannitol is of benefit in unconscious patients with cerebral malaria; its use however, is not recommended by the World Health Organisation.¹

### References


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**CLINICAL BOTTOM LINE**

- ECG rarely adds to clinical evaluation of an asymptomatic heart murmur. It rarely leads to a change in diagnosis.
- Chest x-ray examination is often misleading in the evaluation of an asymptomatic heart murmur and interpretation is only poorly to moderately reproducible.
Intravenous mannitol in cerebral malaria

<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>
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<tr>
<td>Newton et al [1997]</td>
<td>23 Kenyan children with confirmed <em>Plasmodium falciparum</em> cerebral malaria had intracranial pressure monitored. The 14 with severe and intermediate intracranial hypertension received intravenous mannitol</td>
<td>Uncontrolled clinical trial</td>
<td>Intracranial pressure</td>
<td>Mannitol lowered the intracranial pressure in all children</td>
<td>Primary focus of study and outcome measured was measurement of intracranial pressure in cerebral malaria</td>
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**Table 2**

**Clinical Bottom Line**
- There are no controlled data supporting the use of mannitol for cerebral malaria. Consensus statements should be followed.

Intracranial hypertension as a feature of cerebral malaria probably contributes to the poor neurological outcome and death of many children with *Plasmodium falciparum* malaria. A likely cause is an increase in cerebral blood volume due to sequestered parasitised erythrocytes. Mannitol is a relatively cheap osmotic agent which appears to lower intracranial pressure. This may potentially improve the survival and neurological outcome of many children with cerebral malaria. Anecdotal evidence suggests that the conscious level of children with cerebral malaria improves with intravenous mannitol; however, when it should be used is unknown. The benefit may only be temporary; however, in resource limited settings where intensive nursing care may not be optimal, shortening the duration of a coma may have benefits for neurological outcome.

The WHO emphasise that none of the ancillary treatments for cerebral malaria have sufficient supporting evidence to be used. No controlled study for the use of mannitol in paediatric or adult cerebral malaria could be identified and its use cannot be recommended. Further studies are necessary to determine its value and potential side effects.

**References**


**Do antipyretics prevent febrile convulsions?**

**Report by**

A Sahib El-Radhi, W Barry, Queen Mary’s Hospital, Sidcup, Kent, UK

An 1-year-old child is admitted following their first febrile seizure (FS). We wish to prevent recurrences during further febrile episodes. The nursing staff ask you to prescribe an antipyretic. Later you come to advise the parents on methods of preventing further febrile seizures.

**Structured clinical question**

In children who have experienced a febrile seizure [patient] does prescribing antipyretics [intervention] reduce recurrences of febrile seizures [outcome]?

**Search strategy**

Secondary sources

- Cochrane Library and DARE—“febrile convulsions/seizures and antipyretics”, “febrile convulsions/seizures and paracetamol”, “febrile convulsions/seizures and ibuprofen”; one systematic review found (paracetamol for treating fever in children); two protocols.
- Prodigy Evidence Based Clinical guidance—“febrile convulsions”; nil relevant found.

**Primary resources**

PubMed clinical queries (1966 to Jan 2003): “antipyretics and febrile convulsions”—80 references. Of these, three were randomised controlled trials but one was irrelevant (investigating antipyretic effects rather than subsequent seizure reduction).

**Commentary**

As the essential precursor of a febrile seizure is a fever, physicians and paediatric nurses have concluded that antipyretic measures should prevent febrile seizures. Antipyretics continue to be among the most commonly prescribed medications, especially for children at risk of such seizures. Parents are usually advised that the administration of antipyretics to at-risk children may reduce the risk of further convulsions. When asked, the majority of medical trainees and paediatric nurses in our unit replied that the reason for giving paracetamol to children who were at risk of febrile seizure recurrence was to prevent further convulsions. However, the evidence suggests that antipyretics have no effect on preventing further febrile seizures. At this hospital, 13% of children admitted with their first FS subsequently developed repeated FS soon after admission despite the routine administration of paracetamol to control fever prior to the seizure.1

Children with high risk of recurrences of FS (complex features of FS, family history of FS, age less than 1 year, low grade fever at the onset of FS) develop recurrences in at least 80% while those without these risk factors rarely develop recurrences. Antipyretics are used for both groups of children, suggesting that it is these risk factors, and not antipyretics, which are the crucial determinants of the risk of recurrence.

Controlled studies of antipyretic medications, given during the original acute illness following a febrile seizure or during subsequent febrile episodes have failed to show a preventive effect in children at risk of FS (table 3). A randomised, placebo controlled trial in children at risk of FS found no evidence that paracetamol, with or without diazepam, was effective in preventing FS during subsequent febrile episodes.2 A second
Evidence that paracetamol is effective in reducing fever or pre-concluded that the trials failed to show any convincing evidence that paracetamol is effective in reducing fever or premature cessation. It identified 12 randomised or quasi-randomised controlled trials. It concluded that the trials failed to show any convincing evidence that paracetamol is effective in reducing fever or preventing seizures.

Randomised trial compared the antipyretic effectiveness of paracetamol administered at regular intervals (group 1) versus paracetamol administered at the time of fever (group 2) in children presenting with an FS. Early recurrences of FS (within the first 24 hours) were similar in both groups. Ibuprofen was also evaluated in a randomised, double blind, placebo controlled trial in children at risk of FS. The recurrence rate was similar in both groups. In another open trial, children at risk of FS were offered either ibuprofen or ibuprofen during subsequent febrile episodes or else no medication. The recurrence risk of FS was similar in all groups. These four studies concluded that the antipyretics paracetamol and ibuprofen had no preventive effect on the recurrence of FS. A recent review of trials assessing the effects of paracetamol on the clearance time of fever and on FS identified 12 randomised or quasi-randomised controlled trials. It concluded that the trials failed to show any convincing evidence that paracetamol is effective in reducing fever or preventing seizures.

While antipyretics may have a role in improving comfort and general wellbeing, we should surely not be advocating medication for purposes that have been shown not to work.

REFERENCES

The duck-yak problem. Illustration by Jack Maypole, MD