ARCHIMEDES

Towards evidence-based medicine for paediatricians

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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. In doing this, we are adapting a format that 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, although 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 They make no attempt to statistically aggregate the data, nor search the grey, unpublished literature.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[2] and gaining answers.[3]) A brief report of the search used follows—this has been carried out in a hierarchical way, to search for the best-quality evidence to answer the question (http://www.cebm.net/levels_of_evidence.asp). 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), books by Sackett *et al*[4] and Moyer *et al*[5] 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:

- Are meningeal irritation signs reliable in diagnosing meningitis in children?
- Is immobilisation effective in Osgood-Schlatter's disease?
- Do all children presenting to the emergency department with a needlestick injury require PEP for HIV to reduce HIV transmission?

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 has not 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.

- Is lumbar puncture necessary for evaluation of early neonatal sepsis?
- Does the use of calamine or antihistamine provide symptomatic relief from pruritus in children with varicella zoster infection?
- Is supplementary iron useful when preterm infants are treated with erythropoietin?

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Is more research needed?

''More research is needed'' is a phrase you might have read before. But is more research really needed? Two situations are offered to us in *Archimedes* this month where clinical questions are, as yet, unanswered. Is iron supplementation really necessary for premature infants treated with erythropoietin, and do antihistamines and calamine lotion help in children with chicken pox? How can we decide if these questions really do ''need'' research? It may be worth thinking of how likely benefits and harms may be, what the importance of these outcomes are and finally, how much would you consider reasonable to pay for the answer? For example, what chance is there that antihistamines work in chickenpox? What is the chance that side effects will occur? What is the relative severity of side effects versus the delight of being itch free? If we pay for research and spend hours and hours of time pressing through the increasing regulatory frameworks for clinical trials to define the answer to this question, what will be the opportunity cost? What would we fail to do by looking at this? The same questions can be asked of iron supplementation in premature infants, the salvage treatment of relapsing systemic histocytosis or the promotion of car-seat use in low-income families. Such value judgements are important; they will have different answers from different perspectives; they will be subject to political influences from pressure groups; being aware of them might stop us from frequently expounding ''more research is needed''.

REFERENCES

1 **Moyer VA,** Ellior EJ. Preface. In: Moyer VA, Elliott EJ, Davis RL, *et al*, eds. *Evidence based pediatrics and child health*, Issue 1. London: BMJ Books, 2000.
2 **Richardson WS,** Wilson MC, Nishikawa J, *et al*. The well-built clinical question: a key to evidence-based decisions. *ACP J Club* 1995;**123**:A12–13.
3 **Bergus GR,** Randall CS, Sinift SD, *et al*. Does the structure of clinical questions affect the outcome of curbside consultations with specialty colleagues? *Arch Fam Med* 2000;**9**:541–7.
4 **Sackett DL,** Starus S, Richardson WS, *et al*. *Evidence-based medicine. How to practice and teach EBM*. San Diego: Harcourt-Brace, 2000.
5 **Moyer VA,** Elliott EJ, Davis RL, *et al*, eds. *Evidence based pediatrics and child health*, Issue 1. London: BMJ Books, 2000.

Is lumbar puncture necessary for evaluation of early neonatal sepsis?

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A newborn baby born at 37 weeks is noted to be unwell at 18 h postnatally. The mother gives a history of prolonged rupture of membranes for 36 h. The baby is feeding poorly and is jittery, with a temperature of 38°C. A

Table 1 Studies evaluating the role of lumbar puncture to investigate early neonatal sepsis

Citation	Study group	Study type	Outcome	Key results	Comments
Visser *et al*[2]	Newborn with suspected sepsis evaluated within 72 h of life. Total n = 323	Retrospective case notes review, level 2b	Incidence of meningitis	Total no of meningitis = 6, with the incidence of meningitis being 18/1000	Uncontrolled cohort. Indications of sepsis evaluation are not well described. No mentionwhether all suspected newborns were screened
Eldadah *et al*[3]	All infants admitted with RDS were evaluated for sepsis with LP within 24 h of life. n = 203	Prospective study, level 1b	No of cases with meningitis	No cases of meningitis were found. BC was positive in 17 infants	Study does not indicate any long-term follow-up, so no knowledge about missed cases of meningitis. Only included babies with RDS
Hendricks-Munoz and Shapiro[4]	Newborns <34 weeks admitted with suspected sepsis or those with risk factors for sepsis was evaluated within 6 h. LP was carried out only in BC positive cases. Total no was 1390, of which 32 were BC positive; 15 of them died before CSF evaluation; 12 of these 15 patients had LP after death and 16 of the remaining 17 cases were evaluated with ante-mortem LP	Retrospective case notes review, level 2b	No of cases of meningitis, number of missed/partially treated cases of meningitis	No cases of meningitis were found. No missed or partially treated cases were detected	Uncontrolled cohort. Small study but only looking at BC positive cases. Babies were treated with antibiotic before CSF was obtained, so the early meningeal seeding could be missed. No mention about the timing of follow-up to detect missed cases
Weiss *et al*[5]	All infants admitted with respiratory distress on the first day of life had undergone LP as a part of sepsis screen. n = 1495	Retrospective case notes analysis, level 2b	Frequency of meningitis. Degree of association between meningitis and sepsis	4 cases of meningitis were detected with an incidence of 2.7/1000. BC were positive in 3 of these cases	Study included only babies admitted with respiratory distress on day 1 of life
Ajayi and Mokulu[6]	Phase 1: Newborns with suspected sepsis and those with risk factors for sepsis were evaluated within 72 h of age with lumbar puncture. n = 263. Phase 2: Newborns within 72 h of life with signs of severe sepsis only were evaluated with lumbar puncture. n = 50	Retrospective case notes review level 2b	No of LP done. No of cases of meningitis and no of missed or partially treated cases	3 times fewer LP carried out in phase 2 than in phase 1. No cases of meningitis detected in both phases (95% CI 0 to 1.1). No missed or partially treated cases of meningitis found	Uncontrolled cohort. No mention about timing of follow-up to detect partially treated or missed cases. Estimated maximum risk was considered to avoid the fallacy inherent to zero numerators and the attendant complacency

BC, blood culture; CSF, cerebrospinal fluid; LP, lumbar puncture; RDS, respiratory distress syndrome.

clinical diagnosis of early sepsis is made and lumbar puncture is suggested on the ward round as a part of sepsis evaluation. Several publications on the use of lumbar puncture in late-onset sepsis, including a recent review article by Malbon et al,[1] suggest that lumbar puncture is an important method of investigation and should be considered in babies for >48 h old, with suspected sepsis.

We wonder whether there is sufficient evidence to justify lumbar puncture in early sepsis.

Structured clinical question

In a newborn (patient), is lumbar puncture (intervention) necessary to rule out meningitis in suspected sepsis (outcome) in the first few days of life (0–3 days)?

Search strategy and outcome

Search date: September 2005

Cochrane Library: Nil relevant

Medline: 1950–to date; Embase: 1974–to date; Cinhal: 1982–to date via Dialog Datastar

Search terms: (Neonatal ADJ sepsis *or* Neonatal ADJ septicaemia *or* Neonatal ADJ meningitis *or* meningitis and infant–newborn# *or* Early ADJ sepsis, *or* Early ADJ septicaemia) *and* (Lumbar ADJ puncture *or* LP *or* Spinal ADJ tap *or* CSF ADJ examination). Limit to English language and newborn infants from birth to 1 month.

Total number of hits: 51

Cross-references obtained: 6

Total number: 57, of which 5 studies were eligible.[2–7]

Commentary

Lumbar puncture has always been an invaluable tool to diagnose meningitis. In the neonatal period, septicaemia can be indistinguishable from meningitis. The overall incidence of neonatal meningitis is 0.25–1.0 per 1000 live births.[7 8]

Practice varies between hospital units as regards early sepsis evaluation. Although blood culture has been regarded as an essential component of sepsis screen, the role of lumbar puncture is debatable especially in the first 72 h of life. Previously published data showed that neonatal septicaemia can coexist with meningitis in up to 30% of patients.[2] On the other hand, lumbar puncture can be associated with major risks including hypoxaemia, clinical deterioration and many other hazards in small and sick babies.[9 10] Moreover, in about 30% of patients, the cerebrospinal fluid tap could be traumatic or inadequate.[9 11]

Although many of the studies did not compare the incidence of meningitis between groups with early-onset sepsis presenting with symptoms and groups with suspected sepsis because of perinatal risk factors without any overt symptoms,Please confirm the changes made in the sentence the published literature shows the incidence of meningitis in asymptomatic newborns undergoing evaluation only because risk factors is virtually nil.[12–14]

The study by Visser *et al*[2] observed a very high (1.8%) incidence of meningitis in babies within 72 h of life. This study also noted that in 15% of cases, blood culture was negative. Many of the later studies did not show such a high incidence.[12 15] For example, studies by Ajayi and Mokuolu[6] and Hendricks-Munoz and Shapiro[4] looked at around 1700 babies but found no cases of meningitis. Even their long-term follow-up did not show any case of missed or partially treated meningitis. Two other similar studies,[3 5] which looked at babies admitted with respiratory symptoms within 24 h of birth, also found a very low incidence of meningitis (only four cases of meningitis in > 1700 neonates evaluated with lumbar puncture). The statistically estimated maximum risk of meningitis in suspected early sepsis is only 1.1% and that in blood culture proved sepsis is 0–10.3%.

It seems that there is no need to carry out lumbar puncture in neonates suspected of early sepsis who are being evaluated purely for perinatal risk factors, or in those presenting with mild symptoms. It should still be undertaken in babies with severe illness or obviously where meningitis is strongly suspected.

CLINICAL BOTTOM LINE

- Overall incidence of neonatal meningitis is 0.25–1.0 per 1000 live births (grade A).
- Uncontrolled studies suggest that meningitis is very uncommon in asymptomatic babies with only perinatal risk factors for sepsis, so in this group lumbar puncture can be safely omitted from the early sepsis screen (grade B).
- In strongly suspected cases, lumbar puncture should be included in an examination of sepsis (grade B).

REFERENCES

1 **Malbon K,** Mohan R, Nicholl R. Should a neonate with possible late onset infection always have a lumbar puncture? *Arch Dis Child* 2006;**91**:75–6.
2 **Visser VE,** Hall RT. Lumbar puncture in the evaluation of suspected neonatal sepsis. *J Pediatr* 1980;**96**:1063–7.
3 **Eldadah M,** Frenkel LD, Hiatt IM, *et al*. Evaluation of routine lumbar punctures in newborn infants with respiratory distress syndrome. *Paediatr Infect Dis J* 1987;**6**:243–6.
4 **Hendricks-Munoz KD,** Shapiro DL. The role of the lumbar puncture in the admission sepsis evaluation of the premature infant. *J Perinatol* 1990;**10**:60–4.
5 **Weiss MG,** Ionides SP, Anderson CL. Meningitis in premature infants with respiratory distress: role of admission lumbar puncture. *J Paediatr* 1991;**119**:973–5.
6 **Ajayi OA,** Mokuolu OA. Evaluation of neonates with risk factor for infection/suspected sepsis: is lumbar puncture necessary in the first 72 hours of life? *Trop Med Int Health* 1997;**2**:284–8.
7 **Wiswell TE,** Baumgart S, Gan on CM, *et al*. No lumbar puncture in the evaluation for early neonatal sepsis: will meningitis be missed? *Pediatrics* 1995;**6**:95.
8 **Shattuck KE,** Chonmaitree T. The changing spectrum of neonatal meningitis over a fifteen year period. *Clin Pediatr* 1992;**31**:130–6.
9 **Weisman L,** Emrenstein GB, Steenbarger JR. The effect of lumbar puncture position on sick neonates. *Am J Dis Child* 1983;**137**:1077–9.
10 **Speidel BD.** Adverse effects of routine procedures on preterm infants. *Lancet* 1978;**1**:864–5.
11 **Schreiner RL,** Kleiman MB. Incidence and effect of traumatic lumbar punctures in the neonate. *Dev Med Child Neurol* 1979;**21**:483–7.
12 **Kumar P,** Sarkar S, Narang A. Role of lumbar puncture in neonatal infection. *J Paediatr Child Health* 1995;**31**:8–10.
13 **Fielkow S,** Reuter S, Gotoff SP. Cerebrospinal fluid examination in symptom free infants with risk factor for infection. *J Paediatr* 1991;**119**:971–3.
14 **Prabhakar BR,** Campe J, Prabhakar K, *et al*. Lumbar puncture in suspected neonatal sepsis. *Children's Hosp Q* 1999;**11**:15–17.
15 **Schwersenski J,** Mcintyre L, Bauer CR. Lumbar puncture frequency and cerebrospinal fluid analysis in the neonate. *Am J Dis Child* 1991;**145**:54–8.

Does the use of calamine or antihistamine provide symptomatic relief from pruritus in children with varicella zoster infection?

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A 2-year-old girl presents with chickenpox. The girl has typical vesicular lesions but has no evidence of complications on examination. Her mother reports that she is scratching continuously and has had very little sleep over the past few days as a result of the pruritus. Considering the therapeutic options, we wonder whether there is any evidence to support the use of either calamine lotion or antihistamines to alleviate pruritus in varicella zoster infection.

Structured clinical question

In a child with varicella zoster infection [patient], can calamine lotion or antihistamines [interventions] reduce pruritus [outcome]?

Search strategy and outcome

Cochrane Library using ''varicella *and* calamine'', ''varicella *and* antihistamine'', ''chickenpox *and* anitihistamine'' and ''chickenpox *and* calamine'': no relevant results.

PubMed (no limits set) using the search terms given above. The search produced the same results irrespective of whether ''chickenpox'' or ''varicella'' was used. Three publications related to ''varicella *and* calamine'': none were relevant (one case report and two cross-sectional surveys). Twenty two publications related to ''varicella *and* antihistamines'': only one study was relevant.[1] Table 1 summarises the report.

In addition, PubMed was searched for ''varicella'' or ''chickenpox'', respectively, in combination with (*and*) the proprietary names of all antihistamines currently licensed for use in the UK (based on *British National Formulary 51*, March 2006 and *British National Formulary for Children 2005*). For topical antihistamines: antazoline, diphenhydramine and mepyramine. For systemic antihistamines: acrivastine, alimemazine (trimeprazine), brompheniramine, chlorpheniramine (chlorphenamine), cetirizine, cinnarizine, clemastine, cyclizine, cyproheptadine, desloratidine, diphenhydramine, diphenylpyraline, doxylamine, fexofenadine, hydroxyzine, levocetirizine, loratidine, mizolastine, promethazine, terfenadine and triproledene. Fourteen studies were found: one each related to cetirizine, doxylamine, and promethazine, and 11 related to diphenhydramine—none were relevant (search date 14 April 2006).

Commentary

No studies were found that evaluated the effect of calamine lotion on pruritus associated with varicella zoster infection. Nevertheless, the drug—a basic zinc silicate—has a good safety profile and in our personal experience, many patients (or their parents) report symptomatic relief. A study investigating the effectiveness of calamine lotion in varicella zoster infection is desirable.

Only one trial has examined the use of one particular systemic antihistamine in this context—dimethindene maleate (DMM), a non-sedating H1 blocker,[2] which is not available in the UK. Two different regimens were used in this trial—a dose of 0.1 mg/kg/day, which is the standard recommended dose and a ''low-dose'' treatment with 0.05 mg/kg/day. The study showed considerable improvement in severity of itching in both treatment groups, as well as some improvement in appetite and sleep disturbance. However, neither the method of randomisation nor the blinding process is described. The blinding process seems particularly relevant, as the primary outcome measure—the itching severity score—is composed of subjective measures rated by the patient's parents.

Although other systemic antihistamines would probably produce a similar effect, there is currently no definite evidence to support their use. Given that antihistamines are a heterogenic group of drugs—with the shared property of H1 receptor binding but variable antiadrenergic, anticholinergic and antiserotoninergic properties—it is uncertain whether the results of this study can be extrapolated to the use of other antihistamines.[3]