

Towards evidence based medicine for paediatricians

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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. 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 They make no attempt to statistically aggregate the data, nor search the grey, unpublished literature.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,² and gaining answers.³) 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.⁴ 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 Sackett⁵ and Moyer⁶ 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 linked to the original article when they are available. This month an electronic update on “Inhaled steroids in the treatment of mild to moderate persistent asthma in children once or twice daily administration” has been published.

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.

- Should we screen every child with otitis media with effusion for allergic rhinitis?
- Should we treat infantile seborrhoeic dermatitis with topical antifungals or topical steroids?
- Is routine EEG helpful in the management of complex febrile seizures?

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Beyond the evidence

It would be a wonderful thing if every treatment we used had been tested in trials where the populations matched ours exactly. Sadly, this isn't the case. In paediatrics, the evidence we have may be in the “wrong” population: including lots of adults or children of the wrong age. Or the outcomes recorded may only be surrogates, rather than clinically important changes. In order to use the best evidence in practice, we need to consider how far we can take the results “beyond the evidence”.

Fortunately, as with many aspects of critical appraisal, there are guides as to how to think about the issues related to using studies which don't directly apply to our population.¹ It is suggested that first, we should ask if there are biological differences between the populations. For example, does the same process produce cradle cap in babies as seborrhoeic dermatitis in adults? Here it may be relevant to look at pathological data, or compare the results of studies of alternative treatments in the populations under suspicion.

Second, it is appropriate to consider whether differences in psychology, social setting, or economy will stop the data being applicable. When we turn to psychological differences it is clearly inappropriate to use a cognitive-behavioural therapy in infants, but how should we appraise a trial which shows improved quality of life in adults? If there are significant differences in economic or social setting, it may strongly affect the family's adherence to a therapy.

If the treatment seems to be feasible and sensible, we are suggested to address issues of risk and co-morbidity. If COX-2 inhibitors do reduce the chance of gastrointestinal bleeding,² should we be using them in children with juvenile arthritis? We need to know the basic risk of GI bleeding in our population, in order to estimate the benefit they may gain from using the new drugs.

The last issue to consider is that of outcomes. What is the information on side effects? Is there any information about adverse events in children? Are the outcomes we are given directly relevant to our patients (such as improved function in JIA) or surrogate outcomes (such as reduced serum CRP)?

As with everything in evidence based practice, these guides don't give you the rules to act on, but tools to think through. When considering if you can go “beyond the evidence”, look at biological and psychological differences, consider the inherent risk and co-morbidities, and examine all the outcomes closely. Then you'll have a better idea of how far you can apply “best evidence” to your practice.

References

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

Should we screen every child with otitis media with effusion for allergic rhinitis?

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Spiro, a 12 year old boy, was referred to the Allergy Clinic of Department of Pediatrics because of otitis media with effusion (OME) that had been present for the past four years. A paediatrician and an otolaryngologist advised a consultation with an allergist because they

believed that Spiro had OME because he suffered from allergic rhinitis (AR). Should we look for AR in every child with OME?

Structured clinical question

Do children with OME [population] have an increased risk of AR [outcome] than children without OME [comparison]?

Search strategy and outcome

Our search strategy (extended to 2 August 2003) was:

- Cochrane Database of Systematic Reviews using: "otitis media AND allergy"; 13 references (none relevant).
- Medline, via Pubmed: "otitis media with effusion AND allergic rhinitis"; 62 references (four relevant).

See table 1.

Commentary

The full text of two relevant studies^{3 4} was not accessible to us (one was published in Japanese, the other in Turkish); however, the abstract furnished sufficient details for a summary evaluation of their validity and utility for our question.

The studies that we examined in full text^{1 2} showed marked difference in the prevalence of AR in children with OME: 16.3% versus 89%. Trying to explain this discrepancy, it can be noted that the study of Alles and colleagues² is affected by some methodological imperfections that seriously compromise its validity. It lacks a well defined control group and the study definitions of AR and OME are weak. For AR, neither the appearance of the symptoms after exposure to an allergen nor the demonstration, necessarily, of sensitisation to an allergen through measurement of the specific IgE is required. Even the definition of OME was not strong: an unconfirmed history of OME was sufficient for enrolment. The prevalence of the AR in children with OME in the study of Caffarelli and colleagues¹ gives the more reliable estimates; because of the fact that their study is prospective, and the authors have adopted rigorous diagnostic criteria for both the illness studied (AR and OME), have included an adequate control population, and have enrolled a sufficient number of children.

Table 1 Allergic rhinitis in children with otitis media

Citation	Study group	Study type (level of evidence)	Outcome	Key results	Comments
Caffarelli <i>et al</i> (1998)	172 children with OME referred because of symptoms to the Centre for the Study of OME. 200 healthy children as controls	Case-control study (level 2b)	Prevalence of allergic rhinitis	16.3% in children with OME; 5.5% in controls. OR = 3.34 (95%CI 1.6 to 6.3), p<0.001	Well defined and rigorous diagnostic criteria of OME and AR. Presence of an adequate random control population. Sufficient sample size
Kayhan <i>et al</i> (2002)	22 children with OME; 21 children with no symptoms of otolaryngological disease as controls	Case-control study (level 2b)	Prevalence of allergic rhinitis	23% in children with OME; 4.8% in controls. OR = 5.9 (95% CI 0.6 to 55.4), p>0.05	Good quality of definition of diagnosis of OME and AR. Small numbers. Article in Turkish
Alles <i>et al</i> (2001)	209 children with OME	Case series (level 4)	Prevalence of atopy and allergic disease (rhinitis, asthma, eczema)	Prevalence of AR = 89%	Poor quality of definition of diagnosis of OME and AR. Lack of a control population
Ogawa (2002)	185 children with OME	Case series (level 4)	Description of various outcomes (allergic and non-allergic)	Prevalence of AR = 14%	Unknown quality of definition of diagnosis of OME and AR. Lack of a control population. Article in Japanese

The prospective design of the study reduces the recall bias and the possibility of differences in the management of the patients. A rigorous definition of allergic rhinitis allows avoiding its overdiagnosis and the inclusion of patients with non-allergic rhinitis. OME was defined prospectively with tympanometry performed on all the patients (to define cases and controls). The presence of a control group allows us to quantify the parameter we consider the most interesting—that is, the difference (absolute risk increase) in the prevalence of the allergic rhinitis between the children with OME and the ones without. And finally, the presence of a large sample makes the estimate of the absolute risk increase more accurate, tightening its confidence interval.

The duration of OME is an important variable in management decisions: studies of children in day care note that many will have brief periods of time (one or several days) with OME that spontaneously clears; in contrast other children will have OME for months. Only for the latter children would any intervention have the potential to be useful.

However, the studies on the efficacy of antiallergic therapy in the treatment of children with OME are few, methodologically weak, and inconclusive. “Irrespective of the theoretical mechanism, the relation between allergy and otitis media with effusion will remain controversial until well controlled clinical studies are conducted documenting that in select populations antiallergic therapy is efficacious in preventing or limiting the duration of otitis media with effusion”.⁵ Today, the situation is unchanged.

CLINICAL BOTTOM LINE

- The prevalence of allergic rhinitis is significantly higher in children with otitis media with effusion (16.3%) than in healthy controls (5.5%).
- Allergologic screening is not necessary in children with OME as all children with allergic rhinitis present all or some of the characteristic symptoms.
- Treatment for allergic rhinitis has not been shown to improve otitis media with effusion.
- If there are signs or symptoms of allergic rhinitis, further evaluation is justified, because of the potential benefit of treatment for the rhinitis.

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Should we treat infantile seborrhoeic dermatitis with topical antifungals or topical steroids?

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A mother brings her 2 month old child to you with unsightly seborrhoeic dermatitis on his/her scalp. You prescribe 1% hydrocortisone but the mother expresses her unhappiness at using steroids. You remember that the dermatologists at your hospital like to use an antifungal cream and you decide to find out more.

Structured clinical question

In infants with seborrhoeic dermatitis [patient] is there any advantage to using topical antifungals [intervention] over steroids [comparison] to cure seborrhoeic dermatitis of the scalp and prevent recurrences [outcome]?

Search strategy

Primary source

Medline 1966–2003 (Ovid).

Subject heading “seborrhoeic dermatitis” + subheadings “therapy AND drug therapy”; 556 articles produced and sorted manually: 5 relevant; see table 2.

Secondary source

Cochrane database and Best Bets website under keyword “seborrhoeic”. No further papers.

Commentary

Seborrhoeic dermatitis is a common benign condition of childhood. Often the most appropriate treatment is to do nothing; however, children with scalp seborrhoeic dermatitis still make regular presentations to paediatric outpatient clinics with disease burden enough to warrant treatment.

The link between the excessive presence of *Pityrosporum ovale* yeast to seborrhoeic dermatitis is well documented in the literature and it is intuitive that using a pityrosporicidal agent would not only treat the condition, but help prevent recurrences. Both fungicides and steroids have been shown to be effective in the treatment of seborrhoeic dermatitis when compared to placebo.

Five trials of good quality were found directly comparing topical steroids with topical fungicides. At one month of treatment, four of the trials showed good effectiveness of both treatments and no significant differences between them. One trial (Ortonne *et al*) showed a very slight improvement in the ketoconazole group over the steroid group.

The trials reviewed are all on adults as there are no comparable trials in infants. However, the extrapolation to this age group is viable as the disease is similar. Only one paper (Zeharia *et al*), with a specifically paediatric age group could be found and the quality was too low to allow meaningful analysis.

The three studies which also looked at the recurrence rate showed similar results in two and a slight advantage in using ketoconazole in one. Two trials noted low and similar incidence of side effects and one (Ortonne *et al*) showed a much better tolerance of the antifungal over the steroid.

There is no clear consensus on treatment regimen. However, a four week course was shown to be effective in four of the trials using a once or twice a day regimen.

There has been a paper published on the safety of ketoconazole in infants (Brodell *et al*) which showed that a course of ketoconazole twice a week for four weeks produced no detectable serum ketoconazole levels and no change in LFTs.

CLINICAL BOTTOM LINE

- Ketoconazole is at least as effective at treating seborrhoeic dermatitis as steroid creams and may be better at preventing recurrences, providing a good alternative to using steroid creams in infants.

Table 2 Steroids versus antifungals in the treatment of seborrhoeic dermatitis

Citation	Study group	Study type (level of evidence)	Outcome	Key results	Comments
Pari <i>et al</i> (1988)	36 adult patients with face and trunk seborrhoeic dermatitis. Randomised to 2% ketoconazole v 0.05% clobetasol BD for 4 weeks	Randomised double blind trial (level 1b)	Resolution at 4 weeks Recurrence at 3 months	Effective remission in both groups (ketoconazole 64.7%, clobetasone 63.2%). ARR -0.015 95% CI -0.33 to 0.30 Recurrence rates 30% ketoconazole and 50% steroid. ARR 0.180 95% CI -0.13 to 0.49	Not applied to scalp (coal tar shampoo given if scalp affected). No comparison of patient characteristics. Small numbers in trial
Ortonne <i>et al</i> (1992)	62 adult patients with scalp seborrhoeic dermatitis and other locations. Randomised to 2% ketoconazole foaming gel or betamethasone in reducing course over 4 months.	Randomised single blind trial (level 1b)	Resolution at 1 and 4 months Recurrence	Effective remission in both groups at 1 month (ketoconazole 90%, betamethasone 73%). ARR 0.226 95% CI -0.44 to 0.90 At 4 months ketoconazole 89%, betamethasone 62%. ARR 0.290 95% CI 0.09 to 0.49 Recurrence rates similar 70% ketoconazole and 86% betamethasone. ARR 0.153 95% CI -0.08 to 0.38	Adverse effects greater in betamethasone group (52% v 16%) NNT 3
Stratigos <i>et al</i> (1988)	78 adult patients with seborrhoeic dermatitis. Randomised to 2% ketoconazole cream or 1% hydrocortisone cream OD for 4 weeks	Randomised double blind trial (level 1b)	Response of seborrhoeic dermatitis at 2 and 4 weeks	At 4 weeks effective remission in both groups (ketoconazole 81%, hydrocortisone 94%). ARR -0.139 95% CI -0.29 to 0.01	2 week result similar. Low incidence of side effects in both groups.
Faergemann (1986)	70 adult patients with scalp seborrhoeic dermatitis. Randomised to 2% miconazole, 1% hydrocortisone or Daktacort combination OD for 3 weeks and then if no cure for a further 3 weeks	Randomised double blind trial (level 1b)	Resolution at 3 and 6 weeks Recurrence after using same solution in patients achieving remission twice monthly for 3 months	At 3 weeks poor remission in all groups (miconazole 33%, hydrocortisone 33%). ARR -0.116 95% CI -0.15 to -0.01 Risk of recurrence higher in miconazole group (hydrocortisone 82%, miconazole 33%). ARR 0.452 95% CI 0.22 to 0.67	No details of randomisation. Interesting look at steroid-fungicide combination
Katsambas <i>et al</i> (1989)	50 adult patients with seborrhoeic dermatitis. Randomised to 2% ketoconazole cream or 1% hydrocortisone cream BD for 4 weeks	Randomised double blind trial (level 1b)	Response at 4 weeks	Effective response in both groups (ketoconazole 83%, hydrocortisone 96%). ARR -0.128 95% CI -0.30 to 0.04	Low incidence of side effects in both groups. No details of randomisation. No comparison of patient characteristics
Zeharia <i>et al</i> (1995)	36 children from 1 month to 10 years (mean 17 months) with scalp seborrhoeic dermatitis treated with bifonazole 1% shampoo 3 times a week for 4 weeks	Poor quality cohort study (level 4)	Resolution at 4 weeks	71% patients cured at 4 weeks	No randomisation or placebo comparator. Experimenters assumed in conclusion that the high rate of cures makes analysis "straightforward and self-evident"

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Is routine EEG helpful in the management of complex febrile seizures?

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A previously healthy 16 month old girl attends with the first episode of a complex febrile seizure (prolonged more than 15 minutes). She is neurologically normal, and examination reveals otitis media as the source of her fever. According to local protocol, her evaluation includes an EEG. One cannot but wonder as to the value of this routine practice.

Structured clinical question

In a 16 month old neurologically healthy girl [patient] with the first episode of a complex febrile seizure [risk factor] what is the probability of abnormalities after postictal EEG [outcome]?

Search strategy and outcome

Secondary sources—nil.

Search strategy—“(febrile, seizures, complex)” [MeSH] AND “EEG”.

Search results—68 individual articles found, one relevant. See table 3.

Commentary

A febrile seizure is defined as a seizure accompanied by fever without central nervous system infection. Complex febrile seizures, also called atypical or complicated, were defined as focal, prolonged more than 15 minutes, or repetitive.

The purpose of an EEG in the evaluation of complex febrile seizures is to help identify the nature of underlying acute or remote cerebral pathology and predict the risk of future afebrile seizures; no published study has shown that early EEG after a first episode of febrile seizures in postictal neurologically normal children will predict the occurrence of afebrile seizures.

Studies that investigate the relations of signs or symptoms with EEG abnormalities or between clinical subgroups of

complex febrile seizures, for example, focal, prolonged or recurrent, have not been found.

Only one small and non-independently validated descriptive report with 33 patients has specifically answered the question (Maytal *et al*). This study addressed the value of an early postictal sleep EEG to detect the prevalence of abnormalities in neurologically normal children with the first complex febrile seizures, up to one week after the seizure. The study was retrospective and did not indicate whether EEGs were repeated over a follow up period. Twenty four patients were qualified as complex cases based on one factor (prolonged in nine, repetitive in 13, and focal in two). Nine other patients had two complex factors (in six the seizures were long and repetitive, in two focal and repetitive, and in one the seizures were long, focal, and repetitive), which reduced the actual useful number of patients comparable to our patients in a clinical scenario.

The study was uncontrolled and included only neurologically normal children. Maytal and colleagues made no differences between complex febrile seizure clinical subgroups. An important number of patients experienced prior febrile seizures; not all patients were therefore assembled at a common point in the course of the disease.

The rate of abnormalities after an early postictal EEG in these patients was low and similar to the reported rate of abnormalities in children with simple febrile seizures, a fact that could be confirmed on a larger number of patients.

EEG should be considered in all children with complex febrile seizures who recur with afebrile convulsions, or in those children who recur with febrile seizures and exhibit developmental delays or abnormal neurological signs and symptoms.

CLINICAL BOTTOM LINE

- Abnormal EEG was uncommon in children with complex febrile seizures (95% probability less than 8.6%).
- The current local practice of EEG in neurologically normal children with complex febrile seizures does not appear to be evidence based. There is some limited evidence to suggest that it may not be useful.

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Table 3 EEG in the management of complex febrile seizures

Citation	Study group	Study type (level of evidence)	Outcome	Key results	Comments
Maytal <i>et al</i> (2000)	33 patients with complex febrile seizures. Mean age 17.8 months. Neurologically normal children	Retrospective chart review (level 4)	EEG	100% normal (95% CI 89.6–100)	Thirteen (39%) patients experienced prior febrile seizures

An update to “Inhaled steroids in the treatment of mild to moderate persistent asthma in children: once or twice daily administration?” (*Arch Dis Child* 2002;**87**:415–16) has been posted online at <http://www.archdischild.com/supplemental>.