ARCHIMEDES

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 They make no attempt to statistically aggregate the data, nor search the grey, unpublished literature.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 Sackett[5] and Moyer[6] 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.

- Is gradual introduction of feeding better than immediate normal feeding in children with gastroenteritis?
- Are follow up chest *x* ray examinations helpful in the management of children recovering from pneumonia?
- Should preterm neonates with a central venous catheter and coagulase negative staphylococcal bacteraemia be treated without removal of the catheter?

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How do we measure agreement?

How do we measure agreement—clinical agreement between observers—in order to indicate how good or bad at it we are? It's a problem which is raised in the interpretation of chest *x* rays in the second of this month's Archimedes topics.

The statistic chosen to show the degree of agreement is kappa (κ). This statistic tells us how much agreement there is *beyond chance*. Take the situation of two observers reporting chest *x* rayssay, and classifying them as abnormal or normal. If they were to report an equal number of abnormal and normal films, then we would expect by chance alone the two observers to agree 50% of the time. Kappa tells you how much the agreement is beyond chance: in this instance 75% agreement would be a kappa = 0.5; 75% agreement is 25% beyond chance, and this is half of the "perfect" extra of 50%. (The reason we use kappa, rather than just taking 50% off the simple agreement between two observers and using that value is that agreement due to chance varies with how often the observers classify the chest *x* rays as abnormal or abnormal. If they were to report three normal to one abnormal, then we'd expect them to agree—by chance—62.5% of the time.)

Exactly how to calculate kappa is a bit irrelevant, but for a rough guide to interpretation see table 1.

Table 1 Interpretation of kappa

Value of κ	Strength of agreement
<0.20	Poor
0.21–0.40	Fair
0.41–0.60	Moderate
0.61–0.80	Good
0.81–1.00	Very good

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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 **http://cebm**. jr2.ox.ac.uk/docs/levels.htm (accessed July 2002).

5 **Sackett DL**, Starus S, Richardson WS, *et al*. *Evidence-based medicine. How to practice and teach EBM*. San Diego: Harcourt-Brace, 2000.

6 **Moyer VA**, Elliott EJ, Davis RL, *et al*, eds. *Evidence based pediatrics and child health*, Issue 1. London: BMJ Books, 2000.

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

Is gradual introduction of feeding better than immediate normal feeding in children with gastroenteritis?

Report by

Nico Grunenberg, *General Practitioner, Coupar Angus, Fife, UK*

A mother with her 11 month old daughter attends the surgery. The child has gastroenteritis and is mildly dehydrated. Mum has been starving the child the past 24 hours as "everything comes back up". She has read this and also that milk feeds should be avoided, in her health manual at home. Having read a paper once on continuous milk feeding as opposed to gradual regrading of milk, I decide to investigate which approach would be better.

Structured clinical question

In [children with gastroenteritis] is [gradual introduction of feeding better than immediate normal feeding] with regard to [symptom control and time to resolution]?

Search strategy and outcome

Medline 1966–09/01 using the OVID interface.

[exp Gastroenteritis] AND [exp bottle feeding OR exp breast feeding OR exp feeding methods OR "feeding".mp] LIMIT to human AND (newborn infant OR infant OR preschool child OR child).

A total of 145 papers were found, of which 133 were irrelevant or of insufficient quality. The remaining 12 are shown in table 2.

Table 2 Gradual introduction of feeding versus normal feeding in children with gastroenteritis

Citation, country	Study group	Study type (level of evidence)	Outcome	Key results	Study weaknesses
Dugdale *et al* (1982), Australia	59 inpatients older than 6 months (average 22 months) with acute gastroenteritis were given clear fluids and then allocated either to half strength milk for 24 h and then full strength milk and food or immediate normal milk and food	RCT	Hospital stay (days) Weight	Immediate group 4.7; graduated group 5.4, p>0.5 During first 24 h of refeeding immediate group lost 0.02 (0.25) kg and the graduated group lost 0.14 (0.21), p> 0.05	Small numbers ? length of clear fluids
Haque *et al* (1983), Saudi Arabia	150 inpatients, all stages of dehydration between 1 month and 2 years of age randomised to three different feeding regimens: (1) clear fluids (6–24h) then gradual 1/4 strength milk reintroduction (2) clear fluids (6–24h) then full strength milk (3) continuing full strength milk	RCT	Increase in weight at discharge Diarrhoea length (days) Vomiting length (days) Length in hospital (days)	(1) 0.4 (0.1) (2) 0.8 (0.2) (3) 1.2 (0.7) Not stat significant (1) 3.0 (1.4) (2) 3.0 (1.3) (3) 3.8 (1.2) Not stat significant (1) 1.0 (1.1) (2) 1.8 (1.3) (3) 1.6 (1.2) Not stat significant (1) 3.1 (1.4) (2) 3.6 (1.2) (3) 3.8 (1.2) Not stat significant	Large proportion malnourished
Placzek and Walker-Smith (1984), UK	48 inpatients less than 18 months of age with gastro enteritis, >5% dehydration were after 24 h of GEM allocated to immediately full strength milk or gradual reintroduction	RCT	Complicated clinical course = recurrence of ether severe vomiting or watery diarrhoea with 2% or more reducing substances	70% (16) of full strength group uncomplicated; 96% (24) of gradual group uncomplicated	Small numbers Alternate allocation = randomisation 20% not thriving
Rajah *et al* (1988), South Africa	72 male black inpatients between 6 weeks and 2 years with prolonged dehydrating gastroenteritis (needing more than 72 h IV fluids) assigned to 4 different feeds; partially modified cows' milk formula, a lactose free casein containing formula, a lactose free soy protein formula, a lactose free whey- hydrolysate formula	RCT	Stool weights in 3 days following formula change	Significant drop in stool weight AL110 p<0.01 Alfare p<0.05 Alsoy p<0.05 No change with Lactogen	Only male black children
Bhan *et al* (1988), India	60 outpatients <5% dehydration between 3 and 24 months were fed either cereal based formula(A) or cows' milk (B)	RCT	Duration of diarrhoea post intervention (days)	Gr A 11.0 (10.0) > gr B 7.6 (10.8) NS p>0.05	Small numbers Difficulty comparing two preparations Selection criteria (close to hospital) ? compliance to treatment at home

Table 2 continued

Citation, country	Study group	Study type (level of evidence)	Outcome	Key results	Study weaknesses
		Mean weight gain (g/kg/24h)	GrA 2.0 (4.2) < grB 5.8(7.8) significant p<0.05		
Conway and Ireson (1989), Leeds	200 well hydrated inpatients, formula fed, ages 6 weeks to 12 months, acute gastroenteritis Gr1: 24h dextrolyte and gradual reintroduction of SMA gold Gr2: special full strength HN25 untill stools normal, gradual substitution by SMA gold Gr3: continued full strength SMA gold cap Gr4: continued formula S	RCT	Time to discharge Duration of diarrhoea (h) Severity of diarrhoea Weight gain	Gr1 6.9 (3.2); Gr2 6.9 (1.9); Gr3 6.9 (2.2); Gr4 7.1 (3.6); NS Gr1 64 (53.7); Gr2 47 (53.7); Gr3 68 (43.6); Gr4 51 (41.5) NS Gr2 0.8 (1.7) < Gr3 1.8 (1.5), p=0.05; group1 1.6 (1.7), gr4 1.4 (1.9) intermediate positions Day 2 Gr2,3,4 > Gr1 p=0.01; remains significant on day 5 p=0.05	117 had ORS before treatment, so is this immediate or delayed full strength feeding
Ooi *et al* (1989), Singapore	70 inpatients mild/ moderate dehydration, age 1 week to 50 months, either graduated milk feeds or full strength soy feed	CT	Duration of hospitalisation (days)	Soy 2.8; milk group 2.5, not statistically different	Small numbers ?randomised ?effect on symptoms ?received clear fluids
Armitstead *et al* (1989), UK	68 children, admitted or gastroenterology casualty, bottle fed, mild acute gastroenteritis dioralyte 24h plus: (1) gradual milk reintroduction (2) full strength milk (3) rapid regrade to whey hydrolysate formula	RCT	Hospital stay (days) Reducing substances Weight gain Stool frequency	Gr1 4 (0.2); gr2 3.6 (0.6); gr3 3.5 (0.4) NS None in all three groups Day 1–4: gr1 –0.35 (0.5); gr2 +0.65 (0.6); gr3 +0.15(0.2) Day 1–4: grp1 4–2.2; grp2 3.7–1.6; grp3 4.3–2.5	? sufficient number Bottlefed only (sponsored by Nestlé) Most mild dehydration
Haffejee (1990), South Africa	309 hospital patients age 3days to 28 months, acute diarrhoea, all stages of dehydration Formula fed children were randomised to their formula or soy based formula; breast fed children continued this and were divided in breast feeding only and breast feeding plus supplement	RCT	Recovery time (hrs) when hydration, weight and nature of stools were normal	Formula 70.5 (60.3); breast 60.9 (44.8); breast plus supplement 64.8 (43.3); soya 61.4 (43.5) p>0.05 NS	?blinded No patient chracteristics (race, % dehydration)
Lifschitz *et al* (1991), USA	8 children <5 months, mild to moderate dehydration, addition of 13C labelled rice at 6–22h and repeat at 14–17d later. Breath test measurement	CT	13C in breath when ill and after recovery	Apparent absorption not different, 13 C diarrhoea 86.6%- recovery 94%. NS	Small numbers Boys only Mild/moderate dehydration only
Hoghton *et al* (1996), UK	59 outpatient children <3 years old, <7 d gastroenteritis, <5% dehydrated; either immediate modified feeding + ORT (2) or ORT only for 24–48h after which modified food (no milk/wheat) (1)	PRCT, single blind	Median duration of diarrhoea Median % weight change Complication rate	Grp1 66.5 h; grp2 56h p=0.4 not significant Grp 1 0.005- grp 2 0.96 p=0.24 NS Similar, NS	Small numbers Mild dehydration only Parents assessed and charted symptoms (bias)
Sandhu *et al* (1997), Europe	230 weaned European children under the age of 3 admitted to hospital; rehydrated with ORS for 4 hours, then Group A: immediate normal diet, Group B 20h of ORS then normal diet, breast feeding continued throughout	RCT	Weight gain Complications	After rehydration weight gain grA 95g, grB 2g p=0.01; during hospitalisation grA> 200g, grB < 100g p=0.001; weight gain similar by day 5 and 14 No significant diffences re complications	No severely dehydrated children

Commentary

Nearly all studies showed no significant difference in length of symptoms and hospital stay. Two larger studies showed a significant increase in weight in the initial stages with immediate full strenth feeding. One larger study also showed an increase in severity but not in length of diarrhoea with immedaite feeding. This was associated with faster weight gain. One study showed benefit of lactose free feeds in severe dehydrating gastroenteriris. One smaller study showed more complicated clinical courses with immediate feeding; this was

a small study and 20% of the children needed intravenous hydration, possibly related to a more severe illness. In two smaller studies children had solids as well and did not do worse.

CLINICAL BOTTOM LINE

- In children with gastroenteritis, gradual reintroduction of feeding is no better than immediate normal feeding with regard to time to resolution and symptom control.

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Are follow up chest *x* ray examinations helpful in the management of children recovering from pneumonia?

Report by

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A 4 year old boy with a cough and a fever is referred by his general practitioner. On auscultation of his chest there are focal signs suggestive of a lower respiratory tract infection; a chest *x* ray examination confirms right lower lobe collapse and consolidation. He is started on oral antibiotics and discharged home within 24 hours. He is given a follow up appointment in four weeks time in the "registrar clinic" to be reviewed after having a repeat chest *x* ray examination according to your unit's protocol.

At the follow up appointment he is clinically well and has a normal radiograph. After discharging him you wonder whether the "routine" exposure to radiation outweighs the detection of persistent radiological changes.

Structured clinical question

In asymptomatic children with prior radiological evidence of pneumonia [patient] are routine follow up chest radiographs [intervention] necessary to assist in management decisions [outcome]?

Search strategy and outcome

Cochrane Database of Systematic Reviews—none relevant.

Pubmed—"pneumonia" AND "radiography" AND "follow-up"—480 references (four pertinent articles, three in English).

See table 3.

Commentary

There were only two studies, Heaton and Arthur, and Gibson *et al*, which looked at both clinical and radiological features at

Table 3 Follow up chest *x* ray examinations in children recovering from pneumonia

Citation	Study group	Study type (level of evidence)	Outcome	Key results	Comments
Heaton and Arthur (1998)	65 children with pneumonia (history, clinical and radiological diagnosis); mean age 3.5 years (0.4–13)	Retrospective cohort (level 4)	Chest radiograph findings at follow up	37/41 children asymptomatic: 35 (95%) normal CXR (95% CI 87% to 100%) 2 improved (5%) CXR	Only 41/65 children followed up fully; 11 were not offered follow up and a further 13 were lost to follow up
Gibson *et al* (1993)	77 children with pneumonia (history, clinical and radiological diagnosis)	Prospective cohort (level 4)	Clinical symptoms, signs and chest radiograph findings at follow up	59/72 children asymptomatic: 51 (87%) normal CXR 8 (13%) improved CXR	5 patients defaulted follow up.; 7 of the 8 patients with symptoms, signs, and radiological findings at follow up had pleural effusions on their original chest *x* ray
Grossman *et al* (1979)	129 children with a radiological diagnosis of pneumonia. (6 weeks – 15 years)	Prospective cohort (level 4)	Chest radiograph findings at follow up	56/70 (80%) children normal CXR by 4 weeks; 9/9 (100%) children with residual CXR changes at 4 weeks had normal CXR by 3 months	59 were lost to first follow up; no data regarding clinical symptoms and signs was collected at follow up

follow up. The study by Grossman *et al* provided no information about clinical features at follow up but gave similar overall resolution rates.

The studies by Heaton and Arthur, and Gibson *et al* came to similar conclusions despite significant differences in study design. The study by Heaton and Arthur was retrospective; Gibson *et al*'s prospective. Heaton and Arthur's study included children with asthma as it was felt that their exclusion would compromise the practical value of the study. By contrast, Gibson *et al* excluded children with "pre-existing disease"—which may have included asthma—and excluded children presenting with acute asthma, even if radiological findings suggested pneumonic consolidation.

The issue of interobserver variation in the interpretation of *x* rays was raised in both studies. In Gibson *et al*'s study a paediatric radiologist (Hollman) described minor, but improved radiological findings in eight chest *x* rays of asymptomatic children. When viewed by other radiologists four were reported as clear and four with minor changes; and when viewed by clinicians seven were reported clear and one with minor changes. This has practical implications for the paediatrician reviewing the child at follow up.

CLINICAL BOTTOM LINE

- In asymptomatic children with prior radiological evidence of pneumonia, routine chest radiology provides no benefit.

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Should preterm neonates with a central venous catheter and coagulase negative staphylococcal bacteraemia be treated without removal of the catheter?

Report by

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A 10 day old neonate (corrected gestation 29 weeks, birth weight 960 g) has been slow to establish feeds. Intravenous access is difficult and he is receiving parenteral nutrition through a central venous catheter (CVC). He develops temperature instability and hyperglycaemia. You decide to start empirical intravenous antibiotics but keep the CVC in situ as the infant is relatively stable. Peripherally taken blood cultures grow coagulase negative staphylococci (CoNS). Should the CVC be removed, knowing that a future replacement may be very difficult?

Structured clinical question

In a preterm neonate, with a central venous catheter in situ, who is bacteraemic with coagulase negative staphylococcus [patient], can catheter sterilisation [intervention] be achieved without increased morbidity or mortality [outcome]?

Search strategy and outcome

Secondary sources

Cochrane Database of Systematic Reviews, Cochrane Controlled Trials Register, Database of Abstracts of Reviews of Effectiveness: none relevant.

Primary sources

Pubmed.

"Catheterization, Central Venous"[MESH] AND "Staphylococcus"[MESH], limit (newborn: birth–1 month). There were 22 hits—one relevant study found.[5]

"Central venous catheter" AND "neonate" and "CONS" [all textwords]. There were seven hits—two relevant studies, one previously found above.

See table 4.

Commentary

Catheter related sepsis in preterm infants is a common neonatal problem (up to 15.3 infections per 1000 catheter

Table 4 Coagulase negative staphylococcal bacteraemia in preterm neonates with a central venous catheter

Citation	Study group	Study type (level of evidence)	Outcome	Key results
Benjamin *et al* (2001)	NICU inpatients with central venous catheter and CoNS bacteraemia (single positive culture)	Retrospective case notes review (level 4)	Prevalence of end organ damage (meningitis, osteomyelitis, abscess, death) Complicated bacteremia = end organ damage or >2 positive cultures	Sterilisation of catheter was attempted in 72 of 84 neonates with CoNS bacteremia with salvage achieved in 51% without complications Attempt at sterilisation did not significantly increase complicated bacteremia; OR 7.9 (95% CI 0.97–64.5) Significant increased risk of end organ damage after 4 positive blood cultures *v* 3 or less; OR 29.6 (95% CI 4.7–186.1)
Karlowicz *et al* (2002)	NICU admission with CVC and CoNS bacteraemia (2 +ve culture, same organism)	Observational cohort (level 4)	Persistent bacteraemia (>3 days) Death	63 of 119 infants had attempted sterilisation of CVC with salvage in 46%; but a 30% absolute increase in persistent bacteraemia, NNH 3.3 (95% CI 2.2–6.8) No increase in death or recurrent bacteraemia None of 19 patients with bacteremia >4 days achieved catheter salvage

days[1]). Inspite of this there is no good quality data informing the decision to remove central catheters in bacteraemic neonates. Both papers cited are retrospective case notes reviews. As a result the criteria for removal of catheters was not standardised and the management and follow up of the two groups (catheter retained versus removed) may have differed.

Benjamin *et al* did not distinguish between contaminated blood cultures, catheters colonised with CoNS and true catheter related CoNS sepsis. This is a practical problem for clinicians and researchers alike and has been recently reviewed[2]. Karlowicz *et al*[4] used two positive peripheral cultures of the same organism within three days as their definition of CoNS bacteraemia consistent with US Center for Disease Control guidelines.[3]

Karlowicz *et al* found that attempting CVC sterilisation did increase the risk of prolonged bacteraemia, but the numbers were too small to detect a difference in end organ infection and mortality. The concern that bacteraemia may ultimately seed to end organs appears to be supported by Benjamin *et al*. If the CVC was not removed after four positive cultures there was a significant increase in end organ damage. As the number of positive cultures or the duration of bacteraemia increased, CVCs were less likely to be successfully salvaged.[4 5] These studies suggest that catheters should be removed in infants who remain bacteraemic on treatment as the morbidity increases and the chances of line salvage diminishes with time. It is still unclear exactly how long clinicians should wait before abandoning sterilisation attempts and actually removing the catheter.

CLINICAL BOTTOM LINE

- CVCs infected with coagulase negative staphylococcus can be successfully salvaged in ~50% of cases.
- Attempting sterilisation of infected lines increases the risk of persistent bacteraemia, NNH = 3. End organ damage may be increased if the CVC is retained despite repeated positive cultures.
- Prospective randomised studies are required to convincingly address the risks versus benefits of treating infected CVCs in situ.

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