Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary

Edited by K Mackway-Jones

Best evidence topic reports (BETs) summarise the evidence pertaining to particular clinical questions. They are not systematic reviews, but rather contain the best (highest level) evidence that can be practically obtained by busy practising clinicians. The search strategies used to find the best evidence are reported in detail in order to allow clinicians to update searches whenever necessary. The BETs published below were first reported at the Critical Appraisal Journal Club at the Manchester Royal Infirmary or placed on the BestBETs web site. Each BET has been constructed in the four stages that have been described elsewhere. The BETs shown here together with those published previously and those currently under construction can be seen at http://www.bestbets.org. Six BETs are included in this issue of the journal.

- Biphasic or monophasic defibrillation for adult ventricular fibrillation
- Ascorbate for alkali burns to the eye
- Leucovorin (calcium folinate) in “antifreeze” poisoning
- Vasopressin or adrenaline (epinephrine) in cardiac resuscitation
- Is the central venous pressure reading equally reliable if the central line is inserted via the femoral vein
- Oucher or CHEOPS for pain assessment in children

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Clinical scenario
An adult is brought into the emergency department following an out of hospital ventricular fibrillary arrest. Ventricular fibrillation persists despite repeated shocks. You remember reading about biphasic defibrillation and wonder if it offers any advantages.

Three part question
In [an adult in ventricular fibrillation] is [external biphasic shock better than monophasic shock] at [achieving defibrillation]?

Search strategy
Medline 1966–06/03 using the OVID interface. Biphasic.mp AND (defib$.mp OR shock$.mp OR exp electric countershock) LIMIT to human AND English.

Search outcome
Altogether 337 papers were found of which seven related to out of hospital studies relevant to the original question.

Comment(s)
The studies shown in table 1 represent two independent groups of patients. The first two studies are a prospective randomised controlled trial (PRCT) and subsequent subgroup analysis of data from it. The last five studies represent ongoing investigation by a group of researchers with some overlap of patient groups between each study because of differing selection criteria and differing dates of study.

The PRCT provides good evidence for the superiority of biphasic defibrillation over monophasic. Analysis of the data from this study gives an NNT of three for successful defibrillation with first shock, and an NNT of four for successful defibrillation within the first three shocks by biphasic compared with monophasic waveforms. These out of hospital studies follow on from extensive in hospital and animal studies showing the superiority of biphasic defibrillation.

All the studies reported used the Heartstream Forerunner defibrillator with non-escalating 150 J shocks. This device uses an impedance compensating biphasic truncated exponential waveform. Laboratory and hospital based studies show the superiority of biphasic waveforms to be broadly applicable and not confined to this specific example of a biphasic waveform. Work is ongoing to refine which parameters of the waveform influence effectiveness. Evidence should be appraised for the effectiveness of the specific waveform used when selecting a defibrillator. Local considerations will determine when biphasic devices replace monophasic defibrillators.

FEATURED TOPIC REPORTS

Biphasic or monophasic defibrillation for adult ventricular fibrillation

Report by Rob Torok, Specialist Registrar
Checked by Jeremy Till, Staff Grade

A short cut review was carried out to establish whether biphasic defibrillatory shocks were superior to monophasic shocks in patients in ventricular fibrillation. Altogether 337 papers were found using the reported search, of which seven presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of these best papers are tabulated. A clinical bottom line is stated.
Ascorbate for alkali burns to the eye

Report by Kevin Mackway-Jones, Consultant
Checked by Janet Marsden, Senior Lecturer

Abstract

A short cut review was carried out to establish whether ascorbate drops are useful in the management of alkali burns to the eyes. Altogether 33 papers were found using the reported search, of which one presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of this best paper are tabulated. A clinical bottom line is stated.

Clinical scenario

A 22 year old man has been cleaning out an old chemical drum. He attends the emergency department with severe burning in his eyes. He says the drum was marked as NaOH 20%. You arrange for copious irrigation and oral pain relief. You contact the duly ophthalmologist who asks to start mydriatics, antibiotic ointement, and ascorbate drops. You do not have the ascorbate drops and wonder whether there is any evidence for their use.

Three part question

In [patients with alkali eye burns] do [ascorbate drops] [reduce short-term symptoms and long-term sequelae]?

Search strategy

Medline 1966- week 1 06/03 using the OVID interface. ([injury.mp OR exp “wounds and injuries” OR exp burns OR burn$.mp) AND (eye$mp OR exp eye$) OR (eye injury.mp OR eye injuries.mp OR exp eye injuries OR eye burn$.mp OR exp eye burns$) AND (alkali$.mp OR exp alkalis) AND (ascorbate$.mp OR ascorbic acid.mp OR exp ascorbic acid OR vitamin C.mp)
Search outcome
Altogether 33 papers were found of which one was relevant (table 2).

Comment(s)
Ascorbate (and citrate) treatment have been extensively investigated in rabbits but there are no good human data. A randomised controlled trial is mentioned as being underway in papers in 1980, but has not been reported.

CLINICAL BOTTOM LINE
There is no good evidence for the routine use of ascorbate in alkali burns in humans. A well designed randomised controlled trial should be performed.

Leucovorin (calcium folinate) in “antifreeze” poisoning
Report by Angaj Ghosh, Senior Clinical Fellow
Checked by Russell Boyd, Consultant

Abstract
A short cut review was carried out to establish whether the addition of intravenous calcium folinate to standard (ethanol) therapy reduced the visual complications of antifreeze (methanol and ethylene glycol). Altogether 12 papers were found using the reported search, of which one animal study presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of this best paper are tabulated. A clinical bottom line is stated.

Clinical scenario
A man attends the emergency department having deliberately taken 150 ml of “antifreeze”. The can of antifreeze has conveniently been brought along and you find it consists of a mixture of methanol and ethylene glycol. The Poisons Centre is contacted. In addition to treatment with ethanol it is suggested that intravenous Leucovorin (calcium folinate) is given. You wonder if there is any evidence to support this recommendation.

Three part question
In [an adult with methanol/ethylene glycol poisoning] is [the addition of intravenous calcium folinate better than ethanol alone] at [reducing the incidence of reduced acuity and retinal oedema]?  

Search strategy
Medline 1996–06/03 using the OVID interface. [exp leucovorin OR folinic acid.mp OR Calcium folinate.mp] AND [exp methanol OR methanol.mp OR exp ethylene glycol OR ethylene glycol.mp OR antifreeze.mp] LIMIT to English.

Search outcome
Altogether 12 papers were found, none of which were relevant to humans. One paper published in two different journals described studies on monkeys and suggested that the results could be extrapolated to humans (table 3).

Comment(s)
In humans methanol toxicity is characterised by a metabolic acidosis and an ocular toxicity that occur coincident with an accumulation of formate in blood. After experimental studies on monkeys, Noker and Tephly hypothesised that folate compounds could decrease formate accumulation after methanol by stimulating formate oxidation or utilisation and suggested a possible use for folates in the treatment of certain cases of human methanol poisoning.

CLINICAL BOTTOM LINE
There is no direct evidence of the usefulness of folates in methanol poisoning in humans. Local policy should be followed.

Vasopressin or adrenaline in cardiac resuscitation

Report by Kerstin Hogg, Clinical Research Fellow

Checked by Reddy Mahu, Clinical Fellow and Ian Crawford, Research Fellow

Abstract
A short cut review was carried out to establish whether vasopressin is more effective than adrenaline after cardiac arrest. Altogether 44 papers were found using the reported search, of which two presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of these best papers are tabulated. A clinical bottom line is stated.

Clinical scenario
A 67 year old man has been brought into the emergency department by paramedic ambulance. He was initially in ventricular fibrillation, but now has pulseless electrical activity. He collapsed 15 minutes ago and received immediate bystander basic life support. You wonder whether intravenous vasopressin would be better than adrenaline in this situation.

Three part question
In [cardiac resuscitation] is [vasopressin more effective than adrenaline] at achieving [return of spontaneous circulation and longterm survival]?

Search strategy
Medline 1966–06/03 using the OVID interface. [(exp vasopressins OR vasopressin.mp OR ADH.mp OR antidiuretic hormone.mp) AND (exp epinephrine OR epinephrine.mp OR adrenaline.mp) AND (exp resuscitation OR exp cardiopulmonary resuscitation OR exp Heart arrest OR arrest.mp OR exp ventricular fibrillation OR VF.mp OR ventricular fibrillation.mp OR asystole.mp OR EMD.mp OR electromechanical dissociation.mp OR PEA.mp OR pulseless electrical activity.mp)] LIMIT to human AND English.

Search outcome
Altogether 44 papers were found, only two papers compared the effects of adrenaline and vasopressin (table 4).

Comment(s)
The total number of patients studied remains small. The only RCT looking at hospital inpatients has shown no benefit in administering vasopressin during cardiac arrest.

> CLINICAL BOTTOM LINE
Vasopressin and adrenaline are equally efficacious after cardiac arrest.


Is the central venous pressure reading equally reliable if the central line is inserted via the femoral vein

Report by Joel Desmond, RCS Research Fellow

Checked by Mahmoud Megahed, Specialist Registrar

Abstract
A short cut review was carried out to establish whether femoral central venous lines were as reliable as subclavian or jugular lines at assessing right atrial filling pressure. Altogether 141 papers were found using the reported search, of which seven presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of these best papers are tabulated. A clinical bottom line is stated.

Clinical scenario
You have been called to the resuscitation room to see a 67 year old woman who has walked out in front of a bus while shopping in town. She has an obvious closed fracture of her left arm and she is complaining of abdominal pain and central neck pain. You elicit from her husband that she has had two heart attacks in the past and the drugs in her handbag are bendrofluazide, frumil, and lisinopril. Her blood pressure is 90/52 and her pulse is 105. You are concerned that she may be hypovolaemic, but you are aware of the dangers of giving too

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### Table 4

<table>
<thead>
<tr>
<th>Author, date and country</th>
<th>Patient group</th>
<th>Study type (level of evidence)</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Study weaknesses</th>
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<tbody>
<tr>
<td>Lindner KH et al, 1997, Germany</td>
<td>40 prehospital VF arrests Randomised to receive either initial dose vasopressin (40 U) or adrenaline (1 mg)</td>
<td>Prospective randomised double blind trial</td>
<td>Restoration of spontaneous circulation GCS on discharge Survival to discharge Spontaneous circulation on admission to hospital 24 hour survival</td>
<td>55% adrenaline vs 80% vasopressin patients (p=0.18) 10.7 adrenaline vs 11.7 vasopressin 15% adrenaline vs 40% vasopressin (p=0.16) 35% adrenaline vs 70% vasopressin (p=0.06) 20% adrenaline vs 60% vasopressin (p=0.02)</td>
<td>Only looked at VF Small patient sample All out of hospital arrests with mean emergency team response times of six minutes</td>
</tr>
<tr>
<td>Stiell IG et al, 2001, Canada</td>
<td>200 patients treated for cardiac arrest in three hospitals Randomised to receive either initial dose vasopressin (40 U) or adrenaline (1 mg)</td>
<td>Prospective randomised double blind trial</td>
<td>Survival to discharge Presence of pulse and BP for one hour after resuscitation 30 day survival Neurological function at discharge Vasopressin 12% adrenaline 14% Vasopressin group 39% Adrenaline group 35% (not significant) No difference between groups No difference between groups</td>
<td></td>
<td>Powered only to show a 20% difference in one hour survival</td>
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<tr>
<td>Murdoch IA et al, 1994, UK</td>
<td>12 children with cardiac pathology undergoing cardiac catheterisation while on assisted ventilation Mean age 13 months range 0.5–56 months SVC, IVC, and right atrial measurements</td>
<td>Observational cohort study</td>
<td>Comparison of IVC pressure readings compared with SVC and right atrial pressures</td>
<td>SVC to IVC readings were all within 1.2 mm Hg. Right atrial pressure to IVC pressure was always less than 0.7 mm Hg apart.</td>
<td>Young children only, small group of healthy outpatients coming for cardiac catheterisation. Supine patients only. Range of readings not given.</td>
</tr>
<tr>
<td>Chapt H et al, 1994, USA</td>
<td>33 paediatric cardiac-surgical patients age 2 days to 9 years Insertion of femoral venous catheter, and transthoracic right atrial catheter Mechanical and spontaneous ventilation</td>
<td>Observational cohort study</td>
<td>Comparison of right atrial and inferior vena caval pressure</td>
<td>23 of 31 paired patient readings were the same. 5 were within 2 mm Hg, 3 within 3 mm Hg. All spontaneously Breathing readings were within 2 mm Hg. IVC pressures were a mean of 0.71 mm Hg higher than RA pressure.</td>
<td>Study contained only children with congenital cardiac abnormalities.</td>
</tr>
<tr>
<td>Reda Z et al, 1995, USA</td>
<td>44 children in ICU with mechanical ventilation Group 1 had no evidence of abdominal distension</td>
<td>Observational cohort study</td>
<td>SVC pressure compared with IVC pressure Normal abdomen</td>
<td>Mean difference 0.93, max difference 3 mm Hg (unaffected by high PEEP or mean airway pressures 50% of SVC to IVC measurements were &gt;3 mm Hg</td>
<td>The diagnosis of abdominal distension was entirely subjective. No attempt was made to measure intra-abdominal pressure.</td>
</tr>
<tr>
<td>Yung M et al, 1995, Australia</td>
<td>39 children with both SVC and IVC central venous catheters in place in a paediatric ICU Age range 5 days to 14 years CVP range 3–17 mm Hg</td>
<td>Observational cohort study</td>
<td>SVC compared with IVC pressure</td>
<td>Mean difference 0.33 mm Hg. 22 of 39 pressure readings were equal. 33 of 39 pressures were within 1 mm Hg, 37 of 39 pressures were within 2 mm Hg. 3 children spontaneously breathing. 36 ventilated.</td>
<td>Position of femoral lines not verified radiologically and short lines used.</td>
</tr>
<tr>
<td>Yazigi A et al, 1996, Lebanon</td>
<td>30 patients post-coronary arterial bypass grafts Common iliac vein catheter placed at L4 level Measurements before and after extubation</td>
<td>Observational cohort study</td>
<td>SVC pressure compared with IVC pressure before intubation</td>
<td>Mean difference was 0.79 mm Hg 0.68 (SD) mm Hg</td>
<td>Common iliac vein rather than IVC measurement.</td>
</tr>
<tr>
<td>Joynt GM et al, 1996, Hong Kong</td>
<td>19 critically ill patients mechanically ventilated in ICU Femoral catheter placed close to right atrium in IVC. Confirmed by chest radiograph</td>
<td>Observational cohort study</td>
<td>SVC pressure compared with IVC pressure Causes of increased difference</td>
<td>Mean difference is 0.45 mm Hg (CI 0.30 to 0.60) Small tendency for increased PEEP and mean airway pressure to increase observed difference</td>
<td>Patients all supine and ventilated. Non-standard—40–70 cm multi-lumen catheters used. Interestingly an intra-abdominal pressure change of 2–22 cm H2O did not significantly change the differences observed.</td>
</tr>
<tr>
<td>Nahum E et al, 1996, Israel</td>
<td>9 children in a paediatric ICU 8 were mechanically ventilated Age 6 months–14 years Measurement of right atrial pressure and abdominal venous occlusion with or without iliac veins VCP ranged from 3–30 mm Hg</td>
<td>Observational cohort study</td>
<td>Right atrial pressure compared with SVC or common iliac vein pressure Causes of increased difference</td>
<td>Mean difference 0.22 mm Hg 1.52 (SD) mm Hg. 99.2% of measurements were &gt;3 mm Hg apart. None of increased CVP, PEEP and mean airway pressure readings were within 1 mm Hg.</td>
<td>This is a study in children only. 1 patient was excluded due to unreliable venous waveform of the right atrial catheter. 7 patients had congenital heart defects.</td>
</tr>
<tr>
<td>Ho KM, et al, 1998, Hong Kong</td>
<td>20 patients who were mechanically ventilated in ICU Simultaneous monitoring of SVC and common iliac vein pressure, all L5 using commonly available 20 cm central venous catheters SVC range 3–36 mm Hg</td>
<td>Observational cohort study</td>
<td>SVC pressure and common iliac vein pressure (CIVP)</td>
<td>Mean difference 0.1 mm Hg 1.06 (SD) mm Hg</td>
<td>Patients all supine and ventilated.</td>
</tr>
<tr>
<td>Walsh JT et al, 2000, UK</td>
<td>60 adult patients undergoing right heart studies or angiography 28 had impaired LV function and 38 had valvular heart disease</td>
<td>Observational cohort study</td>
<td>Difference between end expiratory right atrial pressure and SVC or IVC measurement</td>
<td>SVC mean difference –0.08 mm Hg (CI –2.2 to 0.38) IVC mean difference –0.23 mm Hg (CI –1.2 to 0.58)</td>
<td>The variability to acute changes were not assessed. Range of right atrial pressures found were not reported. Inadequate recordings obtained at all recording sites for 5 patients.</td>
</tr>
</tbody>
</table>
much fluid to a patient with probable heart failure. You elect to insert a central line for central venous pressure monitoring but she has a neck collar on and so you wonder if placing this via the femoral vein would affect your readings.

**Three part question**

In [patients requiring central venous pressure monitoring] is [a femoral vein central line as good as a jugular or subclavian line] at [reliability assessing right atrial filling pressure]?

**Search strategy**

Medline 1966–06/03 using the OVID interface. [(exp Central Venous Pressure OR Central Venous pressure.mp) AND (exp Vena Cava, Inferior OR vena cava.mp)] LIMIT to human.

**Search outcome**

Altogether 141 papers of which nine were found to be relevant. These papers are shown in table 5.

**Comment(s)**

There is extensive and consistent evidence that right atrial pressure can be reliably measured using both inferior vena cava or common iliac venous pressure measurements in supine patients. This has been proved in ventilated and spontaneously breathing adults and children. The readings of inferior vena cava measured pressures seem to be around 0.5 mm Hg lower than superior vena cava measured pressure on average and rarely more than 3 mm Hg different. This may not apply to patients with raised intra-abdominal pressure but applies to patients with high PEEP or raised mean airway pressures.

> **CLINICAL BOTTOM LINE**

Inferior vena cava or common iliac venous pressure can be used reliably to measure right atrial pressure and may be regarded as equivalent to readings of superior vena cava pressure.


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**Table 6**

<table>
<thead>
<tr>
<th>Author, date and country</th>
<th>Patient group</th>
<th>Study type (level of evidence)</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Study weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beyer JE et al, 1990, USA</td>
<td>25 children aged 3–7 who were given morphine or methadone postoperatively had their pain levels assessed using the CHEOPS, Oucher and the analogue chromatic continuous scales.</td>
<td>RCT to assess the effects of giving morphine or methadone postoperatively. All patients had their pain level assessed.</td>
<td>Looked at the postoperative pain scores 2 hourly for 36 hours and the correlation</td>
<td>The Oucher scale and the ACCS were strongly correlated. CHEOPS was only correlated with the Oucher 4 of 26 times and with ACCS 2 of 26 times.</td>
<td>Sample size not justified, only 25 and at each time point not everyone was assessed, ranges from 6–25. Done postoperatively so may not be applicable generally. Preoperative measurement was done 1 to 4 days before, not consistent might forget technique. Order was consistent with CHEOPS then Oucher and then ACCS to prevent the nurses being influenced by the self report scores.</td>
</tr>
<tr>
<td>Sutters KA et al, 1995, Netherlands</td>
<td>87 children post tonsillectomy. Children were given either IM ketorolac or IM saline. All children had their level of pain assessed using CHEOPS and the Oucher scale, if they were able.</td>
<td>RCT for treatment group. All patients had their level of pain assessed.</td>
<td>Changes in the scores over time</td>
<td>CHEOPS score and Oucher scores after analgesia</td>
<td>Does not include ages of children even though it states that the CHEOPS has thus been shown to be less reliable in older children. Does not say why children couldn’t complete the Oucher. Does not say whether the 2 assessments were done by independent people.</td>
</tr>
<tr>
<td>Jacobson SJ et al, 1997, UK</td>
<td>56 children aged 5–17. One group received IV morphine plus placebo and the other oral morphine plus placebo. Both groups were assessed for their pain using the CHEOPS, Oucher scale, Faces scale and a five point clinical assessment scale.</td>
<td>RCT (with respect to allocation to morphine treatment group). All patients were pain scaled.</td>
<td>Relation between the pain scales presented by use of a Pearson’s correlation and linear regression coefficient.</td>
<td>All pain scales correlated significantly</td>
<td>Little information about the pain scales. Does not say if they used the Oucher picture or numerical scale. Does not tell you if any were unable to use the Oucher scale. There was a single investigator for assessing pain and this may have introduced bias. Does not tell you the order of presentation of the pain scales and if this was random. Uses the CHEOPS in an older age range than it was designed for.</td>
</tr>
</tbody>
</table>
Oucher or CHEOPS for pain assessment in children

Report by Fiona Lyon, Senior House Officer
Checked by Debbie Dawson, Clinical Research Nurse

Abstract
A short cut review was carried out to establish which of the Oucher or CHEOPS pain assessments were best for assessing pain in children. Altogether 12 papers were found using the reported search, of which three presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of these best papers are tabulated. A clinical bottom line is stated.

Clinical scenario
A 3 year old child comes into casualty and you need to assess their pain. Would it be better to use the Oucher scale, a self report measure, or CHEOPS, a behavioural pain measure, as at this age using either seems equally valid.

Three part question
In [children] is the [Oucher better than CHEOPS] at [assessing pain]?

Search strategy
Medline 1966-week 1 06/03 using OVID. Cinahl 1982-week 1 06/03 using OVID. {Oucher.mp. AND cheops.mp.} AND [pain.mp. OR exp pain/]} LIMIT to human and English language)

Search outcome
Altogether 12 papers were found. Three of these addressed the subject indirectly, while testing efficacy of analgesia, they are reviewed in table 6.

Comment(s)
The underlying question is whether pain behaviour tools (such as CHEOPS) or self report tools (such as Oucher) are more useable and valid in the assessment of pain in children capable of assessment by both methods. None of the papers addressed the question directly. There seems to be some disagreement as to whether the CHEOPS score correlates to the Oucher score or not. Jacobson et al states that they are correlated, but this may be unreliable as CHEOPS was used in an older age range than was intended. Sutters et al state that CHEOPS is less reliable in older children, though they do not support this with any evidence. The Beyer study uses the two scales in the correct age range but the study is small and conducted postoperatively and general applicability is therefore moot. Further studies using a larger sample of patients in a wide range of clinical situations are needed.

CLINICAL BOTTOM LINE
There is no evidence to show whether Oucher or CHEOPS is better at assessing pain in children. Local policy should be followed.