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

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.

- Oxygen therapy for uncomplicated myocardial infarction
- Gastric lavage in paracetamol poisoning
- Oral corticosteroids in acute urticaria
- Ice, pins, or sugar to reduce paraphimosis
- Intravenous aminophylline or salbutamol in moderate to severe asthma
- Hypertonic or isotonic saline in hypotensive patients with severe head injury

Oxygen in acute uncomplicated myocardial infarction

Report by Richard Body, Senior House Officer
Checked by Kerstin Hogg, Clinical Research Fellow

Abstract
A short cut review was carried out to establish whether supplemental oxygen reduces mortality in patients with uncomplicated acute myocardial infarction. Altogether 290 papers were identified, only one of which was relevant to the question (table 1).

Clinical scenario
A 60 year old man presents to the emergency department with acute severe crushing chest pain. ECG shows changes consistent with acute myocardial infarction. You prescribe aspirin, thrombolysis, nitroglycerin, β blockers, and high flow oxygen. You know that oxygen therapy is traditionally held to be beneficial in this situation, but wonder if there is any evidence that it reduces mortality.

Three part question
In [patients with acute uncomplicated myocardial infarction] does [oxygen therapy] lead to [reduced mortality]?

Search strategy
Medline 1966-10/03 using the OVID interface. [exp myocardial infarction OR myocardial infarct$ OR MI.mp OR heart attack.mp OR exp Coronary Thrombosis OR acute coronary syndrome.mp] AND [exp oxygen OR oxygen.mp OR O2.mp OR exp oxygen inhalation therapy] AND [exp Mortality OR exp Hospital Mortality OR mortality.mp OR exp Death OR death.mp] LIMIT to human AND English.

Search outcome
Altogether 290 papers were identified, only one of which was relevant to the question (table 1).

Comment(s)
The routine use of oxygen in myocardial infarction has been widely advocated for many years. However, the only study to investigate the efficacy of this approach was underpowered to show a difference in mortality.

Clinical bottom line
In patients with uncomplicated acute myocardial infarction there is no evidence that supplemental oxygen reduces mortality. However the there is no evidence of harm. Further research is required before changes in current practice should be recommended.


Gastric lavage in paracetamol poisoning

Report by Stewart Teece, Clinical Research Fellow
Checked by Kerstin Hogg, Clinical Research Fellow

Abstract
A short cut review was carried out to establish whether gastric lavage is better than activated charcoal in cases of poisoning with paracetamol. Altogether 63 papers were found using the reported search, of which four 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 26 year old woman attends the emergency department 40 minutes after having taken 80 x 300 mg paracetamol tablets. As the dose taken is high and within the past hour you wonder whether she would benefit from gastric lavage.

Three part question
In [paracetamol poisoning] is [gastric lavage better than activated charcoal or nothing] at [reducing hepatotoxicity]?  

Search strategy
Medline 1966-10/03 using the OVID interface. [exp acetaminophen OR paracetamol.mp OR paracetamol] AND [exp poisoning OR poison$.mp OR exp overdose OR overdos$.mp] AND [exp gastric lavage OR gastric lavage.mp OR gastric decontamination.mp OR exp gastric emptying OR gastric emptying.mp OR exp irrigation OR washout.mp] LIMIT to human AND English.

Search outcome
Altogether 63 papers found of which 59 were irrelevant or of insufficient quality. Four of the remaining papers are shown in table 2, the fifth is a position statement mentioned in the comments section.

Comment(s)
The 1997 Joint Position Statement by the American Academy of Clinical Toxicology, European Association of Poisons Centres and Clinical Toxicologists stated gastric lavage should not be routinely used for poisoned patients. A similar statement from the British Poisons Centres indicates that gastric lavage is only to be used within 60 minutes of overdose and only with drugs not absorbed by charcoal.

> CLINICAL BOTTOM LINE
Gastric lavage is less effective than charcoal alone after paracetamol poisoning.

<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>Underhill TJ et al, 1990, UK</td>
<td>60 patients taken 5 g or more within 4 hours of attendance. Gastric lavage (14) v placebo(20) v activated charcoal(20) or nothing(5)</td>
<td>RCT</td>
<td>Plasma concentrations at 0, 1, 0.5 and 2.5 hours after treatment</td>
<td>39.3% reduction in concentration compared with 52.2% charcoal</td>
<td>Small Study</td>
</tr>
<tr>
<td>Buckley NA et al, 1999, Australia</td>
<td>981 consecutive paracetamol overdose. Gastric lavage and charcoal v charcoal alone or nothing</td>
<td>Observational study</td>
<td>Patients developing high risk concentrations</td>
<td>No statistically significant improvement with lavage + charcoal than charcoal alone.</td>
<td>Small study. Low dose. Liquid paracetamol only</td>
</tr>
<tr>
<td>Grierson R et al, 2000, Canada</td>
<td>10 volunteers given 4.0 g paracetamol. Gastric lavage at 1 hour compared with no treatment as crossover.</td>
<td>Crossover study</td>
<td>8 plasma concentrations over 8 hours</td>
<td>Reduction of 20% (95% CI 0.3 to 37%)</td>
<td>Small study. Low dose. Liquid paracetamol only</td>
</tr>
<tr>
<td>Christophersen AB et al, 2002, Denmark</td>
<td>12 volunteers given 50 mg/kg paracetamol. Lavage + charcoal v charcoal</td>
<td>Crossover study</td>
<td>12 plasma concentrations over 7 hours</td>
<td>Charcoal 66% reduction in concentration, lavage + charcoal 48.2%</td>
<td>Small numbers Low dose</td>
</tr>
</tbody>
</table>

Oral corticosteroids in acute urticaria

Report by M Poon, Paediatric Registrar
Checked by C Reid, Registrar

Abstract
A short cut review was carried out to establish whether the addition of oral corticosteroids to antihistamines leads to a
more rapid resolution of urticaria. Thirty nine 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 4 year old girl presents to the emergency department with an urticarial rash. Her general practitioner has prescribed an oral antihistamine but the rash has persisted. You wonder if there is a role for oral corticosteroids in this otherwise well child.

**Three part question**
In a [child with acute urticaria] does the [addition of oral corticosteroids to antihistamines] lead to [more rapid resolution of symptoms].

**Search strategy**

**Search outcome**
Cochrane Database of Systematic Reviews—no relevant results. Medline search results—39 articles, of which two were relevant (table 3).

**Comment(s)**
There are no studies specifically aimed at children with acute urticaria. These limited trials demonstrate improvement in symptoms when prednisolone is prescribed, but larger studies are needed.

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> **CLINICAL BOTTOM LINE**

In patients presenting to the emergency department with acute urticaria, the addition of oral prednisolone to an antihistamine results in decreased itch and more rapid rash resolution.


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**Ice, pins, or sugar to reduce paraphimosis**

**Report by Kevin Mackway-Jones, Consultant Checked by Stewart Teece, Clinical Research Fellow**

Abstract

A short cut review was carried out to establish which of the ice glove technique, the multiple puncture technique, or the application of sugar was the best approach for paraphimosis reduction. Thirty three 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**
You are asked to see a 19 year old man who has presented to the emergency department with paraphimosis. He states that he fell asleep after sex the night before and woke up with swelling. Simple traction has failed to cure the problem (but has brought tears to his eyes). A surgeon, a specialist registrar in emergency medicine, and a urologist are already in attendance. The first says that multiple punctures should be made with a needle, the second that an icd glove should be used, and the third that sugar should be applied. You wonder whether any of the suggested methods are evidence based.

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**Table 3**

<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>Pollack CV Jr and Romano TJ, 1995, USA</td>
<td>43 adult outpatients with acute urticaria given IM diphenhydramine then randomised to oral hydroxyzine plus either 20 mg prednisone 12 hourly for four days or placebo</td>
<td>RCT</td>
<td>10 point visual analogue itch score at 48 hours. Itch score at 5 days</td>
<td>Mean 48 hour itch score 1.3 in prednisone group v 4.4 in control group. Five day itch score 0 in prednisone group v 1.6 in control group</td>
<td>Adult patients only</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td>Description of rash at 48 hours and 5 days</td>
<td>No difference between groups at 48 hours. Rash resolved completely at 5 days in prednisone group</td>
</tr>
<tr>
<td>Zuberbier T et al, 1996, Germany</td>
<td>109 adult and paediatric patients with acute urticaria treated with loratadine 10 mg daily or prednisolone 50 mg daily for three days followed by loratadine 10 mg daily until remission of symptoms</td>
<td>Non-randomised prospective cohort study</td>
<td>Days until cessation of whealing</td>
<td>65.9% of had cessation of whealing by 3 days and a further 13.5% by 7 days in loratadine group, compared with 93.8% by 3 days and a further 3.1% by 7 days in the prednisolone group. Resolution in all patients after &gt;21 days. NNT with prednisolone for resolution of symptoms by 3 days = 4</td>
<td>Number of children unstated. Different exclusion criteria between groups (potentially pregnant women excluded from loratadine group). Small study. No power calculation. Rash not described at five days in control group.</td>
</tr>
</tbody>
</table>
Three part question
In [an adult male with irreducible paraphimosis] is [ice better than multiple puncturing or sugar] at [reducing swelling and allowing reduction]?

Search strategy
Medline 1966-10/03 using the OVID interface. [paraphimosis.mp OR paraphimosis.mp OR exp paraphimosis OR (foreskin.mp AND retraction.mp)] AND [reduc.mp OR exp ice OR ice$.mp OR punctures.mp OR exp punctures OR sugar.mp].

Search outcome
Altogether 33 papers found, of which three were relevant (table 4).

Comment(s)
There are no comparative or randomised trials in this area. Current treatment is based wholly on custom, practice, and word of mouth. Further research is warranted.

► CLINICAL BOTTOM LINE
All three methods have been shown to work, but there is no evidence to show which is best. Local guidelines should be followed.


Is intravenous aminophylline better than intravenous salbutamol in the treatment of moderate to severe asthma?

Report by Andrew Munro, Registrar
Checked by Michelle Jacobs, Specialist Registrar

Abstract
A short cut review was carried out to establish whether intravenous salbutamol or intravenous aminophylline offers the quickest and least complicated treatment for patients with moderate to severe asthma not responding to inhaled therapy. Altogether 71 papers were found using the reported search, of which nine 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 20 year old man is brought to the emergency department in acute respiratory distress with asthma. He has a history of poor compliance with unstable asthma and several hospital admissions in the past. His old notes are available and you notice whenever intravenous treatment has been started he has been given aminophylline. You feel that the best drug is a β2 agonist and that if it is not getting to the receptors via the airways then intravenous is the next best route. There is some dismay among the nursing staff when you formulate an intravenous regimen. They say they have never given it before. You wonder whether your approach is evidence based.

Three part question
In [patients with moderate to severe asthma resistant to inhaled β2 agonists] does [IV aminophylline or IV salbutamol] result in [quicker relief with less side effects]?

Search strategy
Medline 1966-10/03 using the OVID interface. [(exp albuterol/OR salbutamol.mp) AND intravenous.mp] AND [exp asthma/OR exp bronchial spasm/OR exp bronchoconstriction/ OR bronchoconstriction.mp] AND [exp aminophylline/OR aminophylline.mp OR exp theophylline/OR theophylline.mp] LIMIT to human AND English.

Search outcome
Altogether 71 papers found of which 62 were considered irrelevant or of insufficient quality for inclusion. The remaining nine papers are shown in table 5.

Comment(s)
Multiple small trials of reasonable quality show intravenous salbutamol to be as good if not better at reversing obstructive airflow in asthmatic patients. Those studies that were equivocal used drug regimens that could be considered subtherapeutic or confounded. Side effects, although present seem to be well tolerated. Recent or high powered trials comparing the two drugs do not exist.

► CLINICAL BOTTOM LINE
Intravenous salbutamol should be considered a first line agent in the acute management of severe asthma in adults.


<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>Houghton GR, 1973, UK</td>
<td>10 patients with paraphimosis aged 8–91 years. Iced glove placed for five minutes</td>
<td>Case series</td>
<td>Reduction</td>
<td>9 of 10</td>
<td>Small numbers</td>
</tr>
<tr>
<td>Gonzalez FM et al, 2001, Spain</td>
<td>Three patients with paraphimosis Application of granulated sugar for one to two hours</td>
<td>Case series</td>
<td>Reduction</td>
<td>All reduced</td>
<td>No controls</td>
</tr>
<tr>
<td>Kumar V and Javle P, 2001, UK and India</td>
<td>45 patients with paraphimosis Multiple puncture in patients with glans engorgement (39)</td>
<td>Case series</td>
<td>Reduction</td>
<td>All reduced if no skin changes</td>
<td>Small numbers</td>
</tr>
<tr>
<td>Author, date and country</td>
<td>Patient group</td>
<td>Study type (level of evidence)</td>
<td>Outcomes</td>
<td>Key results</td>
<td>Study weaknesses</td>
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<tr>
<td>Beswick KE, et al, 1975, UK</td>
<td>20 patients in GP setting with acute bronchospasm</td>
<td>Single blinded randomised trial of IV salbutamol or aminophylline</td>
<td>Vital signs PEFR FEV1 FVC</td>
<td>Same Difference favouring salbutamol at 10 and 20 min but not significant</td>
<td>Small non-ED study (most treated at home)</td>
</tr>
<tr>
<td>Williams SJ, et al, 1975, Wales</td>
<td>20 acute asthmatic patients with peak flow &lt;25% predicted, PaO₂&lt;68 mm Hg</td>
<td>DBRCT One hour infusion of either 500 µg aminophylline or 500 g salbutamol</td>
<td>Peak flow Pulse</td>
<td>Increased but not significant for salbutamol More tachycardia (significant) with salbutamol</td>
<td>Small numbers</td>
</tr>
<tr>
<td>Tribe AE, et al, 1976, Australia</td>
<td>23 acute asthma patients</td>
<td>DBRCT of IV aminophylline v salbutamol</td>
<td>Spirometry Non-significant benefit and peak effect of aminophylline</td>
<td>Suboptimal dose of salbutamol</td>
<td>Variable pre-trial treatment</td>
</tr>
<tr>
<td>Femi-Pearse D, et al, 1977, Nigeria</td>
<td>50 patients with peak flow &lt;165l/min</td>
<td>Single and double blinded trials of salbutamol and aminophylline</td>
<td>Five minute pulse and peak flow measures</td>
<td>Significant benefit in peak flow at 5 min (p&lt;0.005) and 20 min (p&lt;0.05) for single blinded trial only for salbutamol. No difference in pulse rate</td>
<td>Small trial Low dose of salbutamol</td>
</tr>
<tr>
<td>Johnson AJ, et al, 1978, UK</td>
<td>39 of 62 acute asthmatic patients unresponsive to initial IV 10 min aminophylline infusion and nebulised salbutamol</td>
<td>Single blinded RCT Either 1 mg/min aminophylline or 10 µg/min salbutamol</td>
<td>Peak expiratory flow FEV1 FVC</td>
<td>All received IV aminophylline initially No initial bolus of salbutamol</td>
<td>Variable used of nebulised salbutamol acutely</td>
</tr>
<tr>
<td>Evans WV, et al, 1980, UK</td>
<td>21 acute asthma patients</td>
<td>Single blinded RCT comparing aminophylline, salbutamol or combined IV</td>
<td>Spirometry Non-significantly quicker time to improvement with aminophylline and combined infusion</td>
<td>Significant tachycardia in salbutamol group Variable background preventive treatment Small numbers Variable baseline severity</td>
<td>Small group, not acutely unwell</td>
</tr>
<tr>
<td>Sahay JN, et al, 1984, UK</td>
<td>20 adults with FEV₁&lt;70% predicted</td>
<td>Double blinded RCT crossover of aminophylline, terbutaline and salbutamol</td>
<td>Spirometry All produced significant improvement, salbutamol significantly better than aminophylline to 30 min after dose then no difference with better peak effect.</td>
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<tr>
<td>Sharma TN, et al, 1984, India</td>
<td>30 known asthmatic patients with acute bronchospasm</td>
<td>RCT of aminophylline, salbutamol or terbutaline</td>
<td>Spirometry Salbutamol significantly better FEV₁</td>
<td>Blinding not clear</td>
<td></td>
</tr>
<tr>
<td>Grief J, et al, 1985, Israel</td>
<td>21 patients (mean age 38 years) with acute or chronic asthma</td>
<td>Single blinded crossover 20 min infusion of salbutamol or aminophylline</td>
<td>% Increase in peak flow</td>
<td>Significant benefit to 30 min (p&lt;0.01) and 45 min (p&lt;0.05) after infusion</td>
<td>Small study</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>Pulse rate</td>
<td>Salbutamol shows</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>BP</td>
<td>No difference</td>
<td>Not fully blinded</td>
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<td></td>
<td>Plasma [K⁺]</td>
<td>Average drop of 0.6 mmol/l</td>
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<td></td>
<td></td>
<td>Tremor</td>
<td>More in salbutamol group</td>
<td></td>
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</tbody>
</table>
Table 6

<table>
<thead>
<tr>
<th>Author, date and country</th>
<th>Patient group</th>
<th>Study type (level of evidence)</th>
<th>Key results</th>
<th>Outcomes</th>
<th>Study weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wade CE et al, 1997, Sweden</td>
<td>223 patients with severe head injuries and hypotension. 250 ml 7.5% NaCl/6% Dextran 70 (single bolus) v standard care (usually Ringer’s lactate)</td>
<td>Cohort analysis from six previous PRCTs</td>
<td>24 hour survival</td>
<td>Odds ratio of 1.92 (p = 0.06) for survival 24 hours with HS</td>
<td>Heterogenous trials, which were not all designed to assess head injured patients</td>
</tr>
<tr>
<td>Shackford SR et al, 1998, USA</td>
<td>34 patients with severe head injuries and undergoing ICP monitoring. 1.6% NaCl (HS) v Ringer’s lactate (RL) to treat “episodes of haemodynamic instability” during initial resuscitation and for 5 days</td>
<td>PRCT ICP</td>
<td>Discharge Survival</td>
<td>Odds ratio of 2.12 (p = 0.048) for survival until discharge with HS</td>
<td>Long term outcome not assessed</td>
</tr>
<tr>
<td>Simma B et al, 1998, Switzerland</td>
<td>32 children with severe head injury and ICP monitoring. 1.6% NaCl (HS) v Ringer’s lactate (RL) as only IV fluid for 3 days following injury</td>
<td>PRCT ICP and CPP</td>
<td>Number of interventions to control increased ICP</td>
<td>Average of 41 interventions per patient with HS v 11 interventions with RL (p = 0.01)</td>
<td>HS group had more severe injuries</td>
</tr>
</tbody>
</table>

Hypertonic or isotonic saline in hypotensive patients with severe head injury

Report by Rupert Jackson, Consultant
Checked by John Butler, Consultant

Abstract
A short cut review was carried out to establish whether hypertonic or isotonic saline improved the outcome most in patients with severe head injury. Altogether 66 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
You are resuscitating a 30 year old man with a severe closed head injury. His GCS was 3 on admission. He is intubated and ventilated and a CT scan is being organised. His blood pressure is only 90/40 mm Hg. You want to improve cerebral perfusion by giving intravenous fluid but are aware that too much fluid might worsen cerebral oedema. You wonder whether there would be any advantage in giving hypertonic saline.

Three part question
In [patients with severe head injury and low blood pressure] is [hypertonic saline better than isotonic fluids] at [increasing...?]

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cerebral perfusion, reducing intracranial pressure and improving outcome?}

**Search strategy**
Medline 1966-10/03 using the OVID interface. [exp hypertonic solutions/or exp saline solution, hypertonic/or "hypertonic saline".mp.] AND [exp craniocerebral trauma/OR "head injury".mp. OR "HEAD INJURIES".mp. OR exp head injuries, closed/OR "head injured".mp. OR exp brain injuries/ OR "brain injury".mp.]

**Search outcome**
Altogether 66 papers were found of which three were trials of sufficient quality that addressed the three part question. These are displayed in table 6.

**Comment(s)**
All three trials showed some improvements in patients with head injury treated with hypertonic saline compared with standard care. The largest showed a two times survival advantage in those treated with hypertonic saline but this was a cohort analysis rather than a PRCT. It is not established how much hypertonic saline should be given and when. A large randomised controlled trial would help to establish the role of hypertonic saline.

**CLINICAL BOTTOM LINE**
There is insufficient evidence at present to justify the use of hypertonic saline as resuscitation fluid in patients with severe head injury.

