Therapeutic hypothermia after out of hospital cardiac arrest

Bernard A Foëx and John Butler

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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 website. 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, the last two of which are negative.

- **Nebulised magnesium in asthma**
- **Role of flexion/extension radiography in neck injuries in adults**
- **Peripheral pulses to exclude thoracic aortic dissection**
- **Wound closure in animal bites**
- **Therapeutic hypothermia after out of hospital cardiac arrest**
- **Gastric lavage in aspirin and non-steroidal anti-inflammatory drug overdose**

**Nebulised magnesium in asthma**

Report by Jonathan Costello, Specialist Registrar

Checked by Marten Howes, Specialist Registrar

doi: 10.1136/emj.2004.017939

**Abstract**

A short cut review was carried out to establish whether the addition of nebulised magnesium sulphate to \( \beta \) agonist therapy improves outcome in acute asthma. Altogether 69 papers were found using the reported search, of which five 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 known asthmatic patient is brought into the emergency department with signs consistent with acute asthma. Little improvement is noted with nebulised \( \beta \) agonist therapy. You wonder if adjunctive nebulised magnesium sulphate would provide any benefit.

**Three part question**

In [an adult with asthma] is [nebulised \( \beta \) agonist with nebulised magnesium sulphate better than nebulised \( \beta \) agonist alone] at [improving airflow and reducing morbidity]?

**Search strategy**

Medline 1966-05/04 using the Ovid interface. [(Exp magnesium OR magnesium\$.mp OR exp magnesium sulfate OR magnesium sul\$.mp OR exp magnesium compounds OR magnesium compound\$.mp) AND (nebulise\$.mp OR nebulize\$.mp OR vaporise\$.mp OR vaporize\$.mp OR inhal\$.mp) AND (Exp asthma OR asthma\$.mp OR exp bronchial spasm OR bronchial spasm\$.mp OR bronchospasm.mp))] Limit to human AND English language.

**Search outcome**

Altogether 69 articles found of which five were relevant to the original question (see table 1).

**Comment(s)**

Extensive evidence exists regarding efficacy of intravenous magnesium in bronchospasm reversal. Of the few studies that relate to nebulised magnesium in bronchospasm reversal, samples remain small and conflicting results regarding optimal dose magnesium and sole agent efficacy persist. It is empirically suggested such mode of magnesium delivery be considered in cases of severe asthma only.

**CLINICAL BOTTOM LINE**

There is currently insufficient evidence to support the routine addition of nebulised magnesium to standard \( \beta \) agonist therapy in acute asthma exacerbation.

**References**


Role of flexion/extension radiography in neck injuries in adults

Report by Elspeth Pitt, Specialist Registrar
Checked by Shobhan Thakore, Consultant
doi: 10.1136/emj.2004.017947

Abstract
A short cut review was carried out to establish whether flexion-extension radiography is indicated in the investigation of a neurologically intact adult patient with midline neck tenderness and normal 3-view cervical spinal radiographs. Altogether 101 papers were found using the reported search, of which five 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 man attends the emergency department having been involved in a high speed road traffic accident. He complains of neck pain and midline neck spinal tenderness but has no neurological signs or symptoms. Standard 3-view cervical spine radiology (lateral, anteroposterior, and odontoid views) shows no abnormality. You wonder if a flexion/extension radiograph would show any significant injury/instability.

Three part question
In a neurologically intact adult patient with neck pain following trauma but normal plain radiographs do [flexion/extension x-rays] aid [diagnosis of ligamentous or soft tissue injury with instability]?

Search strategy

Search outcome
Altogether 101 papers from Medline and 79 from Embase were found of which five were relevant (see table 2).

Comment(s)
Most studies are retrospective so the evidence base is limited. Flexion-extension cervical spine radiography (FECSR) is safe in the properly selected patient. If the patient has adequate evidence...
movement FECSR rarely adds to investigation if standard cervical spine radiography (SCSR) is normal. FECSR after an abnormal SCSR is of limited value because of the possibility of inadequate studies (because of pain or muscle spasm) and the risk of false negatives.

► CLINICAL BOTTOM LINE
In the acute setting FECSR adds little if CT/MR can be used to seek fractures or ligamentous instability.
Peripheral pulses to exclude thoracic aortic dissection

Report by Stewart Teece, Clinical Research Fellow
Checked by Kerstin Hogg, Clinical Research Fellow
doi: 10.1136/emj.2004.017954

Abstract
A short cut review was carried out to establish whether the absence of a clinical pulse deficit can be used to exclude dissecting thoracic aneurysm in patients with chest pain. Altogether 89 papers were found using the reported search, of which one was a previous systematic literature review. A further two papers published since the review were also found. These three papers 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 63 year old man presents to the emergency department with a one hour history of central chest pain of sudden onset. ECG shows ST elevation in his inferior leads. He has no obvious contraindications to thrombolysis in his history but you wish to ensure he has no evidence of a dissecting thoracic aneurysm before giving streptokinase. To keep your door to the operating theatre open you wish to ensure he has no evidence of a dissecting thoracic aneurysm before giving streptokinase. To keep your door to the operating theatre open you wish to ensure he has no evidence of a dissecting thoracic aortic aneurysm. This is far too low to be considered suitable as a SnOut and other investigations are required.

Three part question
In [patients with acute chest pain] what is the sensitivity of abnormal peripheral pulses for [diagnosing acute dissection of the thoracic aorta]?

Search strategy

Search outcome
Altogether 89 papers found. One was a systematic review of the literature up to 2000. All relevant papers except two that post-dated it were included in this review. These three papers are summarised in the table 3.

Wound closure in animal bites

Report by Freya Garbutt, Specialist Registrar
Checked by Rachel Jenner, Specialist Registrar
doi: 10.1136/emj.2004.017962

Abstract
A short cut review was carried out to establish whether primary closure of animal bites increases wound infection rates. Altogether 74 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 patient presents to the emergency department having been attacked by a dog. He has sustained lacerations to his hand and face. You provide oral analgesia, ensure he is covered for tetanus, and thoroughly clean and irrigate the wounds under local anaesthesia. The patient asks you to close the wounds and you wonder if there is any evidence that this would increase the rate of infection.

Three part question
In [adult patients with animal bites] does [wound closure] increase the [risk of infection]?

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>Klompas M, 2000, USA</td>
<td>16 papers pooling sensitivity of pulse deficit in 1,586 patients</td>
<td>Meta-analysis</td>
<td>Sensitivity</td>
<td>31% (95% CI 24% to 39%)</td>
<td>Most studies lacked control group</td>
</tr>
<tr>
<td>Bossone E et al, 2002, Italy</td>
<td>513 patients with type A aortic dissection confirmed on imaging, surgery, or postmortem examination</td>
<td>Mix of prospective diagnostic trial and retrospective review of case notes</td>
<td>Sensitivity</td>
<td>30%</td>
<td>Most retrospective analysis of signs in patients with known dissection</td>
</tr>
<tr>
<td>Mehta RH et al, 2002, International</td>
<td>550 patients with type A dissection in an international registry</td>
<td>Retrospective analysis of registry</td>
<td>Sensitivity</td>
<td>30.1%</td>
<td>Small study considering five countries</td>
</tr>
</tbody>
</table>

Comment(s)
Few studies use a control group and use a top-down approach of assessing only patients with a dissection. This makes calculation of likelihood ratios difficult. There is yet to be a blinded bottom up trial of pulse deficit in thoracic aorta dissection. Interestingly it appears that pulse deficit may have use in the risk assessment of dissection.

► CLINICAL BOTTOM LINE
Pulse deficit has a sensitivity of around 30% in dissecting thoracic aortic aneurysm. This is far too low to be considered suitable as a SnOut and other investigations are required.

Klompas M. Does this patient have an acute thoracic aortic dissection? JAMA 2002;287:2262-72.
Search strategy
Medline 1966–05/04 using the OVID interface. [exp "bites and stings" OR Bite.mp] AND [suture.mp OR exp sutures OR steristrip.mp OR exp adhesives OR glue.mp] LIMIT to human AND English language.

Search outcome
Altogether 74 papers were found of which one provided the best evidence to answer the clinical question (see table 4).

Comment(s)
Only one PRCT has been performed to directly investigate infection rates in animal bite wounds treated by primary closure compared with non-closure. No antibiotics were used in this study. It excludes puncture wounds, wounds infected at presentation, wounds with other structures involved, and those requiring plastic surgery. The study concludes that there is no significant difference in infection rates between the two groups except in those wounds occurring to the hands. Significantly more hand wounds became infected than wounds elsewhere, and of all hand wounds significantly more became infected in the group treated by closure. The study also noted that a delay to presentation of more than 10 hours was associated with an increased risk of infection but the relevant raw data are not presented.

▲ CLINICAL BOTTOM LINE
Bite wounds to the hand should be left open. Non-puncture wounds elsewhere may be safely treated by primary closure after thorough cleaning.


Therapeutic hypothermia after out of hospital cardiac arrest
Report by Bernard A Foëx, Consultant
Checked by John Butler, Consultant
doi: 10.1136/emj.2004.017970

Abstract
A short cut review was carried out to establish whether therapeutic hypothermia improves outcome in comatose post cardiac arrest patients. Altogether 176 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 46 year old father of three collapses in the street with a cardiorespiratory arrest. He receives five minutes of bystander CPR. When the ambulance crew arrives he is in ventricular fibrillation. Return of spontaneous circulation is achieved after defibrillation. On arrival in the emergency department he is still in coma. You wonder if his chances of survival or of a good neurological outcome would be improved by therapeutic hypothermia?

Three part question
In [adults who have sustained an out of hospital cardiac arrest] does [therapeutic hypothermia] [improve outcome]?

Search strategy

Search outcome
Altogether 176 papers were found in Medline, only four described any sort of comparative study. Four papers were found in Cochrane, none of which were relevant to the three part question (see table 5).

Comment(s)
There are only four trials of mild hypothermia after cardiac arrest, and only two are randomised controlled trials. Treatment could not be blinded. All show a neurological benefit from mild hypothermia. Only two showed a survival benefit. The main inclusion criterion for these two trials was that patients had been in ventricular fibrillation. In study number 3 patients with a non-perfusing ventricular tachycardia were also included. There is no uniform protocol for how long hypothermia should be maintained, or the rate of rewarming.

▲ CLINICAL BOTTOM LINE
Patients remaining unconscious after out of hospital cardiac arrest, from ventricular fibrillation or non-perfusing ventricular tachycardia, should be cooled to 32–34°C for at least 12 hours as part of their post-arrest intensive care to optimise neurological recovery. This therapeutic strategy has been
 endorsed by the International Liaison Committee on Resuscitation.


### Three part question

[In overdose with aspirin or other non-steroidal anti-inflammatory drugs] is [gastric lavage better than activated charcoal] at [reducing toxicity]?

### Search strategy

Medline 1966-05/04 using the Ovid interface. {exp gastric lavage OR gastirc lavage.mp OR exp gastric emptying OR gastric emptying.mp OR exp irrigation OR lavage.mp OR emt$.mp OR irrigat$.af OR washout.af OR wash-out.af} AND {exp poisoning OR exp overdose OR exp suicide OR exp Self-Injurious Behavior/ OR pois$.af OR overdos$.af OR suicid$.af OR (deliberate adj5 self adj5 harm).af OR dsh.af} AND {exp aspirin OR exp anti-inflammatory agents, non-steroidal OR salic$.af OR nsaid.mp OR ketoprofen.af OR diclofenac.af OR acetylsalicylic acid}
azapropazone.af OR celecoxib.af OR dexketoprofen.af OR diltiazem.af OR etodolac.af OR fenbufen.af OR fentanyl.af OR flurbiprofen.af OR indomethacin.af OR indomethacin.af OR ketoprofen.af OR mefenamic acid.af OR meloxicam.af OR nabumetone.af OR naproxen.af OR phenylbutazone.af OR piroxicam.mp OR exp piroxicam OR rofecoxib.af OR sulindac.af OR tenoxicam.af OR tiaprofenic acid.af} LIMIT to human AND English language.

Search outcome
Altogether 72 papers were found 71 of which failed to answer the three part question. A further reference was found after scanning of paper references. The two papers are shown in the 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>Danel V et al, 1988, UK</td>
<td>12 healthy volunteers given 1.5 g aspirin acting as own controls treated with nothing, charcoal and lavage</td>
<td>Prospective controlled study</td>
<td>Salicylate recovered in urine over 24 h</td>
<td>Control 13.3% lavage 8.8% charcoal 7.0%</td>
<td>Statistical significance not assessed Dose fairly small Number of patients small</td>
</tr>
<tr>
<td>Lapatto-Reiniluoto O et al, 1999, Finland</td>
<td>Nine healthy volunteers as own controls given 400 mg ibuprofen. Treated with water (control), charcoal or charcoal followed by lavage</td>
<td>Prospective controlled trial</td>
<td>AUC plasma ibuprofen as % of control</td>
<td>Control 100% charcoal alone 70% (p&lt;0.05) charcoal + lavage 51% (p&lt;0.05). No statistical significance between control groups</td>
<td>Small numbers Therapeutic ibuprofen dose</td>
</tr>
</tbody>
</table>

Comment(s)
There are no large scale trials performed in this area, however those that exist show that at best lavage is no better if not slightly worse than charcoal at reducing salicylate toxicity. Lavage although better than nothing has an element of risk involved in its practice and charcoal must therefore be treatment of choice.

▶ CLINICAL BOTTOM LINE
Gastic lavage is no better than charcoal alone at reducing toxicity after aspirin or NSAID overdose.  