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, 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

K Mackway-Jones, Department of Emergency Medicine, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL, UK; kevin.mackway-jones@man.ac.uk


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 β 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 β agonist therapy. You wonder if adjunctive nebulised magnesium sulphate would provide any benefit.

Three part question

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

Search strategy

Medline 1966-05/04 using the Ovid interface. [(Exp magnesium OR magnesium$$.mp OR exp magnesium sulfate OR magnesium sulphate$$.mp) AND (nebulised$$$.mp OR nebulize$$.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 bronchospasmp.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 β agonist therapy in acute asthma exacerbation.


www.emjonline.com
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 neck pain following trauma but normal plain 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.

Table 1

<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>Meral A et al, 1996, Turkey</td>
<td>40 paediatric patients (age 8–13) with asthmaic exacerbation randomised to nebulised salbutamol or nebulised magnesium sulphate</td>
<td>Prospective observational</td>
<td>PEFR</td>
<td>Higher PEFR values in the b2 agonist group at 5 min (p = 0.01), 60 min (p = 0.05) and at 360 min (p &lt; 0.01)</td>
<td>Small sample size, unclear randomisation and blinding procedure, questionable outcome measure reliability and reproducibility, unknown exclusion criteria</td>
</tr>
<tr>
<td>Mangat HS et al, 1998, India</td>
<td>33 patients (age 12–60) with asthma (new onset or exacerbation) randomised to nebulised salbutamol or nebulised magnesium sulphate</td>
<td>PRCT</td>
<td>PEFR, Fischl index</td>
<td>No statistical difference between both groups (PEFR increase p = 0.34; Fischl index improvement p = 0.76)</td>
<td>Small sample size, no power calculation, pre-treatment with corticosteroids, uncertain randomisation and blinding procedure</td>
</tr>
<tr>
<td>Nannini LJ, et al 2000, Argentina</td>
<td>35 patients (aged &gt;18, Av 40) with asthmaic exacerbation randomised to nebulised salbutamol/normal saline (placebo) or to nebulised salbutamol/magnesium sulphate</td>
<td>PRCT</td>
<td>PEFR (relative change)</td>
<td>Percentage increase in PEFR 30% and 60% higher in magnesium treated group at 10 min (p &lt; 0.03) and 20 min (p &lt; 0.04) respectively</td>
<td>Small sample size, unclear blinding procedure</td>
</tr>
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<td>Bessmertny O et al, 2002, USA</td>
<td>80 patients (age 18–65) with asthma exacerbation randomised to nebulised salbutalor/normal saline (placebo) or nebulised salbutalor/magnesium sulphate</td>
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<td>PRCT PEFR</td>
<td>No significant difference found between the groups</td>
<td>Sample group pre-treatment selection bias</td>
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<td>Hughes R et al, 2003, New Zealand</td>
<td>52 patients (age 16–65) with severe asthma exacerbation randomised to nebulised salbutamol/normal saline (placebo) or nebulised salbutamol/magnesium sulphate</td>
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<td>Sample group pre-treatment selection bias, uncertain randomisation procedure</td>
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Three part question
In a neurologically intact adult patient with neck pain following trauma but normal plain radiographs do flexion-extension x-rays aid diagnose 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

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Three part question
In a neurologically intact adult patient with neck pain following trauma but normal plain radiographs do flexion-extension x-rays aid diagnose 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
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.

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**Table 2**

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<th>Outcomes</th>
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<th>Study weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lewis LM et al, 1991, USA</td>
<td>141 consecutive adult trauma patients who had flexion extension cervical spine radiography (FECSR) after static cervical spine radiography (SCSR) series</td>
<td>Retrospective review</td>
<td>Radiological abnormality on SCSR</td>
<td>11 of 141 instability on FECSR of which four had normal SCSR. Four had equivocal SCSR and three had fractures on SCSR</td>
<td>Retrospective No comment on blinding or not of radiologist</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Instability on FECSR</td>
<td>FECSR (compared with SCSR alone) increased the sensitivity and specificity for recognising injury from 71% to 99% and 89% to 93% respectively but this was not statistically significant because of small numbers</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Neurological sequelae from performing radiographs</td>
<td>No neurological complications from FECSR</td>
<td>Adequacy of radiography not defined</td>
</tr>
<tr>
<td>Wang JC et al 1999, USA</td>
<td>290 patients after trauma—with neck pain, alert, neurologically intact had FECSR</td>
<td>Retrospective review</td>
<td>Instability on FECSR</td>
<td>1 of 290 (0.34%) instability on FECSR</td>
<td>Retrospective</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Adequacy of FECSR</td>
<td>97 of 290 (33.45%) FECSR were inadequate and could not be assessed for instability so evaluated clinically later</td>
<td>Assessment of adequacy—qualitative</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Neurological problems because of FECSR</td>
<td>No neurological changes during FECSR</td>
<td>SCSR not mentioned in study</td>
</tr>
<tr>
<td>Brady WJ et al, 1999, USA</td>
<td>451 patients over age 18 years with blunt trauma undergoing SCSR and FECSR</td>
<td>Retrospective descriptive review</td>
<td>Abnormality on FECSR</td>
<td>372 (82.5%) normal SCSR of whom five (1.3%) had abnormal FECSR</td>
<td>Retrospective Convenience Sample—referral bias Clinical outcome of patients not really addressed No comment on adequacy of radiographs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Complications of FECSR</td>
<td>Patients with blunt trauma and neck complaints and an abnormal SCSR are more likely to have abnormal FECSR showing cervical injury requiring stabilisation than if they had normal SCSR No complications from FECSR</td>
<td></td>
</tr>
<tr>
<td>Pollack CV Jr et al, 2001, USA</td>
<td>86 patients who had FECSR with radiographically demonstrated cervical spine injury from blunt trauma from NEXUS database (patients also had SCSR and CT/MR as deemed necessary)</td>
<td>Subgroup analysis on prospective observational database</td>
<td>Incidence of diagnostic FECSR in patients with normal SCSR</td>
<td>6 of 86 had normal SCSR but abnormal FECSR but none of these were deemed to be clinically significant</td>
<td>No statistics performed No comment on adequacy of radiographs Past hoc subgroup analysis CT/MR used—confounding results Small numbers</td>
</tr>
<tr>
<td>Inska EK et al, 2002, USA</td>
<td>106 cases aged 17–85, within 12 hours of blunt trauma, evaluated with FECSR—awake, had pain and normal SCSR</td>
<td>Retrospective review</td>
<td>Interpretation and adequacy of CSR radiographs, Clinical outcome on follow up</td>
<td>9 of 106 patients had cervical spine injury (CSJ) on basis of radiograph, clinical diagnosis, and follow up. 74 of 106 (70%) had adequate FECSR of whom five had CSJ (no false negatives). 32 (30%) had inadequate FECSR of whom four (12.5%) had CSJ subsequently found on CT or MRI</td>
<td>Retrospective No statistics performed Not all patients had the same imaging—varied number and types of plain radiography and CT/MR Excluded 228 patients because of inadequate follow up or radiograph taken after 12 hours</td>
</tr>
</tbody>
</table>

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**References**


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 aortic aneurysms 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 needle time below 20 minutes you wonder whether excluding a pulse deficit clinically is sensitive enough to avoid waiting for radiography.

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.

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 aneurysms. This is far too low to be considered suitable as a SnOut and other investigations are required.


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 Most retrospective analysis of signs in patients with known dissection</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% (24% to 37%)</td>
<td>No pulse deficit</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 Retrospective review of diagnosed patients May include patients from Bossone et al paper.</td>
</tr>
</tbody>
</table>
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 adhesive 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, 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 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.

Table 4

<table>
<thead>
<tr>
<th>Author, date and country</th>
<th>Patient group</th>
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<tbody>
<tr>
<td>Maimaris C and Quinton DN, 1988, UK</td>
<td>96 ED patients with 169 dog bite lacerations (punctures excluded) randomised to primary closure or leaving wound open</td>
<td>PRCT</td>
<td>Infection</td>
<td>Seven infections in sutured group (7.6%), compared with six in open group (7.7%) (not significant)</td>
<td>Randomisation method not stated</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Significantly more infections in hand wounds in both groups than elsewhere (p&lt;0.01)</td>
<td>Uncertainty about the adherence to standard wound toilet in early stages of study</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>5 of 30 infections of hand wounds sutured (16%), 4 of 45 infections of hand wounds left open (8%)</td>
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<td></td>
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<td></td>
<td></td>
<td>Cosmesis good or fair in both groups (scar width 2–6 mm in open compared with 1–5 mm in closed)</td>
<td></td>
</tr>
</tbody>
</table>

> **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.


Clinical scenario
A 53 year old widow attends the emergency department having taken 20 aspirin and 20 ibuprofen 1.5 hours previously. You remember that NSAIDs slow gastric emptying and wonder whether gastric lavage would be of use in toxicity reduction.

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 gastric lavage.mp OR exp gastric emptying OR gastric emptying.mp OR exp irrigation OR lavage.mp OR empt$.$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 pois0$.$af OR overdos$.$af OR suicid$.$af OR (deliberate adj5 self adj5 harm$.$).af OR ds$.$af) AND (exp aspirin OR exp anti-inflammatory agents, non-steroidal OR salic$.$af OR nsaid$.$mp OR ketoprofen$.$af OR diclofenac$.$af OR acemetacin$.$af OR acemefacn$.$af OR}

Gastric lavage in aspirin and non-steroidal anti-inflammatory drug overdose

Report by Stewart Teece, Clinical Research Fellow
Checked by Ian Crawford, Clinical Research Fellow
doi: 10.1136/emj.2004.017988

Abstract
A short cut review was carried out to establish whether gastric lavage was better than activated charcoal alone at reducing toxicity after aspirin or other non-steroidal anti-inflammatory drug (NSAID) overdose. Altogether 72 papers were found using the reported search, of which one presented the best evidence to answer the clinical question. A further relevant paper was found on scanning the references of papers identified. 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.
azapropazone.af OR celecoxib.af OR dexketoprofen.af OR diflunisal.af OR etodolac.af OR fenbufen.af OR feno-profen.af OR flurbiprofen.af OR indometacin.af OR indo-methacin.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.

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<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.
