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 practicing clinicians. The search strategies used to find the best evidence are reported in detail in order to allow clinicians to update searches whenever necessary. Each BET is based on a clinical scenario and ends with a clinical bottom line which indicates, in the light of the evidence found, what the reporting clinician would do if faced with the same scenario again.

The BETs published below were first reported at the Critical Appraisal Journal Club at the Manchester Royal Infirmary1 or placed on the BestBETs website. Each BET has been constructed in the four stages that have been described elsewhere.2 The BETs shown here together with those published previously and those currently under construction can be seen at http://www.bestbets.org.3 5BETs are included in this issue of the journal, the last two of which are negative:

- Glucagon infusion in refractory anaphylactic shock in patients on beta-blockers
- Topical analgesia for pain reduction in arterial puncture
- Antifibrinolytics for the initial management of subarachnoid haemorrhage
- Anticoagulation before cardioversion of acute atrial fibrillation in the emergency department
- Anticoagulation post-cardioversion of acute atrial fibrillation in the emergency department

### Glucagon infusion in refractory anaphylactic shock in patients on beta-blockers

**Report by Martin Thomas, Specialist Registrar**

**Checked by Ian Crawford, Senior Clinical Fellow**

doi: 10.1136/emj.2005.023507

**Abstract**

A short cut review was carried out to establish whether a glucagon infusion is of benefit in patients with refractory anaphylaxis. 62 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 53 year old man attends the emergency department with a severe allergic reaction, having been stung by a wasp. You note that he takes atenolol for angina. Despite adequate treatment with adrenaline and intravenous fluids, he remains hypotensive and subsequently dies. Afterwards, you hear that a glucagon infusion may have been of benefit and wonder if there is any evidence for this.

**Three part question**

In [anaphylactic shock for patients on regular beta-blockers] does [the use of a glucagon infusion] improve [outcome]?

**Search strategy**

Medline 1966-12/04 using the OVID interface. ([exp Glucagon OR glucagon.af] AND [exp Hypersensitivity OR anaphyla$.af. OR allerg$.af]) LIMIT to human AND English language.

<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>Zaloga OP et al, 1986, USA</td>
<td>A 75 year old white male with refractory anaphylactic shock following injection of a radiocontrast dye. Daily medications included atenolol 50 mg daily.</td>
<td>Case report</td>
<td>Improvement in BP following administration of glucagon</td>
<td>Resolution</td>
<td>Case report</td>
</tr>
<tr>
<td>Javeed N et al, 1996, USA</td>
<td>A 52 year old white male with refractory anaphylactic shock following injection of a radiocontrast dye. Daily medications included atenolol 50 mg daily.</td>
<td>Case report</td>
<td>Improvement in BP following administration of glucagon</td>
<td>Resolution</td>
<td>Case report</td>
</tr>
</tbody>
</table>
**Search outcome**
Altogether 62 papers were found, of which two were directly relevant to the three part question.

**Comment(s)**
Although there is a pathophysiological rationale for the use of glucagon in anaphylactic patients on beta-blockers the clinical evidence is limited to case reports only. This is not surprising as the situation rarely arises and it is probably unlikely that large series will be published. Although the two reports indicate success, such reports are subject to publication bias and as such should be interpreted with caution.

**Clinical Bottom Line**
Although the evidence is of limited quality, a glucagon infusion may be of benefit in anaphylactic shock for patients on regular beta-blockers when all other, more well-recognised, treatments have failed.


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**Topical analgesia for pain reduction in arterial puncture**

Report by Debbie Dawson, Clinical Research Nurse
Checked by Kerstin Hogg, Clinical Research Fellow
doi: 10.1136/emj.2005.023515

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<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>
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<tbody>
<tr>
<td>Tran NQ et al, 2002, Australia</td>
<td>Topical use of 4% amethocaine gel applied for 30 mins prior to arterial puncture for blood gas analysis</td>
<td>RCT</td>
<td>Primary outcome was pain experienced (measured on a visual analogue scale, 0-100)</td>
<td>Amethocaine group-mean score 16.0 (SD 23.3) Placebo group-mean score 20.7 (SD 18.5)</td>
<td>Amethocaine can cause blanching to the skin, which may affect blinding by introducing bias, though this was not commented on in the paper as one of the reported side effects. Women of &quot;child bearing potential&quot; were excluded from the study. Does this mean that all pre-menopausal women were not included, and if so why?</td>
</tr>
<tr>
<td>Heart rate before, during and after arterial puncture</td>
<td>Number of passes through the skin</td>
<td>These differences were not statistically significant</td>
<td></td>
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<tr>
<td>81 adult patients. 42 received amethocaine gel and 39 received a placebo gel</td>
<td>Side effects of the gel</td>
<td>Small number of minor irritations reported in both groups. Tetracaine group-mean score 25.2 +/- 32.6 The placebo group-mean score 23.8 +/- 27.4 (p = 0.78)</td>
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<tr>
<td>Aaron AD, et al, 2003, Canada</td>
<td>Fifty patients randomised, 24 to receive tetracaine and 26 placebo, 45 minutes prior to elective radial arterial puncture</td>
<td>RCT</td>
<td>Patient’s perception of pain (visual analogue scale, 0-100)</td>
<td>Mean time from skin puncture to procurement of 1 ml of arterial blood</td>
<td>Tetracaine group-mean time 70 +/- 103 seconds. Placebo group-mean time 49 +/- 48 seconds (p = 0.40)</td>
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<td>Difficulty performing the test (graded scale)</td>
<td>Identical for both groups (p = 0.86)</td>
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</tbody>
</table>
blood gas analysis OR exp blood specimen collection OR arterial blood.mp) NOT (BestBETs paediatric filter)] LIMIT to English language AND human.

**Search outcome**
Altogether 431 papers were identified, of which 429 were found not to answer the question directly, the remaining two papers were found to be relevant.

**Comment(s)**
Previous studies looking at the use of EMLA in pain reduction with venepuncture have highlighted that an application time of 60–90 minutes is necessary for adequate anaesthesia; the manufacturers of tetracaine recommend 45 mins application prior to venepuncture. It may be necessary that longer application times are needed for deeper structures.

> **CLINICAL BOTTOM LINE**
The papers found in this search provide little evidence for the effectiveness of topical analgesia in reducing the pain and discomfort of arterial puncture. Further studies with longer application times would be useful.


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**Antifibrinolytics for the initial management of sub arachnoid haemorrhage**

*Report by Simon Carley, Locum Consultant in Emergency Medicine*

*Checked by Ayan Sen, Clinical Fellow*

*doi: 10.1136/emj.2005.023523*

**Abstract**
A short cut review was carried out to gather the evidence for and against the use of tranexamic acid to patients who have suffered subarachnoid bleeding. 267 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 24 year old man presents to the emergency department following a sudden headache and collapse. He is GCS 14 on arrival with no localising signs. CT scan demonstrates a subarachnoid haemorrhage. In a previous hospital you were advised to give tranexamic acid to prevent rebleeding. You suggest this to the neurosurgical SpR on call who thinks you are talking rubbish and strongly advises against it.

You wonder if he is an evidence based neurosurgeon ... or whether he is behind the times?

**Three part question**
[In patients with confirmed SAH] are [antifibrinolytics better than placebo] at [reducing rebleeding, improving survival, or improving morbidity]

**Search strategy**

Medline: [exp Subarachnoid Hemorrhage/OR subarachnoid haemorrhage.mp OR exp Aneurysm, Ruptured/OR SAH.mp] AND [exp Antifibrinolytic Agents/OR antifibrinolytics.mp OR exp Tranexamic Acid/OR tranexamic acid.mp OR exp Aminocaproic Acid/OR aminocaproic acid.mp OR exp 6-Aminocaproic Acid/OR epsilon aminocaproic acid.mp OR epsilon amino-caproic acid.mp OR antifibrinolytics$] AND Cochrane: subarachnoid hemorrhage OR subarachnoid haemorrhage.

**Search outcome**
Altogether 267 references found including one recent Cochrane review. No papers after the publication of the Cochrane review were found. The summary of the Cochrane review is presented here.

**Comment(s)**
A well constructed review article answers the question. Although there appears to be a reduction in the rate of rebleeding this is not matched by an improvement in patient outcome. The authors of this review postulate that the increase in cerebral ischaemia seen in most of the trials may account for this.

From a clinical perspective there appears to be little to be gained from the administration of antithrombolytics in confirmed SAH.

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<table>
<thead>
<tr>
<th>Patient group</th>
<th>Author, date, and country</th>
<th>Study type (level of evidence)</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Study weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roos YB/WEM et al, 2003, Netherlands</td>
<td>9 trials involving 1,399 patients included. Papers sourced through electronic and hand searching methods. RCTs of IV or oral agents included. Only confirmed SAH patients.</td>
<td>Systematic review and Meta analysis</td>
<td>Poor outcome (defined as death, vegetative state or severe disability)</td>
<td>Non significant OR of 1.12 (CI 0.88–1.43) for poor outcome with treatment</td>
<td>This is a well researched review. The studies match the clinical problem well. Of 21 trials found only 9 satisfied the quality filter of the authors which suggests some rigour in the approach used. One of the review authors’ own study was included in the review.</td>
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<td></td>
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<td>Rebleeding at end of follow up</td>
<td>Less with treatment OR = 0.55 (CI 0.42–0.71)</td>
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<td>Risk of cerebral ischaemia</td>
<td>Worse with treatment OR = 1.39 (CI 1.07–1.82)</td>
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<td>Risk of death</td>
<td>Non significant. OR = 0.99 (CI 0.79–1.24)</td>
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<td>Rate of hydrocephalus</td>
<td>Non significant. OR = 1.14 (CI 0.86–1.51)</td>
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</table>
Anticoagulation before cardioversion of acute atrial fibrillation in the emergency department

Report by Katherine Potier, Specialist Registrar in Emergency Medicine
Checked by Richard Parris, Locum Consultant
doi: 10.1136/emj.2005.023549

Abstract
A short cut review was carried out to establish whether anticoagulation is indicated prior to emergency department cardioversion of a patient with acute onset atrial fibrillation. 54 papers were found using the reported search, of which none presented any evidence to answer the clinical question. It is concluded that there is no evidence available to answer this question. Further research is needed.

Clinical scenario
A 58 year old man presents to the emergency department with a 24 hour history of new onset AF. You decide to cardiovert him in the department (chemically or electrically) and wonder whether he needs to be anticoagulated prior to this to reduce any thromboembolic risks.

Three part question
In a patient with [acute atrial fibrillation undergoing cardioversion in the emergency department] does [anti-coagulation immediately before cardioversion] [reduce the incidence of thrombo-embolism]?

Search strategy
Medline: [exp Atrial fibrillation OR AF.mp OR atrial fibrillation.mp] AND [exp electric countershock OR cardioversion.mp OR exp anti arrhythmia agents/OR chemical cardioversion.mp] AND [exp heparin OR heparin.mp OR exp heparin, low molecular weight OR low molecular weight heparin.mp OR fractionated heparin.mp OR bemiparin.mp OR certoparin.mp OR dalteparin.mp OR oxaparin.mp OR reviparin.mp OR tinzaparin.mp OR fragmin.mp OR clexane.mp] LIMIT to human AND English language.
Cochrane: (atrial fibrillation) AND (anticoagulation) AND (cardioversion)

Search outcome
Altogether 54 papers were found, of which none are relevant to the question.

Relevant paper(s)
No relevant papers given.

Comment(s)
Anticoagulation is recommended before cardioversion of AF lasting more than 2 days to avoid thromboembolic complications. However there is little evidence from the literature to support its use in AF of shorter duration.

Anticoagulation post-cardioversion of acute atrial fibrillation in the emergency department

Report by Katherine Potier, Specialist Registrar, Emergency Medicine

Abstract
A short cut review was carried out to establish whether anticoagulation is indicated after emergency department cardioversion of a patient with acute onset atrial fibrillation. 243 papers were found using the reported search, of which none presented any evidence to answer the clinical question. It is concluded that there is no evidence available to answer this question. Further research is needed.

Clinical scenario
A 45 year old man who presented to your emergency department with new onset AF has been successfully chemically cardioverted. You wonder whether he needs anti-coagulating on discharge to prevent any longer term thromboembolic complications.

Three part question
In a [patient with acute atrial fibrillation who has cardioverted to sinus rhythm] does [anticoagulation post-cardioversion] [reduce the incidence of thromboembolic complications]?

Search strategy
Cochrane: (atrial fibrillation) AND (anticoagulation) AND (cardioversion)

Search outcome
A total of 243 papers were found, none of which answered the three part question.

Relevant paper(s)
No relevant papers given.

Comment(s)
It has been recommended that patients with AF lasting more than 2 days should be anticoagulated for at least 1 month post cardioversion. This is because of the formation of
intratrial thrombus and the potential for embolic events with atrial stunning. However, there is no evidence to support this approach in AF of shorter duration as the likelihood of cardioversion related thromboembolism is thought to be very low.

**Clinical Evidence—Call for contributors**

Clinical Evidence is a regularly updated evidence-based journal available worldwide both as a paper version and on the internet. Clinical Evidence needs to recruit a number of new contributors. Contributors are healthcare professionals or epidemiologists with experience in evidence-based medicine and the ability to write in a concise and structured way.

**Areas for which we are currently seeking authors:**
- Child health: nocturnal enuresis
- Eye disorders: bacterial conjunctivitis
- Male health: prostate cancer (metastatic)
- Women’s health: pre-menstrual syndrome; pyelonephritis in non-pregnant women

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**Being a contributor involves:**
- Selecting from a validated, screened search (performed by in-house Information Specialists) epidemiologically sound studies for inclusion.
- Documenting your decisions about which studies to include on an inclusion and exclusion form, which we keep on file.
- Writing the text to a highly structured template (about 1500–3000 words), using evidence from the final studies chosen, within 8–10 weeks of receiving the literature search.
- Working with Clinical Evidence editors to ensure that the final text meets epidemiological and style standards.
- Updating the text every six months using any new, sound evidence that becomes available. The Clinical Evidence in-house team will conduct the searches for contributors; your task is simply to filter out high quality studies and incorporate them in the existing text.
- To expand the topic to include a new question about once every 12–18 months.

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If you are interested in becoming a peer reviewer for Clinical Evidence, please complete the peer review questionnaire at www.clinicalevidence.com or contact Klara Brunnhuber (kbrunnhuber@bmjgroup.com).

**CLINICAL BOTTOM LINE**

There is no evidence to support the anticoagulation of patients with new onset AF on discharge, who have been successfully cardioverted in the emergency department (whether this be chemically, electrically, or spontaneously).