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.1 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 Six topics are covered in this issue of the journal:

- Frusemide or nitrates in acute left ventricular failure
- Bypass or external rewarming after hypothermic cardiac arrest
- Using intravenous adenosine in asthmatics
- First ECG in chest pain
- Timing of aspirin administration in acute myocardial infarction
- CPAP in acute left ventricular failure


Frusemide or nitrates in acute left ventricular failure

Report by Annette Johnson, Specialist Registrar
Search checked by Kevin Mackway-Jones, Consultant

Clinical scenario
An 80 year old man is brought into the emergency department in the early hours of the morning with acute shortness of breath. He is pale, clammy and very distressed. You diagnose acute left ventricular failure. You have heard that frusemide may increase vascular resistance and wonder whether nitrates should be used instead.

Three part question
In [patients with acute left ventricular failure] is [frusemide better than nitrates] at [reducing symptoms and avoiding the need for intubation]?

Search strategy
Medline 1966–09/00 using the OVID interface. ([exp heart failure, congestive OR exp ventricular dysfunction, left OR exp left ventricular failure.mp OR exp pulmonary edema.mp OR pulmonary oedema.mp] AND [nitrate$.mp OR exp nitroglycerin OR nitroglycerin.mp OR gtn.mp OR glyceryl trinitrate.mp OR exp isosorbide dinitrate.mp OR exp isosorbide dinitrate.mp OR isosorbide mononitrate.mp] AND [exp furosemide OR furosemide.mp OR frusemide.mp OR exp bumetanide OR bumetanide.mp OR exp diuretics OR loop diuretic$.mp]) LIMIT to human AND english.

Search outcome
Altogether 116 papers found of which 112 were irrelevant or of insufficient quality. The remaining four papers are shown in table 1.

Comments
There are still no large trials looking directly at this question. The majority of this work was carried out on patients with recent myocardial infarction.

Clinical bottom line
Nitrates have some benefit as the first line pharmacological treatment of acute pulmonary oedema.

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>Nelson GI et al, 1983</td>
<td>28 men with radiographic and haemodynamic evidence of left ventricular failure following acute myocardial infarction Frusemide (1 mg/kg) iv, isosorbide dinitrate (50–200 µg/kg/h)</td>
<td>PRCT</td>
<td>PRCT</td>
<td>PRCT</td>
<td>PRCT</td>
</tr>
<tr>
<td>Verma SP et al, 1987</td>
<td>48 men with transmural myocardial infarction and a pulmonary artery wedge pressure over 20 mm Hg within 18 h of admission to CCU Frusemide (12) iv isosorbide dinitrate (ISDN) (12) iv, hydralazine (12) iv, prenalterol (12)</td>
<td>PRCT</td>
<td>PRCT</td>
<td>PRCT</td>
<td>PRCT</td>
</tr>
<tr>
<td>Cotter G et al, 1998, Israel</td>
<td>110 patients with acute severe pulmonary oedema. All treated with oxygen at 10 l/min and frusemide 40 mg. Isosorbide dinitrate 3 mg every 5 min (56); frusemide 80 mg every 15 min and isosorbide dinitrate 1 mg/h (54).</td>
<td>PRCT</td>
<td>PRCT</td>
<td>PRCT</td>
<td>PRCT</td>
</tr>
</tbody>
</table>


Bypass or external rewarming after hypothermic cardiac arrest

Report by Claudia Webster-Smith, Medical Student
Search checked by Angaj Ghosh, Senior Clinical Fellow

Clinical scenario
A 24 year old woman is brought into the emergency department having fallen into a frozen lake. Passers by heard her cries for help and alerted the emergency services who rescued her 15 minutes later. On the way to hospital she suffered a cardiac arrest. Her core temperature on arrival is 25 degrees centigrade. You know that she needs rewarming but wonder whether her eventual outcome will be improved by cardiopulmonary bypass rather than external rewarming.

Three part question
In [severely hypothermic patients who have suffered cardiac arrest] is [core rewarming by cardiopulmonary bypass better than external rewarming] at [re-establishing spontaneous circulation and leading to eventual discharge]?

Search strategy
Medline 1966–09/00 using the OVID interface. ([exp heart arrest OR cardiac arrest.mp] AND [exp hypothermia OR hypothermia.mp OR hypothermic.mp OR exp body temperature] AND [exp heat OR exp heating OR exp rewarming OR warming.mp OR warming.mp]) LIMIT to human AND english.

Comments
None of the studies directly answer the question. It seems that there is a significant functional recovery after severe hypothermic cardiac arrest, and cardiopulmonary bypass seems to be an efficacious treatment. The number of patients treated by external rewarming is very small and more work will be needed before this can be recommended in preference to bypass.

Table 2

<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>Vretar DF et al, 1994, Canada</td>
<td>68 hypothermic patients with a mean core temperature of 21°C of whom 61 were in cardiac arrest. All patients placed on cardiopulmonary bypass</td>
<td>Review</td>
<td>Review</td>
<td>Review</td>
<td>Review</td>
</tr>
<tr>
<td>Koller R et al, 1997, Switzerland</td>
<td>Data derived from 34 reports. 5 patients with core temperature below 30°C of whom 2 were in cardiac arrest</td>
<td>Cohort</td>
<td>Cohort</td>
<td>Cohort</td>
<td>Cohort</td>
</tr>
<tr>
<td>Walpoth BH et al, 1997</td>
<td>32 of 46 patients in cardiac arrest with core temperature below 28°C. All patients placed on cardiopulmonary bypass</td>
<td>Prospective cohort</td>
<td>Prospective cohort</td>
<td>Prospective cohort</td>
<td>Prospective cohort</td>
</tr>
</tbody>
</table>

www.emjonline.com
Clinical bottom line
In severely hypothermic patients in cardiac arrest cardiopulmonary bypass should be considered.


Using intravenous adenosine in asthmatics
Report by Polly Terry, Specialist Registrar
Search checked by Gail Lumsden, Specialist Registrar

Clinical scenario
A 32 year old woman with asthma presents to the emergency department with a 20 minute history of palpitations. On examination she is cardiovascularly stable, there is no bronchospasm and the ECG shows a supraventricular tachycardia (SVT) that fails to respond to vagal manoeuvres. You would like to use intravenous adenosine but you are aware that asthma is a contraindication treatment. You wonder what evidence there is that intravenous adenosine will cause bronchospasm.

Three part question
[In an asthmatic patient with a SVT] is [treatment with adenosine] associated with [an increased risk of bronchospasm]?

Search strategy
Medline 1966–09/00 using the OVID interface. ([exp tachycardia OR exp tachycardia, supraventricular OR narrow complex tachycardia.mp OR exp arrhythmia OR exp tachycardia OR dysrhythmia.mp] AND [exp asthma OR asthma.mp OR exp respiratory sounds OR wheezing.mp OR exp bronchial spasm OR bronchospasm.mp] AND (exp adenosine OR adenosine.mp OR adenosine.ae.ct)) LIMIT to human AND english.

Search outcome
Altogether 16 papers were found of which 14 were irrelevant or of insufficient quality for inclusion. The remaining two papers are shown in table 3.

Comments
There is very little evidence recording the effect of intravenous adenosine on asthmatic airways. Many studies have documented that inhaled adenosine is a potent bronchoconstrictor in the asthmatic but not normal patients. In the literature there are four case reports of patients with asthma or COAD developing bronchospasm following treatment with intravenous adenosine. This level of evidence has many limitations. Similarly there are many studies looking at the efficacy of adenosine that report no “significant side effects” some specifically mention no patients reported bronchospasm.

Clinical bottom line
At worst adenosine is only relatively contraindicated in the treatment asthmatic patients with supraventricular tachycardia.


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>Larsson K and Sollevi A, 1988, Sweden</td>
<td>5 well subjects with a previous diagnosis of asthma. Increasing doses of adenosine v placebo</td>
<td>Crossover placebo trial</td>
<td>HR Pulmonary function</td>
<td>No significant difference</td>
<td>Children only, Retrospective chart review</td>
</tr>
<tr>
<td>Losek JD et al, 1999, USA</td>
<td>82 patients aged 18 yrs or less who received iv adenosine in the ED for the treatment of SVT. 13 had documented evidence of asthma</td>
<td>Survey</td>
<td>Successful cardioversion Adverse effects</td>
<td>72% cardioversion success rate 22 adverse patient events, no bronchospasm but 2 complaints of “dyspnoea” in non-asthmatic patients</td>
<td>Dose of adenosine very different to that used clinically, Subjects well, and in normal sinus rhythm</td>
</tr>
</tbody>
</table>

First ECG in chest pain
Report by Doug Speake, Medical Student
Search checked by Polly Terry, Specialist Registrar

Clinical scenario
A 55 year old man with cardiac sounding chest pain presents to the emergency department. The first ECG is normal. Just before you
discharge him you stop to wonder what the sensitivity of the initial 12 lead ECG is in predicting acute myocardial infarction.

Three part question
In [patients presenting to the ED with cardiacoercing chest pain] what is the [sensitivity] of the [initial 12 lead ECG]?

Search strategy
Medline 1966–09/00 using the OVID interface. ([exp myocardial infarction OR myocardial infarction.mp OR AMI.mp OR MI.mp] AND [exp electrocardiography OR electrocardiogram.mp OR ECG.mp OR EKG.mp] AND [initial.mp OR first.mp OR single.mp OR premier.mp]) AND maximally sensitive diagnostic study filter LIMIT to human AND engl ish.

Search outcome
Altogether 543 papers found of which 533 were irrelevant or of insufficient quality for inclusion. The remaining 10 papers are shown in table 4.

Comments
At presentation history, clinical findings and ECG are all that are available to aid clinicians in the diagnosis of AMI. These studies have shown that the first ECG is between 13–69% sensitive for AMI.

Clinical bottom line
The first ECG is not sensitive enough to rule out AMI in the emergency department.

Timing of aspirin administration in acute myocardial infarction
Report by Polly Terry, Specialist Registrar
Search checked by Mark Davies, Senior Clinical Fellow

Clinical scenario
A 49 year old man presents to the emergency department with a three hour history of central crushing chest pain. An ECG reveals an acute inferior myocardial infarction. You know that the administration of aspirin reduces future morbidity and mortality but wonder if the administration of aspirin is as time critical as thrombolysis.

Three part question
In [adults with an acute myocardial infarction] does [early administration of aspirin] decrease [mortality]?

Search strategy
Medline 1966–09/00 using the OVID interface. ([exp myocardial infarction OR myocardial infarction.mp OR heart attack.mp]) AND
### Table 5

<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>ISIS-2, 1988, multinational</td>
<td>17 187 patients within 24 hours of suspected MI. IV streptokinase or aspirin or both or neither. Subgroup analysis mortality vs time of aspirin administration from onset of symptoms at 0–4 h, 5–12 h, 5–24 h</td>
<td>PRCT</td>
<td>Overall vascular mortality vs placebo Odds of death at 5 weeks</td>
<td>4% relative risk reduction (0–4 h v 5–12 h v 13–24 h, p=NS)</td>
<td>Not the primary aim of the study, so very hard to extract data.</td>
</tr>
<tr>
<td>Lin M et al, 1998, Taiwan</td>
<td>22 patients with acute cardiogenic pulmonary oedema. Pao₂ &lt;80 mm Hg. CPAP (11) vs control (11)</td>
<td>PRCT</td>
<td>Need for intubation Shunt size</td>
<td>12/20 vs 14/20 (NS) 2/25 vs 7/30 (p&lt;0.05)</td>
<td>Small numbers. Unblinded</td>
</tr>
</tbody>
</table>

### Search outcome

Altogether 295 papers found of which 294 were either irrelevant or of insufficient quality. The remaining paper is shown in table 5.

### Comments

While this paper does not reach statistical significance it does show a trend in reduction of mortality with early aspirin administration. Taking this into account and the large standard deviations given a true difference may indeed exist. Other available data look at the combined effect of early thrombolysis and aspirin on the reduction of mortality and the data here are clear that the earlier the administration the greater the reduction in mortality and morbidity: Evidence exists to show that pharmacologically aspirin has maximal effect within one hour of oral administration, although whether this translates into the clinical setting is unclear. The availability of aspirin, its cost, ease of administration, and the minimal risks associated with a single dose make it an ideal immediate treatment to be given prehospital admission. The available data however suggest that this is not so time critical, that other factors cannot be taken into consideration, for example, gastrointestinal upset, respiratory contraindications, etc.

### Clinical bottom line

In an acute myocardial infarction, aspirin should be given as early as possible.

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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>Rasanen J et al, 1985, Finland</td>
<td>40 patients with acute cardiogenic pulmonary oedema. RR &gt;25 and Pao₂ &lt;200 mm Hg. CPAP (20) vs control (20)</td>
<td>PRCT</td>
<td>Need for intubation</td>
<td>6/20 vs 12/20 (NS)</td>
<td>Small numbers. Unblinded</td>
</tr>
<tr>
<td>Bersten A et al, 1991, Australia</td>
<td>39 patients with acute cardiogenic pulmonary oedema. Pao₂ &lt;70 mm Hg and Paco₂ &gt;45 mm Hg CPAP (19) vs control (20)</td>
<td>PRCT</td>
<td>Need for intubation</td>
<td>0/19 vs 7/20 (p&lt;0.005)</td>
<td>Small numbers. Unblinded. Randomisation not concealed.</td>
</tr>
<tr>
<td>Lin M et al, 1991, Taiwan</td>
<td>100 patients with a clinical diagnosis of acute cardiogenic pulmonary oedema. CPAP (50) vs control (50)</td>
<td>PRCT</td>
<td>Shunt size</td>
<td>Significantly improved in CPAP group 8/30 vs 18/50 (p&lt;0.01)</td>
<td>Unblinded</td>
</tr>
<tr>
<td>Takeda S et al, 1998, Japan</td>
<td>349–60.</td>
<td>PRCT</td>
<td>Hospital mortality Need for intubation</td>
<td>4/50 vs 6/50 (NS) 2/11 vs 8/11 (p&lt;0.03)</td>
<td>Small numbers. Unblinded</td>
</tr>
</tbody>
</table>

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**CPAP in acute left ventricular failure**

Report by Simon Carley, Specialist Registrar Search checked by Simon Carley, Specialist Registrar

**Clinical scenario**

A 76 year old man is brought into accident and emergency in a collapsed state. He has a history of ischaemic heart disease. He is agitated, tachypnoeic and sweating profusely. His neck veins are distended and there are widespread coarse crepitations in his chest. He has a diminished oxygen saturation. You make a clinical diagnosis of acute cardiogenic pulmonary oedema. In addition to vasodilator treatment and opioids, you wonder whether you should administer non-invasive continuous positive airways pressure (CPAP).

**Three part question**

[In patients with acute LVF] is [CPAP better than O₂ via normal mask] at [avoiding intubation and improving mortality]?

**Search strategy**

Medline 1966–09/00 using the OVID interface. ((exp pulmonary edema OR pulmonary oedema.mp OR exp ventricular dysfunction, left OR exp heart failure, congestive OR exp myocardial infarction OR left ventricular failure.mp OR LVF.mp) AND (exp positive-pressure respiration OR CPAP.mp OR continuous positive airway pressure$ .mp OR PEEP.mp OR positive end expiratory pressure.mp))
pressure$\text{.mp}$ | AND maximally sensitive randomised controlled trial filter) LIMIT to human AND English language

**Search outcome**
Altogether 114 papers were found of which 109 were either irrelevant or of insufficient quality for inclusion. The remaining five papers are shown in table 6.

**Comments**
All of these trials have shown significant reductions in the need to intubate patients in acute pulmonary oedema. In these small trials a reduction in mortality could not be seen. The numbers in the trials are not large and there is not yet absolute evidence of benefit from CPAP. A large, well designed PRCT may provide this. In the meantime it would seem that patients with severe LVF will benefit from CPAP.

**Clinical bottom line**
Patients presenting with severe acute pulmonary oedema should be treated with CPAP.

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