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

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$.mp OR exp nitroglycerin OR nitroglycerin.mp OR gtn.mp OR glyceryl trinitrate.mp OR exp isosorbide dinitrate OR isosorbide dinitrate.mp OR isosorbide mononitrate.mp] AND [exp furosemide OR furosemide.mp OR frusemide.mp OR exp bumetanide OR bumetanide.mp OR exp diuretics OR loop diuretic$.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>Vretnar 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>Overall survival: 60% Survival if core temperature &lt;15 degrees Return to previous function: 60% of survivors</td>
<td>60%</td>
<td>Publication bias likely as success more likely to be reported than failure.</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>Overall survival: 100% Return to previous function: 100%</td>
<td>100%</td>
<td>Small numbers.</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>Overall survival: 15/32 (45%)</td>
<td>15/32 (45%)</td>
<td>Unclear why patients selected for bypass.</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.**

### Search outcome

Altogether 114 papers found of which 111 were irrelevant or of insufficient quality. The remaining three papers are shown in table 2.

### 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.

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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.


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
Table 4

<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>McGuinness JB et al., 1976; Scotland</td>
<td>898 patients admitted to CCU. 400 with AMI. 221 ED chest pain patients. 39 with AMI.</td>
<td>Prospective diagnostic cohort</td>
<td>Sensitivity of initial ECG</td>
<td>51%</td>
<td>No raw cardiac enzyme data confirming how AMI diagnosed.</td>
</tr>
<tr>
<td>Starck M and Vacek JL, 1987, USA</td>
<td>34 patients admitted to CCU. 34 with AMI. 440 ED chest pain patients. 100 with AMI. 918 ED chest pain patients. 811 with AMI.</td>
<td>Prospective diagnostic cohort</td>
<td>Sensitivity of initial ECG</td>
<td>61%</td>
<td>Small population size.</td>
</tr>
<tr>
<td>Fesmire F et al, 1989, USA</td>
<td>616 ED chest pain patients. 108 with AMI.</td>
<td>Prospective diagnostic cohort</td>
<td>Sensitivity of initial ECG</td>
<td>36%</td>
<td>Recruitment criteria unclear.</td>
</tr>
<tr>
<td>Rouan G et al, 1989, USA</td>
<td>222 ED chest pain patients. 43 with AMI. 149 ED chest pain patients. 34 with AMI.</td>
<td>Retrospective survey</td>
<td>Sensitivity of initial ECG</td>
<td>28%</td>
<td>Study population mostly elderly</td>
</tr>
<tr>
<td>Gibler WB et al., 1989, USA</td>
<td>1000 ED chest pain patients. 204 with AMI. 3027 ED chest pain patients. 1149 with AMI.</td>
<td>Prospective diagnostic cohort</td>
<td>Sensitivity of initial ECG</td>
<td>55.4%</td>
<td>Unclear if series or selection of patients recruited</td>
</tr>
<tr>
<td>Zaleski R et al, 1993, USA</td>
<td>324 patients with AMI. 248 with non-diagnostic ECGs.</td>
<td>Prospective diagnostic cohort</td>
<td>Sensitivity of initial ECG</td>
<td>69%</td>
<td>Initial ECG taken by paramedics, not in ED.</td>
</tr>
<tr>
<td>Fesmire F, 1998, USA</td>
<td>34 patients had AMI following admission to ED.</td>
<td>Prospective diagnostic cohort</td>
<td>Sensitivity of initial ECG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kudenchuk PJ et al, 1998, USA</td>
<td>400 with AMI.</td>
<td>Prospective diagnostic cohort</td>
<td>Sensitivity of initial ECG</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 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 English.

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.

### 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</td>
<td>PRCT</td>
<td>Overall vascular mortality</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>Subgroup analysis mortality v time of aspirin administration from onset of symptoms at 0–4 h, 5–12 h, 13–24 h</td>
<td>Odds of death at 5 weeks v placebo</td>
<td>0–4 h 5–12 h 13–24 h</td>
<td>0.75 (SD=0.07) 0.79 (SD=0.07) 0.79 (SD=0.12)</td>
<td></td>
<td></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

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) v control (20)</td>
<td>PRCT</td>
<td>Need for intubation</td>
<td>6/20 v 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) v control (20)</td>
<td>PRCT</td>
<td>Need for intubation</td>
<td>17/20 v 14/20 deaths in hospital (NS) 0/19 v 7/20 (p&lt;0.005)</td>
<td>Small numbers. Unblinded. Randomisation not concealed.</td>
</tr>
<tr>
<td>Lin M and Chiang HT, 1991, Taiwan</td>
<td>55 patients with acute cardiogenic pulmonary oedema. RR &gt;20 CPAP (25) v control (30)</td>
<td>PRCT</td>
<td>Hospital mortality Shunt size</td>
<td>Need for intubation 7/25 v 17/30 (p&lt;0.05) Need for intubation 2/25 v 4/30 (NS) Significantly improved in CPAP group</td>
<td>Significantly improved in CPAP group</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) v control (50)</td>
<td>PRCT</td>
<td>Hospital mortality Need for intubation</td>
<td>4/50 v 6/50 (NS) 2/11 v 8/11 (p=0.03)</td>
<td>Small numbers. Unblinded</td>
</tr>
<tr>
<td>Takeda S et al, 1998, Japan</td>
<td>22 patients with acute cardiogenic pulmonary oedema. Pao2 &lt;80 mm Hg. CPAP (11) v control (11)</td>
<td>PRCT</td>
<td>Hospital mortality</td>
<td>1/11 v 7/11 (p=0.02)</td>
<td></td>
</tr>
</tbody>
</table>
pressure$.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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K Mackway-Jones

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