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. Five BETs are included in this issue of the journal together with another five that inform the accompanying accumulator BET.

**Accuracy of negative urine analysis in ruling out urinary tract infection in adults**

**Venous blood gas in adult patients with diabetic ketoacidosis**

**Antithrombotic treatment of below knee deep venous thrombosis**

**Buccal nitrates in left ventricular failure**

**Oral methionine compared with intravenous n-acetyl cysteine for paracetamol overdose**

**Clinical probability scoring and pulmonary embolism**

**Accuracy of combining clinical probability score and simpliRED d-dimer for diagnosis of pulmonary embolism**

**IL d-dimer test in the diagnosis of pulmonary embolism**

**Outpatient investigation of pulmonary embolism**

**Outpatient treatment of pulmonary embolism**

**Accuracy of negative dipstick urine analysis in ruling out urinary tract infection in adults**

**Report by Nick Ohly, Senior House Officer**

**Checked by Stewart Teece, Clinical Research Fellow**

**Abstract**

A short cut review was carried out to establish whether negative dipstick urine analysis is sensitive enough to rule out urinary tract infection (UTI) in adults with urinary symptoms. Altogether 75 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 20 year old student presents to the emergency department with a three day history of urinary frequency, dysuria, and lower abdominal pain. Examination is unremarkable and dipstick urine analysis is normal. You wonder whether normal dipstick urine analysis is sufficient to rule out a UTI or whether antibiotics anyway should be prescribed whatever the result.

**Three part question**

In [adults with symptoms of a urinary tract infection] does [negative dipstick urine analysis] rule out a [UTI]?

**Search strategy**

Medline 1966–04/03 using the OVID interface. [(exp Urinalysis OR exp Indicators and Reagents OR exp Reagent Strips OR stix.af OR urinalysis.af) AND (exp Urinary Tract Infections OR (urin$ adj5 infect$).af OR UTI.af OR exp Bacteriuria OR bacteriur$.af) AND (dysuria.af OR frequency.af OR haematuria.af OR hematuria.af OR stranguria.af OR urgency.af)] LIMIT to human AND English language AND all adult <19 plus years>

**Search outcome**

Altogether 75 papers were found. Of these, two were identified as answering the three part question. One of these was a meta-analysis containing nine papers not identified by the original search as they did not consider dipstick urine analysis (table 1).

**Comment(s)**

The meta-analysis shows that the prevalence of UTI in patients who present with symptoms of UTI is around 50%. The probability of UTI is even higher (around 90%) with a convincing history. Dipstick urine analysis is a quick and inexpensive test however sensitivity (and therefore negative
predictive value) were found to be as low as 75%. Some studies included in the meta-analysis were of low quality and further studies need to be done in this field.

**CLINICAL BOTTOM LINE**

Dipstick urine analysis is of insufficient sensitivity to be used to rule out UTI in patients with one or more symptoms.


Bent S et al, 2002, USA

Adult women from nine original studies involving patients with symptoms of an UTI presenting to outpatient clinics. Total number of patients 2331

Prospective observational study

Sensitivity 92% Only women

NPV 83% No sample size analysis

Positive dipstick defined as detectable nitrite or leucocyte esterase

Prevalence 45.9% Gold standard urine culture


Venous blood gas in adult patients with diabetic ketoacidosis

Report by Ziauddin Hassan, Devasena M Subramonyam, Registrars

Checked by Shobhan Thakore, Specialist Registrar

Abstract

A short cut review was carried out to establish whether venous blood gas measurement accurately demonstrates the degree of acidosis in patients with diabetic ketoacidosis. A total of 27 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 22 year old insulin dependent diabetic presents to our emergency department with a raised blood sugar and urine dipstick showing +++ of ketones. You suspect diabetic ketoacidosis and would like the know the degree of his acidosis, but the patient refuses arterial blood gas sampling due to a previous bad experience. You wonder whether venous blood would accurately show the degree of his metabolic acidosis.

Three part question

In [an adult patient with diabetic ketoacidosis] do [venous blood gases] accurately demonstrate [the degree of acidosis]?

Search strategy

Medline 1966–04/03 using the OVID interface. [(venous blood.mp OR exp blood specimen collection OR exp blood gas analysis) AND (exp diabetic ketoacidosis OR diabetic ketoacidosis.mp OR exp diabetic coma) AND (exp acidosis OR acido-sis.mp OR exp hydrogen-ion concentration)] AND LIMIT to human AND English language.

Search outcome

Altogether 27 papers were found of which only two are relevant and of sufficient quality for inclusion (table 2).

Comment(s)

There are only a limited number of studies on this subject and these have involved small numbers of patients. Further studies with large series of patients are necessary.

### 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>Lammers RL et al, 2001, USA</td>
<td>331 adult women presenting to ED or intermediate care centre with more than one symptom of a UTI. Positive dipstick defined as detectable nitrite or leucocyte esterase. Prevalence 45.9%. Gold standard urine culture</td>
<td>Prospective observational study</td>
<td>Sensitivity</td>
<td>92%</td>
<td>Only women</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NPV</td>
<td>83%</td>
<td>No sample size analysis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Positive dipstick defined as detectable nitrite or leucocyte esterase</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Prevalence 45.9%</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Gold standard of positive urine culture</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bent S et al, 2002, USA</td>
<td>Adult women from nine original studies involving patients with symptoms of an UTI presenting to outpatient clinics. Total number of patients 2331</td>
<td>Meta-analysis</td>
<td>Sensitivity</td>
<td>75%</td>
<td>Some studies only included women</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Likelihood of UTI in presence of dysuria and frequency without vaginal discharge is high</td>
<td>&gt;90%</td>
<td>Only able to use data from some studies</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Difference in cut off level for positive urine culture (range 100–100,000 CFU/ml)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Prevalence 48%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gold standard of positive urine culture</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 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>Brandenburg MA and Dire DJ, 1998, USA</td>
<td>38 patients with DKA presented to emergency department</td>
<td>Prospective</td>
<td>Mean difference in pH</td>
<td>−0.03</td>
<td>Small numbers</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No control group</td>
</tr>
<tr>
<td>Gokel Y et al, 2000, Turkey</td>
<td>152 samples, from 100 uraemic patients, 21 patients with DKA and 31 healthy volunteers</td>
<td>Prospective</td>
<td>Mean difference in pH</td>
<td>−0.05</td>
<td>Small numbers</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Unequal number of patients in each group</td>
</tr>
</tbody>
</table>
CLINICAL BOTTOM LINE
There is no clinically significant difference between arterial and venous pH estimates in patients with diabetic ketoacidosis.


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Antithrombotic treatment of below knee deep venous thrombosis
Report by Kerstin Hogg, Clinical Research Fellow
Checked by Andrew Ashton, Senior Clinical Fellow

Abstract
A short cut review was carried out to establish whether oral anticoagulation is necessary to prevent pulmonary embolization in patients with below knee deep venous thrombosis. A total of 425 papers were found using the reported search, of which 11 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 50 year old man attends the emergency department with a plethoric, swollen left calf. Ultrasound examination reveals a posterior tibial vein thrombosis. You wonder what the risk of a pulmonary embolus is and whether he should be anticoagulated.

Three part question
In [a patient with a below knee venous thrombosis], is [oral anticoagulation necessary] to prevent [a pulmonary embolus]?

Search strategy
Medline 1966–04/03 using the OVID interface. [((DVT.mp OR exp venous thrombosis OR “deep vein thrombosis”-mp) AND (“below knee“-mp OR calf.mp OR popliteal.mp OR exp popliteal vein OR fibular.mp OR peroneal.mp OR posterior tibial.mp) OR “deep calf venous thrombosis”-mp OR “calf vein thrombosis”-mp) AND (therapy.mp OR exp therapeutics OR treatment.mp OR exp heparin OR exp heparin, low-molecular-weight OR heparin.mp OR exp warfarin OR warfarin.mp OR exp coumarins OR coumarin.mp)] LIMIT to human and English.

Search outcome
Altogether 425 papers were found, only 10 original papers and one literature review addressed the question. Some studies included other patients with PE or thigh DVTs—only the one literature review addressed the question. Some studies could have been more thorough in their diagnostic criteria and/or follow up. However, despite the flaws it is clear that pulmonary emboli do result from below knee thrombi.

CLINICAL BOTTOM LINE
All patients with calf thrombosis should receive oral anticoagulation.

Buccal nitrates in left ventricular failure
Report by Dhurga Gnanasegaram, Senior Clinical Fellow
Checked by Jon Argall, Senior Clinical Fellow

Abstract
A short cut review was carried out to establish whether buccal and intravenous nitrates are equally effective at preload reduction in patients with left ventricular failure. Seven 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 is tabulated. A clinical bottom line is stated.

Clinical scenario
You are called to see a 60 year old man who has been increasingly breathless for a week. Examination reveals him to be mildly dyspnoeic at rest with a raised JVP and bicuspid creps. There is evidence of ischaemia on his ECG. The chest radiograph shows upper lobe diversion and Kerley B lines. You wonder whether buccal suscard would be an appropriate alternative to a GTN infusion.

Three part question
In [a patient with left ventricular failure] are [buccal nitrates equivalent to a nitrate infusion] for [preload reduction]?

Search strategy
Medline 1966–04/03 using the OVID interface. [((exp nitrates OR nitrate.mp OR exp nitroglycerin OR nitroglycerin.mp OR exp vasodilator agents OR GTN.mp OR glyceryl trinitrate.mp OR exp isosorbide dinitrate OR ISOKET.mp OR SUSTCARD.mp) AND ((buccal.mp OR exp mouth mucosa OR exp administration, buccal) AND (exp injections, intravenous OR intravenous.mp OR IV.mp)) AND (exp heart failure, congestive OR heart failure.mp OR LVF.mp OR exp left ventricular failure.mp OR congestive cardiac failure.mp OR exp ventricular dysfunction, left OR exp ventricular dysfunction OR exp pulmonary oedema)] LIMIT to human AND English language.

Search outcome
Altogether seven papers were found, of which five were reviews of nitrates rather than comparative studies. The two

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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>Philbrick JT et al, 1988, USA</td>
<td>All studies of sufficient quality identified from literature search over years 1944 to 1986</td>
<td>Literature review</td>
<td>Incidence PE</td>
<td>6 of 163 patients receiving no anticoagulation (Strength of evidence weak). 9 of 208 patients receiving a range of anticoagulation (0 of 32 in only study with strong evidence, all other studies, weak)</td>
<td>No controlling of postmortem procedures—unclear if all legs veins thoroughly examined. Only 23 of 152 considered to die from PE actually had a PM and had the source of the embolus confirmed.</td>
</tr>
<tr>
<td>Giachino A, 1988, Canada</td>
<td>152 patients who died in Ottawa hospitals over a five year period, with PE listed as the cause of death.</td>
<td>Retrospective study</td>
<td>Source of thrombosis in fatal pulmonary emboli.</td>
<td>82 had no postmortem examination. 23 postmortem examinations confirmed PE as the cause of death, and identified the source of the embolus. 3 of 23 postmortem examinations revealed the calf veins as the source of the thrombi. 15% propagated to involve the popliteal or larger veins. A further 17% propagated within the calf veins</td>
<td>Publication bias—all of these patients may have been included in the study by Pellegrini V et al, 1993. No information regarding the length of follow up, or the effect of varying therapies. Two of the PE's were diagnosed on the strength of sudden collapse and cardiac arrest—no postmortem examination carried out</td>
</tr>
<tr>
<td>Lahr J et al, 1991, USA</td>
<td>75 patients with ultrasound diagnosed calf thrombosis. Treatment left to physician’s discretion.</td>
<td>Prospective study with follow up serial ultrasound examination.</td>
<td>Thrombus propagation</td>
<td>53 of 139 thrombi propagated</td>
<td>Publishing bias—the cohort appears to include all of the patients included in the previous Lohr study (see study in this table) Paper does not establish rate of PE Venography not used to diagnose initial calf DVT. Apparently, no attempts were made to actively seek the diagnosis of PE throughout the follow up period. No adequate description of the positive VQ scans.10 patients lost to follow up at six months. No account taken of the effect of treatment</td>
</tr>
<tr>
<td>Pellegrini V et al, 1993, USA</td>
<td>25 patient with isolated calf DVT and 12 patients with superficial or muscular calf thrombosis, diagnosed by venography on postoperative screening of total hip arthroplasty patients. Only 12 calf DVTs and one superficial/muscular calf thrombosis were anticoagulated</td>
<td>Prospective study following up at 6, 12, 24 and 52 weeks</td>
<td>Incidence of PE</td>
<td>4 of 13 untreated calf DVT patients were diagnosed with PE. 0 of 1 treated calf DVT patient and none of the superficial/muscular calf thrombosis developed PE</td>
<td>No information regarding exact criteria for diagnosing PE from VQ scan alone—probably over-estimation of incidence. VQ scans were performed at 10 and 60 days, however no information regarding the breakdown of subsequent PEs between proximal and isolated calf DVT groups.</td>
</tr>
<tr>
<td>Nielsen HK et al, 1994, Denmark</td>
<td>15 patients with venographically diagnosed calf DVTs.</td>
<td>Prospective study</td>
<td>VQ scan result at presentation</td>
<td>5 of 15 had positive VQ scans. No information regarding which symptoms would prompt investigations for PE. Method’s description implies that a VQ scan alone would diagnose PE—no information as to how this PE was diagnosed</td>
<td></td>
</tr>
<tr>
<td>Lahr JM et al, 1995, USA</td>
<td>192 patients with ultrasound diagnosed below knee DVTs. Treatment left to physicians discretion.</td>
<td>Prospective study with serial ultrasound for four weeks</td>
<td>Thrombus propagation</td>
<td>53 of 139 thrombi propagated</td>
<td>Patients were not identified using venography. Retrospective study, therefore unable to detect silent PEs or those that did not present to medical services. One PE diagnosed on strength of high probability VQ scan alone. No description of frequency of follow up ultrasound scans. Therapy at the discretion of physician. No information regarding anticoagulant therapy for patient with extension to thigh DVT. 28 patients were not followed up for the full 6 months as they died. Diagnosis did not always use venography. No information regarding which symptoms would prompt investigations for PE.</td>
</tr>
<tr>
<td>O'Shaughnessy AM et al, 1997, Ireland</td>
<td>50 patients with ultrasound diagnosed DVTs, 43 treated with anticoagulation and 7 without</td>
<td>Prospective study, using repeat ultrasound at one week, one month, six months and one year.</td>
<td>“Outcome” of isolated calf thrombosis.</td>
<td>3 patients presented initially with a “positive” VQ scan. One fatal PE within the first month.</td>
<td>No information regarding which symptoms would prompt investigations for PE. Method’s description implies that a VQ scan result of intermediate probability would diagnose PE—no information as to how this PE was diagnosed</td>
</tr>
<tr>
<td>Gottlieb RH et al, 1999, USA</td>
<td>238 patients with ultrasound diagnosed below knee DVTs</td>
<td>Retrospective study</td>
<td>Incidence of diagnosed PEs</td>
<td>2 of 56 patients not receiving anticoagulant therapy had PE. 1 of 227 receiving anticoagulant therapy had documented extension to thigh DVT.</td>
<td></td>
</tr>
<tr>
<td>Finnell L, et al, 2001, France</td>
<td>105 patients with calf DVTs treated for six weeks with warfarin. 92 patients with calf DVTs treated for 12 weeks with warfarin</td>
<td>Prospective study</td>
<td>Incidence of PE</td>
<td>1 of 197 (patient from 12 week warfarin group) had documented PE</td>
<td>Gold standard venography not used</td>
</tr>
<tr>
<td>Schwarz T et al, 2001, Germany</td>
<td>84 patients with isolated calf muscle thrombosis. 52 received LMWH for 10 days, 32 received no anticoagulation</td>
<td>Prospective cohort with serial ultrasound examinations</td>
<td>Progression to deep veins of calf PE</td>
<td>Study discontinued as 8 of 32 non-anticoagulated patients progressed to deep veins thrombosis, compared with 0 of 52 anticoagulated patients</td>
<td>No information regarding which symptoms would prompt investigations for PE. VQ scan results interpreted in isolation</td>
</tr>
<tr>
<td>Sharpe RP et al, 2002, USA</td>
<td>85 trauma patients with below knee DVTs</td>
<td>Prospective cohort</td>
<td>Thrombus propagation PE</td>
<td>4 of 85 thrombi propagated proximally. 1 of 85 did not propagate but had a PE</td>
<td>Gold standard investigations not applied for DVT or PE</td>
</tr>
</tbody>
</table>
remaining publications consisted of a summary report and full article relating to the same trial. The results of this trial are shown in table 4.

**Comment(s)**
There is very limited evidence available to allow direct comparison between intravenous and buccal routes.

> **CLINICAL BOTTOM LINE**
Buccal nitrates produce an immediate reduction in preload (comparable with intravenous GTN).


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**Oral methionine compared with intravenous n-acetyl cysteine for paracetamol overdose**

**Report by Walid Alsalim, Specialist Registrar**
**Checked by Mohamed Fadel, Specialist Registrar**

**Abstract**
A short cut review was carried out to establish whether methionine was better than n-acetyl cysteine at reducing the severity of liver damage after paracetamol overdose. Thirty nine 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 19 year old woman brought to the emergency department six hours after paracetamol overdose. She is fully conscious and admits ingestion of 32 tablets of paracetamol. She is complaining of abdominal discomfort but no nausea or vomiting. Her examination is unremarkable. You arranged blood investigations. Intravenous access and n-acetyl cysteine infusion started as per protocol. You wonder whether oral methionine would have been as effective as n-acetyl cysteine in her treatment.

**Three part question**
In a [patient with paracetamol overdose within eight hours] is [methionine as good as or better than n-acetyl cysteine] at [reducing liver damage]?

**Search strategy**

**Search outcome**
Altogether 39 papers were found, of which two were relevant (table 5).

**Comment(s)**
There have been no randomised controlled trials and only two prospective observational studies comparing these two drugs. However, patients in these two studies had the antidote within eight hours.

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### 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>Verma SP et al, 1989, UK</td>
<td>36 male patients with acute LVF secondary to recent MI (&lt;10 hours) in CCU</td>
<td>PRCT</td>
<td>Left heart filling pressures</td>
<td>All three groups reduced</td>
<td>Only 36 patients</td>
</tr>
<tr>
<td></td>
<td>IV v buccal v transdermal GTN</td>
<td></td>
<td>Cardiac output</td>
<td>No reduction in any group</td>
<td>Different doses of buccal, IV and dermal GTN (based on previous studies)</td>
</tr>
<tr>
<td></td>
<td>Average doses over 90 min: IV 12.9 mg, buccal 5 mg, dermal 20 mg</td>
<td></td>
<td>BP</td>
<td>3 patients had BP falls in buccal group but with no clinical deterioration</td>
<td>IV dose individually titrated; buccal and dermal doses predetermined</td>
</tr>
</tbody>
</table>

### 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>Vale JA, 1981, UK</td>
<td>158 patients with paracetamol overdose. Mean age: 26 y: 1.2 M, F ratio</td>
<td>Prospective observational</td>
<td>Liver damage:</td>
<td>NSD</td>
<td>No randomisation</td>
</tr>
<tr>
<td></td>
<td>High risk patients defined as paracetamol level: &gt;300 mg/l at 4 h</td>
<td></td>
<td>Methionine within 10 h (n=96)</td>
<td>7%</td>
<td>Small study</td>
</tr>
<tr>
<td></td>
<td>IV n-acetyl cysteine within 10 h (n=62)</td>
<td></td>
<td>In high risk patients methionine. within 10 h (n=43)</td>
<td>14%</td>
<td>2 of 7 vomited the first dose</td>
</tr>
<tr>
<td></td>
<td>In high risk patients IV n-acetyl cysteine. within 10 h (n=33)</td>
<td></td>
<td></td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Prescott LF, 1981, UK</td>
<td>104 patients with paracetamol overdose. Mean age 33 y: 1.5 M, F ratio</td>
<td>Prospective observational</td>
<td>Liver damage:</td>
<td>NSD</td>
<td>No randomisation</td>
</tr>
<tr>
<td></td>
<td>High risk patients defined as paracetamol level: &gt;300 mg/l at 4 h</td>
<td></td>
<td>Methionine. Within 10 h, (n=42) 57% of them were high risk</td>
<td>7%</td>
<td>Small study</td>
</tr>
<tr>
<td></td>
<td>IV n acetyl cysteine within 10 h (n=62)</td>
<td></td>
<td>33 of 62 (53%) of them were high risk</td>
<td>2%</td>
<td></td>
</tr>
</tbody>
</table>
Intravenous acetylcysteine (parvolex) is more effective than methionine in preventing liver damage in patients after paraacetamol overdose.


Clinical probability scoring and pulmonary embolism

Report by Ged Brown, Specialist Registrar
Checked by Kerstin Hogg, Clinical Research Fellow

Abstract
A short cut review was carried out to establish the diagnostic utility of clinical probability scoring in stratifying the risk of pulmonary embolus. A total of 938 papers were found using the reported search, of which three 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 30 year old man presents to the department with a spontaneous onset of atraumatic pleuritic chest pain. He has no previous medical history and has no shortness of breath or haemodynamic compromise. You wonder whether his clinical features and risk factors can help to safely exclude a pulmonary embolus.

Three part question
In [a patient presenting with features suggestive of pulmonary embolus] what is [the diagnostic utility of clinical probability scoring] in [stratifying risk of pulmonary embolus]?

Search strategy
Medline 1966–04/03 using the OVID interface. (exp Pulmonary Embolism OR exp Thromboembolism OR PE.mp OR pulmonary infarct$mp OR Pulmonary Embolism.mp) AND (exp Risk Assessment OR risk assessment.mp OR risk stratification.mp OR probability.mp) LIMIT to human AND English language.

Search outcome
Altogether 938 papers were found of which 935 papers were irrelevant to the question, of insufficient quality or did not report a mathematically derived scoring systems. The remaining three are included in table 6.

NB The clinical scoring systems have not been represented in the table. Please refer to the individual papers for these details.

Comments
There is evidence to suggest a variety of clinical models can be used to stratify patients into different levels of risk for PE. It is possible that these may be combined with other tests to give an acceptably low post-test probability of PE.

Accurancy of combining clinical probability score and simpliRED D-dimer for diagnosis of pulmonary embolism

Report by Russell Boyd, Consultant
Checked by Kerstin Hogg, Clinical Research Fellow

Abstract
A short cut review was carried out to establish whether bedside clinical examination and simpliRED D-dimer are
sufficiently sensitive to rule out pulmonary embolus. A total of 272 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 34 year old woman presents with a two day history of pleuritic chest pain. There are no abnormal physical signs and her only risk factor is that she is taking oral contraceptives long term. You wonder if a combination of clinical examination and the available d-dimer test (SimpliRED) would be suitable to rule out pulmonary embolism.

Three part question
In [suspected PE] is [bedside clinical examination and simpliRED d-dimer sufficiently sensitive] at [ruling out PE]?

Search strategy

Search outcome
Altogether 272 papers were identified of which five were relevant and of sufficient quality. These are shown in table 7.

Comment(s)
Use of a bedside clinical decision rule for PE probability with the additional use of latex agglutination d-dimer testing results in high levels of sensitivity and high negative predictive values in the low PE risk groups. It is this group of patients that makes up the bulk of patients with a putative diagnosis of PE. However, latex agglutination d-dimers do not perform well in high or even moderate risk groups.

Clinical bottom line
Patients at low clinical risk with a negative bedside d-dimer can have pulmonary embolus ruled out.


Table 7

<table>
<thead>
<tr>
<th>Author, date and country</th>
<th>Patient group</th>
<th>Study type (levels of evidence)</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Study weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginsberg JS et al, 1998, Canada</td>
<td>1250 consecutive referred patients to teaching hospital thromboembolic clinic with putative diagnosis of PE (73 lost to follow up)</td>
<td>Cohort</td>
<td>Diagnostic utility of a combination of low clinical probability of PE on clinical assessment with –ve SimpliRED d-dimer</td>
<td>Negative predictive value of 99%</td>
<td>Exclusion criteria “lost” 484 of original 1881 patients screened then further 147 excluded because of non-consent</td>
</tr>
<tr>
<td>Wells PS et al, 2000, Canada</td>
<td>1211 patients with presumptive diagnosis of PE broken into derivation and validation set</td>
<td>Diagnostic test</td>
<td>Sensitivity of clinical decision rule with addition of SimpliRED D-dimer</td>
<td>87.8%–88.3% (validation-derivation)</td>
<td>Actual methodology not fully demonstrated, for example, gold standard definition predictive values and likelihood ratios not given</td>
</tr>
<tr>
<td>Farrell S, 2000, USA</td>
<td>198 patients presenting to US ED with suspected thromboembolic disease</td>
<td>Diagnostic test</td>
<td>Diagnostic utility of a combination of low clinical probability of PE on clinical assessment with –ve SimpliRED d-dimer</td>
<td>Negative predictive value 97% Sensitivity 84%</td>
<td>Estimation of clinical probability was with implicit not explicit methods</td>
</tr>
<tr>
<td>MacGillavry MR, 2001, Netherlands</td>
<td>404 adults, both in and outpatients in teaching hospitals with putative diagnosis of thromboembolic disease</td>
<td>Diagnostic test</td>
<td>Sensitivity and specificity of using a clinical probability and SimpliRED d-dimer test</td>
<td>Sensitivity 98% Specificity 11%</td>
<td>Over 50% exclusion rate for entry into study. Implicit methods only for determining clinical probability</td>
</tr>
<tr>
<td>Wells P, 2001, Canada</td>
<td>946 adult patients referred for assessment of PE</td>
<td>Cohort</td>
<td>Diagnostic utility of a combination of low clinical probability of PE on clinical assessment with –ve SimpliRED d-dimer</td>
<td>Negative predictive value 99.5%</td>
<td>Investigation protocol violations occurred in nearly 10% of the patients</td>
</tr>
</tbody>
</table>

IL D-dimer test in the diagnosis of pulmonary embolism

Report by Kerstin Hogg, Clinical Research Fellow

Checked by Russell Boyd, Consultant

Abstract
A short cut review was carried out to establish whether a negative IL D-dimer test alone could be used to rule out a diagnosis of pulmonary embolus. Six 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 30 year old woman presents to the emergency department with distressing, left sided pleuritic chest pain. She may have had a pulmonary embolism and you request a D-dimer test. You know the laboratory in your hospital uses the IL D-dimer test and wonder whether a normal result would be sufficiently sensitive to rule out a pulmonary embolus.

Three part question
In a [patient with suspected pulmonary embolus] does a [negative IL D-dimer test] adequately [rule out the diagnosis]? In a [patient with suspected pulmonary embolus] does a [sensitive IL D-dimer test] adequately [rule out the diagnosis]? In a [patient with suspected pulmonary embolus] does a [specific IL D-dimer test] adequately [rule out the diagnosis]?

Search strategy
Medline 1966–04/03 using the OVD interface. ([D-dimer.mp or exp Fibrin Fibrinogen Degradation Products or FDP.mp] AND [IL test.mp] AND [exp Thromboembolism or exp Pulmonary Embolism or pulmonary embol$.mp or PE.mp or pulmonary infarct$.mp or exp venous thromboembolism]).

Search outcome
Six papers were found from the above search. Four were relevant. One further paper was found from hand searching journals and references. These five papers are shown in table 8.

Comments
To date there have been few studies measuring the accuracy of this D-dimer test. Of note, there is almost no research looking in particular at patients presenting with symptoms of PE. The sensitivity of the IL test for ruling out DVT seems to lie somewhere between 90% and 100%. It is worth noting that all of these studies used a comparatively low cut off level and it is worth being aware what the cut off level is in your hospital laboratory.

> CLINICAL BOTTOM LINE
The IL D-dimer test alone is not sufficiently sensitive to rule out pulmonary embolus. It must be used in conjunction with another test.

**Table 8**

<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>Legani C et al, Italy 1999</td>
<td>105 consecutive outpatients 7DVT</td>
<td>Prospective cohort</td>
<td>ROC curve to define max sensitivity of IL test</td>
<td>230 ng/ml cut off sensitivity 100% specificity 77.2%</td>
<td>Patients DVT not PE. High prevalence DVT. Would not reflect an average emergency department population</td>
</tr>
<tr>
<td>van der Graaf F, 2000</td>
<td>99 DVT outpatients. Comparison of 13 different D-dimer tests</td>
<td>Prospective cohort</td>
<td>IL test</td>
<td>Sensitivity specificity</td>
<td>90% 78%</td>
</tr>
<tr>
<td>Villa P et al, Spain 2000</td>
<td>86 patients with a moderate or high clinical suspicion DVT</td>
<td>Prospective cohort</td>
<td>Sensitivity Specificity</td>
<td>Illet using 255 ng/ml cut off</td>
<td>98.4% 33.3%</td>
</tr>
<tr>
<td>Harper P et al, New Zealand 2001</td>
<td>235 patients presenting to emergency department with DVT</td>
<td>Prospective cohort</td>
<td>Sensitivity IL test (250 ng/ml cut off) and SimpliRED</td>
<td>94.1% 66%</td>
<td></td>
</tr>
<tr>
<td>Kovacs MJ et al, Canada 2001</td>
<td>All patients with suspected DVT (468 patients) or PE (525 patients), presenting to four hospitals</td>
<td>Prospective cohort</td>
<td>Sensitivity of</td>
<td>SimpliRED, IL test and Acculog</td>
<td>80% 91% 91%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Specificity of</td>
<td>SimpliRED, IL test and Acculog</td>
<td>79% 74% 76%</td>
</tr>
</tbody>
</table>


www.emjonline.com
Outpatient investigation of pulmonary embolism

Report by Kerstin Hogg, Clinical Research Fellow

Checked by Debbie Dawson, Clinical Research Nurse

Abstract

A short cut review was carried out to establish whether outpatient investigation of suspected pulmonary embolus is a safe strategy. A total of 198 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 38 year old man presents to the emergency department with left posterior pleuritic chest pain. He had a DVT eight years ago and his D-dimer levels are raised. He is haemodynamically stable with normal oxygen saturations, ECG, and chest radiograph. You would like to rule out a pulmonary embolism, but it is 8 pm. You wonder whether it would be safe to discharge the patient home overnight before his VQ scan tomorrow.

Three part question

In a [patient with suspected pulmonary embolism] is [outpatient investigation] [safe]?

Search strategy

Medline 1966–04/03 using the OVID interface. [(pulmonary embol$.mp OR exp Pulmonary Embolism OR PE.mp OR exp Thromboembolism OR pulmonary infarct$.mp) AND (diagnosis.mp OR exp Diagnosis) AND (outpatient.mp OR exp Outpatients OR clinic.mp OR exp Outpatient clinics, hospital)] LIMIT to human AND English.

Search outcome

Altogether 198 papers were found, one of which looked at outpatient investigation of patients with suspected PE. This is shown in table 9.

Comments

This is the only published study looking at outpatient investigation of PE and is small. Further research is needed.

> CLINICAL BOTTOM LINE

It may be safe to investigate selected patients with suspected pulmonary embolus at home.


Outpatient treatment of pulmonary embolism

Report by Kerstin Hogg, Clinical Research Fellow

Checked by Debbie Dawson, Clinical Research Nurse

Abstract

A short cut review was carried out to establish whether outpatient treatment of patients with pulmonary embolus is a safe strategy. Sixty six papers were found using the reported

Table 9

<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>Bauld DL et al, Canada, 1999</td>
<td>128 emergency department patients—50 with suspected PE, the rest suspected DVT. All given one dose of dalteparin and discharged overnight before investigations</td>
<td>Prospective cohort</td>
<td>Adverse events</td>
<td>6% had bruising at injection site</td>
<td>Small study numbers</td>
</tr>
</tbody>
</table>

Table 10

<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>Wells PS et al, 1998, Canada</td>
<td>184 patients with either DVT or PE [54 had PE] deemed at low risk of complications randomised to self administration dalteparin or homecare nurse administration. All treated at home</td>
<td>Prospective cohort</td>
<td>Recurrent thromboembolic event in three month follow up</td>
<td>3.6%</td>
<td>Small number of patients with PE</td>
</tr>
<tr>
<td>Kovacs MJ et al, 2000, Canada</td>
<td>81 patients treated at home for pulmonary embolism. Further 27 managed at home after average 2.5 days in hospital.</td>
<td>Prospective cohort</td>
<td>Recurrent thromboembolic event in three month follow up Major haemorrhage Death</td>
<td>5.6% 2.0% 5.1%</td>
<td>Comparatively small numbers</td>
</tr>
<tr>
<td>Labas P et al, Slovakia, 2001</td>
<td>28 patients diagnosed with concurrent PE and DVT treated at home</td>
<td>Prospective cohort</td>
<td>Death</td>
<td>None</td>
<td>No details given regarding diagnostic criteria for PE</td>
</tr>
</tbody>
</table>
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 40 year old woman presents to the emergency department with pleuritic chest pain. She comments that she has had “cramp” in her left leg since discharge from the surgical ward after hysterectomy. Her ventilation-perfusion scan shows a high probability of pulmonary embolism. You have scored her as a high clinical probability of PE and therefore diagnose pulmonary embolic disease. She is comfortable, has normal oxygen saturations and is keen to return home to her family. You wonder whether treating her as an outpatient would be a safe option.

**Three part question**
Is it [safe] to treat a patient with [pulmonary embolic disease] as an [outpatient]?

**Search strategy**
Medline 1966–04/03 using the OVID interface. 

\[(\text{pulmonary embol$.mp OR exp Pulmonary Embolism OR PE.mp OR exp Thromboembolism OR pulmonary infarct$.mp}) \text{ AND (treatment.mp OR exp Therapeutics OR LMWH.mp OR exp Heparin, Low-Molecular-Weight OR low molecular weight.mp OR exp Anticoagulants} \text{ AND (outpatient.mp OR exp Outpatients OR clinic.mp OR exp Outpatient clinics, hospital)}) \text{ LIMIT to human AND English.}\]

**Search outcome**
Altogether 282 papers were found, of which three were relevant (table 10).

**Comment(s)**
There are no large studies validating this approach to the treatment of pulmonary embolism.

**CLINICAL BOTTOM LINE**
It may be safe to treat a low risk group of patients with pulmonary embolic disease at home.

Accumulator BET: a traumatic pleuritic chest pain

- **Patient with pleuritic chest pain**
  - **SaO₂, ECG, Chest radiograph**
    - **Clinical risk assessment**
      - **d-Dimer**
        - **Consider for OP investigation**
          - **Raised**
            - **Normal**
          - **Chronic cardiac or respiratory problem**
            - **Yes**
              - **CT pulmonary angiography**
                - **No PE**
                  - **Consider for OP investigation**
                    - **PE**
                      - **Interpret VQ with clinical risk assessment**
                        - **Low/low**
                          - **Admit anticoagulate**
                      - **High/High**
                        - **Other**
                          - **BB 178 Abnormal**
                            - **Other diagnosis requiring admission**
                              - **Yes**
                                - **Admit for treatment**
                              - **No**
                                - **Home**
                    - **No PE**
                      - **Interpret VQ with clinical risk assessment**
                        - **Low/low**
                          - **Admit anticoagulate**
                        - **High/High**
                          - **Other**
                            - **BB 178 Abnormal**
                              - **Other diagnosis requiring admission**
                                - **Yes**
                                  - **Admit for treatment**
                              - **No**
                                - **Home**
          - **Normal**
            - **Other diagnosis requiring admission**
              - **Yes**
                - **Admit for treatment**
              - **No**
                - **Home**


**BB 178.** Combining clinical probability and ventilation-perfusion scan for diagnosis of pulmonary embolism. [http://www.bestbets.org/cgi-bin/bets.pl?record=178](http://www.bestbets.org/cgi-bin/bets.pl?record=178)

**BB 271.** Diagnostic utility of ECG for diagnosing pulmonary embolism. [http://www.bestbets.org/cgi-bin/bets.pl?record=271](http://www.bestbets.org/cgi-bin/bets.pl?record=271)


**BB 463.** Outpatient investigation of pulmonary embolism. [http://www.bestbets.org/cgi-bin/bets.pl?record=463](http://www.bestbets.org/cgi-bin/bets.pl?record=463)


**BB 490.** IL-d-dimer test in the diagnosis of pulmonary embolism. [http://www.bestbets.org/cgi-bin/bets.pl?record=490](http://www.bestbets.org/cgi-bin/bets.pl?record=490)

**BB 594.** Accuracy of CT pulmonary angiogram in the diagnosis of pulmonary embolism. [http://www.bestbets.org/cgi-bin/bets.pl?record=594](http://www.bestbets.org/cgi-bin/bets.pl?record=594)

**BB 610.** Can clinical probability score estimate the probability of pulmonary embolism. [http://www.bestbets.org/cgi-bin/bets.pl?record=610](http://www.bestbets.org/cgi-bin/bets.pl?record=610)

**BB 611.** Diagnostic utility of chest x-ray for investigation of pulmonary embolism. [http://www.bestbets.org/cgi-bin/bets.pl?record=00611](http://www.bestbets.org/cgi-bin/bets.pl?record=00611)

Prepared by K Hogg, G Brown, K Mackway-Jones
Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary

K Mackway-Jones

doi: 10.1136/emj.20.4.362

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- Urinary tract infections (25)
- Urinary tract infections (25)
- Diabetes (75)
- Poisoning (245)
- Poisoning/Ingestion (245)
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