BEST EVIDENCE TOPIC REPORTS

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] Eight topics are covered in this issue of the journal

- Lorazepam or diazepam for generalised convulsions in adults
- Capillary blood gases in COPD
- Salbutamol and ipratropium in COPD
- Nebulised epinephrine or corticosteroids in croup
- SimpliRed and diagnosis of deep venous thrombosis
- Prophylactic magnesium in myocardial infarction
- Monophasic or biphasic defibrillation
- Antibiotics for otitis media

1 Carley SD, Mackway-Jones K, Jones A, *et al*. Moving towards evidence based emergency medicine: use of a structured critical appraisal journal club. *J Accid Emerg Med* 1998;**15**:220–2.
2 Mackway-Jones K, Carley SD, Morton RJ, *et al*. The best evidence topic report: a modified CAT for summarising the available evidence in emergency medicine. *J Accid Emerg Med* 1998;**15**:222–6.
3 Mackway-Jones K, Carley SD. bestbets.org: Odds on favourite for evidence in emergency medicine reaches the worldwide web. *J Accid Emerg Med* 2000;**17**:235–6.

Lorazepam or diazepam for generalised convulsions in adults

Report by John Butler, *Specialist Registrar*
Search checked by Mark Lewis, *Specialist Registrar*

Clinical scenario
A 45 year old woman epileptic presents after sustaining a grand mal convulsion at home. She starts fitting again on arrival in the emergency department; the fit does not stop spontaneously after five minutes. The paramedics have secured intravenous access before arrival but have not given any anticonvulsants. You wonder whether lorazepam is more effective than diazepam as a first choice drug to safely terminate this convulsion.

Three part question
In [an adult epileptic patient suffering a grand mal fit] is [intravenous lorazepam safer and more effective than intravenous diazepam] at [safely terminating the convulsions].

Search strategy
Medline 1966–09/00 using the OVID interface. [(exp epilepsy OR exp epilepsy, generalised OR exp epilepsy, tonic-clonic OR epilepsy.mp OR fits.mp OR exp convulsions OR convulsion$.mp OR exp seizures OR exp alcohol withdrawal seizures OR seizure$.mp) AND (exp lorazepam OR lorazepam$.mp)] LIMIT to human AND english.

Search outcome
Altogether 133 papers found of which 131 were irrelevant or of insufficient quality. The remaining two papers are shown in the table 1.

Comments
The incidence of status epilepticus is given as 15–30 per 100 000 per year. It carries a considerable mortality (approximately 10%). The best first line treatment remains controversial. The use of diazepam is limited by its rapid redistribution out of the CNS. The duration of action of diazepam is approximately 20–30 minutes. Pharmacokinetic studies of lorazepam have shown it has an elimination half life of 13 hours. Lorazepam has a much longer duration of anticonvulsant action than diazepam and has an equivalent onset of action. Studies in healthy volunteers suggest it has reduced cardiorespiratory side effects compared with other benzodiazepines. There may be an increased risk of thrombophlebitis when compared with intravenous diazemuls.

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Table 1

Author, date and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Leppik *et al*, 1983, USA	78 adult patients with status epilepticus. iv Lorazepam (4 mg) *v* iv diazepam (10 mg)	PRCT	Clinical control of seizure activity:	Lorazepam 89% within 2 doses *v* diazepam 76% within 2 doses	Small numbers Many different types of seizure activity
Treiman *et al*, 1998, USA	384 patients with generalised convulsions from 570 patients with status epilepticus. iv diazepam (0.15 mg/kg) plus phenytoin (0.1 mg/kg) *v* iv lorazepam (0.1 mg/kg) *v* iv phenobarbitone (15 mg/kg) *v* iv phenytoin (18 mg/kg)	PRCT	Stopping all motor seizure activity / EEG activity in <20 minutes.	55.8% *v* 64.9% *v* 58.2% *v* 43.6% In an intention to treat analysis the differences between treatment groups were not significant (p=0.12).	Some patients were treated prior to inclusion in trial. No long term follow up of patients.

Clinical bottom line

Intravenous lorazepam is effective and safe in the treatment of status epilepticus. It should be the first line of treatment.

1 Leppik IE, Derivan AT, Homan RW, *et al*. Double-blind study of lorazepam and diazepam in status epilepticus. *JAMA* 1983;**249**:1452–4.
2 Treiman DM, Meyers PD, Walton NY, *et al*. A comparison of four treatments for generalized convulsive status epilepticus. *N Engl J Med* 1998;**339**:792–8.

Capillary blood gases in COPD

Report by Ross Murphy, *Senior Clinical Fellow*
Search checked by Magnus Harrison, *Clinical Research Fellow*

Clinical scenario

A 60 year old man presents to the emergency department with an acute exacerbation of COPD. Analysis of blood gases is required. You wonder whether a capillary blood sample will be as accurate as an arterial blood sample.

Three part question

In [a patient with an acute exacerbation of COPD] is [a capillary blood sample as good as an arterial blood sample] at measuring [Pa_{O_2}, Pa_{CO_2} and pH]?

Search strategy

Medline 1966–11/00 using the OVID interface. {[Capillar$.mp AND (exp blood gas analysis OR blood gas$.mp OR blood gas$.mp)] AND [(exp arteries OR arter$.mp) AND (exp blood gas analysis OR blood gas$.mp OR blood gas$.mp)]} LIMIT to human AND english.

Search outcome

Altogether 280 papers found of which 276 were irrelevant or of insufficient quality. The remaining four papers are shown in table 2.

Comments

Different studies have given slightly different results. There have been no statistically significant differences identified. Moreover the differences that have been seen are clinically insignificant as well. Further research in patients with COPD would be useful.

Clinical bottom line

Properly taken capillary blood samples accurately reflect arterial blood gas measures of P_{O_2}, P_{CO_2} and pH.

1 Langlands JH, Wallace WF. Small blood samples from ear-lobe puncture. *Lancet* 1965;ii:315–17.
2 Begin R, Racine T, Roy JC. Value of capillary blood gas analysis in the management of acute respiratory distress. *Am Rev Resp Dis* 1975;**112**:879–81.
3 Pitkin AD, Roberts CM, Wedzicha JA. Arterialised earlobe blood gas analysis: an underused technique. *Thorax* 1994;**49**: 364–6.
4 Dar K, Williams T, Aitken R, *et al*. Arterial versus capillary sampling for analysing blood gas pressures. *BMJ* 1995;**310**: 24–5.

Table 2

Author, date and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Langlands JH and Wallace WF, 1965, UK	14 patients under investigation for pulmonary disease and 2 normal patients. Arterial blood *v* capillary blood from ear	Diagnostic test	P_{O_2}	Mean difference 0.62 mm Hg (SD 4.1) NS	Small numbers. No power calculation. Do not know if any patients were suffering from COPD
			P_{CO_2}	Mean difference 1.05 mm Hg (SD 1.6) NS	
			pH	Mean difference 0.006 (SD 0.01) NS	
Begin R *et al*, 1975, USA	45 patients in acute respiratory distress without circulatory shock. 15 were below age 16. Arterial blood *v* capillary blood from finger.	Diagnostic test	P_{O_2}	Mean difference 2.1 mm Hg (SD 4.4) $r = 0.97$	Small numbers. No power calculation. Do not know if any patients were suffering from COPD
			P_{CO_2}	Mean difference 1.4 mm Hg (SD 3.2) $r = 0.98$	
			pH	Mean difference 0.006 (SD 0.016) $r = 0.98$	
Pitkin AP *et al*, 1994, UK	40 patients with chronic lung disease and a variety of arterial blood gas tensions. 29 had COPD and bronchiectasis. Arterial blood *v* capillary blood from ear.	Diagnostic test	P_{O_2}	Mean difference 0.17 kPa (CI −1.09 to +0.75)	Small numbers. No power calculation. Patients suffered from a variety of underlying illnesses.
			P_{CO_2}	Mean difference 0.21 kPa (CI −0.24 to +0.67)	
			pH	Mean difference 0.007 (CI −0.008 to +0.022)	
Dar K *et al*, 1995, UK	55 patients requiring measurement of blood gases. 22 had exacerbations of COPD. Arterial blood *v* capillary blood from ear.	Diagnostic test	P_{O_2}	Mean difference 0.09 kPa (SD 0.59)	Small numbers. No power calculation.
			P_{CO_2}	Mean difference 0.01 kPa (SD 0.3)	
			pH	Mean difference 0.007 (SD 0.02)	

Salbutamol and ipratropium in COPD

Report by Magnus Harrison, *Clinical Research Fellow*
Search checked by Ross Murphy, *Senior Clinical Fellow*

Clinical scenario
A 59 year old man presents with an exacerbation of COPD. You wonder whether it is better to nebulise salbutamol or ipratropium bromide alone, or a combination of the two.

Three part question
In [patients presenting with an acute exacerbation of COPD] is nebulisation of [a beta 2 agonist alone, ipratropium bromide alone or a combination of the two] more effective at [controlling and improving symptoms].

Search strategy
Medline 1966–11/00 using the OVID interface. {{[(exp chronic disease OR exp hospitals, chronic disease OR chronic.mp) AND (exp lung disease, obstructive OR obstructive.mp)] OR exp emphysema OR exp pulmonary emphysema OR emphysema.mp OR exp bronchitis OR bronchitis.mp OR exp COPD.mp OR COAD.mp OR airway obstruction.mp)} AND (acute.mp or exacerbation.mp)} AND (exp ipratropium OR ipratropium bromide.mp OR atrovent.mp OR antimuscarinic.mp OR exp. muscarinic antagonist OR exp brochodilators agents OR bronchodilators.mp OR exp albuterol OR salbutamol.mp OR beta 2 agonist.mp OR exp terbutaline) AND (exp nebulisers OR vaporises.mp OR exp respiratory therapy OR nebulisers.mp) NOT (exp child OR children.mp OR exp paediatrics OR paediatric.mp) LIMIT to human AND english.

Search outcome
Altogether 162 papers found of which 157 were irrelevant or of insufficient quality. The remaining five papers are shown in table 3.

Comments
There are five randomised trials that address the three part question. All of the studies are of reasonable quality.

Clinical bottom line
Initial treatment can be either salbutamol or ipratropium nebulisers alone. There is no evidence to suggest that using both has additional benefit.

1 Rebuck AS, Chapman KR, Abboud R, *et al*. Nebulised anticholinergic and sympathomimetic treatment of asthma and chronic obstructive airways disease in the emergency room. *Am J Med* 1987;**82**:59–64.
2 O'Driscoll BR, Taylor RJ, Horsley MG, *et al*. Nebulised salbutamol with and without ipratropium bromide in acute airflow obstruction. *Lancet* 1989;i:1418–20.
3 Shrestha M, O'Brien T, Haddox R, *et al*. Decreased duration of emergency department treatment of chronic obstructive airways disease exacerbations with the addition of ipratropium bromide to beta-agonist therapy. *Ann Emerg Med* 1991; **20**:1206–9.
4 Moayyedi P, Congleton J, Page RL, *et al*. Comparison of nebulised salbutamol and ipratropium bromide with salbutamol alone in the treatment of chronic obstructive pulmonary disease. *Thorax* 1995;**50**:834–7.
5 Koutsogiannis Z, Kelly A-M. Does high dose ipratropium bromide added to salbutamol improve pulmonary function for patients with chronic obstructive airways disease in the emergency department? *Aust N Z Med J* 2000;**30**:41–7.

Table 3

Author, date and country	*Patient group*	*Study type (level of evidence)*	*Outcomes*	*Key results*	*Study weaknesses*
Rebuck AS *et al*, 1987, Canada	51 patients with an acute exacerbation of COPD (148 asthmatics also recruited)	PRCT	FVC, FEV_1, MMEFR, PEFR, cardiovascular markers at 45 min	No significant difference	No sample size calculation.
	Ipratropium *v* fenoterol *v* both (all nebulised).		FVC, FEV_1, MMEFR, PEFR, cardiovascular markers at 90 min	No significant difference	Small groups in each of the treatment arms, thus small differences may go undetected.
O'Driscoll BR *et al*, 1989, UK	47 patients with COPD (an asthmatic group also recruited)	PRCT	PEFR on arrival and at one hour	No difference in improvement (p>0.55)	No sample size calculation, small groups in each treatment arm, thus important effects can be overlooked. No defined inclusion or exclusion criteria. 20 patients admitted, excluded from study. No actual figures given.
	Salbutamol *v* salbutamol plus ipratropium bromide				
Shrestha M *et al*, 1991, USA	55 COPD patients with an acute exacerbation (FEV_1 <40% of predicted)	PRCT	Times to discharge from ED	Time to discharge 91 minutes less in the salbutamol plus ipratropium group (p<0.05)	No sample size calculation.
	Isoetharine plus placebo *v* isoetharine plus ipratropium bromide (inhaled)		FVC, FEV_1	No difference	Small numbers. Inhaled therapy
Moayyedi P *et al*, 1995, UK	62 COPD patients with an acute exacerbation	PRCT	Length of hospital stay Duration of nebuliser therapy	No significant difference No significant difference	Power study retrospectively completed
	Salbutamol *v* salbutamol plus ipratropium bromide (nebulised)		FVC, FEV_1 Subjective improvement on days 1, 3, 7 and 14	No significant difference No significant difference	
Koutsogiannis Z and Kelly A-M, 2000, Australia	50 patients presenting to ED with an acute exacerbation of COPD.	PRCT	Absolute and percentage change in FEV_1 at 90 min	No difference between the 2 groups.	No sample size calculation. Groups are small thus any differences may be overlooked. All patients had both drugs initially.
	All patients started with salbutamol and ipratropium nebulisers and then salbutamol *v* ipratropium *v* salbutamol plus ipratropium.			(p=0.36 for absolute change, p=0.56 for % change)	

Nebulised epinephrine or corticosteroids in croup

Report by Angaj Ghosh, *Senior Clinical Fellow*
Search checked by Rosemary Morton, *Consultant*

Clinical scenario
A 4 year old girl attends the emergency department with moderately severe croup. You have heard that croup responds to corticosteroid therapy, but wonder whether it is more effective than nebulised epinephrine

Three part question
In a [child with croup] is [nebulised epinephrine or nebulised budesonide] more effective at [reducing croup score and length of stay].

Search strategy
Medline 1966–11/00 using the OVID interface. [(exp croup OR croup.mp OR exp tracheitis OR laryngotracheitis.mp OR laryngotracheobronchitis.mp OR Stridor.mp) AND (exp epinephrine OR adrenaline.mp OR exp budesonide OR budesonide.mp)] LIMIT to human AND english.

Search outcome
Altogether 119 papers found of which 118 were irrelevant or of insufficient quality. The remaining paper is shown in table 4.

Comments
This study shows that there are no significant clinical differences between the two treatments. In such a case the relative cost of the treatment is an important factor in deciding which should be prescribed.

Clinical bottom line
Nebulised epinephrine and nebulised budesonide are as effective as each other in moderately severe croup.

1 Fitzgerald D, Mellis C, Johnson M, *et al*. Nebulized budesonide is as effective as nebulized adrenaline in moderately severe croup. *Pediatrics* 1996;**97**:722–5.

Table 4

Author, date and country	*Patient group*	*Study type (level of evidence)*	*Outcomes*	*Key results*	*Study weaknesses*
Fitzgerald D *et al*, 1996, Australia	66 hospitalised children with viral or spasmodic croup. Budesonide 2 mg *v* epinephrine 4 mg	PRCT	Change in total croup symptom score Duration of croup attack in hours Side effects	7.1 (1.2) *v* 7.7 (1.1) (not significant) 31 (21) *v* 26 (21) (not significant) No significant difference	Sample size calculated to be 66 but only 53 completed the 24 h study. No follow up

Prophylactic magnesium in myocardial infarction

Report by Mark Davies, *Senior Clinical Fellow*
Search checked by Angaj Ghosh, *Senior Clinical Fellow*

Clinical scenario
You see a 50 year old man with a two hour history of cardiac chest pain and an ECG suggestive of acute myocardial infarction. You decide to thrombolyse. The cardiology registrar suggests that you also give intravenous magnesium to reduce the incidence of ventricular fibrillation. You wonder whether there is any evidence to support this.

Three part question
In [patients with suspected acute myocardial infarction] is [magnesium] effective at [reducing the incidence of ventricular fibrillation].

Search strategy
Medline 1966–11/00 using the OVID interface. [(exp myocardial infarction OR myocardial infarction.mp OR MI.mp) AND (exp magnesium sulfate OR magnesium sulfate.mp OR magnesium sulphate.mp OR exp magnesium OR exp magnesium.mp OR exp magnesium chloride OR magnesium chloride.mp) AND (exp arrhythmia OR arrhythmia.mp OR dysrhythmias.mp OR exp ventricular fibrillation OR ventricular fibrillation.mp OR (VF.mp) or (exp. mortality/ or mortality.mp)] AND maximally sensitive RCT filter LIMIT to human AND english.

Search outcome
Altogether 103 papers found of which 86 were irrelevant and 12 of insufficient quality for inclusion. The remaining five papers are shown in table 5.

Comments
A number of small studies published have suggested that magnesium therapy significantly improves mortality following myocardial infarction. While the two larger studies show a trend to reduction in the incidence of ventricular fibrillation but also demonstrates that this benefit is outweighed by an increased incidence of detrimental effects.

Clinical bottom line
Routine prophylactic magnesium in patients with myocardial infarction is not indicated.

1 Abraham AS, Rosenmann D, Kramer M, *et al*. Magnesium in the prevention of lethal arrhythmias in acute myocardial infarction. *Arch Intern Med* 1987;**147**:753–5.
2 Roffe C, Fletcher S, Woods KL. Investigation of the effects of intravenous magnesium sulphate on cardiac rhythm in acute myocardial infarction. *Br Heart J* 1994;**71**:141–5.
3 Bhargava B, Chandra S, Agarwal VV, *et al*. Adjunctive magnesium infusion therapy in acute myocardial infarction. *Int J Cardiol* 1995;**52**:95–9.
4 Anonymous. ISIS 4: A randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58050 patients with suspected acute myocardial infarction *Lancet* 1995;**345**:669–85.
5 Gyamlani G, Parikh C, Kulkarni AG, *et al*. Benefits of magnesium in acute myocardial infarction: timing is crucial. *Am Heart J* 2000;**139**:703.

Table 5

Author, date and country	*Patient group*	*Study type (level of evidence)*	*Outcomes*	*Key results*	*Study weaknesses*
Abraham AS *et al*, 1987, Israel	94 patients with proven MI 2.4 g $MgSO_4$ daily for 3 days *v* glucose	PRCT	Incidence of : Ventricular triplets R-on-T VT VF Total of above	 8 *v* 13% p=NS 0 *v* 2% p=NS 7 *v* 15% p=NS 0 *v* 4% p=NS 14 *v* 34% p=0.05	Analysed by group sequential design (interim analysis)
Ro *e C et al, 1994, UK*	2316 patients with suspected MI 8 mmol $MgSO_4$ stat and 65 mmol over 24 h *v* equal volume of saline	PRCT	Odds ratio (95% CI) VF VT SVT AF Heart block Sinus bradycardia	 0.74 (0.46,1.20) p=NS 0.87 (0.63,1.20) p=NS 0.69 (0.38,1.26) p=NS 0.92 (0.69,1.23) p=NS 1.17 (0.83,1.65) p=NS 1.38 (1.03,1.85) p=0.02	Clinical significance of arrhythmias not described
Bhargava B *et al*, 1995, India	78 patients with proven MI 73 mmol $MgSO_4$ over 24 h *v* saline	PRCT	Incidence of : Sustained VT Non-sustained VT VF SVT Bradycardia Asystole Mortality at 28 days In hospital mortality	 10 *v* 20% p=NS 23 *v* 50% p<0.02 5 *v* 8% p=NS 0 *v* 6% p=NS 5 *v* 3% p=NS 0 *v* 3% p=NS None 7.5 *v* 8% p=NS	Small numbers
ISIS-4 investigators, 1995, multinational	58 050 patients 80 mmol mg over 24 h *v* no infusion	PRCT	Incidence of : VF Other cardiac arrest 2nd or 3rd degree heart block Heart failure Cardiogenic shock profound hypotension 5 week mortality	 3.5 *v* 3.8% 3.2 *v* 2.9% 3.9 *v* 3.7% 0.01<p<0.05 17.8 *v* 16.6% p<0.001 4.6 *v* 4.1% p<0.01 16.8 *v* 15.1% p<0.0001 7.64 *v* 7.24% p=NS	
Gyamlani G *et al*, 2000, India	100 patients with proven MI 50 mmol mg in 1st 24 h then 12 mmol mg in next 24 h *v* glucose	PRCT	Incidence of : SVT Sustained VT Non-sustained VT VF Total arrhythmias Mortality	 2 *v* 8% p=NS 2 *v* 10% p=NS 4 *v* 12% p=NS 0 *v* 4% p=NS 8 *v* 34% p<0.01 4 *v* 20% p<0.05	Small numbers

SimpliRed and diagnosis of deep venous thrombosis

Report by Steve Jones, *Clinical Research Fellow*
Search checked by Magnus Harrison, *Clinical Research Fellow*

Clinical scenario

A patient attends the emergency department with signs and symptoms consistent with a deep venous thrombosis. Somebody suggests that there is a new bedside blood test, called SimpliRed, that may help to rule out the diagnosis in your patient. You know that ruling out a diagnosis is possible by having a test with a high sensitivity or negative predictive value. You wonder what evidence there is to suggest that SimpliRed fulfils these criteria?

Three part question

In a [patient with a suspected DVT] does the [SimpliRed test] reliably [rule out the diagnosis]?

Search strategy

Medline 1966–11/00 using the OVID interface. [(exp thrombosis or exp venous thrombosis or thrombosis.mp OR venous thrombosis.mp deep venous thrombosis.mp) AND (exp fibrin fibrinogen degradation products or simplired.mp OR d-dimer$.mp)] LIMIT to human and english language OR Medline 1966–11/00 using the OVID interface. simplired.mp.

Search outcome

Altogether 741 and 37 papers found of which 13 were relevant and of sufficient quality. These 13 remaining papers are shown in table 6.

Comments

The "gold standard" investigation for DVT is contrast venography. This has now been replaced in many centres with a strategy of single or serial compression ultrasound, hence the use of different reference standard tests.

If an investigation is to be used in order to rule out a diagnosis, then it must have a sensitivity of 95% or above. In some of the studies mentioned this is the case, however such is the variability of the results obtained in the other studies the safety of SimpliRed as a lone exclusionary test must be in question. The reasons for this variability may include the operators of the assay or the various techniques used. Many of the results however are still inadequate.

Clinical bottom line

It is not safe to use SimpliRed as a lone exclusionary test for a patient presenting to the emergency department with a possible DVT.

Table 6

Author, date and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Wells PS *et al*, 1995, Canada	214 consecutive patients referred for investigation of ?DVT.	Prospective cohort	Prevalence Sensitivity Specificity NPV NLR	25% 88% (CI 77, 96) 77% (CI 63, 80) 95% (CI 89, 98) 0.16	No sample size calculation Excluded patients with inconclusive venograms or plethysmogram
Brenner B *et al*, 1995, Israel	86 consecutive patients referred for investigation of ?DVT	Prospective cohort	Prevalence Sensitivity Specificity NPV NLR	58% 94% 61% 88% 0.1	Small patient numbers. No sample size calculation. No confidence intervals
Turkstra F *et al*, 1996, Netherlands	234 consecutive patients referred for ?DVT or ?PE	Prospective cohort	Prevalence Sensitivity Specificity NPV	27% 100% (CI 95, 100) 58% (CI 50, 65) 100% (CI 96, 100)	No sample size calculation (but good numbers)
Janssen MC *et al*, 1997, Netherlands	132 patients referred to ED or OPD for investigation of ?DVT	Prospective cohort	Prevalence Sensitivity Specificity NPV NLR	67% 61% (CI 51, 71) 90% (CI 81, 99) 52% (CI 29, 75) 0.43	No sample size calculation. Technique of assay may have affected results. Reference standard not applied to all patients
Ginsberg FS *et al*, 1997, Canada	398 consecutive patients referred to thromboembolic OPD as first episode of ?DVT	Prospective management study	NPV D-dimer alone NPV D-dimer and plethysmography together	97.1% (CI 94.5, 98.8) 98.5% (CI 96.3, 99.6)	No sample size calculation. Reference standard not applied to all patients
Mayer W *et al*, 1997, Austria	108 consecutive patients referred to vascular laboratory as ?DVT	Prospective cohort	Prevalence Sensitivity Specificity NPV	31% 100% (CI 89, 100) 75% (CI 63, 84) 100% (CI 94, 100)	Small patient numbers. No sample size calculation. Used single ultrasound as reference standard
Wildberger JE *et al*, 1998, Germany	250 consecutive patients referred for venography	Prospective cohort	Sensitivity Specificity NPV NLR	96% 59% 97% 0.06	No sample size calculation. Patient selection bias. No confidence intervals
Wells PS *et al*, 1998, Canada	496 consecutive outpatients referred with ?DVT	Prospective cohort	Overall sensitivity Overall specificity NPV NLR *Low pretest probability* Sensitivity Specificity NPV NLR *Medium pretest probability* Sensitivity Specificity NPV NLR *High pretest probability* Sensitivity Specificity NPV NLR	94% 71% 98% (CI 96, 99) 0.08 87% 76% 99% (CI 97, 100) 0.17 89% 64% 97% (CI 90, 99) 0.17 98% 54% 86% (CI 42, 97) 0.04	No sample size calculation. Patient selection bias. No confidence intervals
Mauron T *et al*, 1998, Switzerland	45 consecutive outpatients referred with ?DVT.	Prospective cohort	Prevalence Sensitivity Specificity NPV NLR	33% 53% (CI 28, 78) 70% (CI 54, 86) 75% (CI 59, 91) 0.67	Small patient numbers. No sample size calculation. Wide confidence intervals
Carter CJ *et al*, 1999, Canada	200 consecutive patients referred to diagnostic radiology department with ?DVT. Inpatients and outpatients	Prospective cohort	Prevalence Sensitivity Specificity NPV NLR	28% 87% (CI 80, 96) 79% 94% 0.16	No sample size calculation. Used single ultrasound as reference standard. Wide confidence intervals
Lennox AF *et al*, 1999, UK	200 consecutive patients referred to diagnostic radiology department with ?DVT. Inpatients and outpatients	Prospective cohort	Prevalence Sensitivity Specificity NPV NLR	23% 91% 82% 97% 0.11	No sample size calculation. Incorrect test procedure likely to give falsely high sensitivities. No confidence intervals
Farrell S *et al*, 2000, USA	173 consecutive patients referred to ED with ?DVT (48) or ?PE (125)	Prospective clinical trial	Prevalence Sensitivity NPV NLR	33% 56% (CI 32, 81) 77% (CI 62, 92) 0.61 (CI 0.34, 1.11)	Did not recruit all patients required. Used single ultrasound as reference standard. Wide confidence intervals
Van der Graaf F *et al*, 2000, Netherlands	112 outpatients referred to department	Prospective cohort	Prevalence Sensitivity Specificity NPV Likelihood ratio for negative result (NLR)	50% 80% (CI 66, 90) 94% (CI 83, 99) 82% (CI 70, 91) 0.21	Small patient numbers. No sample size calculation. Wide confidence intervals

NPV = Negative predictive value, NLR = Likelihood ratio for negative result.

1 Wells PS, Brill-Edwards P, Stevens P, *et al*. A novel and rapid whole-blood assay for D-dimer in patients with clinically suspected deep vein thrombosis. *Circulation* 1995;**91**:2184–7.
2 Brenner B, Pery M, Lanir N, *et al*. Application of a bedside whole blood D-dimer assay in the diagnosis of deep vein thrombosis. *Blood Coagul Fibrinolysis* 1995;**6**:219–22.
3 Turkstra F, van Beek EJ, ten Cate JW, *et al*. Reliable rapid blood test for the exclusion of venous thromboembolism in symptomatic outpatients. *Thromb Haemost* 1996;**76**:9–11.
4 Janssen MC, Heebels AE, de Metz M, *et al*. Reliability of five rapid D-dimer assays compared to ELISA in the exclusion of deep venous thrombosis. *Thromb Haemost* 1997;77:262–6.

5 Ginsberg JS, Kearon C, Douketis J, *et al*. The use of D-dimer testing and impedance plethysmographic examination in patients with clinical indications of deep vein thrombosis. *Arch Intern Med* 1997;**157**:1077–81.
6 Mayer W, Hirschwehr R, Hippmann G, *et al*. Whole-blood immunoassay (SimpliRED) versus plasma immunoassay (NycoCard) for the diagnosis of clinically suspected deep vein thrombosis. *Vasa* 1997;**26**:97–101.
7 Wildberger JE, Vorwerk D, Kilbinger M, *et al*. Bedside testing (SimpliRED) in the diagnosis of deep vein thrombosis. Evaluation of 250 patients. *Invest Radiol* 1998;**33**:232–5.
8 Wells PS, Anderson DR, Bormanis J, *et al*. SimpliRED D-dimer can reduce the diagnostic tests in suspected deep vein thrombosis. [Letter]. *Lancet* 1998;**351**:1405–6.
9 Mauron T, Baumgartner I, Z'Brun A, *et al*. SimpliRED D-dimer assay: comparability of capillary and citrated venous whole blood, between-assay variability, and performance of the test for exclusion of deep vein thrombosis in symptomatic outpatients. *Thromb Haemost* 1998;**79**:1217–19.
10 Carter CJ, Serrano K, Breen DJ, *et al*. Rapid fibrin D-dimer testsfor deep venous thrombosis: factors affecting diagnostic utility. *J Emerg Med* 1999;**17**:605–10.
11 Lennox AF, Delis KT, Serunkuma S, *et al*. Combination of a clinical risk assessment score and rapid whole blood D-dimer testing in the diagnosis of deep vein thrombosis in symptomatic patients. *J Vasc Surg* 1999;**30**:794–803.
12 Farrell S, Hayes T, Shaw M. A negative SimpliRed D-dimer assay result does exclude the diagnosis of deep venous thrombosis or pulmonary embolus in emergency department patients. *Ann Emerg Med* 2000;**35**: 121–5.
13 van der Graaf F, van den Borne H, van der Kolk, *et al*. Exclusion of deep venous thrombosis with D-dimer testing—comparison of 13 D-dimer methods in 99 outpatients suspected of deep venous thrombosis using venography as reference standard. *Thromb Haemost* 2000; **83**:191–8.

Monophasic or biphasic defibrillation

Report by Russell Boyd, *Consultant*
Search checked by Angaj Ghosh, *Senior Clinical Fellow*

Clinical scenario
You have just finished an unsuccessful cardiac resuscitation in a patient who had an initial presenting rhythm of ventricular fibrillation. You wonder if one of the new biphasic defibrillators would have increased the possibility of successful defibrillation.

Three part question
In [an adult patient with ventricular fibrillation] is [biphasic or monophasic D/C shock] better [at restoring sinus rhythm]?

Search strategy
Medline 1966–11/00 using the OVID interface. (biphasic.mp OR monophasic.mp) AND (exp.defibrillation OR exp electric counter shock OR cardioversion.mp).

Search outcome
Altogether 316 papers found of which 313 were irrelevant or of insufficient quality. The remaining three papers are shown in table 7.

Comments
There is some laboratory evidence that biphasic defibrillation has higher first shock success rates for defibrillation of VF/VT. A theoretical advantage exists with biphasic devices but there is no clinical evidence of increased survival in cardiac arrest occurring outside the cardiac arrhythmia laboratory.

Clinical bottom line
The advantages of biphasic devices are currently mainly theoretical. No real world data exist that would suggest an immediate conversion to using biphasic devices.

1 Greene HL, DiMarco JP, Kudenchuk PJ, *et al*. Comparison of monophasic and biphasic defibrillating pulse waveforms for transthoracic cardioversion. *Am J Cardiol* 1995;**75**:1135–9.
2 Mittal S, Ayati S, Stein K, *et al*. Comparison of a novel rectilinear biphasic waveform with a damped sine wave monophasic waveform for transthoracic ventricular defibrillation. *J Am Coll Cardiol* 1999;**34**:1595–601.
3 Bardy G, Marchlinski F, Arjun D, *et al*. Multi-center comparison of truncated biphasic shocks and standard damped sine wave monophasic shocks for transthoracic ventricular defibrillation. *Circulation* 1996;**94**:2507–14.

Table 7

Author, date and country	*Patient group*	*Study type (level of evidence)*	*Outcomes*	*Key results*	*Study weaknesses*
Greene HL *et al*, 1995, USA	171 patients undergoing electrophysiological studies for ventricular arrhythmias with induced VT and VF requiring external defibrillation. Monophasic *v* biphasic	PRCT	Success of first shock in VT	85.2% (75/88) *v* 97.6% (81/83)	Laboratory conditions for fresh arrhythmias
			Success of first shock in VF	78.6% (22/28) *v* 100% (25/25)	
Mittal S *et al*, 1999, USA	184 patients undergoing electrophysiological testing for ventricular arrhythmias producing an induced VF Monophasic *v* biphasic	PRCT	Success of first shock	93% (80/86) *v* 99% (97/98) (p=0.05)	Laboratory conditions for fresh arrhythmias
Bardy G *et al*, 1996, USA	294 patients with induced VF/VT during implantation of cardioversion devices Monophasic *v* biphasic	PRCT	Success of first shock	86% (143/166) *v* 86% (144/167)	Laboratory conditions for fresh arrhythmias Results for VF and VF combined

Antibiotics for otitis media

Report by Angaj Ghosh, *Senior Clinical Fellow*
Search checked by Rupert Jackson, *Specialist Registrar*

Clinical scenario
A 2 year old child is brought into the emergency department with general malaise and irritability for the past 24 hours. Examination of the right ear reveals a diffusely red bulging ear drum.A diagnosis of acute otitis media is made. You wonder whether there is any evidence that oral antibiotics would decrease the time to recovery and prevent secondary complications.

Three part question
In [a systemically well child with otitis media] are [oral antibiotics better than placebo] at [decreasing time to recovery and reducing the incidence of secondary complications]?

Search strategy
Medline 1966–11/00 using the OVID interface. Cochrane database. [(exp otitis media OR otitis media.mp OR acute otitis media.mp OR acute red ear.mp) AND (exp antibiotics OR antibiotic$.mp OR exp amoxycillin OR amoxycillin.mp OR exp amoxicillin-potassium clavulanate combination OR augmentin.mp OR co-amoxyclav.mp OR exp erythromycin OR exp erythromycin estolate OR erythromycin.mp OR exp penicillins OR penicillin.mp OR non-antibiotic treatment.mp OR placebo.mp)] AND maximally sensitive RCT filter LIMIT to human AND english.

Search outcome
Altogether 865 papers found of which 10 were relevant and had been meta-analysed by the Cochrane review group, which was last updated on the 28 April 2000. No further relevant papers have been published since. A meta-analysis done in 1994 was also selected. Details are shown in table 8.

Comments
Most cases of otitis media will spontaneously resolve.

Clinical bottom line
There is some benefit from the use of antibiotics in otitis media.

1 Rosenfeld RM, Vertrees JE, Carr J, *et al*. Clinical efficacy of antimicrobial drugs for acute otitis media: metaanalysis of 5400 children from thirty-three randomized trials. *J Pediatr* 1994;**124**:355–67.
2 Glasziou PP, Del Mar CB, Hayem M. Antibiotics for acute otitis media in children (Cochrane Review). In: *The Cochrane Library, Issue 4, 2000*. Oxford: Update Software.

Table 8

Author, date and country	*Patient group*	*Study type (level of evidence)*	*Outcomes*	*Key results*	*Study weaknesses*
Rosenfeld RM *et al*, 1994, USA	33 trials including 5400 children with acute otitis media Antibiotics *v* no antibiotics	Meta-analysis	Complete clinical resolution of signs (primary control)	Compared with placebo or no drug, antimicrobial therapy increased primary control by 13.7% (8.2% to 19.2%) (NNT=7)	Outcome not patient oriented
Glasziou PP *et al*, 2000, UK	7 trials with patient related outcomes. Total inclusion of 2202 children with acute otitis media Antibiotics *v* no antibiotics	Systematic review	Pain at 24 hours Pain between 2 and 7 days Hearing between 1 and 3 months	No difference 28% (CI 15%, 38%) relative reduction with antibiotics (NNT=17) No significant difference	Only one episode of mastoiditis in all the trials