

BEST EVIDENCE TOPIC REPORTS

Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary

Edited by K Mackway-Jones

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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 Infirmary¹ or placed on the BestBETs web site. 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 Five BETs are included in this issue of the journal.

- ▶ Amiodarone or flecainide for cardioversion in acute onset atrial fibrillation
- ▶ The sensitivity of a normal chest radiograph in ruling out aortic dissection
- ▶ Antibiotics in acute exacerbations of chronic obstructive pulmonary disease
- ▶ Intravenous magnesium in chronic obstructive pulmonary disease
- ▶ Intra-articular corticosteroid injections in acute rheumatoid monoarthritides

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- 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](http://www.bestbets.org): Odds on favourite for evidence in emergency medicine reaches the worldwide web. *J Accid Emerg Med* 2000;17:235–6.

Amiodarone or flecainide for cardioversion in acute onset atrial fibrillation

Report by Jon Argall, *Senior Clinical Fellow*
Checked by Ian Crawford, *Clinical Research Fellow*

A short cut review was carried out to establish whether amiodarone is better than flecainide at restoring sinus rhythm in patients with atrial fibrillation. Altogether 42 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 50 year old woman presents to the emergency department with acute onset of palpitations of less than two hours duration. She does not have chest pain, her heart rate is about 140–160 with a good systolic blood pressure, and respiratory examination is normal. An ECG confirms the rhythm to be atrial fibrillation. You consider which method of pharmacological cardioversion would be most suitable as the medical and cardiological opinions differ between amiodarone and flecainide.

Three part question

In [acute onset atrial fibrillation] is [amiodarone better than flecainide] at [restoring normal sinus rhythm]?

Search strategy

Medline 1966-11/03 using the Ovid interface. [exp Atrial Fibrillation OR (atrial adj5 fibrillation).af OR af.af] AND [exp Amiodarone OR amiodarone.af OR cordarone.af] AND [exp Flecainide OR flecainide.af OR tambacor.af] AND [Maximally Sensitive RCT Filter] LIMIT to human AND English.

Search outcome

Altogether 42 papers were found of which four were directly relevant to the three part question (see table 1).

Comment(s)

There were no significant differences in the patient groups or adverse effects in all studies. Most adverse effects were mild and self limiting, with no fatal events reported.

▶ CLINICAL BOTTOM LINE

In the stable patient with acute onset atrial fibrillation and uncompromised left ventricular function, flecainide is the most efficacious drug at restoring normal sinus rhythm expeditiously. However about 60% of patients will revert with no treatment.

Capucci A, Lenzi T, Boriani G, *et al.* Effectiveness of loading oral flecainide for converting recent-onset atrial fibrillation to sinus rhythm in patients without organic heart disease or with only systemic hypertension. *Am J Cardiol* 1992;70:69–72.

Donovan KD, Power BM, Hockings BE, *et al.* Intravenous flecainide versus amiodarone for recent-onset atrial fibrillation. *Am J Cardiol* 1995;75:693–7.

Boriani G, Biffi M, Capucci A, *et al.* Conversion of recent-onset atrial fibrillation to sinus rhythm: effects of different drug protocols. *Pacing Clin Electrophysiol* 1998;21:2470–4.

Martinez-Marcos FJ, Garcia-Garmendia JL, Ortega-Carpio A, *et al.* Comparison of intravenous flecainide, propafenone, and amiodarone for conversion of acute atrial fibrillation to sinus rhythm. *Am J Cardiol* 2000;86:950–3.

The sensitivity of a normal chest radiograph in ruling out aortic dissection

Report by Kerstin Hogg, *Clinical Research Fellow*
Checked by Stewart Teece, *Clinical Research Fellow*

A short cut review was carried out to establish the sensitivity of a normal chest radiograph as a rule out test for aortic

Table 1

Author, date and country	Patient group	Study type (level of evidence)	Key results	Outcomes	Study weaknesses
Capucci A <i>et al</i> , 1992, Italy	62 patients with recent onset atrial fibrillation (≤ 7 days), placebo versus amiodarone iv bolus followed by infusion or flecainide po	Randomised single blind trial	Conversion to sinus rhythm	as a percentage	Small numbers
			at 3 hours	placebo 29, amiodarone 16, flecainide 68	Placebo group discontinued monitoring after 8 hours
			at 8 hours	placebo 48, amiodarone 37, flecainide 91	
Donovan KD <i>et al</i> , 1995, Australia	98 patients with acute onset atrial fibrillation (≤ 72 h), placebo versus amiodarone iv or flecainide iv	RCT	at 12 hours Conversion to sinus rhythm	amiodarone 47, flecainide 91 amiodarone 89, flecainide 95 placebo 7/32, amiodarone 11/32, flecainide 20/34	Small numbers
			<2 hours	placebo 18/32, amiodarone 19/32, flecainide 23/34	Power not shown
Boriani G <i>et al</i> , 1998, Italy	417 patients with recent onset atrial fibrillation (≤ 7 days), placebo versus amiodarone iv, flecainide po, propafenone iv or propafenone po	Cohort	>2 and <8 hours Conversion to sinus rhythm	as a percentage	
			at 1 hour	placebo 9, amiodarone 6, flecainide 13	
			at 3 hours	placebo 18, amiodarone 25, flecainide 57	
			at 8 hours	placebo 37, amiodarone 57, flecainide 75	
Martinez-Marcos FJ <i>et al</i> , 2000, Spain	150 patients with acute onset atrial fibrillation (≤ 48 hrs). Amiodarone iv versus flecainide iv or propafenone iv	Randomised single blind trial	Conversion to sinus rhythm	as a percentage	
			at 1 hour	amiodarone 14, flecainide 29	
			at 8 hours at 12 hours	amiodarone 42, flecainide 82 amiodarone 64, flecainide 90	

aneurysm. Altogether 557 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 52 year old man attends the emergency department with central chest tightness and left arm heaviness. ECG shows anterior ST elevation of 3 mm in three consecutive leads. He has a normal mediastinum on chest radiograph, but as you administer the thrombolytic agent, you wonder just how sensitive this investigation is in ruling out an aortic dissection.

Three part question

In a [patient with chest pain] what is the [sensitivity of a normal chest radiograph] in ruling out [aortic dissection]?

Search strategy

Medline 1966-11/03 using the OVID interface. [exp Aneurysm, Dissecting OR dissecti\$.mp OR aneurysm.mp] AND [exp AORTA OR exp AORTA, THORACIC OR aort\$.mp.] AND [X-ray.mp OR exp X-Rays OR exp Radiography, Thoracic OR radiograph\$.mp] LIMIT to human AND English.

Search outcome

Altogether 557 papers were found. One recent literature review included the relevant papers with the exception of three additional papers (see table 2).

Comment(s)

All these studies are of poor quality. There is an enormous lack of quality prospective studies recruiting consecutive patients presenting to the emergency department with chest pain.

► CLINICAL BOTTOM LINE

The classic chest radiological findings of a wide mediastinum or abnormal aortic contour do not seem sufficiently sensitive to rule out aortic dissection in a patient with chest pain.

Hartnell GG, Wakeley CJ, Tottle A, et al. Limitations of chest radiography in discriminating between aortic dissection and myocardial infarction: implications for thrombolysis. *J Thorac Imaging* 1993;**8**:152–5.

Vu KH, Young N, Soo YS. Imaging of thoracic aortic dissection. *Australas Radiol* 1994;**38**:170–5.

Hennessey TG, Smith D, McCann HA, et al. Thoracic aortic dissection or aneurysm: clinical presentation, diagnostic imaging and initial management in a tertiary referral centre. *Ir J Med Sci* 1996;**165**:259–62.

Klompas M. Does this patient have an acute thoracic aortic dissection? *JAMA* 2002;**287**:2262–72.

Antibiotics in acute exacerbations of chronic obstructive pulmonary disease

**Report by Ross Murphy, Specialist Registrar
Checked by Martin McKechnie, Specialist Registrar,
Joel Dunning, RCS Fellow**

Table 2

Author, date and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Hartnell GG <i>et al</i> , 1993, UK	Chest radiographs from 18 patient with aortic dissection, and 25 patients with acute myocardial infarction Chest radiographs reviewed by consultant radiologists	Case control study	Sensitivity of chest radiographs interpretation	88.9%	Unclear how MI chest radiographs were obtained
			1st observer	72.2%	Only two radiologists interpreted the radiographs. There was a large interobserver variability. It would have been more informative if a larger number of radiologists had been used. Radiologists knew that around half the patients had a dissection and half an MI This study does not use A&E doctors Gold standard not applied to all patients— only 16 had confirmation of dissection at surgery or on postmortem examination. No information given regarding the diagnostic imaging for the other 26. Retrospective review open to bias Chest radiographs reported by a senior radiologist—not A&E doctors Unclear how patients were identified retrospectively
			Sensitivity observer 2		
Vu KH <i>et al</i> , 1994, Australia	42 patients with diagnosis of aortic dissection	Retrospective cohort	The following results are calculated using 19 patients with dissection (16 confirmed by surgery/necropsy, but also includes three patients who died without necropsy)	52.6%	Retrospective review using case notes.
			Sensitivity wide mediastinum	47%	
			Sensitivity dilated aortic arch	17%	
			Sensitivity displacement of calcified aortic plaques	5%	
Hennessy TG <i>et al</i> , 1996, Ireland	55 consecutive patients referred with suspected thoracic dissection to a cardiology department 35 of 55 had a dissecting thoracic aneurysm	Retrospective cohort	Sensitivity tracheal deviation	15%	Unclear who reported chest radiographs Only includes those referred to cardiology department. It is unclear which investigations each patient had undergone before referral Not clear whether gold standard applied to all patients Search terms not clearly stated. It would not be possible to repeat this search from the information given
			Sensitivity pleural effusion	21%	
			Sensitivity cardiomegally		
			Sensitivity wide mediastinum	65.7%	
			Normal chest radiograph	14 of 35 normal	
Klompas M, 2002, USA	Patients with clinically suspected aortic dissection or confirmed dissection	Literature review including prospective and retrospective cohorts in 21 studies	Abnormal aortic contour	Sensitivity 61% (CI 56 to 84)	Vast majority of papers are retrospective reviews of patients with known dissections, unblinded and heavily open to bias Not all studies looked at the same chest radiograph findings
			Pleural effusion	Sensitivity 16% (CI 12 to 21)	
			Displaced intimal calcification	Sensitivity 9% (CI 6 to 13)	
			Wide mediastinum Abnormal chest radiograph	Sensitivity 64% (CI 44 to 80) Sensitivity 90% (CI 87 to 92)	

A short cut review was carried out to establish whether antibiotics improve recovery in patients with acute exacerbations of COPD. Altogether 200 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 78 year old man with a history of COPD attends the emergency department with a recent increase in shortness of breath, cough, and wheeze. You diagnose him as suffering

from an exacerbation of COPD and treat him with oxygen, nebulised salbutamol, and corticosteroids. You wonder if a course of antibiotics would also be of benefit.

Three part question

In [a patient with an acute exacerbation of COPD] does [administration of a course of antibiotics] improve [outcome and hasten recovery]?

Search strategy

Medline 1966-11/03 using the Ovid interface. In addition the Cochrane Database of Systematic Reviews was searched and the National Institute of Clinical Excellence web site was searched for relevant guidelines. [(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 [exp acute disease OR

acute.mp OR exacerbation.mp] AND [exp antibiotics OR antibiotic\$.mp] AND [exp Meta-analysis OR meta-analysis.mp OR exp review literature OR Review.mp OR systematic review.mp OR guideline\$.mp OR exp clinical protocol OR protocol.mp]

Table 3

Author, date and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Saint S <i>et al</i> , 1995, USA	9 randomised trials (n=1101) including npatients and outpatients with exacerbations of COPD	Meta-analysis	Mortality benefit of antibiotics v placebo, (effect size transformed into units of standard deviation) Change in peak expiratory flow rate	0.22 (95% CI 0.10 to 0.34). Small but significant improvement 10.75 l/min (95% CI, 4.96 to 16.54l/min) (6 trials 836 patients) When two of the following three are present:	English language search only Variety of antibiotics combined to produce these figures
British Thoracic Society 1997	Initiated by the Standards of Care Committee of the British Society. A core group of individuals produced background papers that were collated into a single document. This was discussed over a two day period by a larger group which included respiratory physicians from both teaching and teaching and district general hospitals across the UK, geriatricians, general practitioners, nurses, and public health physicians	Systematic review and guideline	Situations in which antibiotics are proven to be of use in hospital and non-hospital settings Duration of treatment Antibiotic of choice	(1) increased breathlessness (2) increased sputum volume (3) development of purulent sputum Any patient with pH<7.35 should also receive antibiotics A maximum of 7 days should always be sufficient Oral treatment with common antibiotics such as amoxicillin or tetracycline should be considered first choice	Paper search strategy may not have been systematic, search methods not fully described
Mcroy DC <i>et al</i> , 2001	Systematic review conducted by a joint panel from the American College of Physicians (ACP)- American Society for Internal Medicine (ASIM) and the American College of Chest Physicians (ACCP)	Systematic review	Findings from 11 RCTs looking at antibiotics v placebo (They found two additional papers to the meta-analysis of Saint <i>et al</i>) Number of days of administration	Three papers found a statistical benefit, 3 papers found a non-significant benefit and the remainder showed no benefit. Benefits were larger, the more severe the exacerbation Days of administration ranged from 3 to 10 days in these studies	Study effects were not summarised by meta-analysis
NICE 2003	Full NICE guideline for the management of patients with COPD Note: currently only in its 2nd draft. 270 received antibiotics, 92 did not.	Systematic review	Grade A recommendations Grade B recommendations	Antibiotics should be used to treat exacerbations of COPD associated with a history of purulent sputum Antibiotics are more likely to be helpful in patients with more severe underlying disease Patients with exacerbations without purulent sputum do not need antibiotic therapy unless there is consolidation on a chest radiograph or clinical signs of pneumonia	

Search outcome

Altogether 200 papers were found of which four meta-analyses or systematic reviews provided the highest level of evidence (see table 3).

Comment(s)

A large number of papers have addressed this question in hospital and community settings. A well conducted meta-analysis by Saint *et al* found nine randomised controlled trials in this area and found a statistically significant mortality benefit in patients receiving antibiotics. In addition they showed a significant benefit in terms of peak expiratory flow rate. Several large groups have published guidelines. The American Colleges joint statement found an additional two papers to Saint *et al*, and concluded that antibiotics were of benefit and that the more severe the exacerbation the greater the benefit.

The British Thoracic Society Guidelines state that antibiotics should be used for anyone with two of: increased breathlessness, increased production of sputum, or purulent sputum.

NICE are currently in their second draft for producing new guidelines in this area. In addition to the 11 papers used above they have found three more studies of interest. They recommend that all patients with purulent sputum should have antibiotics and that there is greater benefit in patients with more severe underlying disease.

► CLINICAL BOTTOM LINE

Antibiotics improve outcome in acute exacerbations of COPD, especially when associated with purulent sputum, more severe exacerbations, or severe underlying disease.

Saint S, Bent S, Vittinghoff E, *et al*. Antibiotics in chronic obstructive pulmonary disease exacerbations. A meta-analysis. *JAMA* 1995;273:957–60.

British Thoracic Society Nebulizer Project Group. Nebulizer therapy. Guidelines. *Thorax* 1997;52:suppl 24.

McCroory DC, Brown C, Gelfand SE, *et al*. Management of acute exacerbations of COPD: a summary and appraisal of published evidence. *Chest* 2001;119:1190–209.

National Institute of Clinical Excellence. Chronic obstructive pulmonary disease: management of adults with chronic obstructive pulmonary disease in primary and secondary care, 2003. <http://www.nice.org.uk/article.asp?a=91784>

Intravenous magnesium in chronic obstructive pulmonary disease

Report by Rachel Jenner, *Specialist Registrar*
Checked by Richard Body, *Senior House Officer*

A short cut review was carried out to establish whether the addition of intravenous magnesium to standard treatments improved outcome in patients with exacerbations of COPD. Altogether 465 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 65 year old man presents to the emergency department with an exacerbation of COPD. You are aware that intravenous magnesium is used as a bronchodilator in acute severe asthma and wonder if it would benefit this patient.

Three part question

In [patients with an exacerbation of COPD] does [the addition of intravenous magnesium to conventional treatments] improve [PEFR or discharge rate or morbidity or mortality]?

Search strategy

Medline 1966-11/03 using the Ovid interface, including non-indexed citations and Medline in progress. [exp Magnesium or magnesium.mp] AND [exp Pulmonary Disease, Chronic Obstructive OR COPD.mp OR COAD.mp OR exp Lung Diseases] LIMIT to human AND English

Search outcome

Altogether 465 papers were found of which one was relevant (see table 4).

Comment(s)

There is only one small study addressing this question and it excludes patients with acute infection, which is one of the commonest causes of exacerbation of COPD. However, it does show a small significant improvement in PEFR with intravenous magnesium. The clinical significance of this change may be small but seems to show a non-significant trend towards a reduced rate of admission. A larger trial including patients with signs of acute infection would be helpful.

► CLINICAL BOTTOM LINE

Intravenous magnesium is worth considering in patients with an exacerbation of COPD.

Skorodin MS, Tenholder MF, Yetter B, *et al*. Magnesium sulfate in exacerbations of chronic obstructive pulmonary disease. *Arch Intern Med* 1995;155:496–501.

Table 4

Author, date and country	Patient group	Study type (level of evidence)	Outcome	Key results	Study weaknesses
Skorodin MS <i>et al</i> , 1995, USA	72 adults (70 male) presenting to ED with exacerbation COPD randomised to 1.2 g magnesium sulphate or placebo after receiving 2.5 mg nebulised salbutamol	Double blinded PRCT	Change in PEFR at 30 min and 45 min	25.1 l/min better for MgSO ₄ at 30 min, 7.4 l/min better for MgSO ₄ at 45 min (p=0.03)	Male bias
			Change in % PEFR at 30 min and 45 min	22.4% for MgSO ₄ at 30 min, 6.1% at 45 min (p=0.01)	Patients with high temperature or radiological signs of infection excluded
			Need for hospitalisation	28.1% for MgSO ₄ group v 41.9% for placebo (p=0.25)	Three patients received 3 g magnesium sulphate instead of 1.2 g

Table 5

Author, date and country	Patient group	Study type (level of evidence)	Outcomes	Key results	Study weaknesses
Van Vliet-Daskalopoulou E <i>et al</i> , 1987, Netherlands	137 patients with classic or definite RA involving at least one knee joint requiring local treatment. Single intra-articular injection of rimexolone. 34 given placebo, 32 given 10 mg, 33 given 20 mg, 31 given 40 mg. 7 patients did not fulfil protocol requirement	Placebo controlled double blind multicentre clinical trial	Assessment of pain, tenderness, morning stiffness, swelling, range of movement and walking ability at days 7, 28, 56, and 84 after injection	Statistically superior clinical improvement for most variables with rimexolone at 20 mg and 40 mg than placebo. With the 10 mg dose of rimexolone only reduction of tenderness was significantly superior. Duration of improvement longest with 40 mg rimexolone. One single intra-articular injection of this dose significantly reduces pain, tenderness and stiffness and improved range of movement and walking ability for 8–12 weeks	There was a significant drop out rate (66% of 10 mg group, 72% of 20 mg, and 71% of 40 mg groups remained for rimexolone groups at the end of the study. Only 44% of placebo treated patients were still under study with the rest not accounted for. 130 patients distributed over four groups with no sample size calculation No indication of effort made to standardise clinical variables. As this is a multicentre trial questionable reliability and validity

Intra-articular corticosteroid injections in acute rheumatoid monoarthritides

Report by Jane Sholsberg, *Medical Student*
Checked by Rupert Jackson, *Consultant*

A short cut review was carried out to establish whether intra-articular corticosteroid injections were effective at reducing pain in patients with acute rheumatoid monoarthritis. Altogether 215 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 42 year old woman known to suffer from rheumatoid arthritis presents to the emergency department with an acutely inflamed swollen knee. The patient is given an intra-articular corticosteroid injection. You know this is a standard treatment but wonder how effective it actually is.

Three part question

In [patients with acute rheumatoid monoarthritis] are [intra-articular corticosteroid injections] effective in [reducing pain and swelling and improving mobility]?

Search strategy

Medline 1966-11/03 using the Ovid interface, including Medline in progress and non-indexed citations. (exp arthritis,

rheumatoid/OR monoarthritis.mp. OR exp arthritis OR exp rheumatic diseases/OR monoarthropathy.mp.) AND (exp steroids/or steroid\$.mp. OR exp methylprednisolone/OR methylprednisolone.mp OR exp hydrocortisone/OR hydrocortisone.mp OR exp prednisolone/OR prednisolone.mp) AND (exp injections, intra-articular/) LIMIT to human AND English AND abstracts.

Search outcome

Altogether 215 papers found of which 214 were irrelevant or of insufficient quality. The remaining paper is shown in table 5.

Comment(s)

Acute rheumatoid monoarthritides are commonly treated with intra-articular corticosteroid injections. Although this paper indicates a favourable outcome using intra-articular rimexolone injections particularly at 40 mg, the small number used in each group may have introduced bias and the high drop out rate in the placebo group in the later stages of the study prevents efficacious comparisons to be made.

► CLINICAL BOTTOM LINE

The available evidence suggests that a single intra-articular injection of 40 mg rimexolone significantly reduces pain, tenderness and stiffness, and increases mobility in patients with acute rheumatoid arthritis.

van Vliet-Daskalopoulou E, Jentjens T, Scheffer RT. Intra-articular rimexolone in the rheumatoid knee: a placebo-controlled, double blind, multicentre trial of three doses. *Br J Rheumatol* 1987;26:450–3.