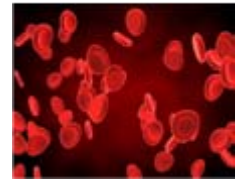


The GP Update Handbook



Spring 2010

(Pages 14-19)

www.gp-update.co.uk

Abbreviations used in the GP Update Handbook

We try to avoid using abbreviations except where they are universally recognised (MI, COPD). The only exceptions to this are the abbreviations of some of the journals we use:

Ann Int Med	Annals of Internal Medicine
Arch Int Med	Archives of Internal Medicine
BJGP	British Journal of General Practice
BMJ	British Medical Journal
DTB	Drugs and Therapeutics Bulletin
MeReC	National Prescribing Centre Bulletins (<i>not exactly an abbreviation!</i>)
NEJM	New England Journal of Medicine
NICE	National Institute for Health and Clinical Excellence
SIGN	Scottish Intercollegiate Guidelines Network

Statistical abbreviations are listed in the statistics chapter.

A note on Cochrane references

Cochrane reviews are referenced as: Cochrane 2005;CD002946. Go to the Cochrane website (www.cochrane.org) and type the 'article number' without the date (eg. CD002946) into the search engine and it will find the correct article for you. *NB if you go to www.cochrane.co.uk you must specify that you want to search Cochrane.org or you will generate no search results. It's obvious how to do this when you get there.*

We make every effort to ensure the information in these pages is accurate and correct at the date of publication, but it is of necessity of a brief and general nature, and this should not replace your own good clinical judgement, or be regarded as a substitute for taking professional advice in appropriate circumstances. In particular check drug doses, side effects and interactions with the British National Formulary. Save insofar as any such liability cannot be excluded at law, we do not accept any liability for loss of any type caused by reliance on the information in these pages.

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Welcome to the GP Update Handbook!

Keeping up to date as a GP or practice nurse isn't easy. Every week another few journals land on our doormat. And despite our best intentions, they often end up joining the ever increasing pile of unread paperwork in the corner of our study or consulting room.

We, like you, are just ordinary GPs, but we have dedicated time to read the journals. We draw together all the latest evidence and guidelines. We focus on what is relevant to us in the consulting room; what GPs and practice nurses need to know, how we can incorporate the new evidence into our practice, and answering the questions our patients may ask us.

So where do we get our information from? We read all the main journals (the BMJ, BJGP, Lancet, NEJM, Family Practice etc.) as well as material from bodies such as the Drug & Therapeutics Bulletin and the National Prescribing Centre. We also read any relevant guidelines, including from NICE and SIGN. All the time we focus on material that is relevant to primary care, asking the important question 'So what does all this mean in practice?'

Revalidation is looming on the horizon. Because many GPs are uncertain exactly what revalidation will involve, we have summarised the latest from the RCGP on page 6. Part of this involves earning CPD credits to show evidence of ongoing learning. So we've developed the **Revalidation Action Pack** to help you earn your credits. By picking a few of the activities in the Revalidation Action Pack over the next year you can start to earn CPD credits whilst, at the same time, ensuring that the new evidence in the Handbook gets embedded into your practice.

We have no involvement whatsoever with the pharmaceutical industry, because we think it would be unethical to do so, and we feel very uncomfortable that so much GP and practice nurse education is sponsored by the pharmaceutical industry. We want to be able to tell you the facts as they are, not as Big Pharma might like you to hear them!

Who are the GP Update Team?

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James Cave has been a partner at the Downland Practice in Berkshire for 20 years. Outside the practice he writes for the local paper, has been involved in the development of PCGs/Ts, Lord Darzi's Next Stage review and the charity CRUSE. He still belongs to a young principal group – now in its 20th year. In 2009 James was awarded an OBE for services to medicine.

We believe general practice is a great job! We hope GP Update will give you a new enthusiasm for the work you do, greater confidence in your knowledge base and the inspiration and practical support to make changes to your practice.

We welcome your feedback; do email us at: feedback@gp-update.co.uk

Lucy, Peter, Caroline and James.

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Syncope in adults

BMJ 2010;340:c880

Fainting is common, especially in women. But when should we worry about serious causes?

Causes of syncope

Syncope refers to sudden onset, brief loss of consciousness because of reduced cerebral perfusion, loss of tone, collapse and then rapid recovery.

- **Cardiac causes.** These are the more serious causes and the ones, as GPs, we worry we may be missing. Causes include arrhythmias, ischaemia, structural heart disease, steal syndromes etc. Long QT syndrome is discussed in the next section.
- **Neurally mediated syncope.** Common and benign. Described as neurally mediated because characterised by vasodilatation or vagal stimulation causing bradycardias or (brief, recoverable) asystole causing collapse. Examples are:
 - Vasovagal syncope (simple faint, reflex anoxic seizures in children)
 - Respiratory syncope (with cough or sneeze)
 - Urinary (micturition) syncope
 - Laughter syncope
 - Valsalva induced syncope (weight lifter's syncope, trumpet blower's syncope).
- **Orthostatic (postural hypotension)** which includes that caused by autonomic failure. May be either primary or secondary (eg. to diabetes).
- **The older you are the less likely the cause is neurally mediated** (and benign). Neurally mediated syncope accounts for over 90% of syncope in people under the age of 40, but only about 50% of syncope in the over 60s.

How do we investigate syncope?

There are two important aspects:

Firstly is this syncope (not another condition such as epilepsy)?

Secondly, is this a cardiac syncope or not?

This is not to say that orthostatic syncope is entirely benign, it can result in both morbidity and mortality because of the underlying condition, but the significant risk of death from cardiac syncope means that this must be identified and treated.

- **Take a detailed history, examine (with lying & standing BPs) and an ECG. Remember to ask about sudden unexplained death in family members.** For more on the important features in the history and what diseases they suggest, see the table in the appendix. The BMJ review suggests that history, examination (including lying and standing blood pressures) and ECG should identify a cause in up to 66% of patients!
- If a cause is established with these simple tests (possible in 66% of cases), then treat the cause. **If not, the patient needs referral for more detailed investigations**, guided by the history. This might include tilt table testing, carotid sinus massage test, echo, ambulatory ECG and, if the cause is still unclear, coronary angiograms, exercise ECGs and brain scanning may be suggested.
- There are risk scoring tools that aim to detect those at greatest risk of serious pathology but they need more validation before they are used in clinical practice.

How to do lying and standing blood pressures

- The patient must be lying (not sitting) for 10 minutes.
- Record baseline pulse and blood pressure (BP).
- **Check BP 3 minutes after standing up.** Ask if symptoms reproduced on standing.
- **Orthostatic hypotension is clinically important if:**
 - drop in SBP of 20mmHg or a drop in DBP of 10mmHg at 3minutes
 - original symptoms are reproduced.
- **Also note that heart rate should rise on standing:** an excessive rise (≥ 30 bpm) or a rise to ≥ 120 bpm suggests postural orthostatic tachycardia syndrome. Failure to make pulse rise suggest autonomic failure or rate limiting drugs (eg. betablockers).

What should prompt urgent referral/admission?

- Consider urgent referral or admission:
 - In those with syncope associated with:
 - No warning (Stokes-Adams attack)
 - Palpitations
 - Chest pain/breathlessness
 - Being supine
 - Those with a cardiac history
 - Signs of heart failure
 - Abnormal ECG
 - Family history of sudden death.

Treatment

- Treatment depends on underlying cause.
- For those with neurally mediated and orthostatic hypotension advice on avoidance is important. Beta-blockers are no longer used for neurally mediated syncope.

Driving and syncope

Simple faints to which the '3Ps' (postural, prodrome provocation) apply do not need to notify DVLA and can continue to drive (ordinary & vocational drivers) (that is if they are unlikely to occur when sitting, have a prodrome and are provoked). For everyone else, see the DVLA guidance. Cough syncope is taken particularly seriously.

Take home messages: Syncope

- **Common. Important to exclude serious causes, especially cardiac causes.**
- **Always ask about family history of sudden death.**
- **History critical. Detailed history, examination, postural BPs and ECG should give you a diagnosis in many.**

Useful websites**For professionals:**

The DVLA guidance is available at: <http://www.dft.gov.uk/dvla/medical/ataglance.aspx>

Long QT syndrome

BMJ 2010;340:b4815

This was the subject of the BMJs 'easily missed' series. Here I'll look from a GP perspective.

As the review points out, it is easily missed because the main presenting symptom (syncope) is common, or because it is mis-diagnosed as epilepsy (the hypoperfusion of syncope may result in epileptic type movements). The review illustrates this with a recent study showing that almost 40% of people with long QT syndrome had a delayed diagnosis because the cause was labelled as fits.

Why does it matter?

- It is rare (prevalence in the order of 1 in 2 000-3 000 (so just less than 1/GP!) but long QT syndrome causes avoidable sudden cardiac death, often in young people.

Causes

- The cause is abnormal repolarisation (lengthening the Q-T interval) due to abnormalities in sodium and potassium ion channels.
- **Long QT may be congenital or acquired.**
- Congenital long QT syndrome is inherited in an autosomal dominant pattern (so if one of your parents have it you have a 1 in 2 chance (50%) of inheriting the gene). However variable expression of the gene means some may never experience symptoms whilst in others it causes death in utero.
- Acquired long QT syndrome may be due to drugs, metabolic disturbance, brain injury, cardiac disease or hypothermia.
- All the causes of acquired long QT syndrome listed above may unmask congenital long QT in a previously asymptomatic individual.
- **Because it may be inherited, if you identify one affected person, other (often asymptomatic) affected family members should be sought out.**
- **There are 3 subtypes of congenital long QT syndrome:**
 - **LQT1:** triggered by exercise, esp. swimming. Symptoms frequent but low mortality.
 - **LQT2:** often triggered by emotional stress or because of auditory stimuli, especially when waking from sleep (eg. alarm clock, the phone ringing).
 - **LQT3:** tends to occur at rest. Rare but higher mortality.

Diagnosis can be difficult, but here are some pointers

- **Always ask about family history** – sudden unexplained death including in children, recurrent syncope or refractory epilepsy (it may not be epilepsy after all).
- **An accurate and detailed history from the patients and a witness is needed.** Remember normal vasovagal syncope is usually associated with a warm environment, prolonged standing, insufficient food intake or pain. **Are there atypical features?**
- **Exertional syncope: this should always make you suspicious of a sinister cause.**
- **Sudden syncope associated with unusual features** eg. dizziness, sweating, visual disturbance before loss of consciousness. In normal individuals symptoms of a vasovagal attack may be associated with tachycardia, but it is usually a compensatory mechanism, coming on *after* the other symptoms, whereas in long QT syndrome, palpitations may be the first feature (hence the need for a very careful history!)
- **Rapid recovery.** After cardiac syncope (but not epilepsy) there should be rapid recovery without drowsiness or confusion.
- **Always ask about drugs** (and see list below for some common culprits).
- **Clinical examination will be normal as the heart is structurally normal. If it is not, consider cardiomyopathy as a cause of the syncope.**

Investigations

- **The first line investigation is obviously the ECG, but can be difficult to interpret. A 24 hour tape or exercise test may be needed to give more accurate results.**
- **Do not rely on automated calculations of QT interval.** The BMJ review reminds us that QT interval is difficult to assess and that automated calculations are often wrong, giving rise to both false positive and false negative. **They recommend manual calculation with correction for heart rate using Bazett's formula.**

So how do you measure QT interval? You need to measure from the onset of the Q wave to the intersection between the baseline and a tangent taken from the steepest part of downsweep of the T wave, not where the T wave reaches the baseline. Then correct for heart rate with Bazett's formula: corrected QT = $\frac{QT}{\sqrt{RR(\text{in seconds})}}$

- **Abnormal is a corrected QT interval of >450ms in males and >460ms in females.**

Now I don't know about you, but I don't feel that confident about calculating the QT interval.

- **So I would recommend that if you have any concerns at all, based on the history, you should ask a cardiologist to review the ECG (+/- the patient!).**

Treatment

- **Beta-blockers are the main treatment. Treatment is life long.** Long QT 1 responds best to beta-blockers, long QT3 shows least benefit, although they should still be used.
- If betablockers are not an option (eg. in asthma) or QT interval is particularly long, or if patients have survived a cardiac arrest, an **implantable defibrillator may be used.**
- **Ensure patients avoid all drugs that prolong QT interval.** There is an (extensive) list of these on the website listed below, but here are the commonest ones:

Antibiotics	Antihistamines	Antiarrhythmics	Antidepressants
Erythromycin	Terfenadine	Amiodarone	Fluoxetine
Clarithromycin		Sotalol	Sertraline
Ciprofloxacin			Amitriptyline

- **Once diagnosed, a specific mutation can be identified in about 70%, which then means family members can be screened for the disorder more easily.**

Take home messages: Long QT syndrome

- **A cause of preventable death in young people.**
- **Rare, and difficult to diagnose. Take a careful history from the patient and witnesses, looking for unusual features that separate this event from normal vasovagal faints and other conditions such as epilepsy.**
- **ECG is the investigation of choice but 24hr tapes/exercise ECG may be needed.**
- **Expert help may be needed to correctly calculate the corrected QT interval to avoid false positives and negatives.**
- **Treatment is with beta-blockers (for life) in the first instance.**
- **Ensure patients are aware of the long list of drugs that should not be used.**
- **Consider looking for other affected family members if long QT is diagnosed.**

Useful websites

For patients and professionals:

A full list of drugs that can increase the QT interval and must be avoided by patients with long QT syndrome is available from the Arizona Centre for Education and Research on Therapeutics: www.azcert.org/medical-pros/drug-lists/drug-lists.cfm

Aspirin & cardiovascular disease

The role of aspirin in CVD prophylaxis in diabetics is discussed in the chapter on diabetes.

Aspirin for cardiovascular disease prevention

Lancet 2009;373:1849

Comment Lancet 2009;373:1821

No one doubts the role of aspirin in secondary prevention; the initial Antithrombotic Trialists' Collaboration trials showed this (BMJ 1994;308:81 and BMJ 2002;324:71).

The question is whether aspirin works in primary prevention of CV events. Now the Antithrombotic Trialists' Collaboration (ATTC) have produced a meta-analysis of the use of aspirin in both primary prevention (95 000 people) and secondary prevention (17 000 people). All compared aspirin use with placebo (Lancet 2009;373:1849). The main outcomes were CV events (MI, CVA, vascular death) plus the rate of haemorrhagic stroke and significant GI and extra-cranial bleeds.

- **For all groups, benefits (and harms) seemed similar for men and women.**
- **Benefit did not change significantly with age (although of course older people have a higher baseline risk of CV events).**

For secondary prevention:

- Aspirin prevents one CV event a year for every 66 people treated. Vascular deaths are reduced by 1 for every 344 people treated.
- There was insufficient data to report on GI/extra-cranial bleeds or haemorrhagic CVAs.

For primary prevention:

- **Aspirin does not reduce CV mortality when used as primary prevention.**
- **Aspirin does reduce CV events, but the absolute risk reduction is very small. You need to treat 1666 people with aspirin for 1 year to prevent 1 CV event (NNT 1666).**
- Significant GI/extra-cranial bleeding would occur in one person for every 3 333 people treated over 12 months.
- High risk individuals (eg. those with hypertension) do not get significantly more benefit than low risk individuals.

What does this mean in practice?

For men and women of all ages:

- **Aspirin should be used for secondary prevention of CVD.**
- **In primary prevention absolute benefits of aspirin are small, even in those at high risk of CV events, and must be balanced against risks.**
- **The authors do not recommend widespread use of aspirin as primary prevention, even in high risk groups.**
- A further larger RCT (almost 30 000 people) looked at those with low ankle brachial pressure index (an independent marker for cardiovascular disease) but with no CV disease. Over 8 years aspirin did not reduce CV events (JAMA 2010;303:841-47).
- Our biggest problem is that many patients (and doctors!) think aspirin 'is a good thing'!

And the Drugs and Therapeutics Bulletin agree that:

- **Aspirin should not be started for primary prevention of CVD (including those with diabetes or hypertension).**
- **In those already taking it there should be a discussion with each patient explaining the current evidence showing limited benefit.** (DTB 2009;47:122-4)

How much aspirin for CVD protection?

JAMA 2007;297:2018-24

This large systematic review looked at the evidence for the differing doses and found that there was no evidence that using more than 75mg/day offered any greater protection BUT did increase GI haemorrhage risks.

- **In the UK, 75mg of aspirin od is the recommended dose for CV protection.**

What are the risks of combination therapy? Lancet 2009;374:1967-74

Some have suggested that if single agents reduce CV events, why not try using several agents together. Would this reduce CV events still further? Would there be harms?

This retrospective analysis of records in Denmark does exactly this. It identifies those on single and combination therapy and calculates the benefits and harms. By following people after an MI they were able to see what agents were prescribed and look at the risk of admissions for bleeding and death. Analysis was done on average 1.5 years after the MI.

Importantly such a method will include a form of bias: there will be clinical reasons why some were offered monotherapy as opposed to dual or triple therapy, that relate in part to clinicians perception of bleeding risk. That will make these figures more conservative than if you did this trial again but as an RCT rather than a retrospective review (although you would struggle to get this past an ethics committee!).

Numbers need to harm (NNH) are quoted. NNHs are calculated in comparison with aspirin therapy alone, over a 12m period. Remember that the lower the NNH the more harm you do!

Aspirin & clopidogrel	NNH = 89	<i>An NNH of 50 for clopidogrel means that for every 50 patients treated with clopidogrel instead of aspirin, 1 will have a fatal or non-fatal major haemorrhagic event in the year who would not have had it if they had been on aspirin instead.</i>
Warfarin	NNH = 60	
Clopidogrel	NNH = 50	
Aspirin & warfarin	NNH = 40	
Clopidogrel & warfarin	NNH = 10	
Aspirin & clopidogrel & warfarin	NNH = 10	

How do you explain these results?

- Aspirin is associated with the lowest risk of bleeding.
- Warfarin appears to perform relatively well in this analysis probably because of selection bias; this group included many patients who were on warfarin before their MI so they had a proven track record of being on warfarin and not having problems with it.
- Interestingly aspirin and clopidogrel in combination is associated with a lower risk of harm than clopidogrel alone. This data is in line with other studies showing similar rates of bleeding from combination therapy, and the fact it appears to be 'safer' than aspirin may be related to bias, as I have discussed.

So what does this mean in practice?

Despite the problems with this study it still gives us some useful information.

- **Aspirin alone is the safest drug in terms of risks of major haemorrhage & death.**
- **Aspirin & clopidogrel, if needed in combination, appear to be reasonably safe.**
- **The authors suggest that triple therapy or a clopidogrel/warfarin combination (both NNH=10) should not be used unless there is a very strong indication.**

Take home messages: Aspirin and cardiovascular disease

- **Aspirin should be used for secondary prevention of CVD (NNT 66).**
- **Aspirin is not recommended for primary prevention, even in those at highest risk, because the absolute benefits are very small (NNT 1 666).**
- **The aspirin dose for CVD protection is 75mg od.**
- **If needed, aspirin and clopidogrel appear to be a reasonable combination, but triple therapy with clopidogrel, warfarin and aspirin, or double therapy with warfarin and clopidogrel in combination, should not be used.**

CPD Ideas

There is an activity in the Revalidation Action Pack on the use of aspirin in primary and secondary prevention which is suitable for all practitioners.