bestpractice

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PARKINSON'S DISEASE

HEADACHE

AUGMENTIN-FREE OFFICE

bpac nz
better medicine

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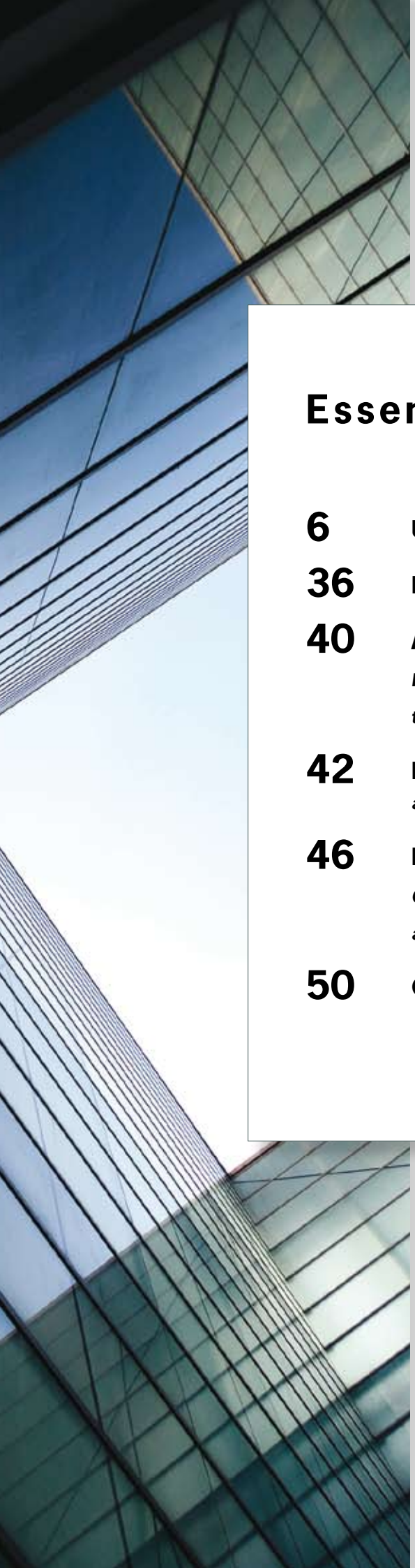

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UPFRONT

THE AUGMENTIN-FREE OFFICE

Bruce Arroll MBChB, PhD, FRNZCGP
Professor of General Practice and Primary Health Care
University of Auckland

What is the augmentin-free office?

A few years ago my clinic colleagues and I got fed up with our students wanting to give every patient amoxicillin clavulanate, available in New Zealand as augmentin; no matter what sort of infection they had, bacterial or viral!

The same thing happened in hospital. Although, according to my hospital teaching colleagues, this has now evolved from amoxicillin clavulanate to using third generation cephalosporins, at great cost and usually no particular advantage.

Amoxicillin clavulanate and third generation cephalosporins are important medications. If they continue to be overused, bacteria will become resistant to them. We want to preserve these antibiotics for occasions they are really needed. In our clinic, we were aware that there is usually a good alternative to amoxicillin clavulanate and came up with the concept of the augmentin-free office.

In our clinic you now 'need' to ask a colleague if it is okay to give a prescription for amoxicillin clavulanate before prescribing it. We even have a former trainee who calls me to get 'permission' to use amoxicillin clavulanate. Clearly our policy is not an absolute prohibition and we are not entirely augmentin-free, but it does control the amount we use.

Join the augmentin-free office movement today

We invite all primary care prescribers to join the movement. You don't have to call me. Preferably find a colleague to act as your 'permitter' and call him or her to check out the need for amoxicillin clavulanate. This is one way to preserve this useful medication for our grandchildren.

My history with amoxicillin clavulanate

This goes back to 1996 when my brother-in-law went to his doctor with a cold and was given amoxicillin clavulanate. Two days later he was no better but had developed diarrhoea. Diarrhoea is one of the common complications of this antibiotic, in that up to 25% of patients will get it. I resolved then to reduce the amount of antibiotics used in New Zealand. Fortunately this seems to be happening. The profession is aware of the growth of resistance to antibiotics and the current overuse.

www.bpac.org.nz keyword: "**Augmentin**"

The antibiotic state of the nation

This has not been good in the past, but is getting better. In 1996 there were about 1.2 million prescriptions of amoxicillin clavulanate and 0.6 million prescriptions of amoxicillin. Thus between these two medications there were about 1.8 million prescriptions for antibiotics. This seems an extraordinary figure given that there are only 4 million people in the country.

In 2003 this had fallen to about 1.2 million for the two medications combined (0.6 million amoxicillin clavulanate, and 0.6 million amoxicillin). One could only hope it would fall further. However, the Pharmac Annual Report 2005–6 showed that there were 0.74 million prescriptions for amoxicillin clavulanate, and 0.72 for amoxicillin. In that report it was the 4th most commonly prescribed medication after paracetamol, simvastatin and omeprazole. This would suggest that there has been a drop in the use of amoxicillin clavulanate and small increase in the use of amoxicillin.

A study conducted in a small New Zealand town found that 42% of the population received an antibiotic in the year 2002.[1] The National Medical Care study (2001) conducted in New Zealand general practice supported these figures. It reported that 53.7% of patients with respiratory infections received an antibiotic.

In 2006, I asked Professor Chris van Weel from the Netherlands what was happening in his country and he said the population antibiotic prescribing rate was about 3%. He thought that even that was too high.

Interestingly the Netherlands has a very low level of bacterial resistance to antibiotics.

Ad watch is an Australian website that challenges the advertising around amoxicillin clavulanate.
http://snipurl.com/1o3nc

Experience to date with the augmentin-free office

The augmentin-free office idea is being kept alive by frequent mentioning that this is an augmentin-free office. Being asked if it is appropriate to use amoxicillin clavulanate or asking someone else if it is appropriate, also reinforces the message.

My clinic colleagues feel pleased to be working in an augmentin-free clinic. They feel they are making a contribution to mankind. We have been 'overwhelmed' at the acceptance by parents that antibiotics are no longer routinely given. One patient did get very upset that we were 'augmentin-free.' She clearly had been very medicalised by overuse of augmentin.

When I talk to groups of doctors there are usually a few horrified faces in the audience. This suggests to me they are high users of amoxicillin clavulanate. There is usually someone who gives a challenge, such as the child with impetigo who cannot take oral flucloxacillin. My response is that the augmentin-free office concept is not an absolute and that it is quite reasonable to give amoxicillin clavulanate in such a situation. I do suggest that discussion occurs with parents so that they know that diarrhoea is a potential problem with amoxicillin clavulanate versus difficulty with palatability of oral flucloxacillin.

Amoxicillin clavulanate in middle ear infections after amoxicillin has been tried and failed.

This is a condition where some authorities feel amoxicillin clavulanate has a place. However, I could find no trials of amoxicillin clavulanate versus amoxicillin in patients who had not improved from an initial treatment with amoxicillin. In my own experience I have never seen a case where amoxicillin has not worked i.e. a child is still in pain or febrile after about 4–5 days. Most ears are still red and bulging at that stage, but that is part of the disease.

The evidence suggests that amoxicillin clavulanate is no better than other antibiotics and in some cases inferior. A head-to-head study of amoxicillin and amoxicillin clavulanate found no clinical benefit in terms of otitis media.[6] Another study found no difference, but the elimination of the initially occurring pathogens was equal in the two study groups with the exception of *B. catarrhalis* which was eliminated to a significantly higher extent with amoxicillin clavulanate.[7] Another study found that co-trimoxazole was significantly more effective than amoxicillin clavulanate and had fewer side effects.[8]

A recent meta-analysis of antibiotic versus placebo in acute otitis media reported that antibiotics were most effective in children <2 years with bilateral otitis media (NNT = 4).[9] For unilateral otitis media in this age group, NNT = 20. The measure was improvement in fever and pain at about 3–7 days, so if parents are willing to control the pain and fever with paracetamol and monitor the child for deterioration, very few children should need antibiotics.

Table 1: Indications for amoxicillin clavulanate use in common conditions

Condition	Amoxicillin clavulanate indicated	Comment
Acute bronchitis	No, usually no indication for any antibiotics as this is a viral infection	Check the diagnosis: i.e. has the patient got asthma, pneumonia or COPD with an acute exacerbation[2]
Acute cystitis in non-pregnant women	No	Trimethoprim 300 mg daily for 3 days. Norfloxacin or nitrofurantoin are alternatives
Acute cystitis in children	Yes	Alternatives are trimethoprim, cefaclor, nitrofurantoin
Bites and clenched fist injury with no established infection but a high risk of infection	Yes	Penicillin and metronidazole together are an alternative
Community acquired pneumonia	No	Amoxicillin just as good. Systematic review by G Mills et al[3]
Epididymo-orchitis	No	Young men: treat as for urethitis with azithromycin Older men: Ciprofloxacin 500 mg bd for 10 to 14 days
Impetigo	Yes, in children if they will not take oral flucloxacillin and the parents are not too concerned about diarrhoea	Alternatives would be oral cefaclor or oral erythromycin but both of these medications also have adverse effects. Consider offering parents the choice
Middle ear infection	No need for antibiotics initially unless the child is under 6 months or looking very sick	Delayed prescriptions have shown a 75% reduction in antibiotic usage.[4] (see previous page)
Acute sinus pain	No	Antibiotics only indicated in severe cases and then amoxicillin is recommended. A recent trial of amoxicillin clavulanate versus placebo in rhinoscopically diagnosed bacterial sinusitis found no benefit[5]

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HEADACHE
IN PRIMARY CARE*

Key Advisers: Dr Neil Whittaker - GP, Nelson
Dr Alistair Dunn - GP, Whangarei

Expert Reviewer: Dr Alan Wright - Neurologist, Dunedin

Every headache presentation is unique and challenging, requiring a flexible and individualised approach to headache management.

- Most headaches are benign **primary** headaches
- A few headaches are **secondary** to underlying pathology, which may be life threatening

Primary headaches can be difficult to diagnose and manage. People, who experience severe or recurrent primary headache, can be subject to significant social, financial and disability burden.

We cannot cover all the issues associated with headache presentation in primary care; instead, our focus is on assisting clinicians to:

- Recognise presentations of secondary headaches
- Effectively diagnose primary headaches
- Manage primary headaches, in particular tension-type headache, migraine and cluster headache
- Avoid, recognise and manage medication overuse headache

DIAGNOSIS OF HEADACHE IN PRIMARY CARE

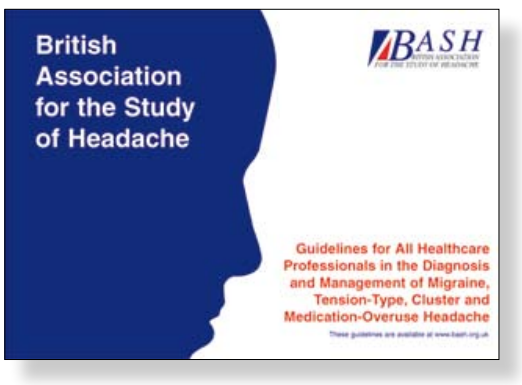
The keys to headache diagnosis in primary care are:

- Ensuring occasional presentations of secondary headache do not escape notice
- Differentiating between the causes of primary headache
- Addressing patient concerns about serious pathology

RECOGNISE SERIOUS SECONDARY HEADACHES BY BEING ALERT FOR RED FLAGS AND PERFORMING FUNDOSCOPY

Although primary care clinicians worry about missing serious secondary headaches, most people presenting with secondary headache will have alerting clinical features. These clinical features, red flags, are not highly specific but do alert clinicians to the need for particular care in the history, examination and investigation.

An exception to this may be slow growing intracranial tumours. For this reason fundoscopy, even though positive findings are rare, is essential for every initial headache presentation and periodically thereafter. Slow growing frontal lobe tumours are particularly liable to be silent. They may present with non-specific headache and subtle personality changes, resulting in treatment for depression. In these situations, non-response to treatment may prompt further investigation.



Red Flags in headache presentation

Red Flags in headache presentation include:

Age

- Over 50 years at onset of new headache
- Under 10 years at onset

Characteristics

- First, worst or different from usual headache
- Progressive headache (over weeks)
- Persistent headache precipitated by Valsalva manoeuvre (cough, sneeze, bending or exertion)
- Thunderclap headache (explosive onset)

Additional features

- Atypical or prolonged aura (>1 hour)
- Aura occurring for the first time in woman on combined oral contraceptive
- New onset headache in a patient with a history of cancer or HIV
- Concurrent systemic illness
- Neurological signs
- Seizures
- Symptoms/signs of Giant Cell Arteritis (e.g. jaw claudication)

*Much of this article is adapted from:British Association for the study of headache, Guidelines for all healthcare professionals in the diagnosis and management of migraine, tension-type, cluster and medication-overuse headache. January 2007. The guideline can be downloaded from: **http://snipurl.com/1nzel**

Causes of secondary headache

The presence of red flags prompts consideration of a wide range of diagnoses. Some of these are listed below.

- **Vascular**
  - Subdural hematoma
  - Epidural hematoma
  - Subarachnoid haemorrhage
  - Venous sinus thrombosis
- **Tumour**
- **Toxins** (e.g. carbon monoxide)
- **Infectious causes**
  - Meningitis
  - Encephalitis
  - Abscess
- **Giant cell arteritis**
- **Hydrocephalus**
  - Obstructive
  - Acute
- **Metabolic disorders**

MINIMAL EXAMINATION FOR HEADACHE PRESENTATION

For all initial presentations of headache, examination includes:

- Fundoscopy
- Visual acuity
- Blood pressure measurement
- Examination of the head and neck for muscle tenderness, stiffness, range of movement and crepitation.

The presence of red flags or other features suggesting secondary headache indicate the need for more detailed examination. The question of whether a neurological examination should be performed, and in how much detail, is more problematic when there are no suspicious features and the history is characteristic of a primary headache.

Even when there are no red flags, a brief neurological examination, although unlikely to be positive, is a strong source of reassurance to patients and will save time in future consultations with still-worried patients. A suggested routine for a short neurological examination in these circumstances is available on a brief video on our web site, ***www.bpac.org.nz*** ***keyword:*** *'Neuroexam'*

DIAGNOSIS OF PRIMARY HEADACHE

Primary headache is usually caused by tension-type headache, migraine, with or without aura, or cluster headache. Mixed headache types do occur, for example many people experience both migraine and tension-type headaches. Differentiation between the primary headaches is important because there are effective interventions available for each of them.

Headache diaries are useful diagnostic tools, which help the diagnosis of headaches and identification of any predisposing or precipitating factors.

Tension-type headache is the commonest form of primary headache

Most people will have at least one episode of tension-type headache during their lifetime. It is the commonest form of primary headache. The headache is usually described as tightness or pressure, like a tight band, around the head and often spreads to, or appears to arise from, the neck.

Tension-type headache is usually episodic, of low frequency and short duration but chronic tension-type headache can occur on more days than it is absent. Photophobia or exacerbation by movement can occur but these are usually less prominent features than in migraine.

Tension-type headaches are associated with stress and functional or musculoskeletal problems of the neck and often these occur together. Muscles of the head or neck are often tight and tender.

It is often useful to explain to patients that the pain is related to tension in the muscles of the head and neck and is often made worse by stress. This helps exploration of stressors without the patient feeling the clinician thinks 'it is all in my mind'.

Features of Migraine

Adults with migraine usually have a family history of migraine and experience recurrent episodes of moderate or severe headaches (which may be unilateral and/or pulsating) lasting for several hours or up to 3 days. These are typically associated with gastrointestinal symptoms, limitation of activity and avoidance of light and noise. There is often a preceding aura. People with migraine are free from symptoms between attacks.

When considering a differential diagnosis between migraine and tension headache, ***the following features are common in migraine but not usually seen in tension headache.***

- Aura
- Unilateral headache
- Hypersensitivity, such as to light and noise
- Gastrointestinal symptoms, such as nausea or vomiting

The diagnostic criteria for migraine are reproduced in Table 1. These may be useful in the diagnosis of headache when there is some doubt about the diagnosis, particularly when there is no aura. When migraine is accompanied by aura the diagnosis is easier and only two episodes are required to make the diagnosis.

Table 1: Diagnostic criteria for migraine without aura

A	At least 5 attacks fulfilling criteria B–D
B	Headache attacks lasting 4–72 hours* (untreated or unsuccessfully treated)
C	Headache has at least two of the following characteristics: 1. Unilateral location* 2. Pulsating quality (i.e. varying with the heartbeat) 3. Moderate or severe pain intensity 4. Aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)
D	During headache at least one of the following: 1. Nausea and/or vomiting* 2. Photophobia and phonophobia
E	Not attributed to another disorder (history and examination do not suggest a secondary headache disorder or, if they do, it is ruled out by appropriate investigations or headache attacks do not occur for the first time in close temporal relation to the other disorder).

*__In children__, attacks may be shorter-lasting, headache is more commonly bilateral, and gastrointestinal disturbance is more prominent.

One third of people with migraine have preceding aura

Approximately one third of people who get migraine, experience preceding aura. Usually auras last for between 5 to 60 minutes before the onset of migraine headache and settle as headache commences. The most frequently reported auras are visual disturbance, such as flickering or jagged lines or blind spots. Visual blurring or spots before the eyes are non-specific symptoms and do not represent aura. Other transient focal neurological symptoms, such as unilateral paraesthesia of a hand, arm or the face, and dysphasia, can also occur as aura in migraine.

Visual or other transient focal neurological signs presenting for the first time in older people always raise the possibility of Transient Ischaemic Attacks (TIAs). Prolonged aura in all age groups, especially continuing after resolution of headache and aura which involve muscular weakness, are indications for specialist investigation to exclude other causes.

Headache in migraine is not always unilateral

Although migraine headache is often unilateral it is not always so and the diagnosis of migraine should not be abandoned when headache is bilateral. The headache of tension-type headache is usually bilateral, but may be unilateral.

Migraine is usually accompanied by hypersensitivity

Hypersensitivity to stimuli, which are not normally noxious, is a common feature of migraine. Photophobia and phonophobia are the most frequently reported but hypersensitivity to touch (allodynia), smell (osmophobia), movement and pulsation of the arteries are also often experienced.

Hypersensitivity in migraine appears to be related to the central sensitisation and resulting peripheral sensitisation that occur in migraine.

Gastrointestinal upsets often prominent in migraine

Nausea and vomiting in migraine may be related to vestibular hypersensitivity and can be a prominent disabling feature of migraine episodes. Although anorexia and mild nausea may occur in tension-type headache, it is not usually a major feature.

Visual or other transient focal neurological signs presenting for the first time in older people always raise the possibility of Transient Ischaemic Attacks (TIAs).

Features of Cluster Headache

Cluster headache, unlike migraine, affects mostly young men (male:female = 6:1). Typically, the headaches occur in bouts for 6 to 12 weeks, once every year or two. The pain is severe, unilateral and disabling. During bouts, headache usually occurs daily, at a similar time each day.

Associated autonomic features include ipsilateral conjunctival injection, lacrimation, rhinorrhea, nasal congestion and ptosis. These do not always occur but the presence of one or two of these together with a typical cluster headache pattern clinch the diagnosis.

MANAGEMENT OF TENSION-TYPE HEADACHE

Management of tension-type headache includes general exercise, stress reduction, treatment of any underlying musculoskeletal problems and analgesia. Episodic use of aspirin or ibuprofen is usually sufficient. Paracetamol appears less effective. Complementary therapies such as yoga, meditation and acupuncture may help some people.

Although treatment sounds easy, in practice, implementation may be complicated. Patients may be expecting high-tech investigations to rule out serious pathology, physiotherapy and counselling may be unaffordable and often the stressors associated with the headaches are not amenable to change. This can result in over-reliance on medication.

Chronic use of medication for pain relief carries high risk of medication overuse headache. Analgesia use, should therefore, preferably be limited to no more than two days per week. Opiates, such as codeine, carry particularly high risk of medication overuse headache.

Chronic use of medication for pain relief carries high risk of medication overuse headache. Analgesia use, should therefore, preferably be limited to no more than two days per week.

A three-week course of an NSAID, such as naproxen, may break the cycle of continuing pain and cover the early management of predisposing and precipitating factors, such as musculoskeletal problems and stress.

If this fails, the prophylactic medication of choice is amitriptyline; starting very low (5–10 mg at night) and increasing slowly every three weeks until symptoms are controlled, up to 75–150 mg at night. As in other chronic pain syndromes, the effectiveness of amitriptyline does not depend on its antidepressant activity. If amitriptyline is not well tolerated, nortriptyline has fewer side effects and may be an effective alternative.

A randomised controlled trial of botulinum toxin for chronic tension-type headache showed it to be ineffective.

MIGRAINE MANAGEMENT REQUIRES A SYSTEMATIC APPROACH

Migraine management can be complicated and requires a systematic approach to:

1. Management of predisposing factors
2. Trigger identification and avoidance
3. Acute pain relief
4. Prophylaxis

MANAGING PREDISPOSING FACTORS IN MIGRAINE

Several factors are known to predispose people to migraine. These include stress, depression, anxiety, head or neck trauma and hormonal changes such as around menstruation or menopause. Management of these factors can have a significant impact on migraine frequency and severity. Keeping a diary will help to identify any predisposing and triggering factors.

IDENTIFICATION AND AVOIDANCE OF TRIGGER FACTORS IN MIGRAINE

Unfortunately, most migraine episodes have no obvious trigger, but if triggers can be identified, avoidance is often very effective. Frequently reported triggers include:

- Relaxation after stress
- Change in habit, such as a missed meal, late night or travel
- Bright lights and loud noise
- Dietary triggers, such as certain alcoholic drinks, some cheeses
- Unaccustomed strenuous exercise

A systematic, three-tiered approach to the management of acute migraine headache is useful. Additional measures for emergency treatment at home and treatment of a relapse may be needed.

Using a systematic approach ensures each treatment modality is given a reasonable trial of effectiveness and highlights which treatments are effective for particular patients. BASH suggests that failure of treatment on one tier on three occasions should be the criterion for moving onto the next tier.

These tiers should all preferably be combined with rest and sleep; a stat dose of temazepam may be useful to achieve this

- ***Tier one*[1]*:*** analgesic +/- antiemetic
- ***Tier two:*** specific anti-migraine drugs
- ***Tier three:*** combination therapies
- ***Emergency treatment:*** intramuscular NSAID and antiemetic
- ***Relapse:*** repeat symptomatic analgesics from step one and two and consider repeat of triptan

Footnotes

1. Tier one incorporates stages one and two of the BASH recommendations, which split oral and rectal analgesia +/- antiemetic into separate stages.
2. This is naproxen 250 mg plus naproxen 500 mg, or naproxen sodium 275 mg plus naproxen sodium 550 mg.
3. Cataflam or voltaren rapid. These appear to be more rapidly absorbed than diclofenac sodium.
4. EBM Reviews - Cochrane Central Register of Controlled Trials Di Monda V, Nicolodi M, Aloisio A, et al Efficacy of a fixed combination of indomethacin, prochlorperazine, and caffeine versus sumatriptan in acute treatment of multiple migraine attacks: a multicenter, randomized, crossover trial. Headache. 2003; 43(8):835–44

Tier one: analgesic +/- antiemetic

Step one consists of analgesia with aspirin or other NSAID, with the best evidence for ibuprofen and naproxen. These are usually given orally with **standard release** preparations at **higher doses**, taken **early in the attack** to avoid delayed absorption due to gastric stasis. **Delayed release preparations are not suitable**.

Recommended doses for adults are:

Aspirin: 600–900 mg, up to four doses in 24 hours
Ibuprofen: 400–600 mg, up to four doses in 24 hours
Naproxen[2]*:* 750–825 mg, with further 250–275 mg up to twice in 24 hours
Diclofenac-potassium[2]*:* 50–100 mg up to a total of 200 mg in 24 hours

General contraindications to NSAIDs must always be kept in mind but there is little evidence for paracetamol use on its own in migraine. In practice, paracetamol does appear to be useful, especially when combined with metoclopramide.

Metoclopramide promotes gastric emptying. Even when nausea and vomiting are not present, this is likely to improve absorption of analgesics and there is some evidence that metoclopramide on its own gives relief in migraine.

When nausea or vomiting render oral administration problematic, rectal preparations of analgesics and anti-emetics may be more suitable. Diclofenac suppositories, 100 mg, used up to twice in 24 hours are recommended by BASH.

Anti-emetic suppositories are useful if nausea and vomiting is a problem. Prochlorperazine, 25 mg, is available as a suppository in New Zealand.

There has been a recent resurgence of interest in the use of preparations containing fixed drug combinations. In a randomised controlled trial, a fixed combination suppository of indomethacin, prochlorperazine and caffeine, was as effective as sumatriptan.

Opiates and opioids should, in general, be avoided during acute migraine. They provide little additional benefit, have potential for addiction and, as discussed on page 22, can be associated with medication overuse headache. Any history of alcohol or drug abuse or dependency is a strong warning that problems are likely.

2 *Tier two: specific anti-migraine drugs*

The triptans are serotonin agonists used in acute migraine management. Sumatriptan is the only funded triptan in New Zealand.

Unlike symptomatic treatment, triptans should not be taken too early. They appear to be ineffective if given during aura and most effective, whilst pain is still mild or at the onset of hypersensitivity. Unfortunately, triptans are associated with return of symptoms within 48 hours in 20–50% of patients who initially respond.

Sumatriptan should not be repeated if the first dose has been ineffective but can be repeated if it was initially effective but the headache has recurred (see page 19).

Sumatriptan, 50 mg orally, is usually tried in the first instance combined with metoclopramide. If this is not effective, 100 mg orally, can be tried in future attacks. Sumatriptan can, if necessary, be given subcutaneously at a dose of 6 mg.

Contraindications to triptans include:

- Ischaemic heart disease
- Prinzmetal's angina/coronary vasospasm
- Cerebrovascular disease (CVA) or transient ischaemic attack (TIA)
- Uncontrolled hypertension
- Severe hepatic impairment
- Concurrent use or use within two weeks after discontinuation of monoamine oxidase inhibitors

Ergotamine use, for migraine, is limited by a significant risk of toxicity and drug interactions. Major side effects include: nausea, vomiting, paresthesia, and the convulsive and gangrenous effects of ergotism. Contraindications are cardiovascular and cerebrovascular diseases, Raynaud's disease, arterial hypertension, renal failure, pregnancy and breastfeeding.

Ergotamine is thought to have significantly lower relapse rates than sumatriptan and may be useful if relapse is a major problem and cannot be managed with other medications. It should not be used for at least 12 hours after sumatriptan (see page 19).

Ergotamine is available in New Zealand combined with caffeine in Cafergot. One tablet contains 1 mg of ergotamine and 100 mg of caffeine. For first time users, two tablets are taken initially with a further tablet half hourly if needed. Subsequently three tablets can be taken initially, if needed, with a further tablet half hourly. The **maximum dose** in any 24 hour period is six tablets and a maximum of ten tablets in any week.

Tier three: combination therapies

There is some evidence that a combination of naproxen and sumatriptan is superior to either drug alone and it can be worth trying this combination as Tier Three.

Emergency treatment: intramuscular NSAID and antiemetic

Emergency management of acute migraine is difficult, especially on house calls to patients not seen previously. Injections of opiates, e.g. pethidine or morphine, are best avoided. Rebound headache, potential side effects and risk of dependency generally outweigh the potential for additional pain relief.

BASH recommends for adults, when there are no contraindications, diclofenac, 75 mg, intramuscularly. However, diclofenac injections can cause serious tissue damage and it is preferable to avoid them if possible. Medsafe recommends they be given by deep intragluteal injection into the upper outer quadrant, if required.

NSAIDs by suppository are a safer alternative, and are often effective. Concurrent administration of prochlorperazine, 25 mg as a suppository is useful to control nausea and vomiting.

Chlorpromazine, 25–50 mg intramuscularly is useful as an anti-emetic and sedative in the emergency management of acute migraine.

Relapse: repeat analgesics and consider repeat of triptan

Relapse is recurrence of headache within the same episode of migraine despite initial efficacy. Management is difficult because repeated doses, especially of triptans or opiates, if they have been used, can give rise to repeated rebound over several days.

Repeat of previously used analgesics may be effective. A second dose of triptan is usually effective but does increase the risk of further rebound. A minimum of two hours is required between doses. Ergotamine may be an alternative but must be given at least 12 hours after sumatriptan.

The maximum dose of sumatriptan in any 24 hour period is:

- Oral dosage in 24 hours, 300 mg
- Sub-cutaneous dosage in 24 hours, 12 mg

Limit use of acute migraine therapy to two days per week

Regular use of acute migraine therapies for more than two days per week carries significant risk of initiating or escalating medication overuse headache and should be avoided. Regular requirement of acute migraine therapy for more than one day per week is an indication to evaluate how the medication is being used and review the diagnosis.

MIGRAINE PROPHYLAXIS

Migraine prophylaxis is indicated when symptoms cannot be adequately controlled with acute therapy. As migraine is cyclical, permanent use of prophylaxis is not usually required; it can be tapered off, after 4-6 months, to test the need for continued use.

The choice of medication for prophylactic therapy for individual patients is guided by:

- Evidence of effectiveness
- Potential benefits
- Potential risks
- Ease of use
- Comorbidities

The medications most useful in primary care are shown in Table 2. In general, prophylactic therapies are started at low doses and gradually increased to avoid side effects. Once a full dose is achieved, a reasonable trial of therapy is approximately 6–8 weeks.

Table 2: Medications for migraine prophylaxis in primary care

	Evidence	Additional benefits	Risks	Dose	Comorbidities to consider
Beta blockers Good evidence base	RCTs for metoprolol, propanolol, nadolol and atenolol		Cold extremities, reduced exercise tolerance, dizziness	Metoprolol 50–100 mg BD Propanolol LA 80 mg daily to 160 mg BD	Asthma, heart failure, peripheral vascular disease, depression
Tricyclics Adequate evidence base	Evidence for effectiveness from small RCTs of amitriptyline	Helps with co-existent tension headache, other pain conditions, disturbed sleep and depression. Some evidence of synergy with beta blockers	Sedation, dry mouth, dizziness, nausea Less side effects with nortriptyline	10–150 mg at night	Concurrent use of other anti-cholinergic medications
Sodium valproate Good evidence base	RCTs		Nausea, weight gain, alopecia, spontaneous bruising, liver dysfunction	300–1000 mg BD	Contra-indicated in pregnancy

RCT = Randomised Controlled Trial

Pizotifen and clonidine have little evidence of effectiveness and are now superseded for the prophylaxis of migraine in adults. There is some evidence for the effectiveness of verapamil and the evidence for the use of fluoxetine is inconclusive.

Acupuncture is often used for migraine and trials have shown reduction in the severity and frequency of episodes. However, the quality of these trials has been questioned. There are the usual problems associated with testing complementary therapies. Medications are subject to trials before introduction, whereas complementary therapies are not usually subject to trial until they have been used for many years and positions have become entrenched. Decisions will depend on the enthusiasm of individual clinicians and patients for this modality of treatment.

MIGRAINE IN CHILDREN

In children, migraine attacks may be shorter-lasting, headache is more commonly bilateral and gastrointestinal disturbance is more prominent.

Generally, children with migraine, which cannot be controlled with simple analgesics, are best referred for specialist care. Anti-emetics are not recommended.

MANAGEMENT OF MIGRAINE DURING PREGNANCY AND BREAST-FEEDING

There are no clinical trials specifically evaluating the drug treatment of migraine during pregnancy. Fortunately, migraine frequency is usually reduced during this time. (Ever et al, 2006)

Table 3: Management of migraine during pregnancy

Paracetamol	Can be used throughout pregnancy and breast-feeding
NSAIDs	Avoid in the third trimester to avoid fetal renal damage and patent ductus. In the first and second trimester short acting NSAIDs, such as ibuprofen, are preferred
Metoclopramide	Unlikely to cause harm through pregnancy and breast-feeding
Triptans and ergotamine	Contraindicated However, women who have taken sumatriptan inadvertently in pregnancy can be reassured current evidence suggests they are at no greater risk of birth defects than the general population
Propanolol	Beta blocker with best evidence of safety during pregnancy
Amitriptyline	Lowest effective dose may be used

MANAGEMENT OF CLUSTER HEADACHE

Cluster headache is excruciatingly painful and symptomatic treatment is seldom adequate. Patients often benefit from the involvement of a specialist who has experience in the prophylactic management of cluster headache.

Sumatriptan, 6 mg subcutaneously, is the only proven highly effective treatment for acute cluster headache. Oxygen 100% for 10–20 minutes helps some people. Analgesics have no place in treating cluster headache. Ergotamine and oral triptans are not effective.

Prophylactic therapy is commenced as early as possible when a new cluster starts and alcohol should be avoided completely during cluster episodes. Verapamil, prednisone and lithium all appear to be effective prophylactic therapies for cluster headache. Cluster headache is rare and GPs are unlikely to develop experience in its management. Referral to an appropriate specialist in this area is usually the best option.

AVOIDANCE, RECOGNITION AND MANAGEMENT OF MEDICATION OVERUSE HEADACHE

Medication overuse headache occurs most frequently from chronic overuse of analgesics, such as aspirin, NSAIDs, paracetamol and codeine, to treat headache. Frequent lower doses appear to carry greater risk than higher weekly doses. It also occurs because of rebound headache following triptan use.

Medication overuse headache may take a long time to resolve after the medication is withdrawn. Re-introduction of headache medication may resolve the headache in the short term but escalates the long-term problem.

There is no specific type of headache associated with medication overuse but patients often describe them as oppressive, often worse on wakening and aggravated by physical exercise. They are not usually accompanied by nausea or vomiting.

Headaches evolve over weeks or longer, with increased frequency of the headache, often accompanied by increased analgesia use, until eventually, medication is taken in anticipation of headaches. Prophylactic medication is ineffective. Often the pattern of headaches and medication use can only be understood with the help of an accurate headache and medication diary.

Other forms of primary and secondary headache should be carefully excluded.

There are four objectives in the management of medication overuse headache:

- Withdrawal from the overused medication
- Recovery from the headache
- Re-assessment of any underlying primary headache
- Prevention of relapse

WITHDRAWAL OF OVERUSED MEDICATION

Motivation: For people who experience medication overuse headache, the outcome of withdrawal is usually good. The alternative is ever-worsening headache.

Warning: Headaches may worsen for three to seven days following withdrawal of medication. Patients need encouragement and support over this time and absence from work may be required.

Diary: Recording symptoms and medication use during medication withdrawal, allows a more objective assessment of the results of withdrawal.

Good hydration: This is thought to help.

Abrupt withdrawal: This is more successful than gradual withdrawal. When withdrawal cannot be achieved, it may be effective to offer regular naproxen 250 mg tds or 500 mg bd for three weeks to cover the withdrawal period. The aim is to prevent people responding to headache by taking medication.

RECOVERY FROM HEADACHE

The time to recovery from the headache depends on the medication type.
Triptan: 7–10 days
Simple analgesics: 2–3 weeks
Opiates: 2–4 weeks

When recovery does not follow a reported withdrawal, the headache may have other causes, or medication overuse may be continuing.

RE-ASSESSMENT OF UNDERLYING PRIMARY HEADACHE

An underlying primary headache, usually tension-type or migraine, often becomes apparent within two months. This should be managed systematically. The analgesics, which were implicated in the overuse headache, can be re-introduced after two months, if required, but care has to be taken that these are used appropriately.

PREVENTION OF RELAPSE

There is a high risk of relapse and good support will be required.

BRIEF UPDATE ON THE PATHOPHYSIOLOGY OF MIGRAINE AND ANTI-MIGRAINE DRUGS

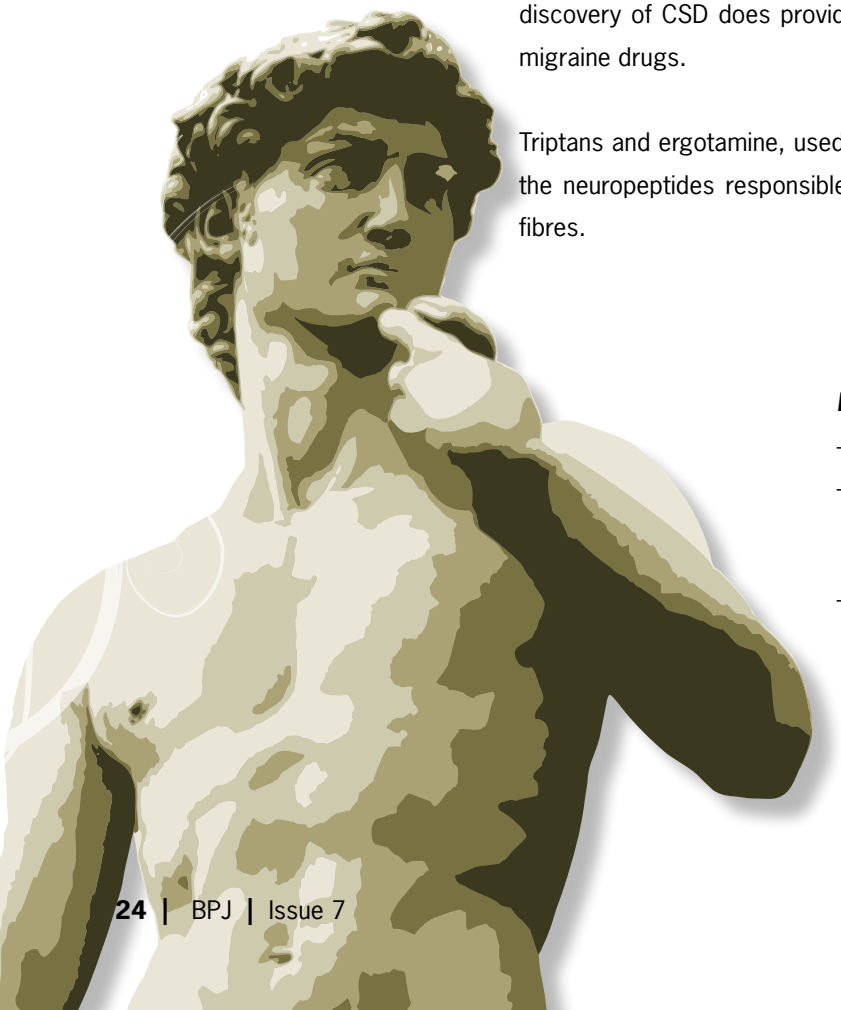
Migraine is a group of familial disorders; individual susceptibility is conferred by genetics and exposure to triggering factors.

Migraine aura is strongly associated with a slowly spreading wave of decreased electrical activity that travels across the cortex at approximately 2–3 mm per minute. This is termed Cortical Spreading Depression (CSD). CSD is thought to also occur in migraine without aura, but is clinically silent.

An episode of CSD is followed by long-lasting suppression of neuronal activity and activation of the trigeminovascular system. Consequent release of neuropeptides produces vascular dilation and neurogenic inflammation. Headache results because of meningeal irritation and the sensitisation of nerve fibres to previously innocuous stimuli, such as the pulsing of blood vessels.

Beta blockers, valproate and amitriptyline, the first choice drugs for migraine prophylaxis in primary care, have all been demonstrated to reduce the number of CSDs in animal experiments. The mechanism by which this occurs has not yet been demonstrated, but the discovery of CSD does provide an avenue for the development of new prophylactic anti-migraine drugs.

Triptans and ergotamine, used in acute migraine, reduce headache by blocking release of the neuropeptides responsible for meningeal irritation and sensitisation of central nerve fibres.



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DIAGNOSIS AND MANAGEMENT OF PARKINSON'S DISEASE

KEY POINTS

1. ***The diagnosis of Parkinson's disease is still based on careful history taking and clinical examination, despite ongoing advances in neuro-imaging and laboratory testing.***
2. ***One of the first challenges is to differentiate between Parkinson's disease and Parkinsonism – any group of nervous system disorders characterised by muscular rigidity, tremor and impaired motor control.***
3. ***Management of Parkinson's disease and co-existent health problems is a long journey, requiring a multidisciplinary team approach.***
4. ***Initiation of drug treatment for early Parkinson's disease is usually delayed until functional problems develop.***
5. ***Levodopa is the drug of choice for Parkinson's disease but approximately half of patients will experience fluctuations in motor control after 5 to 10 years of treatment.***
6. ***Long-term management of Parkinson's disease involves careful adjustment of medications and their doses along with other strategies such as education, exercise, speech therapy and nutrition.***

Key Adviser: Dr Wendy Busby - Consultant Geriatrician, University of Otago

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www.bpac.org.nz keyword: **"Parkinson"**

Parkinson's disease is one of the most common neurodegenerative diseases, with prevalence ranging from 100–180 per 100,000 population and an incidence of 4–20 cases per 100,000. There is a male to female predominance of 1.3:1. It typically presents in those over 60 years and the prevalence will increase with the ageing population.

While most cases of Parkinson's disease are thought to be sporadic in onset, mutations in six nuclear genes have been associated with autosomal dominant or recessive Parkinson's disease. A number of aetiologic factors have been considered including infections, toxins, head trauma, coffee and alcohol consumption. The strongest association is that non smokers are at greater risk of developing Parkinson's disease.

The diagnosis of Parkinson's disease is based upon careful history taking and examination, despite ongoing advances in neuro-imaging and laboratory testing. Computerised tomography (CT) and Magnetic Resonance Imaging show no specific changes but may help to exclude other conditions. Positron emission tomography and single photon emission CT may help in diagnosis but are not routinely available.

Ideally, patients should be managed jointly with GP, specialist and other health professionals including nurse specialist, physiotherapists, occupational therapists, social workers, speech-language therapists and the Parkinson's Society field worker. Effective communication and team work are paramount for optimal management.

This is often a long journey which also requires the management of co-existent health problems and may culminate in end stage Parkinson's disease and palliative care.

MAKING THE DIAGNOSIS

Getting the diagnosis correct underpins the best management of patients and a specialist opinion is usually helpful, ideally before starting any medications.

Careful history taking is essential and often provides a clear guide to the diagnosis. The duration of symptoms is important, as is any family history of either Parkinson's disease or tremor.

The error rate in diagnosing idiopathic Parkinson's disease has been reported as around 50% in general practice, 25% in general specialist clinics and 8% in specialised Parkinson's disease clinics.[1]

Differentiating Parkinson's disease from Parkinsonism

One of the first challenges is differentiating Parkinson's disease from Parkinsonism as the management is usually quite different.

Parkinsonism is any of a group of nervous system disorders with symptoms similar to Parkinson's disease, characterised by muscular rigidity, tremor, and impaired motor control. There is often a specific cause, such as the use of certain drugs or frequent exposure to toxic chemicals.

It is essential to check for medications which interfere with dopamine release in the brain and hence cause Parkinsonism (neuroleptics, metoclopramide, prochlorperazine).

Features of Parkinson's disease

Tremor: (Table 1) The most common presenting symptom is tremor, although the majority of those with tremor do not have Parkinson's disease. Tremor in Parkinson's disease usually presents as a unilateral, pill rolling hand tremor. It may affect other limbs and the head. Always query the diagnosis if tremor is absent.

The pattern of any tremor should be clarified, for example, whether it is worse on activity or at rest or if there are any relieving factors. Past medical history may indicate other diseases. A careful medication history is essential to exclude drug induced tremor.

- Essential tremor is relatively common, affecting 0.4 to 4% of the population and approximately 2.5% of those over 60 years. It is often bilateral, progressive and not associated with other extrapyramidal signs.
- Cerebellar tremor may be unilateral or bilateral depending upon its aetiology. It is worse on movement, often with a stuttering or saccadic character and worse at the beginning and end of movement. There may be other cerebellar signs including nystagmus and ataxia.

Table 1: Characteristics of Tremor

Tremor	*Character*	*Tone*	*Reflexes*
Extrapyramidal	Resting	Cogwheel/ Lead pipe	Normal range
Cerebellar	Action, Past pointing	Hypotonic	Pendular
Essential	Action	Normal	Normal
Action	Action	Normal	Normal

Rigidity and Bradykinesia: Bradykinesia and rigidity, micrographia, stiffness and slowness, may be features of other conditions including ageing, depression, dementia, arthropathies, polymayalgia rheumatica, and hypothyroidism, as well as Parkinson's disease.
At first presentation of Parkinson's disease, patients may complain of a general slowing up and stiffness which can be attributed to ageing or osteoarthritis. There may be difficulties in turning over in bed, which may contribute to sleep disturbance. Speech may be slower, quieter and more monotonous. Patients may have expressionless faces and be less spontaneous.

The increased tone is classically present throughout movement (lead pipe) or has a cog-wheeling component to it. This can be thought of as the additive effects of tremor upon the lead pipe rigidity.

Gait disorder, postural changes and falls: These occur later in the disease course and if present early, should alert the clinician to an alternative diagnosis.

In Parkinson's disease, the characteristic features usually begin with unilateral loss of arm swing and it is often helpful to watch the patient walk along a corridor. The gait is typically small-stepped and shuffling, described as festinating. The posture becomes stooped, and arms flexed. Patients turn en bloc, shuffling around on the spot. Postural stability becomes impaired and the risk of falling increases. Postural hypotension as a result of autonomic dysfunction and/or medication can contribute to falls.

Examination

Assessment should include:

- Anaemia
- Cognitive function
- Gait
- Lying and standing blood pressure
- Musculoskeletal conditions
- Thyroid disease
- Weight

Neurological assessment should include checking for red flags for alternative diagnoses.

Red Flags

There are some "red flags" (Table 2) which should always alert the clinician to an alternative diagnosis (Table 3).

Table 2: Red Flag alerting clinicians to an alternative diagnosis

No tremor at time of diagnosis
Bilateral signs at onset
Dementia or hallucinations early in the disease course
Early onset of postural hypotension and autonomic failure
Reduced range of eye movements at diagnosis
Falls or drop attacks early in history
Up-going plantar reflex
No response to levodopa

Parkinsonian Syndromes

Include the following:

Progressive Supra-nuclear palsy is rare neurodegenerative condition, usually presenting after the age of 40 years. It is characterised by vertical gaze paralysis, truncal and neck rigidity, postural instability and unexplained falls. Tremor is rare.

Dementia with Lewy bodies is characterised by sudden falls or dropping to the ground associated with cognitive deficits in attention, visual spatial and loss of executive function, insight and judgment. Hallucinations occur relatively early in the disease course and patients often have marked intolerance to neuroleptic agents.

Normal pressure hydrocephalus is associated with the triad of an ataxic gait, urinary incontinence and cognitive loss.

Vascular Parkinsonism is often distinguishable from the history and accompanying cognitive loss. Tremor is not usually present. Examination of the patient and a CT headscan should help to confirm the diagnosis. The use of levodopa does not improve symptoms and may exacerbate cognitive problems. Unilateral Parkinsonism may be difficult to distinguish from a CVA.

Multi-systems atrophy includes the conditions known as olivopontocerebellar atrophy, nigrostriatal degeneration and Shy-Drager syndrome which often presents with early and severe autonomic dysfunction including postural hypotension. There may be a combination of extra-pyramidal signs without tremor, pyramidal and cerebellar signs.

Table 3: Parkinsonian Syndromes

Drug Induced Parkinsonism
Alzheimer's Disease or Vascular Dementia
Dementia with Lewy Bodies
Multiple Systems Atrophy/ Shy Drager Syndrome
Corticobasal degeneration
Progressive Supra-nuclear Palsy
Normal Pressure Hydrocephalus
Vascular Parkinsonism

See opposite panel for more details

NATURAL HISTORY

By the time symptoms of Parkinson's disease appear, approximately 70–80% of the dopamine is lost from the substantia nigra indicating a substantial sub-clinical period. While dopamine is the primary neuro-transmitter involved in the pathology of Parkinson's disease it is clear that others are involved including acetylcholine, noradrenaline, adenosine, glutamate and GABA.

The factors which determine prognosis and disease progression in Parkinson's disease are not clearly established.

Initially, patients experience a prompt and even response to medication. Usually within two years, medication doses need to be increased and patients often take a combination of medications.

The lowest dose of medication needed should always be used. The progressive degeneration of dopamine terminals means the concentration of dopamine in the basal ganglia becomes more dependent upon plasma levels. These can fluctuate because of the 90 minute half life of levodopa and its unpredictable absorption. At this time, the consensus is that chronic administration of levodopa does not exacerbate the disease process.

"One of the first challenges is differentiating Parkinson's disease from Parkinsonism"

MOTOR FLUCTUATIONS

Motor fluctuations occur in approximately half of patients after 5 to 10 years of treatment. These often are more severe in younger patients and are associated with the use of levodopa containing preparations. These include wearing off, dyskinesias and dystonias, and on-off episodes.

When the effect of levodopa wears off in less than four hours, this can initially be managed by increasing the dose of medication and/or shortening the dosing interval.

This can progress to on-off episodes (fluctuations between control and no control). Initially the pattern may be predictable with timing of medication and its effectiveness but it may become unpredictable. Patients may find themselves suddenly freezing, often when moving through doorways. Dyskinetic movements may occur typically when patients are in an "on" period. Dystonia, often painful, including dystonic inversion of the foot, may occur when the patient is either "on" or "off"

The treatment of such complications can be difficult and specialist help is usually required.

"Fluctuations in motor control occur in approximately half of patients after 5 to 10 years of treatment with levodopa"

DRUG MANAGEMENT OF PARKINSON'S DISEASE

SUMMARY POINTS

- Levodopa is the principal choice for initial treatment of Parkinson's disease but long term use is limited by motor complications and drug-induced dyskinesias.
- Dopamine agonists are also options for initial treatment and are not usually associated with motor complications. However they are inferior to levodopa in controlling motor symptoms.
- When levodopa related motor complications develop in advanced Parkinson's disease, the addition of a dopamine agonist, catechol-O-methyltransferase inhibitor (COMT) or monoamine oxidase-B inhibitor (MAOI-B) may be beneficial.
- Parkinson's disease is often associated with psychiatric illness such as dementia, depression and psychosis. Psychosis is often drug induced and can be managed by dose reduction of antiparkinsonism medication. Other conditions (e.g. depression) may require active drug management.
- Parkinson's disease is associated with a significant range of non-motor symptoms which should be identified and managed

EARLY PARKINSON'S DISEASE

Early Parkinson's disease refers to people with mild symptoms or who have developed functional disability and who require symptomatic treatment. Late disease refers to people who are already taking levodopa and have developed motor complications.

Initiation of drug treatment for early Parkinson's disease is usually delayed until patients develop functional problems. As the benefit from medications reduces with time, some people prefer to delay initiation of treatment and the advantages and disadvantages should be discussed with the patient. Older patients may have greater disability at the time of onset of symptoms because of the compounding effects of other co-morbidities.

The Unified Parkinson's Disease Rating Scale (UPDRS), a standardized tool, can help in assessing and subsequent monitoring of disability and treatment response. It has four parts measuring;

- Activities of daily living
- Motor impairment
- Psychological/cognitive effects
- Treatment and disease complications

Available from ***http://www.mdvu.org/pdf/updrs.pdf***

Drug treatment in early Parkinson's disease

Once functional impairment develops, drug treatment is usually required. There is no universal first-choice drug for those with early Parkinson's disease (see Table 4).

- Selegiline or an anticholinergic may improve mild symptoms, particularly in younger people, but most people usually require levodopa or a dopamine agonist
- Levodopa is better at improving motor disability and dopamine agonists cause less motor complications
- The long term use of levodopa is limited by motor complications and drug-induced dyskinesias
- Generally, a dopamine agonist is used in younger people with mild symptoms and levodopa used initially in older people with more severe motor symptoms
- Levodopa is the most effective treatment for bradykinesia and rigidity[2,3]

NEUROPROTECTION

The use of neuroprotective agents such as vitamin E, monoamine oxidase inhibitors, co-enzyme Q10 and dopamine agonists, have not been proven to be effective. Early studies of co-enzyme Q10 and dopamine agonists have indicated some slowing of disease progression.[4] NICE generally advises against the use of neuroprotective agents except when part of a clinical trial.[5]

Levodopa is the precursor of dopamine and is used because dopamine does not cross the blood brain barrier. It is given with a dopa-decarboxylase inhibitor (usually 4:1 ratio) to minimize peripheral conversion to dopamine and reduce nausea and hypotension. Sinemet and Madopar are levodopa preparations combined with a dopa-decarboxylase inhibitor. Doses are started low and titrated upwards in response to the therapeutic effect. Particular care needs to be taken with older patients and those with other co-morbidities.

Dopamine agonists include bromocriptine, ropinirole, lisuride and apomorphine. Bromocriptine and lisuride are ergot derivatives, while ropinirole is a non-ergot derivative. These drugs directly stimulate dopamine receptors and are effective alone or combined with levodopa for symptoms of early Parkinson's disease and to help manage motor fluctuations. Bromocriptine and lisuride require regular monitoring (renal function, ESR and chest X-ray) but ropinirole has the advantage of requiring less monitoring and is generally the first choice dopamine agonists.[5]

Response and side effect profiles are the other determinants of drug choice. Apomorphine is only available as subcutaneous injection and is reserved for severe "off" periods and motor fluctuations which are not responding to other treatments.

Selegiline (a MAO-B inhibitor) gives mild symptomatic improvements in patients with early Parkinson's disease.[2] It is also used as adjuvant therapy for patients with Parkinson's disease and motor fluctuations.

Anticholinergic agents (benztropine, procyclidine and orphenadrine) are useful to treat disabling tremors, particularly in younger people with preserved cognitive function. In older people (> 70 years) their use is limited by their side effect profile including a high incidence of postural hypotension, urinary retention, constipation and neuropsychiatric adverse effects.[4]

Amantadine (originally marketed as an antiviral agent) has been shown to reduce tremor, rigidity and akinesia, in people with Parkinson's disease.[4] It may be useful in some patients but supporting evidence is relatively weak.

Table 4: Medication for Parkinson's disease

Medication	Indications and comments	Adverse effects
Anticholinergics: *Benztropine (Cogentin),* *Procyclidine (Kemadrin)* *Orphenadrine (Disipal)*	Useful for symptomatic control of Parkinson's disease (benefits are mild to moderate); associated with more adverse effects than other drugs	Dry mouth, dry eyes, constipation, hypotension, cognitive impairment, urinary retention
Carbidopa/levodopa Immediate and carbidopa/levodopa SR (Sinemet). *Benserazide/levodopa (Madopar – similar to Sinemet – dispersible tablet may be useful for people with swallowing difficulties)*	Levodopa is the most effective medication and remains the primary treatment for symptomatic Parkinson's disease; no added benefit for motor complications with sustained-release versus immediate-release preparations	Nausea, somnolence, dyskinesia, hypotension, hallucinations. Long term use is limited by motor complications and drug-induced dyskinesias.
COMT inhibitors: *Entacapone (Comtan)*	Useful for managing motor fluctuations ('wearing-off' effect) in patients taking levodopa; levodopa dose may need to be reduced if dyskinesia appears.	Diarrhoea; exacerbates levodopa adverse effects; bright red-brown urine
Tolcapone (Tasmar)	Not generally recommended due to hepatotoxicity. Entacapone is preferred.	Diarrhoea, exacerbates levodopa adverse effects; rare liver failure (liver function monitoring needed)
****Dopamine agonists:*** *Bromocriptine (Parlodel)*	Useful for early disease and in patients with Parkinson's disease and motor fluctuations	Nausea, headache, dizziness. Pleuropulmonary changes, CNS effects, retroperitoneal fibrosis (long term use). Regular monitoring required.
Lisuride (Dopergin)	Useful for early disease and in patients with Parkinson's disease and motor fluctuations	Similar to bromocriptine and other ergot derivatives.
Ropinirole (Requip)	Useful for early disease and in patients with Parkinson's disease and motor fluctuations	Nausea, sleep attacks, edema, hallucinations, hypotension
MAO-B inhibitors: *Selegiline (Eldepryl)*	Useful for symptomatic control of Parkinson's disease (benefits are mild to moderate) and as adjuvant therapy for patients with Parkinson's disease and motor fluctuations	Nausea, insomnia, drug interactions with other MAO inhibitors/tyramine
NMDA receptor inhibitor: *Amantadine (Symmeterel)*	Useful for treating akinesia, rigidity, tremor, dyskinesia	Nausea, hypotension, hallucinations, confusion, edema

*Pergolide is another dopamine agonist available in New Zealand but has been associated with significant cardiac and pulmonary fibrosis. Other agents are preferred.

LATE PARKINSON'S DISEASE

Late Parkinson's disease refers to people who are taking levodopa and have developed motor complications, typically with wearing off and on-off phenomena.

The approach to treating motor complications is varied. Adjustment of dosage, use of controlled release preparations and adjusting timing of medications may help.

Long acting levodopa preparations (Sinemet CR, Madopar HBS) can be useful in reducing the frequency of dosing for patients especially overnight, and for addressing wearing off phenomena. If doses need adjustment, this should generally be done one drug at a time to assess response.

The addition of a MAO-B inhibitor (Selegiline), a dopamine agonist or a COMT inhibitor may provide an improvement to motor complications.[2,4]

Dopamine agonists have been shown to significantly reduce off time, improve motor function and reduce the need for levodopa.[4] They are generally useful as adjunct therapy in people already taking levodopa.

COMT inhibitors (entacapone (Comtan) and tolcapone (Tasmar)) are used with levodopa to reduce its breakdown and increase its half-life. Consequently they can be effective in reducing the end of dose wearing-off effect and the duration of off time. Tolcapone should not generally be used due to the risk of hepatotoxicity. Monitoring of liver function tests is required for the first year of treatment.[5]

At some point there may be little benefit from ongoing adjustment of antiparkinsonian medication; doses may need to be reduced and treating associated problems may be more useful. This should be done in discussion with the patients. Some prefer being mobile and tolerating dyskinesia while others find dyskinesia intolerable and prefer to be more bradykinetic.

"Initiation of drug treatment for early Parkinson's disease is usually delayed until functional problems develop"

NON-MOTOR FEATURES OF PARKINSON'S DISEASE

Non-motor symptoms such as depression, psychoses, sleep disturbance and hypotension are commonly associated with Parkinson's disease. These symptoms and their management are outlined in Table 5.

When managing non-motor symptoms or other concurrent conditions, care should be taken to check if drug therapy could aggravate symptoms of Parkinson's disease or interact with existing medication. For example for nausea, prochlorperazine and metoclopramide should be avoided whereas domperidone is very unlikely to cause extrapyramidal effects. An SSRI, selected to treat depression may interact with selegiline causing serotonin syndrome.

"Late Parkinson's disease is associated with motor complications from the levodopa wearing off and on-off phenomena. Adjusting dose, timing and release of medications may help"

Table 5: Management of non-motor features of Parkinson's disease

Symptom	*Management strategies*
Cognitive impairment	Evaluate for and treat medical problems (e.g. dehydration, metabolic disorders, infection); adjust antiparkinsonian medications; decrease or discontinue anticholinergics, dopamine agonists, amantadine (Symmetrel), and selegiline (Eldepryl).
Constipation	Patients should increase fluid and fibre intake; increase physical activity; discontinue anticholinergics; and use a stimulant laxative (e.g. Coloxyl with Senna), stool softeners, or enemas as needed.
Depression	Initiate counseling; consider drug therapy with selective serotonin reuptake inhibitors or tricyclic antidepressants (because of side effect profile, use tricyclic antidepressants with caution).
Dysphagia	Perform a swallowing evaluation and refer the patient to a speech language therapist specialist; increase "on" time (the period when symptoms are decreased), and encourage patients to eat during this time; patient should eat soft foods.
Orthostatic Hypotension	Discontinue antihypertensive medication; the head of the patient's bed should be elevated, and patient's should rise slowly from a prone position; consider support stockings and fludrocortisone (Florinef).
Psychosis, hallucinations or delirium	Decrease or discontinue anticholinergics, dopamine agonists, amantadine, and selegiline; decrease levodopa; consider low-dose quetiapine.
Sleep disturbance	Daytime somnolence and sleep attacks; discontinue dopamine agonists, general methods to improve sleep hygiene. Nighttime awakenings because of bradykinesia; consider a bedtime dose of long-acting Sinemet or Madopar, adjuvant entacapone (Comtan), or a dopamine agonist. Rapid eye movement sleep behaviour disorder; decrease or discontinue night time use of antiparkinsonian drugs, (consider ropinirole for restless leg syndrome).
Urinary urgency	Reduce evening fluid intake; Confirm aetiology of urgency before using an anticholinergic agent such as oxybutynin (Ditropan).

OTHER MANAGEMENT

Education

Patients and their families may be alarmed by the diagnosis of Parkinson's disease. Many have known people who have had disabling symptoms. Care should be taken not to over expose newly diagnosed patients to information regarding all the potential end stage features. Many patients never progress to this stage.

Education should under pin all management decisions. Many patients will be making a series of lifestyle changes to attempt to slow the effects of the disease. Early contact with the Parkinson's society either via the local field officer or through the national office (www.parkinsons.org.nz) may be helpful and provides ongoing information and support.

Exercise and physiotherapy

Regular exercise may encourage a healthy life style in people with Parkinson's disease. Specific help may be obtained from physiotherapists who can develop an individualised exercise programme. This can help to promote flexibility, prevent rigidity and flexed posture and maintain balance and strength to help prevent falls.

Fractures often have devastating consequences for people with Parkinson's disease. Consideration should be given to management of any co-existent osteoporosis. Mobility aids and falls prevention programmes may be needed.

Occupational Therapist

An occupational therapist can assist with promoting leisure, work and home activities. They also can perform cognitive assessments if cognitive loss is becoming apparent. Home based assessments are often helpful and aids, equipment and household modifications facilitated. Silky sheets and night wear and an Adams pole insert on the bed side may help bed mobility.

Social Worker and Needs Assessor

Younger patients should be encouraged to remain actively involved in the work force. A social worker may be able to assist if difficulties arise. With time, many people may struggle to maintain their activities of daily living and a Needs Assessor can help with determining needs and liaising with service providers to co-ordinate support. General practitioners can allocate carer support and a disability allowance.

Speech language therapist

Communication and swallowing problems may occur in time and early referral to a speech-language therapist can provide assessment and exercise programme for patients.

Nutrition

For most people early in the disease course, a normal, healthy diet is appropriate. For patients who begin to develop motor fluctuations, dietary modification to improve drug absorption may be helpful. Theoretically, certain proteins compete with dopamine absorption and hence advice is to take medications on an empty stomach. However some patients may experience nausea and taking medications with food helps. Compliance may be improved by taking medications at meals times. Large meals high in fats may slow gastric emptying and impede medication absorption.

Many patients lose weight as the disease progresses and any dietary restrictions may lead to inadequate caloric intake. Attempts should be made to avoid weight loss and weight should be routinely monitored.

If swallowing is impaired, foods may need to be pureed.

Driving

Care should be taken in monitoring the patient's safety to drive. It is advisable to check with family members if there have been any concerns and to ask about any accidents. Some of the medications used can cause daytime drowsiness or abrupt onset of sleep..

Enduring Power of Attorney (EPOA)

All patients should be encouraged to contact their lawyer to have a welfare guardian and a property manager designated through the EPOA process.

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etc

evidence that counts

Hormone Therapy, Age, and Risk for Heart Disease

Journal Watch May 1, 2007, Vol. 27, No. 9

***Bottom Line:** The trend for CHD seen in these analyses, although nonsignificant, supports the current practice of many clinicians, who counsel patients that HT to control postmenopausal symptoms appears to be acceptable (in terms of CHD risk) for a few years but should then be stopped unless the symptoms are unmanageable. Of course, other risks associated with HT (breast cancer, stroke, and venous thrombosis) also should be kept in mind.*

Women's Health Initiative (WHI) data have suggested that the greatest risk for coronary heart disease associated with hormone therapy — with conjugated equine estrogen (CEE) alone or CEE plus medroxyprogesterone acetate (MPA) — might occur in older women. Because the number of younger women with CHD events was small, the WHI researchers pooled data from both arms of the trial, encompassing a total of 27,347 women aged 50 to 79 who were randomized to CEE or CEE/MPA (depending on uterine status) or placebo.

There was a slight, nonsignificant trend toward decreased CHD risk with HT use (compared with placebo) among younger women and those closer to menopause. For example, there was an absolute decrease of 6 CHD events per 10,000 person-years in women within 10 years of menopause, compared with an absolute increase in risk of 17 events for women 20 or more years since menopause, and a decrease of 2 events per 10,000 person-years for women aged 50 to 59, compared with an increase of 19 events for women aged 70 to 79. The trend toward decreased CHD risk in the early years after menopause was driven mainly by event rates in the CEE-alone arm (and not the CEE/MPA arm). Risk for stroke increased significantly across all categories of age and time since menopause (absolute increase, 9 events per 10,000 person-years).

Reference

Rossouw JE et al. Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause. JAMA 2007 Apr 4; 297:1465-77.

Does Aspirin Lower Mortality in Women?

Journal Watch May 1, 2007, Vol. 27, No. 9

***Bottom Line:** In this large observational study, aspirin use was associated with significant reductions in cardiovascular and cancer deaths in women. In contrast, aspirin did not reduce cardiovascular mortality or a combined cardiovascular endpoint in the previously published Women's Health Study (a randomized trial of 40,000 women with 10 years of follow-up; Journal Watch Mar 18 2005), but it did confer a small reduction in stroke. An accompanying editorial notes that residual confounding could explain the positive results of the current study and believes that they should not trump the results of the more rigorous primary prevention clinical studies. Although the controversy will persist, the cumulative evidence fails to support routine use of aspirin for primary prevention in women.*

The controversy continues about whether aspirin should be prescribed for primary prevention of cardiovascular disease (CVD) and cancer in women. Researchers evaluated the risk for death from CVD or cancer among 79,439 women (mean age, 46; 97% white) in the prospective Nurses' Health Study. Participants were followed biennially and classified according to aspirin use.

During 24 years of follow-up, 6460 deaths were attributed to CVD or cancer. In multivariate analyses, the risks for death from CVD or cancer were significantly lower among current users of aspirin than among women who never used aspirin regularly (relative risks, 0.62 and 0.88, respectively). The association between aspirin use and lower cardiovascular mortality was evident within the first 5 years of use. The association between aspirin and lower cancer mortality was not evident until after 10 years of use.

Reference

Chan AT et al. Long-term aspirin use and mortality in women. Arch Intern Med. 2007 Mar 26;167562-72.
Baron JA. Can aspirin keep mortality at bay? Arch Intern Med 2007 Mar 26; 167:535-6.

Rosiglitazone May Increase Risk for Myocardial Infarction

Journal Watch June 15th, 2007, Vol. 27, No. 12

Bottom Line: This meta-analysis has several methodologic limitations, acknowledged by the authors and editorialists; nonetheless, the results alert us to the possibility that rosiglitazone may increase risk for coronary events. A key question is whether the new findings represent a "class effect" of all thiazolidinedione drugs; perhaps tellingly, another thiazolidinedione (muraglitazar) was associated with increased cardiovascular morbidity (Journal Watch Nov 29 2005) and was not marketed in the U.S.

For now, clinicians have several options. One is to stop rosiglitazone and consider other drug classes, if necessary. A second option is to substitute pioglitazone (Actos), the other thiazolidinedione available in the U.S. This drug was associated with a small reduction in a composite of death, MI, and stroke (but an increase in heart failure) in a recent trial (Journal Watch Nov 8 2005) and is associated with better lipid profiles than rosiglitazone. With this option, patients should understand that a comprehensive analysis of pioglitazone's effect on coronary events has not been undertaken. A third option is to continue rosiglitazone in patients who appear to have benefited from it, as long as patients understand that MI risk may be increased and that alternative treatments are available. The FDA has issued a safety alert on rosiglitazone.

Rosiglitazone (Avandia) is a thiazolidinedione drug used to treat type 2 diabetes. While this drug is known to precipitate congestive heart failure, its effect on coronary events is unclear. This meta-analysis of 42 randomized published and unpublished trials examined the effect of rosiglitazone on myocardial infarction and cardiovascular death. The trials included 28,000 patients, generally lasted 6 to 12 months, and compared rosiglitazone with other glucose-lowering drugs or placebo.

Overall, the incidence of MI was about 0.6%, and the incidence of cardiovascular death was about 0.3%. Rosiglitazone was associated with a significantly increased risk for MI, compared with risk among controls (odds ratio, 1.43; P=0.03). In addition, an increased risk for cardiovascular death in the rosiglitazone group almost reached statistical significance (OR, 1.64; P=0.06).

References

Nissen SE and Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. N Engl J Med 2007 Jun 14; [e-pub ahead of print].

Psaty BM and Furberg CD. Rosiglitazone and cardiovascular risk. N Engl J Med 2007 Jun 14; [e-pub ahead of print].

Adding Inhaled Steroids and Long-Acting B-Agonists to Tiotropium for COPD

Journal Watch May 1, 2007, Vol. 27, No. 9

Bottom line: This relatively small study cannot answer all questions about inhaled therapies for COPD. But its findings are consistent with those of other studies suggesting that the combination of long-acting ß-agonists and inhaled steroids confers benefit — in this case, when added to a long-acting anticholinergic bronchodilator.

Recent studies have suggested possible harm from long-acting ß-agonists, but possible benefit from the combination of ß-agonists and inhaled steroids (Journal Watch Dec 28 2006 and Feb 21 2007). This study, sponsored by the Canadian Institutes of Health, examined the treatment outcomes of 449 patients with moderate or severe chronic obstructive pulmonary disease; the patients all received tiotropium and were randomized to receive placebo, inhaled salmeterol, or fluticasone–salmeterol for 1 year.

Similar proportions of patients in all three groups (60%–65%) had COPD exacerbations, which were defined as a sustained worsening of respiratory condition requiring steroids or antibiotics. However, the tiotropium/fluticasone–salmeterol group (but not the tiotropium/salmeterol group) had significantly greater improvements in FEV1 and a lower rate of hospitalization than the tiotropium/placebo group (incidence rate ratio, 0.53). Furthermore, compared with the tiotropium/placebo group, the other two groups experienced significantly greater improvements in health-related quality of life. Rates of adverse events and deaths were similar in the three groups.

References

Aaron SD et al. Tiotropium in combination with placebo, salmeterol, or fluticasone–salmeterol for treatment of chronic obstructive pulmonary disease. A randomized trial. Ann Intern Med 2007 Feb 19; [e-pub ahead of print].

etc

evidence that counts

Reducing the Intensity of Treatment in Mild Asthma

Journal Watch June 15th, 2007, Vol. 27, No. 12

Bottom Line: These important trials demonstrate the feasibility of step-down therapy in patients whose mild persistent asthma is well controlled with standard twice-daily inhaled corticosteroids. An objective of this research is to minimize cumulative lifetime exposure to inhaled steroids, which may have systemic effects after years of use. The first trial shows that once-daily montelukast or a once-daily combination of an inhaled steroid plus salmeterol are both reasonable alternatives (although treatment failures occurred somewhat more frequently with montelukast). In the second trial, symptom-driven inhaled corticosteroids worked as well as daily therapy in patients with mild asthma.

Many patients with mild asthma take standard daily doses of inhaled corticosteroids indefinitely. Two new industry-supported, placebo-controlled, randomized trials — each with about 500 participants whose mild asthma was controlled with twice-daily inhaled steroids — show that "step-down" therapy may be reasonable for such patients.

One study compared twice-daily inhaled steroid therapy with once-daily oral or inhaled alternatives. Patients received one of three treatments: inhaled fluticasone (Flovent Diskus, 100 µg), twice daily; combined fluticasone/salmeterol (Advair Diskus, 100/50 µg), once daily in the evening; or oral montelukast (Singulair), once daily. At 16 weeks, treatment failure (an endpoint that included several clinical and spirometric outcomes) had occurred in 20% of patients in each inhaled-therapy group and in 30% of montelukast patients, a significant difference. This difference reflected primarily spirometric outcomes, and not differences in need for systemic steroids or urgent asthma care.

The second study examined the relatively novel idea that as-needed inhaled steroids might be as effective as daily maintenance therapy. Patients received one of four treatments: twice-daily inhaled beclomethasone (250 µg) with as-needed albuterol; twice-daily combined beclomethasone/albuterol, with as-needed albuterol; the same beclomethasone/albuterol combination, but only as needed; and as-needed albuterol only. At 6 months, the primary outcome — morning peak expiratory flow rate — was similar in the twice-daily beclomethasone and the as-needed beclomethasone/albuterol groups, and was significantly higher in both groups than in the as-needed albuterol group. Both twice-daily beclomethasone and as-needed beclomethasone/albuterol were associated with fewer exacerbations than as-needed albuterol.

References

The American Lung Association Asthma Clinical Research Centers. Randomized comparison of strategies for reducing treatment in mild persistent asthma. N Engl J Med 2007 May 17; 356:2027-39.

Papi A et al. Rescue use of beclomethasone and albuterol in a single inhaler for mild asthma. N Engl J Med 2007 May 17; 356:2040-52.

Rosiglitazone May Reduce Bone Density

Journal Watch May 15th, 2007, Vol. 27, No. 10

Bottom Line: These findings suggest that rosiglitazone may accelerate bone loss in postmenopausal women. It will be important to determine whether the changes noted in this short-term study persist with longer-term treatment. The results are particularly worrisome because rosiglitazone was associated with a significant increase in fractures, compared with metformin and glyburide, in a recent 4-year diabetes study (N Engl J Med 2006; 355:2427). Until more data become available, clinicians should think about the possibility of accelerated bone loss when considering the use of rosiglitazone (and possibly pioglitazone).

The insulin-sensitizing drugs rosiglitazone and pioglitazone lower glucose in diabetic patients by activating peroxisome proliferator-activated receptor- (PPAR-). These receptors are also found in bone, and animal research suggests that PPAR- activation may induce bone loss by suppressing osteoblast function. In this randomized study from New Zealand, researchers evaluated the effect of rosiglitazone on bone density in humans.

Fifty healthy postmenopausal women (mean age, 68) received either rosiglitazone (8 mg daily) or placebo for 14 weeks. Mean serum levels of two markers of bone turnover (osteocalcin and procollagen type I N-terminal propeptide) decreased significantly in the rosiglitazone group, but not in the placebo group. Moreover, at 14 weeks, mean bone density at the hip had decreased by about 2% in the rosiglitazone group but remained unchanged in the placebo group, a significant difference.

Reference

Grey A et al. The peroxisome proliferator-activated receptor-agonist rosiglitazone decreases bone formation and bone mineral density in healthy postmenopausal women: A randomized, controlled trial. J Clin Endocrinol Metab 2007 Apr; 92:1305-10.

How Long to Treat Venous Thromboembolism

Journal Watch May 15th, 2007, Vol. 27, No. 10

Bottom Line: In this study, 3 months of therapy for venous thromboembolism was as efficacious as 6 months and carried a significantly lower risk for hemorrhage. However, the study included patients with identified transient risk factors as well as patients with no evident cause of VTE. Three months of treatment seems sufficient for patients with transient risk factors; however, for those with idiopathic VTE, other studies have suggested that the benefits of more prolonged anticoagulation may outweigh the risks (Journal Watch Apr 2 1999). A recently published guideline supports this view (Journal Watch Feb 13 2007).

While it is generally accepted that patients with venous thromboembolism (VTE) should receive anticoagulation for at least 3 months, there is continuing debate about whether to continue treatment beyond that time. In this study, 749 adults with proven or highly probable VTE (pulmonary embolism or deep venous thrombosis) were recruited from 46 U.K. hospitals. None of the patients had an identified persistent predisposition to VTE; about half had transient reversible risk factors, and the other half had no evident cause. They were randomized to receive standard anticoagulation for either 3 months or 6 months (target INR, 2.0 to 3.5).

Patients were followed for 12 months. During treatment, VTE extended, failed to resolve, or recurred in 6 patients in the 3-month group and 10 in the 6-month group. After treatment, 23 such events occurred in the 3-month group and 16 in the 6-month group. The combined rate of fatal and nonfatal thrombotic events was 8% in each group. No major hemorrhages occurred in the 3-month group, but eight occurred in the 6-month group.

References:

Campbell IA et al. Anticoagulation for three versus six months in patients with deep vein thrombosis or pulmonary embolism, or both: Randomised trial. BMJ 2007 Mar 31; 334:674.

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ACUTE POST-STREPTOCOCCAL GLOMERULONEPHRITIS

In her UPFRONT article on infectious disease patterns (BPJ Issue 5 p4), Professor Diana Lennon noted the fact that Post-streptococcal glomerulonephritis remains an issue in the upper north island. This article explores its recognition and management.

Post-streptococcal glomerulonephritis persists as a problem in the upper North Island

Although rare, acute post-streptococcal glomerulonephritis (APSGN) is the most common glomerulonephritis affecting children[1,2] particularly those aged 2–12 years.

APSGN is typically a complication of group A streptococcal infection, usually originating from the skin (impetigo, infected scabies) or occasionally, the throat. It was first recognised in the 18th century associated with the convalescence period of scarlet fever.[3] There are links today with overcrowded living conditions, low socio-economic status and areas of close contact e.g. schools and daycare centres. Countries with tropical climates, where skin infections are common, have higher incidence.[3] In New Zealand, the upper North Island has the highest rates.

CLINICAL FEATURES VARY WITH SEVERITY OF THE ILLNESS

There is a latent period between the streptococcal infection and the onset of APSGN — generally 3–4 weeks after skin infection and 1–2 weeks after throat infection, so history taking needs to reflect this.

Presenting symptoms vary, depending on the severity. The classic clinical features are gross haematuria (30–50%)[1], oedema (60–70%)[3] and hypertension (60–80%)[1,3] but cases may range from those with asymptomatic microscopic haematuria, who never reach medical attention, up to the 5% who have hypertensive encephalopathy with seizures, confusion and coma.[1] The dark urine, typical of the condition, may not be noticed by children. Patients may report general malaise, anorexia, nausea, vomiting, headache or pain in the abdomen or back.[2]

On examination, signs are related primarily to volume overload — facial oedema, especially periorbital, generalised oedema or even signs of congestive heart failure (raised JVP, enlarged liver, crepitations in lung bases). Patients may be pale and could have residual signs of the contributing skin infection. BP should be checked.

Urinalysis can show frank blood, red cell casts, leucocytes and proteinuria. Throat swabs are unhelpful as they are rarely positive.[1] Further lab tests may show raised antistreptolysin-O (ASO), decreased complement levels, increased urea and mild normochromic, normocytic anaemia due to haemodilution.[1,2,3]

www.bpac.org.nz keyword: **"Post Strep"**

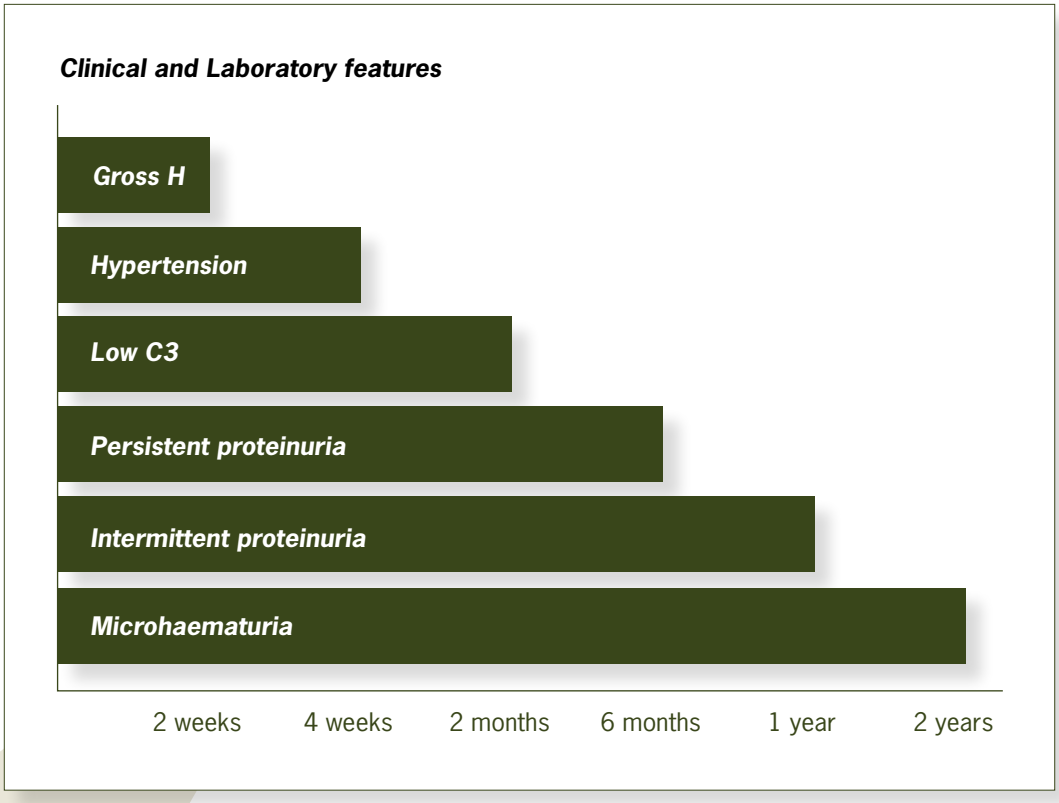
APSGN is usually self limiting but supportive care and careful follow up are required

There is no specific treatment. APSGN is self-limiting – supportive care is needed with the major aims being to control oedema and hypertension, if present. Salt and water restriction may be beneficial but referral to hospital may be required for accurate fluid and electrolyte management, and treatment of hypertension with medication (iv frusemide, isradapine, labetalol or others).[1,3]

Antibiotics can be given to reduce infectivity but they do not help in the actual treatment of APSGN.[1] Family members or other contacts are sometimes given prophylactic antibiotics.

The majority of children will recover spontaneously over 2–3 weeks with resolution of all abnormal symptoms and signs (see Figure 1). Microscopic haematuria can, however, take up to 2 years to resolve.[1] Chronic renal failure is a rare complication in children but it is suggested that urinalysis and BP be rechecked at 3–6 monthly intervals.

Figure 1: Time course to resolution of APSGN[1]



C3 = Complement Protein, Gross H = Gross Haematuria

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3. Geetha D. Glomerulonephritis, Poststreptococcal. 2006. Available on line at http://snipurl.com/1o7v6 Accessed July 2007

Bandolier

Independent evidence-based thinking about health care

Moderate activity reduces diabetes risk

Bandolier 159, Volume 14, Issue 5 *www.ebandolier.com*

Hands up everyone who knows what a MET is? Answer is a Metabolic Equivalent Task, which is the amount of energy expended in performing various activities compared with sitting down doing nothing. It is commonly used in medicine to express metabolic rates measured during a treadmill test. Two definitions of the MET are used, essentially equivalent:

1 MET is equivalent to a metabolic rate consuming 3.5 millilitres of oxygen per kilogram of body weight per minute.
1 MET is equivalent to a metabolic rate consuming 1 kilocalorie per kilogram of body weight per hour.

In more common parlance, a slow walk or promenade is equivalent to about two METs, a brisk walk about four METs, and gym work more like six METs and above. A new systematic review of observational studies links moderate periods of moderate intensity exercise with reduced risk of developing type 2 diabetes in adults [1].

Systematic review

The review sought observational studies up to March 2006 associating moderate exercise with incidence and prevalence of type 2 diabetes. Moderate intensity exercise was that with a MET score of 3-6.

Results

Ten cohorts were found with just over 300,000 persons of both sexes aged mostly between their late-30s to early-60s. Follow up in these studies tended to be long with seven of the studies longer than seven years, and the shortest four years. The mean follow up period, weighted by study numbers, was 8.2 years.

In most of the studies exercise included walking, but cycling and light gardening were also included. The definition of diabetes varied, including glucose tolerance test results, the use of primary care or national registers, and, mostly, by self-report of a diagnosis by a physician, usually validated.

There were 9,400 cases of diabetes, a prevalence of 3.1%. This meant that type 2 diabetes occurred in 0.4% of these older adults every year, a risk of 1 in 263 per year. Compared with sedentary persons, the risk was substantially lower in people who took moderate exercise (by about 30%), whether all activity or only brisk walking was used in the tests of association (Table 1). Because people who take no exercise tend to be fatter, there was adjustment of risk for BMI, and here the reduction of risk was about 17%.

Comment

The amount of exercise examined in this paper was not heroic, amounting to no more than about 2.5 hours of brisk walking every week. The message is that to help avoid developing diabetes, you don't necessarily have to go into the gym, just walk down there and then walk back again. Given that walking does other good things positively affecting heart, and circulation, and bone, and balance, and weight, this is something of a no-brainer. Diabetes is worth avoiding.

References:

1 CY Jeon et al. Physical activity of moderate intensity and risk of type 2 diabetes. Diabetes Care 2007 30: 744-752.

Table 1: Evidence associating physical activity and walking with reduction in risk of developing type-2 diabetes

Observation	Studies	People	Relative risk	Percent risk reduction
Total physical activity				
Development of type 2 diabetes, no BMI adjustment	9	213,314	0.69 (0.58 to 0.83)	31
Development of type 2 diabetes, with BMI adjustment	9	295,231	0.83 (0.76 to 0.90)	17
Walking				
Development of type 2 diabetes, no BMI adjustment	4	152,698	0.70 (0.58 to 0.84)	30
Development of type 2 diabetes, with BMI adjustment	4	234,615	0.83 (0.75 to 0.91)	17

Occult blood tests for colorectal cancer?

Bandolier 149, Volume 13, Issue 7 *www.ebandolier.com*

People get hot under the collar when it comes to screening, and screening for cancer in particular. Two general criticisms are often made of screening trials. First that the design of many studies was compromised, resulting in possible bias, with better studies giving less encouraging results (as for breast cancer screening in Bandolier 72). The other is that results of screening are provided in terms of death reduction for the cancer being screened, not all cause mortality.

For instance, a Cochrane review [1] of occult blood testing for colorectal cancer screening found that biannual occult blood screening reduced colorectal cancer deaths by about 20%, preventing about one death per year per 10,000 people. Comments on that review include the criticism of the failure to analyse overall deaths, but that has now been done [2], and provides interesting reading.

Meta-analysis

The original Cochrane review included four randomised trials, but did not report overall deaths. Two have now published more follow up, allowing the analysis to be done.

Results

Three of the four trials in the original review provided data, on 245,000 people, with 2.8 million years of follow up, and using biannual screening. There were 2,148 colorectal cancer deaths, and 65,000 deaths in total.

The death rate from colorectal cancer was about 1 in 100 people over the whole period, or 1 in 1,250 per year. As in the Cochrane review, colorectal cancer deaths were reduced with screening, though the absolute effect was small, almost 10,000 people needing to be screened for one year to prevent a single colorectal cancer death. Table 1 shows the analysis as per patient, and per patient year.

The death rate from all causes was 1 in 4 over the whole period, about 1 in 40 per year. Neither analysis by patient nor by per patient year showed any difference between the screened and the control population in terms of overall mortality.

Comment

The corollary of all this was that screened persons died more often from other causes, significantly so. How could such a result be possible? It is unlikely that biannual occult blood testing would, in itself, be a cause of death.

The most obvious point is that only 1 death in 30 was a colorectal cancer death. Moreover, the difference between screened and non-screened people was only 1 death in every 300 total deaths. How likely is it, then, that a difference this small would be seen in an analysis of overall mortality. The answer is that it is vanishingly small, even with large numbers of patients observed over many years; it would be washed out by the random play of chance.

It may also just be possible that the fact of screening could give a false sense of health security, with a greater tendency to less healthy lifestyle. Another possibility would be that these open trials could be open to bias, with more intensive investigation for people being screened.

The final word, though, should be on the balance between benefit and risk. We know that over 80% of positive tests were false; the tests were positive but patients did not have cancer [1]. Those patients had the stress of receiving a positive test, and underwent further examination, which is not entirely benign. In 10,000 people an estimated 60-280 would have at least one colonoscopy, with 2-4 perforations or haemorrhages.

Some of these will be fatal. So for occult blood screening for one year, the chance of avoiding dying from colon cancer is 1 in 1,200, while the risk of a perforation or haemorrhage is 1 in 3,000. Maybe it is better and more productive to get people to eat more fibre, especially when we can be pretty sure that screening in practice is unlikely to be as thorough as screening in trials.

Reference:

1 BP Towler et al. Screening for colorectal cancer using the faecal occult blood test, Hemoccult. Cochrane Database of Systematic Reviews issue 2, 1998.

2 P Moayyedi, E Achkar. Does fecal occult blood testing really reduce mortality? A reanalysis of systematic review data. American Journal of Gastroenterology 2006 101: 380-384.

Table 1: Meta-analysis of colorectal cancer deaths and death from all causes, with biannual occult blood screening

Analysis	Number of patients/ patient years	Percent deaths		Relative Risk (95% CI)	NNT to prevent one death from colorectal cancer
		Screening	Control		
Colorectal cancer deaths (n=2,148)					
Per patient	245,217	0.82	0.94	0.87 (0.80 to 0.95)	830 (520 to 2,200)
Per patient per year	2,757,795	0.083	0.073	0.87 (0.80 to 0.95)	9,400 (5,800 to 25,000)
Deaths from all causes (n=64,949)					
Per patient	245,217	26.5	26.5	1.00 (0.99 to 1.01)	not calculated
Per patient per year	2,757,795	2.36	2.35	1.00 (0.98 to 1.02)	not calculated

How good are trials and interventions in knee arthritis?

Bandolier 155, Volume 14, Issue 1 *www.ebandolier.com*

The reason we do systematic reviews is not only to evaluate how good an intervention may be, but also to examine the clinical utility of the trials we do. The bottom line we have to recognise is that almost all drug trials are performed for some registration purpose, and that the requirements of drug registration are far removed from what is needed in clinical practice.

Those of a more practical bent have therefore either to throw up their hands and walk away from the evidence that exists or to look at that evidence with a cold and fishy eye and criticise constructively. A meta-analysis of interventions for knee osteoarthritis provides an excellent example [1].

Systematic review

The review had a wide search strategy that identified randomised, blinded, placebo-controlled trials of interventions in knee arthritis. The inclusion criteria included use of established diagnostic criteria, including symptom duration of more than three months, and an outcome measure of pain intensity both initially and within four weeks scored on WOMAC pain subscale or 100 mm VAS for global or walking pain.

The main analysis was for the difference between active and placebo during weeks 1-4, using the point with the maximum effect.

Results

The authors found 65 trials with information on 14,060 patients (Table 1). Though trials differed in number and number of patients for each intervention, they were generally similar in terms of the initial pain intensity and mean measurement time for maximum effect, though this was somewhat longer for glucosamine and chondroitin. All trials except two for intra-articular glucocorticoid were of adequate quality to avoid most sources of bias (scoring 3 or more on a five point scale for quality).

What the results show is that some interventions (intra-articular glucocorticoids, topical NSAIDs, opioids, and oral NSAIDs) provide pain relief equivalent to 10-15 mm on a 100 mm VAS scale (Table 1), while others (glucosamine, chondroitin, paracetamol) provide under 5 mm.

Comment

What conclusion can we draw from this? One, which the authors draw, is that perhaps a 10 mm difference over placebo just isn't good enough, and they give some reasons for why we might think that. In essence, then, the conclusion is that the interventions are relatively ineffective.

An alternative view, provided by an accompanying editorial [2], is that common experience is that most of these interventions are known to work well for individual patients in clinical practice. Perhaps, then, the problem is that the trials are unable to capture that benefit, especially in terms of averages – when few patients are average. Here the advice is to question how we do trials or analyse them, and to perhaps consider blaming trial design rather than intervention efficacy.

This is exactly what we want from systematic review: argument, challenge, and new thinking. This is a particularly good example, because it will challenge guidelines, especially in the UK, which rate paracetamol as the first intervention to use, and relegates topical NSAIDs back to the shelf. The evidence makes it hard to justify that view: more thinking needed.

References:

1 JM Bjordal et al. Short-term efficacy of pharmacotherapeutic interventions in osteoarthritic knee pain: a meta-analysis of randomised placebo-controlled trials. European Journal of Pain 2007 11: 125-138.

2 H McQuay, A Moore. Utility of clinical trial results for clinical practice. European Journal of Pain 2007 11: 123-124.

Table 1: Results for short-term interventions for knee osteoarthritis. Best mean difference was the greatest difference between intervention and placebo in the period 1-4 weeks

Intervention	Number of		Mean initial pain (mm VAS)	Mean time of measurement (weeks)	Best mean difference from placebo (mm VAS)
	Trials	Patients			
Intra-articular glucocorticoid (methylprednisolone 40 mg or equivalent)	6	221	57	1.5	15
Topical NSAID	9	749	55	1.6	12
Opioids (30 mg morphine sulphate or equivalent)	6	1057	73	2.8	11
Oral NSAIDs (diclofenac 100 mg or equivalent)	27	9964	64	2.3	10
Glucosamine sulphate (1500 mg)	7	401	58	4.0	5
Chondroitin sulphate (800 mg)	6	362	51	3.6	4
Paracetamol (4000 mg)	4	1306	55	1.3	3

Prevalence of aspirin resistance

Bandolier 157, Volume 14, Issue 3 *www.ebandolier.com*

Aspirin probably works by irreversibly inactivating cyclooxygenase-1 in platelets, which means that they cannot produce thromboxane A_2 with a consequent reduction in aggregation. It is worth noting that while NSAIDs also inhibit cyclooxygenase-1, this inhibition is reversible, and so any effect wanes as drug levels diminish, with only a transient reduction, if any, in platelet aggregation.

Aspirin resistance is a simple description of a complex phenomenon, namely the persistence of platelet aggregation despite use of aspirin. That simple statement is deceptive, however, because there is no agreed definition of aspirin resistance. A variety of laboratory tests are used to measure aspirin resistance.

So a moment's reflection demonstrates that trying to measure the prevalence of aspirin resistance is not going to be straightforward. Apart from differences between individuals (due to pharmacokinetic or genomic issues), there will be issues of dose of aspirin, co-medication, medical condition, as well as method of measurement and definition of resistance to contribute to differences in measured prevalence. All of which is made plain by a systematic review [1] that tries to pull some of this together.

Systematic review

The systematic review used a heroic series of searches to find studies. To be included a study had to report the prevalence of aspirin resistance from a survey or cohort study with consecutive patients, have a clear definition of aspirin resistance, in well described patients using aspirin for secondary prevention of cardiovascular events.

Stratified analyses were planned by dose of aspirin and laboratory method used to measure aspirin resistance, according to the populations studied (post myocardial infarction, stroke or TIA, and revascularisation, or other).

Results

The review included 34 full articles and eight abstracts, but we are not told the number of patients studied in total, the number of patients in each study, nor the prevalence in each study. All we have is a series of results of pooled analyses, and it is clear that some individual studies must have reported on more than one group of patents, dose of aspirin, and method of analysis.

Overall aspirin resistance was 24%, with prevalence in individual studies ranging from 0% to 57%. Figure 1 shows the 95% confidence intervals for prevalence of aspirin resistance according to aspirin dose, after some statistical adjustments. There was little difference in aspirin resistance prevalence between different patient groups, or by different methods of measurement, with one exception. Five studies using arachidonic acid as an agonist in light transmission aggregometry reported lower prevalence values of 1% to 12% (average 6%).

Comment

It is a bit of a shame that there is some opaqueness about the review, and this is one of the times to bemoan the lack of accompanying tables with information on the individual studies. If they were there, we might do some sums of our own without retrieving 42 papers and starting from the beginning.

But that is a quibble stemming from the importance of the paper. The authors do their weighting based on patient numbers.

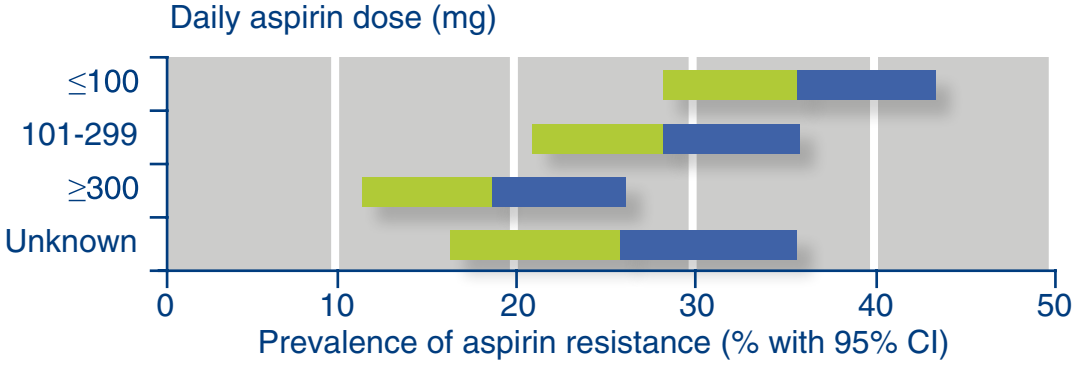
Perhaps the take-home message is that a prevalence of aspirin resistance of 1 person in 4 might be a worst-case scenario. For instance, we have the problems of definition and method, and it may well be that more conservative definitions and defined methods would reduce rather than increase the prevalence. Again, we have no idea about compliance: we know from other sources that compliance with daily aspirin is often poor, and that would certainly contribute to higher apparent aspirin resistance.

These are details that will be sorted out in due course. What we can be pleased about is that this should be the first step on the path of individualising therapy (perhaps measuring resistance after starting at very low doses of aspirin) and improving cardiovascular outcomes.

Reference:

1 MM Hovens et al. Prevalence of persistent platelet reactivity despite use of aspirin: a systematic review. American Heart Journal 2007 153:175-181.

Figure 1: Prevalence of aspirin resistance (failure to inhibit platelet aggregation) with daily aspirin dose



Dear Dave

Dave and other members of the bpac[nz] team answer your clinical questions

Can **SUMATRIPTAN** be used safely with **SSRIs**

Many drug interaction programmes and texts warn against concurrent use or advise caution when sumatriptan is used with an SSRI (fluoxetine, paroxetine or citalopram). What is the basis of this interaction and can these drugs be used safely together?

Migraine and depression are common conditions and often co-exist so there is a significant potential for these drugs to be used together. Sumatriptan is a serotonin agonist and the SSRIs inhibit the re-uptake of serotonin therefore there is a theoretical potential for the drugs to increase serotonergic activity leading to serotonin syndrome. Serotonin syndrome comprises a cluster of symptoms, including altered mental status, autonomic instability, and neuromuscular abnormalities. However, milder symptoms of serotonin 'overload' may occur without the full blown syndrome.

There have been a few reports of symptoms of serotonin syndrome when sumatriptan has been given together with an SSRI.[1] Symptoms attributed to increased serotonergic activity include, restlessness, anxiety, weakness, myoclonus, loss of co-ordination, tachycardia and sweating.[2] Postmarketing surveillance[1,3] has also identified cases of serotonin syndrome but such reports appear to be very rare.

Several studies have looked at the evidence of safety for the use of Sumatriptan with an SSRI. A large prospective study followed over 12,000 patients who were using subcutaneous sumatriptan for migraine. Almost 1800 of these patients also took an SSRI during the study and there was no increase in adverse effects within 24 hours of taking sumatriptan.[4]

www.bpac.org.nz keyword: "sumatriptanssri"

Who is Dave?

Pharmaceutical Programme Manager Dave Woods is a graduate of Manchester University (B.Sc. [Hons]) and the University of Otago (MPharm). Dave has extensive experience in hospital pharmacy, drug information, rational use of drugs and quality assurance. He has published on a range of subjects and holds editorial positions for several international journals.

If you have a clinical question email it to **dave@bpac.org.nz**

If you have a clinical question email it to

dave@bpac.org.nz

Concurrent use of triptans (drugs in the same group as sumatriptan) and SSRIs is widespread and there has been no epidemic of the syndrome in practice even though almost 50,000 people in the USA are taking these drugs at the same time.[5] Our analysis of Pharmhouse data using patient NHI numbers indicates that approximately 10% of people taking sumatriptan (about 1000) are also taking an SSRI.

In other countries, up to six different triptans are available, e.g. zolmitriptan, almotriptan and naratriptan. Some of these may have a greater potential to interact with SSRIs as they have different pharmacokinetic properties. In New Zealand, only sumatriptan and rizatriptan (not subsidised) are available but there is no indication that the latter has a different potential to interact than sumatriptan. Venlafaxine (a serotonin and noradrenaline re-uptake inhibitor) also has the potential to interact with sumatriptan and the same cautions apply, as with the SSRIs.

Other agents which increase serotonin levels, may also interact with sumatriptan. One such agent is St John's Wort which is freely available without prescription and in supermarkets. Authorities in the UK and Sweden have advised that St John's Wort should not be used by people taking triptans.[6]

In summary, there have been reports of serotonergic symptoms and serotonin syndrome when sumatriptan and SSRIs have been used together. In practice, such reports appear to be rare and the drugs can be used safely together in the vast majority of people. However, all people taking this combination should be advised to report symptoms of increased serotonerigic activity (e.g. restlessness, tremor, sweating, shivering) particularly with initiation of treatment or with dose increases. The same cautions apply to the use of venlafaxine and sumatriptan. It is advisable to avoid St John's Wort in people taking sumatriptan or an SSRI and especially if they are taking both.

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Dear Dave

Dave and other members of the bpac^{nz} team answer your clinical questions

Can you ever use **BETA-BLOCKERS** in someone with a history of **ASTHMA**

Media attention has focused recently on the tragic case of a fatal reaction to propranolol, used for migraine in a 37-year-old woman with a history of asthma.

GPs providing advice in this case expressed their unanimous opinion that it was inappropriate to prescribe a beta-blocker to an asthmatic.[1] Drug manufacturers[2] and almost all commonly used texts say that their use is contraindicated in asthma.

The key point in this recent case was that the history of asthma was not obtained from the patient or the notes. The take home message primarily revolves around accurate history and note taking. The HDC commissioner commented that if the information needed is not available in the notes, it is vital that the doctor concerned obtain the relevant history from the patient. "Patients cannot be relied on to volunteer all relevant details, and indeed do not have the training and experience to know what may be important. They rely on their GP to elicit key information."[3]

The question remains though – can a person with asthma safely use a beta-blocker?

The answer is probably that some patients can sometimes safely take some beta-blockers, but this is not a good basis for safe prescribing!

In the 1960's, studies on earlier generations of beta-blockers, which were non-cardioselective, showed acute reductions in FEV1 and led to the recommendation that their use is contraindicated in asthma patients.[4,5] Propranolol is non-cardioselective, that is, it not only blocks beta-1 adrenoceptors but also beta-2 adrenoceptors in the smooth muscle of the airways, potentially leading to bronchospasm.[6]

Most of the recent studies and analyses have focused on the use of cardioselective beta-blockers because of their huge potential in the treatment of cardiovascular disease, particularly in COPD patients.[7,8] Both cardio-selective and nonselective beta-blockers have been shown to increase emergency department visits and hospitalisations in asthma patients while decreasing admissions for COPD patients.[9]

A recent article concludes "current evidence indicates that cardioselective beta-blockers are not contraindicated in patients with airways disease."[10] However, this statement is then followed by the advice that "it is still appropriate to apply certain provisos, which are themselves not evidence-based, to minimise the risk of adverse reactions". The authors also point out that conclusions drawn from meta-analyses apply to populations and not individuals.

There are varying opinions as to whether the contraindication is absolute. In general, beta-blockers, selective or non-selective, should not be used in people with asthma. However, if there is a compelling reason for prescribing a beta-blocker to a person with asthma, such as heart failure, then consultation with a respiratory specialist is recommended. Cardioselective beta-blockers may be used for people with COPD, if they do not have concomitant asthma.

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www.bpac.org.nz keyword: **"Beta-blockerAsthma"**

Correspondence

Microalbuminuria screen in patients on an ACE

Dear Editor,

Thank you for the informative collation of lab tests in diabetes – I read it with interest.

Can I question you over the suggestion of doing at least one microalbuminuria screen on each patient with diabetes each year in the pamphlet?

My understanding is that if the patient is either already on an ACE inhibitor (as this is the treatment if microalbumin +) or they have established microalbuminuria they do not need to be screened.

Can you verify this for me please as that has been my practice to date?

Thank you
David Zarifeh

Dr Rick Cutfield Diabetologist, responds...

I recommend annual screening of microalbumin despite use of an ACE inhibitor. Worsening microalbuminuria will trigger a response to watch blood pressure and glucose control more closely, perhaps adjusting the BP target downwards eg <120/80. It may also trigger a response to emphasise drug compliance.

It is also helpful to see stability or improvement of microalbumin levels while on treatment – to patient and doctors.

Microalbuminuria that steadily progresses to proteinuria should prompt consideration of a referral to diabetes or renal specialist.

Please note: If patients have microalbuminuria - aspirin and statins are mandatory to reduce cardiovascular risk.

Paracetamol in infants less than 2 months of age

Dear Editor,

I have not previously seen recommendations to avoid paracetamol use in infants under 2 months of age as stated in this review (BPJ 5 p24 "Safe Use of Paracetamol In Children"). Considering the relatively wide-spread use of paracetamol for infants receiving immunisations at 6 weeks, and extensive dosing information for infants under 2 months of age, could you please clarify why is such use "best avoided"?

My understanding was that glutathione conjugation is only one pathway for paracetamol clearance (besides the "toxic pathway") and there is apparently a greater degree of sulphation in children. It would seem a shame to unnecessarily avoid paracetamol use in infants having their "jabs" at 6-weeks.

Yours sincerely,
Robert Buckham
Christchurch Drug Information Service

Dr David Reith Paediatrician, reponds...

Paracetamol can be used for the treatment of pain and fever in infants less than 2 months of age. Although in the past paracetamol was used guardedly in this age group, there is recent data on pharmacokinetics, efficacy and safety in the neonatal age group.[1,2] Glucuronidation of paracetamol, the major pathway of elimination in older children and adults, appears to be reduced in neonates resulting in reduced clearance in this age group. This means that doses need to be given less frequently for the same effect, and also to avoid toxicity. Paracetamol toxicity has been described in neonates following excessive dosing and it is important to communicate dosing instructions clearly to parents and caregivers.[3] The BNF for children advises oral doses for term neonates of 20 mg/kg as a single dose, then 15–20 mg/kg every 6 to 8 hours as necessary, up to a maximum daily dose of 60 mg/kg.[4] Over 3 months of age, divided doses of up to 90 mg/kg/day may be given in otherwise healthy children.

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Frequency of testing in patients with diabetes

Dear Editor,

I was interested to get bpac report re. diabetes testing. Many of my diabetic patients are enrolled in a chronic care management scheme with the Counties Manukau DHB. They have minimal requirements for lab testing – these include;

- HbA1c at least every 3 months
- Lipids profile at least every 3 months
- Serum glucose at least every 3 months

These criteria (amongst many others) need to be met if we are to receive payment for managing these patients. If you think these tests are too frequent, I suggest you contact the DHB rather than the GP's who are obliged to order them.

Yours faithfully,
Dr John Allen

Dr Gary Sinclair (Clinical Director Primary Care and Chronic Care Management, Counties Manukau DHB) responds...

The Diabetes CCM programme was initially developed in 2001 based on an expanded version of the Chronic Care Model developed by Ed Wagner, using a Kaiser approach to delivery of service. As part of the delivery system redesign, information systems and decision support, CMDHB developed "templates" in locally used patient management systems for collection of the disease specific dataset for communication to a central "integrated care" server which collects data for decision support, exception reporting and general programme management.

At that time the national guidelines for diabetes and cardiovascular disease were in development, and so the clinical dataset (including required laboratory investigations) was derived on advice from a local programme disease specific advisory group (DSAG) which included physicians from both primary and secondary care in CMDHB.
Given that the CCM programme is targeted at high acuity patients (all patients have to satisfy entry criteria demonstrating poor control of clinical management indicators or signs of advanced end organ damage), and to facilitate ease of programme implementation, the DSAG advised on regular three monthly testing for HbA1c, serum creatinine and albumin-creatinine ratio, lipids being tested every six months.

With the release of national guidelines for the management of diabetes and cardiovascular disease, we noted some variance between guideline based "best practice" and the CCM programme requirements for some of our enrolled patients.

We are currently engaged in the process of integrating the CCM programmes for diabetes and cardiovascular disease, based on the current national guidelines and incorporating requirements for the "Get Checked 2" dataset. At this stage we anticipate migrating to the new platform early in 2008. The new programme will have the IT capability to advise on different management for different individuals (including laboratory investigations) based on individual patient scenarios.

The DSAG has discussed the present laboratory testing protocols, and support the best practice guidelines articulated by bpac[nz]. However in the interests of maintaining programme integrity, DSAG have advised that we continue collecting lab data at the afore mentioned intervals relying on the judgement of our clinicians regarding actual testing intervals until the decision support platform is deployed.

Send your letters to...

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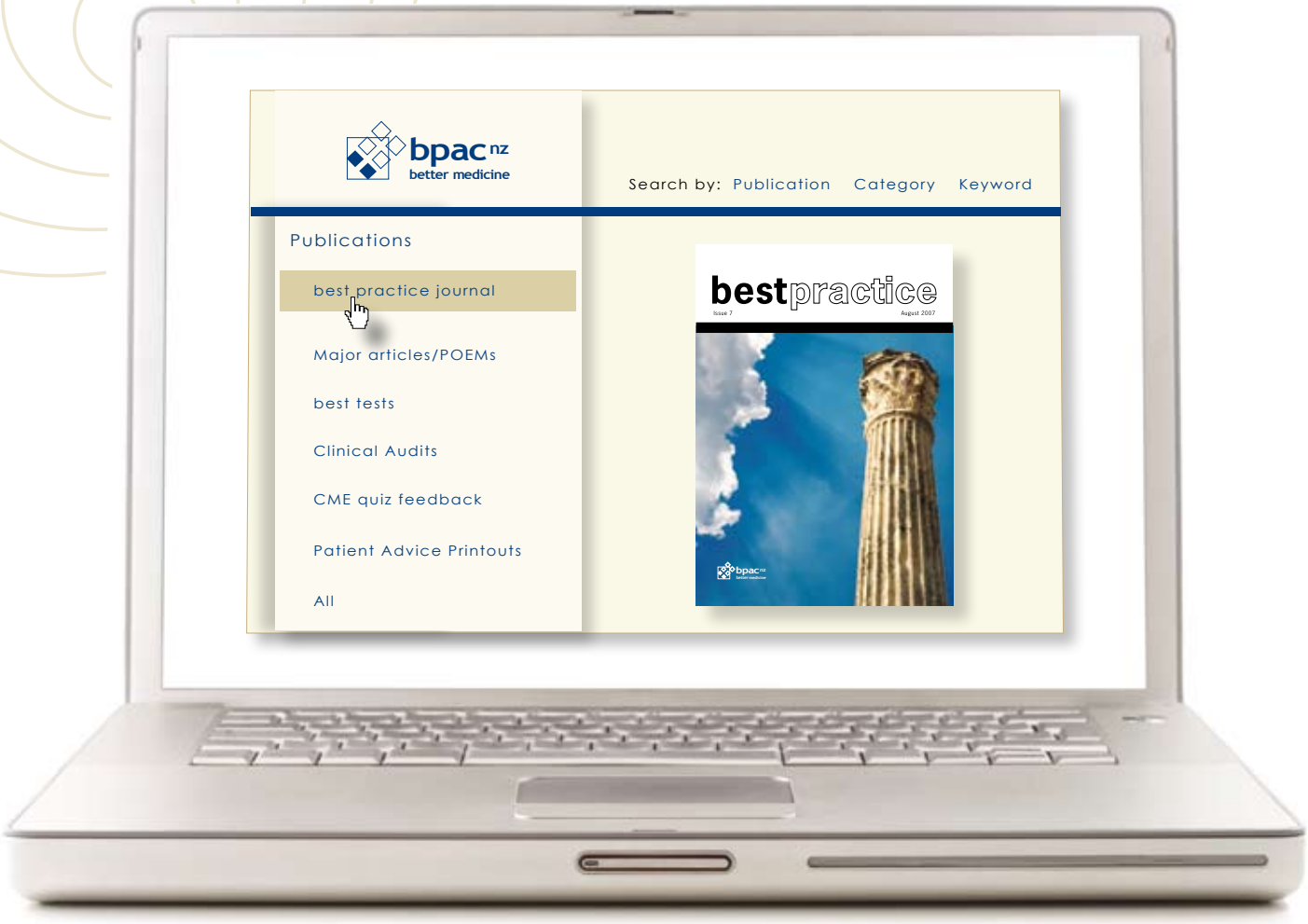

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