PERTUSSIS VACCINE IN PREGNANCY | TALKING ABOUT GOUT | ROLE OF ANKLE BRACHIAL PRESSURE INDEX

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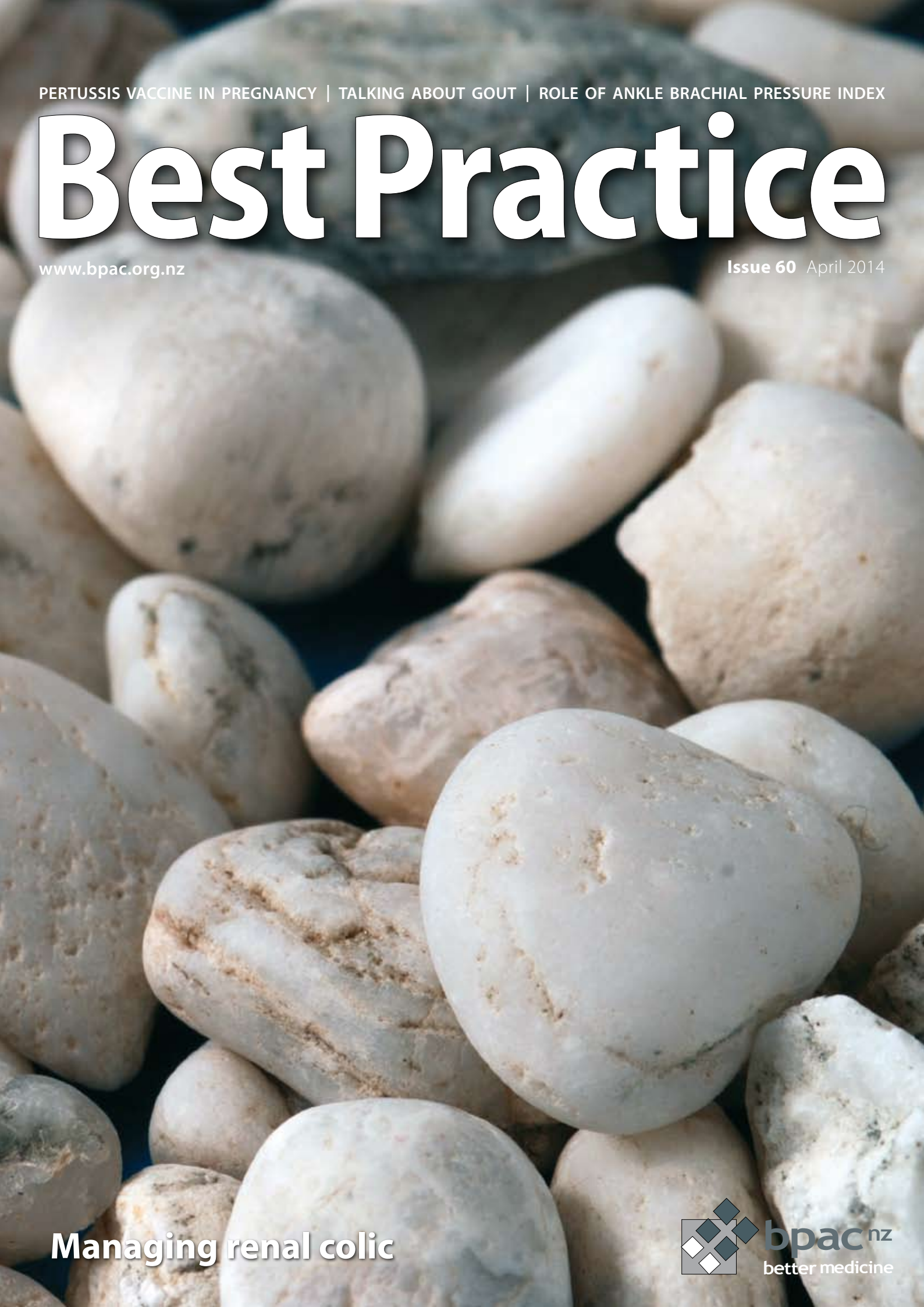

## Managing renal colic

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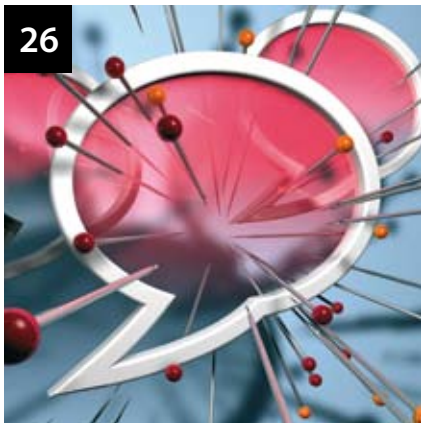
## CONTENTS

**Issue 60** April 2014

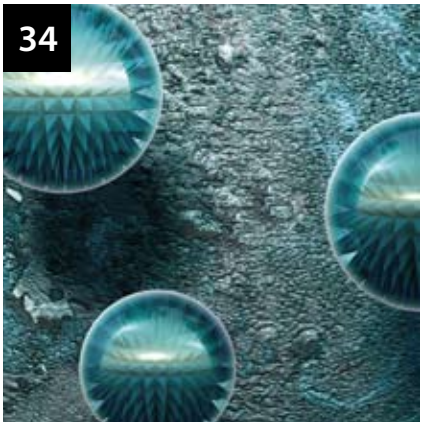



## CONTENTS

**Issue 60** April 2014





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# Azithromycin: use it wisely

*Growing use of azithromycin in New Zealand means that we are in danger of increasing bacterial resistance to macrolide antibiotics, as has been the case in other countries. Macrolides are particularly important in New Zealand given our high rates of pertussis and rheumatic fever. It is not too late to act; azithromycin should only be prescribed for specific indications to make sure it works when we need it the most.*

## Azithromycin is an effective antibiotic, but it's use must be preserved

Azithromycin is a macrolide antibiotic with a broad spectrum of activity. While azithromycin has a number of indications, infectious diseases experts recommend that in New Zealand, azithromycin only be used in the following situations:*

- **First-line indications:** pertussis in children, chlamydia, gonorrhoea (for treatment of presumed co-infection with chlamydia), acute non-specific urethritis
- **Second-line indications:** pelvic inflammatory disease as an alternative to doxycycline when chlamydia is present, pertussis in adults when erythromycin is unable to be tolerated

* bpac$^{nz}$. Antibiotic choices for common infections. 2013. Available from: www.bpac.org.nz

Internationally, particularly in the United States, azithromycin is a widely used antibiotic. This has led to rapidly increasing levels of resistance among some common pathogens, e.g. *Streptococcus pneumoniae*.[1] In December, 2012, PHARMAC widened subsidised access to azithromycin to allow for the treatment of pertussis in children. While this has been beneficial for managing the pertussis epidemic we need to remain cautious with the use of azithromycin to avoid an increase in macrolide resistance in New Zealand, as has been the case overseas.

### How does antimicrobial resistance occur?

All use of antibiotics contributes to resistance, but suboptimal use of antibiotics is the most important cause of the emergence and spread of resistant organisms. Prescribing antibiotics when they are not indicated (e.g. for viral infections), prescribing a broad spectrum antibiotic when a narrow spectrum option would be adequate and prescribing antibiotics at an inappropriate dose or duration of treatment all result in increased resistance.

Azithromycin in particular is more likely to contribute to the development of resistance because of its long half-life of approximately three days.[2] This results in low (i.e. sub-inhibitory) concentrations of the drug at sites of microorganism carriage for several days, which promotes the selection of resistant strains of bacteria. Nasopharyngeal carriage of macrolide-resistant streptococci following treatment with azithromycin has been observed in a number of studies.[3]

## Cardiovascular risks with azithromycin

In March, 2013, the US Food and Drug Administration (FDA) warned that there is an increased risk of QT-prolongation and potentially fatal arrhythmia with azithromycin use, particularly in people who are already at increased cardiovascular risk.[10] Other macrolide antibiotics are associated with cardiovascular adverse effects, but until recently it was thought that azithromycin had minimal cardiotoxicity.[11]

People at risk of azithromycin-induced arrhythmia include those with existing prolonged QT interval, bradycardia, low blood levels of potassium or magnesium and those currently taking antiarrhythmic medicines or other medicines which prolong the QT interval, e.g. antipsychotics, citalopram.

This risk of cardiovascular adverse effects with azithromycin was first raised in 2012 when a United States study found that there was a small increased risk of cardiovascular death and death from any cause during five days treatment with azithromycin compared to treatment with amoxicillin, ciprofloxacin or no medicine.[11] The risk was greatest in those with a high baseline risk of cardiovascular disease.[11] This means that for every 21 000 prescriptions written for azithromycin for patients in the community, one extra cardiovascular death occurred when compared to the same number of amoxicillin prescriptions. This risk increased to one extra cardiovascular death per 4100 prescriptions for azithromycin in patients with existing high cardiovascular risk (compared to amoxicillin).[12] There have been mixed results in subsequent studies of the cardiovascular risk associated with azithromycin, however, the evidence was considered robust enough to prompt the FDA warning.[12]

Along with macrolides, QT-prolongation is associated with other antibiotics such as fluoroquinolones. This should be taken into consideration when making the decision to prescribe any antibiotic, especially in patients with cardiovascular risk factors and cases where antibacterial treatment has limited benefits.[12]

## Azithromycin use in the United States: A cautionary tale

Azithromycin is used much more extensively in the United States, for a wider range of infections, than in New Zealand. Azithromycin is perceived to have potential advantages over other macrolides because it has fewer adverse gastrointestinal effects, requires less frequent dosing (once a day), and it usually requires a shorter duration of treatment (e.g. five days). For these reasons, azithromycin became the most commonly prescribed antibiotic in the United States in 2011.[4] However, resistance is increasingly of concern, with recent studies showing high rates of azithromycin resistance, particularly in pneumococci. Currently 30 – 35 % of pneumococci in the United States are resistant to macrolides.[5] Resistance rates to macrolides began to increase sharply in the 1990s, coinciding with the introduction of clarithromycin in the United States in 1991 and azithromycin in 1992. In the early 1990's rates of macrolide resistance in pneumococci were approximately 10%, however, by the early 2000's resistance rates had reached 30%.[5]

International studies have linked increasing use of macrolides, particularly azithromycin, with the increasing prevalence of resistance in *Streptococcus pyogenes*[6] and in *Streptococcus pneumoniae*.[7] While the direct consequences of increasing rates of macrolide resistance are difficult to quantify, there have been cases of breakthrough bacteraemia in patients treated with macrolides who were subsequently found to be infected with macrolide-resistant strains of *S. pneumoniae*.[8] Other cases highlight problems with macrolide resistance in *Streptococcus pyogenes*, e.g. two cases of children in the United States who developed rheumatic fever following treatment of streptococcal pharyngitis with azithromycin. Macrolide resistance was proven in one case and presumed in the other.[9]

## Azithromycin use in New Zealand: halting the surge

Concerns about increasing macrolide resistance were raised prior to the funding change in December, 2012, which widened access to azithromycin. This change allowed for funded treatment of pertussis using a liquid formulation of azithromycin suitable for children (as well as tablets). Previously, funding for azithromycin had been restricted to a maximum of two 500 mg tablets per prescription, for the treatment of infections due to *Chlamydia trachomatis*. Following consultation, PHARMAC added a restriction of five days supply to the new azithromycin listing.

The number of azithromycin prescriptions in New Zealand has been increasing since the widening of access in December 2012 (Figure 1). While some increase may be expected due to the use of azithromycin for pertussis, Figure 1 shows that pertussis rates began to decrease in early 2013, but dispensed azithromycin did not. Rates of chlamydia and gonorrhoea also appear to be stable or decreasing.

ESR collects annual surveillance data on antimicrobial resistance rates in New Zealand. Data is not reported specifically on azithromycin, but latest figures from 2012 show that 19.2% of *S. pneumoniae* and 3.9% of *S. pyogenes* were resistant to erythromycin.[13]

## The final word

Unlike some other countries where macrolide resistance is already out of control, it is not too late to preserve the effectiveness of macrolides in New Zealand. By prescribing azithromycin only for the conditions it is recommended for (i.e. first-line antibiotic treatment for pertussis in children and first-line treatment for chlamydia, and second-line antibiotic treatment for pelvic inflammatory disease) we can ensure that macrolide antibiotics remain effective when they are needed the most. Wise use of antibiotics means prescribing the right antibiotic, for the right indication, to the right person.

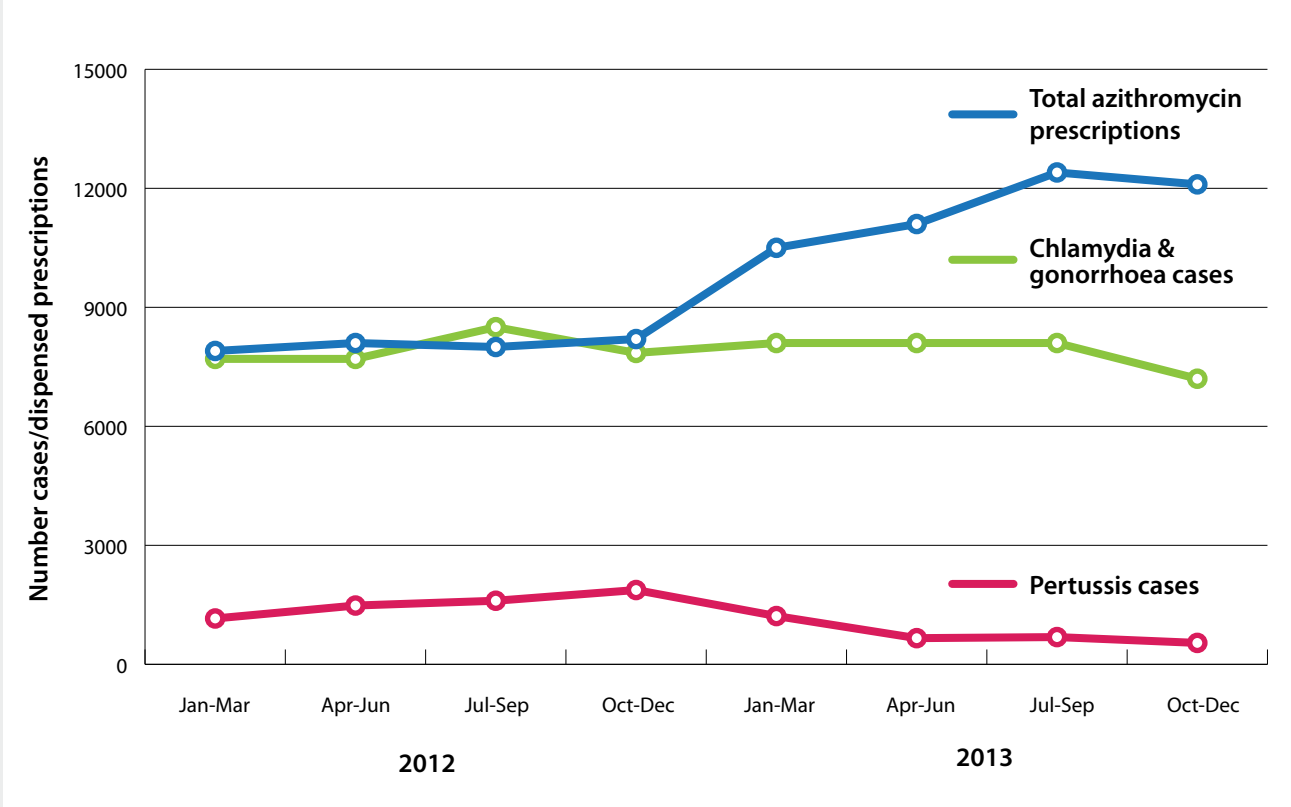


**Figure 1:** Number of dispensed azithromycin prescriptions and number of cases of pertussis and gonorrhoea and *Chlamydia* (combined), 2012 – 2013.

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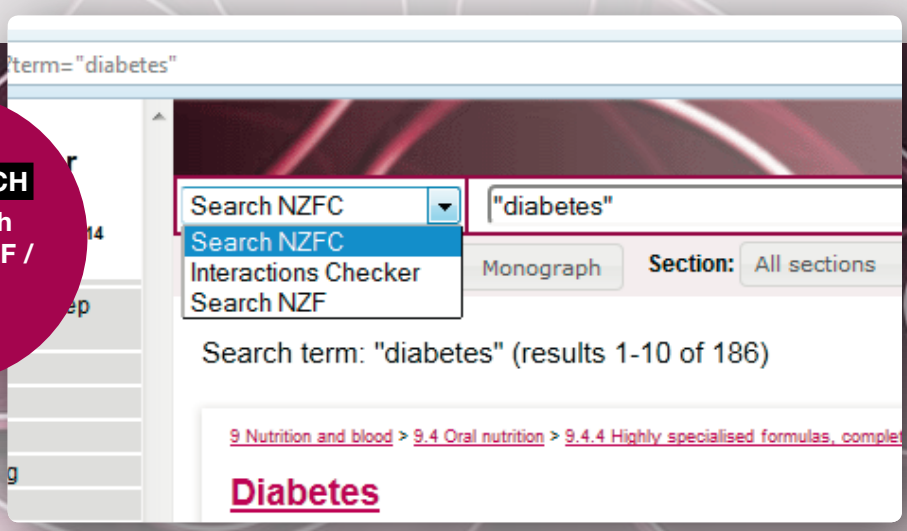


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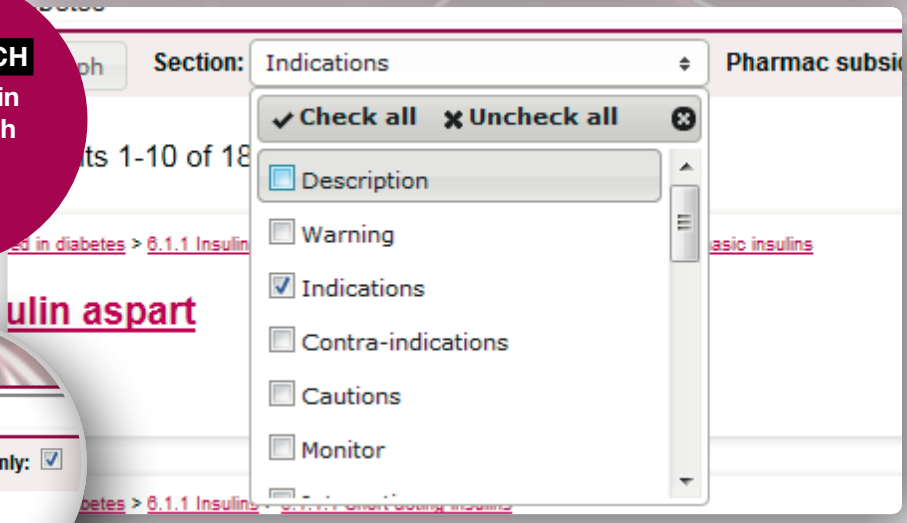


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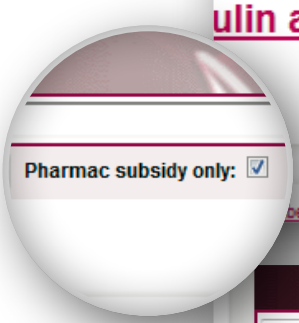


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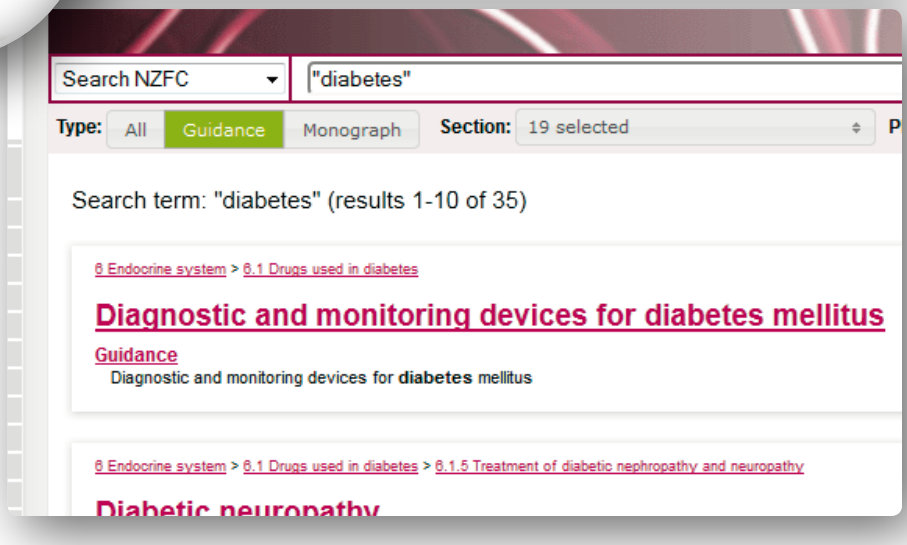


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# Managing patients with **renal colic in primary care: Know when to hold them**

*Approximately one in ten people will be affected by renal colic at some stage in their life. Patients with red flags should be referred for emergency treatment immediately. However, patients with an uncomplicated presentation of renal colic can often be managed in primary care, following prompt referral for imaging to confirm the diagnosis (same-day if possible). Non-steroidal anti-inflammatory drugs (NSAIDs) are generally preferred over morphine for pain management in patients with renal colic. Most urinary stones will pass spontaneously, however, alpha-blockers are now recommended to accelerate their passage.*

## Assessing renal colic

Renal colic is generally caused by stones in the upper urinary tract (urolithiasis) obstructing the flow of urine; a more clinically accurate term for the condition is therefore ureteric colic.[2] The blockage in the ureter causes an increase in tension in the urinary tract wall, stimulating the synthesis of prostaglandins, causing vasodilatation. This leads to a diuresis which further increases pressure within the kidney. Prostaglandins also cause smooth muscle spasm of the ureter resulting in the waves of pain (colic) felt by the patient. Occasionally renal colic will occur due to a cause other than urinary stones, such as blood clots that may develop with upper urinary tract bleeding, sloughed renal papilla (e.g. due to sickle cell disease, diabetes, long-term use of analgesics) or lymphadenopathy.[3]

Individual urinary stones are aggregations of crystals in a non-crystalline protein matrix.[3] Eighty percent of urinary stones are reported to contain calcium, frequently in the form of calcium oxalate.[3] Calcium phosphate and urate are also found in urinary stones in decreasing frequency, although urate may be more prevalent in patients who are obese.[3] Bacteria can also cause the formation of calculi, referred to as infection stones, which contain magnesium ammonium phosphate and may be large and branched; these are also known as staghorn calculi.[3]

The pain of renal colic develops suddenly and is often described by patients as "the worst pain they have ever felt".[4] Despite this severe presentation, the majority of urinary stones pass spontaneously.[4] Therefore many patients with renal colic can be managed in primary care with a watchful waiting approach if there are no red flags present (see over page), their pain can be controlled and a prompt referral for imaging is arranged.[3]

### Which patients are most likely to develop urinary stones?

It is estimated that 12% of males and 6% of females will experience an episode of renal colic at some stage in their life, with incidence peaking between age 40 and 60 years for males, and in the late 20's for females.[3]

Urinary stones are more likely to occur in patients who have:[3]

- Chronic dehydration resulting in concentrated urine production, e.g. less than one litre of urine production per day
- A family history of urinary stones; the risk is increased 2.5 times
- An abnormality of the urinary tract
- Obesity
- Hyperparathyroidism
- Gout
- Idiopathic hypercalciuria
- Exposure to a hot environment, e.g. hot working conditions, causing dehydration

Between 30 – 40% of people will experience reccurrent renal colic within five years of their first episode.[3]

## Diagnosing renal colic

Patients with renal colic classically present with sudden and severe loin pain that occurs in waves of intensity and may be accompanied by nausea and vomiting. Some patients may be symptom-free between these episodes. This description helps to distinguish renal colic from some other conditions causing abdominal pain (see differential diagnosis below). The site of the pain is generally not useful for predicting the location of the stone within the renal tract, however, new onset lower urinary tract symptoms are consistent with a stone migrating distally.[2] If the stone is located at the vesico-ureteric junction patients may experience straining when urinating, with painful and frequent passage of small volumes of urine (strangury), due to the stone irritating the detrusor muscle.[3]

**Examining the patient**

Patients with renal colic typically appear restless and unable to find a comfortable position. Classical renal colic pain is located in the costovertebral angle, lateral to the sacrospinus muscle and beneath the 12th rib.[3] The pain may radiate to the flank, groin, testes or labia majora.[3]

Acute kidney injury is a concern in patients with renal colic. It is important to be aware of a previous nephrectomy or any other cause of renal impairment which would increase the significance of further renal injury and lower the threshold for referral to the emergency department (see "Red Flags").

Assess for signs and symptoms of infection. Another concern in patients with renal colic is the development of pyonephrosis (infection of the renal system above an obstructing stone). If this occurs then the patient can develop life-threatening sepsis.

Diagnostic uncertainty is an indication for referral to hospital as renal colic can be difficult to differentiate from a number of other conditions, including:[3, 5]

- Biliary colic and cholecystitis
- Aortic and iliac aneurysms – particularly in older patients with left-side pain, hypertension or atherosclerosis
- Appendicitis, diverticulitis and peritonitis. N.B. These patients are less likely to appear restless and generally prefer to lie still.
- Gynaecological causes, e.g. endometriosis, ovarian torsion and ectopic pregnancy
- Testicular torsion

**Investigating suspected renal colic**

The following investigations should be performed or requested to detect haematuria, rule-out infection, assess kidney function and assess for the presence of an underlying metabolic condition, such as gout, hyperparathyroidism or renal tubular acidosis: [2, 3, 5]

- Urine dipstick
- Midstream urine culture
- Full blood count
- Serum creatinine
- Electrolytes
- Serum urate
- Serum calcium
- Serum phosphate

Approximately 90% of patients with urinary stones will return a positive test for haematuria on urine dipstick, therefore a negative result is a reason to reconsider the diagnosis.[3] A midstream urine sample should be sent for microscopy to assess for the presence of dysmorphic red blood cells and urinary casts to exclude other causes such as glomerular injury.[2] Patients with reduced kidney function, e.g. creatinine > 160 mmol/L, who are at immediate risk of acute kidney injury (AKI) should be referred to the emergency department.

N.B. the patient's white blood cell count may be elevated in the absence of infection.[2] Serum urate levels may also fluctuate due to acute inflammation.[3]

**Red flags that over-ride requests for testing and require immediate referral** of the patient to the emergency department include:[3, 5]

- Fever or other features, e.g. rigors, consistent with systemic infection which can lead to life-threatening sepsis
- Suspected bilateral obstructing stones
- Known clinically significant renal impairment
- The presence of only one kidney
- Pregnancy (see: "Renal colic during pregnancy", Page 13)

**Non-contrast computed tomography (CT) urogram is the gold standard for diagnostic confirmation** of renal colic.[3] If CT urogram is not available then a kidney-bladder ultrasound

in combination with an x-ray can achieve detection rates for urinary stones that approach those of CT urogram.[3] Ultrasound is the preferred imaging technique for patients who are unable to be x-rayed, e.g. a female who is pregnant, and is also useful for identifying urate stones which cannot be detected with standard x-ray.[2, 3] Patients should have a full bladder when the ultrasound is performed to identify stones at the vesico-ureteric junction.[3] Stones in other regions of the ureter may not be seen, however, dilatation will suggest where the obstruction is located.

## Management of renal colic in primary care

In a patient suspected of having renal colic initial management will generally include:

1. Acute pain control with either a non-steroidal anti-inflammatory drug (NSAIDs or morphine (see below)
2. Laboratory testing, e.g. serum creatinine and full blood count (see previous page)
3. Prompt referral (same-day if possible) for CT urogram or kidney-bladder ultrasound and x-ray (see below)
4. Prescribe an analgesic for ongoing pain management
5. Prescribe an alpha-blocker to accelerate stone passage (see below)
6. Consult with the patient the following day to discuss treatment and referral options

**NSAIDs are the first-line treatment** for renal colic pain because they have been shown to achieve greater reductions in pain scores, have a longer duration of action and result in a reduced need for additional analgesia in the short-term, compared with patients treated with opioid analgesics.[3] The increased efficacy of NSAIDs may be partially explained by the fact that prostaglandin production is part of the pathophysiological process of renal colic. In addition, treatment with NSAIDs has the advantage of circumventing any concerns about drug-seeking behaviour (see: "Identifying drug-seeking behaviour", Page 16).

**Opioid analgesics can be prescribed in addition to, or as an alternative, to NSAIDs** for patients with renal colic who are at risk of NSAID-induced adverse effects, e.g. in patients with chronic renal impairment, who are dehydrated or have a history of peptic ulcers.[3, 5]

N.B. Pethidine is no longer used for the treatment of renal colic because it is no more effective than morphine and is associated with an increased rate of adverse effects such as vomiting.[3] Pethidine is also best avoided in people with impaired renal function as it has a toxic metabolite which can accumulate.

The patient's general health, e.g. the presence of co-morbidities, age and their preference, as well as any history of successful renal colic pain management should be taken into account when considering the most appropriate analgesic regimen.

## Diclofenac is often the first choice NSAID for renal colic

Diclofenac is used for the treatment of renal colic because:[4]

1. It is the NSAID with the strongest evidence of effectiveness in the management of renal colic
2. It is available in immediate and modified release oral, injectable and suppository formulations
3. Both injectable and suppository formulations are available fully subsidised on a Practitioner's Supply Order (PSO)

Diclofenac injectable preparation is indicated for the immediate relief of renal colic pain. It must be administered by deep intragluteal injection in the upper outer quadrant to minimise the risk of abscess formation.[6] The recommended dose is:

- Diclofenac 75 mg (3 mL) injection, IM, repeated once (may be given 30 minutes later if required, in the opposite side)
- May also be combined with oral diclofenac to a maximum of 150 mg, daily, for a maximum of two days[5]

Oral or rectal diclofenac, 75 – 150 mg, daily, can be prescribed for ongoing pain management.[6] Some clinicians recommend NSAID suppositories as the best analgesia for out-of-hospital care for renal colic pain.[2]

Ten diclofenac 50 mg suppositories, and five 75 mg injections are available fully subsidised on a PSO for general practices to have available for acute administration.[6]

Diclofenac may not always be the most appropriate NSAID for treating the pain of renal colic, e.g. if the patient is unable to tolerate diclofenac or has an increased cardiovascular risk. Diclofenac is contraindicated in patients who have had a myocardial infarction in the previous 12 months.[6] Other NSAIDs, e.g. ibuprofen or naproxen, should provide effective pain management for patients with renal colic in these situations.

For further information see: "Non-steroidal anti-inflammatory drugs (NSAIDs): making safer treatment choices", BPJ 55 (Oct, 2013).

## Morphine is an alternative to NSAIDs

Morphine 5 – 10 mg, IM, is an alternative treatment to NSAIDs for acute pain management in patients with renal colic and is preferred over NSAIDs in women who are pregnant (see: "Renal colic during pregnancy", opposite). The concomitant administration of an antiemetic may be considered for the prevention or control of nausea and vomiting.[5]

Once the patient's pain has been controlled, short-term use of oral morphine, 5 – 10 mg, every four hours, adjusted according to response, can be appropriate for patients managed in the community who are unable to tolerate oral NSAIDs.[6]

## Additional pain management options

Paracetamol and a weak opioid, e.g. codeine or tramadol, can be prescribed for ongoing pain management if NSAIDs are not appropriate once any nausea and vomiting has passed.[5] Applying warmth to the lateral abdomen and lower back, e.g. with a wheat bag or hot-water bottle, may provide useful pain relief for patients with renal colic.[3]

## How much fluid should patients drink?

In general, patients should drink sufficient fluid to reduce the risk of developing AKI, especially if they are taking NSAIDs.[3] Advising patients to maintain a lightly coloured urine is a "rule of thumb" for achieving this.[5] Patients who are dehydrated may benefit from intravenous fluids, if the practice has the resources to provide this treatment. However, there is no evidence that increasing hydration assists in pain control or stone movement once the ureter has become obstructed.[3] Excessive fluid intake will increase urine output pressure causing hydroureteronephrosis (distension of the ureter and kidney) which is likely to worsen the patient's pain.[7]

## Alpha-receptor blockers (medical expulsive treatment)

Alpha-receptor blockers, e.g. doxazosin and terazosin, or calcium channel blockers, e.g. nifedipine, can accelerate the passage of urinary stones by relaxing smooth muscle without preventing peristalsis.[3, 8] Alpha-blockers are also thought to reduce pain episodes and the need for analgesia.[3] An alpha-blocker should be prescribed as an off-label indication when patients with renal colic are first seen. Several local guidelines in New Zealand, e.g. Canterbury HealthPathways, recommend doxazosin, 1 – 4 mg, at night, for four weeks or until the stone passes. A lower dose may be more appropriate in older patients or patients who are hypotensive.[6] Doxazosin

is contraindicated in patients with a history of postural hypotension or micturition syncope.[6]

## Interpreting the results of the computer tomography urogram

Patients with renal colic who have not been referred to hospital should be asked to attend a follow-up consultation as soon as is feasible to discuss their imaging and tests results, to confirm pain is being managed and to discuss referral options. The CT urogram is critical when assessing the likelihood of the patient's stone passing without the need for surgery; which will also determine whether they should continue to be managed in secondary care.

**Which stones are most likely to pass without surgery?**

The smaller the stone and the more distal its location the more likely it will pass spontaneously.[3] The presence of anatomical abnormalities in the ureter may also influence the likelihood of stone passage occurring. The average reported time for a stone 2 – 4 mm in diameter to pass is approximately 13 days and approximately 22 days for a stone 6 – 8 mm in diameter.[3] Over half of stones causing symptoms in patients presenting to an emergency department can be expected to be found at the ureterovesical junction and approximately one-quarter in the proximal ureter.[3] Spontaneous passage is reported to occur in 79% of patients with urinary stones located at the ureterovesical junction and in 48% of patients with stones located in the proximal ureter.[11]

## When should patients be referred to an Urologist?

**In general, if there is a single stone less than 4 mm on CT urogram the patient can be managed in the community** if they are able to cope at home and have social support. Follow-up radiology will often not be required as it is likely that the stone will pass without the need for surgery, however, the location of the stone will also influence this. The patient should be monitored for signs of infection and advised to

## Renal colic during pregnancy

The incidence of renal colic is not thought to be increased in women who are pregnant.[1] However, the composition of urinary stones in women who are pregnant may be different, e.g. often containing calcium phosphate.[1] Complications if renal colic does occur during pregnancy include: premature rupture of membranes, pre-term labour and delivery, pregnancy loss, mild pre-eclampsia and infection. All pregnant women with suspected renal colic should therefore be referred to an Urologist or Obstetrician.[1] The possibility of ectopic pregnancy should be excluded during the history and examination. Renal and bladder ultrasound is the investigation of choice in women who are pregnant, but interpretation of imaging may be complicated if the stone is not readily visible due to hydronephrosis, which occurs naturally in up to 90% of pregnant women.[1] Transvaginal ultrasonograpy, simple radiography and intravenous urography are investigations that may also be used if necessary.[1]

The majority of urinary stones in women who are pregnant will pass spontaneously, so management is generally watchful waiting with appropriate pain management. Of the stones that do not pass during pregnancy, many will pass after delivery; usually within the first month.[1] Non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided during the first and third trimester of pregnancy due to potentially teratogenic adverse effects early in pregnancy and an increased risk of miscarriage or premature closure of the ductus arteriosus later in pregnancy.[1] Short-term oral morphine can be used if required for ongoing pain.[6, 12] There is no evidence of alpha-blockers causing teratogenicity.[6] Urinary stone passage may be accelerated by the off-label use of doxazosin if the potential benefits of an early stone passage, which will reduce the need for analgesia, outweighs any risks.[1, 6]

If the urinary stone does not pass or if there are signs of infection, then management depends on the clinical situation, e.g. the stage of pregnancy. Temporary drainage of the ureter with delayed stone treatment, urgent or definitive stone treatment via ureteroscopy, may be considered.[1]

contact the practice once they have passed the urinary stone. Untreated obstruction of the ureter can lead to a permanent loss of renal function and it can be expected that urological follow up will be advised if the patient has not passed a stone after two to three weeks.

A practical tip for patients with smaller stones is to ask the patient to sieve their urine, e.g. through pantyhose fabric, to confirm passage of the stone and to aid retrieval for analysis if required.

**Patients with a stone larger than 4 mm on CT urogram, with a stone in the kidney or multiple urinary stones should be discussed with an Urologist** who will generally arrange for follow-up radiology.

Stones greater than 6 mm in diameter have a low likelihood of spontaneous passage and these patients should be immediately discussed with an Urologist to ensure the patient is prioritised appropriately.[2]

## Surgical treatment of urinary stones

The size of the urinary stone, its position and the general health of the patient will determine which technique is the most appropriate for the removal of stones that require surgery.[2] People with certain occupations, e.g. airline pilots, require complete removal of any urinary stones before they are able to return to full duties.[2]

**Uretero pyeloscopic laser lithotripsy** uses laser pulses to break up ureteric and smaller renal stones. This has high stone-clearance rates but may cause:[2]

- Infection in at least 5% of patients
- Haematuria, which will be problematic in < 1% of patients
- Postoperative pain
- Rarely, significant ureteric injury

Urinary tract infection is the only specific contraindication for this technique, and patients are able to continue to take antithrombotic medicines.[2]

**Shock wave lithotripsy** is the least invasive but also least effective method for removing urinary stones. It is not commonly used to treat urinary stones in the ureter, but may occasionally be used to treat those in the upper ureter. The technique is generally indicated for renal stones in patients who are not troubled by pain or for patients with stones that are inaccessible via retrograde or percutaneous routes.[2] Shock wave lithotripsy is less effective for stones greater than 10 – 20 mm in diameter.[2] The adverse effects of shock wave lithotripsy include:[2]

- Significant pain due to stone fragment passage, experienced by 15% of patients
- Haematuria is to be expected, but is problematic in less than 1% of patients
- Rarely perinephric haematoma can occur

This technique is contraindicated in patients who: are pregnant, have an active UTI, are taking antithrombotic medicines, have an aortic aneurysm or with drainage abnormalities of the kidney.[2]

**Percutaneous nephrolithotripsy** is generally performed on renal stones larger than 20 mm and particularly staghorn calculi.[2] This has an increased risk of bleeding and sepsis, compared with laser treatment, and the patient may require further treatment to remove remaining fragments.[2] Patients may require several nights in hospital following this procedure.[2]

**Open surgery** is performed rarely for patients with urinary stones that have not passed and requires an extended period in hospital and an approximate six week convalescence.[2]

## Preventing stone reoccurrence

Patients can take several steps to reduce the likelihood of future urinary stone formation including:[2]

- Increasing water intake to dilute urine output
- Reducing salt intake
- Maintaining a healthy diet
- Avoiding fructose-containing soft drinks due to their association with increased urate levels

An analysis of stone content can guide dietary and medical interventions for urinary stone prevention. This may be useful for patients with a history of recurrent urinary stones.

Patients with stones containing calcium oxalate can be advised to reduce their salt and oxalate intake.[2] Examples of foods rich in oxalate include: tea, chocolate, spinach, beetroot, rhubarb, peanuts, cola and supplementary vitamin C (most of which is converted to oxalate).[2] Patients should maintain a normal dietary calcium intake of 700 – 1000 mg per day. Potassium citrate is subsidised under Special Authority for patients who

have had recurrent calcium oxalate urinary stones and who have had more than two episodes of urinary stones in the previous two years.[6]

For patients with urate stones, reducing dietary purines by eating less purine-rich meat (e.g. red meat and offal) and seafood (e.g. shellfish and oily fish) is an effective way to decrease urate production.[13] A urinary pH of 6.0 – 6.5 can increase the solubility of urate.

Allopurinol is indicated for the prophylaxis and treatment of patients with either urate or calcium oxalate renal stones.[6] Treatment with allopurinol is recommended if urinary stones reoccur despite lifestyle modifications and adjustment of urinary pH.[13] For patients without renal impairment allopurinol is initiated at 100 mg, once daily, and increased by 100 mg, every four weeks until a target serum urate of < 0.36 mmol/L is achieved.[6] Lower doses of allopurinol are recommended for patients with estimated glomerular filtration rates < 60 mL/min/1.73 $m^2$ (see NZF for details).

If a patient is suspected of having a renal tract abnormality that may predispose them to stone formation or if a patient passes a urinary stone that when analysed has an unusual composition, e.g. marked cystine content, then further investigations and treatment should be discussed with an Urologist.

**ACKNOWLEDGEMENT:** Thank you to **Mr Peter Davidson**, Consultant Urologist, Canterbury DHB for expert review of this article.

## Identifying drug-seeking behaviour

More than one in 30 New Zealanders reported using an opiate for recreational purposes at some stage in their life in the 2007/2008 alcohol and drug use survey.[9] The most common type of opiates used were analgesics such as morphine and oxycodone.[9] As opioids are a known treatment for renal colic this condition can be mimicked by drug-seekers wanting to misuse or on-sell opioids. Therefore in some situations the possibility that a patient's symptoms are fictitious may need to be excluded. Some general features of the patient encounter that increase the suspicion of drug-seeking behaviour include:[10]

- Presenting near closing time without an appointment
- Reporting a recent move into the area, making validation with their previous practitioner difficult
- Obsessive and impatient behaviour, often demanding immediate appointments but not attending follow-up consultations
- An unusual degree of knowledge about analgesics or an insistence on a specific opioid
- An unwillingness to trial non-pharmacological methods of pain relief
- Effuse gratitude when prescribed an opioid

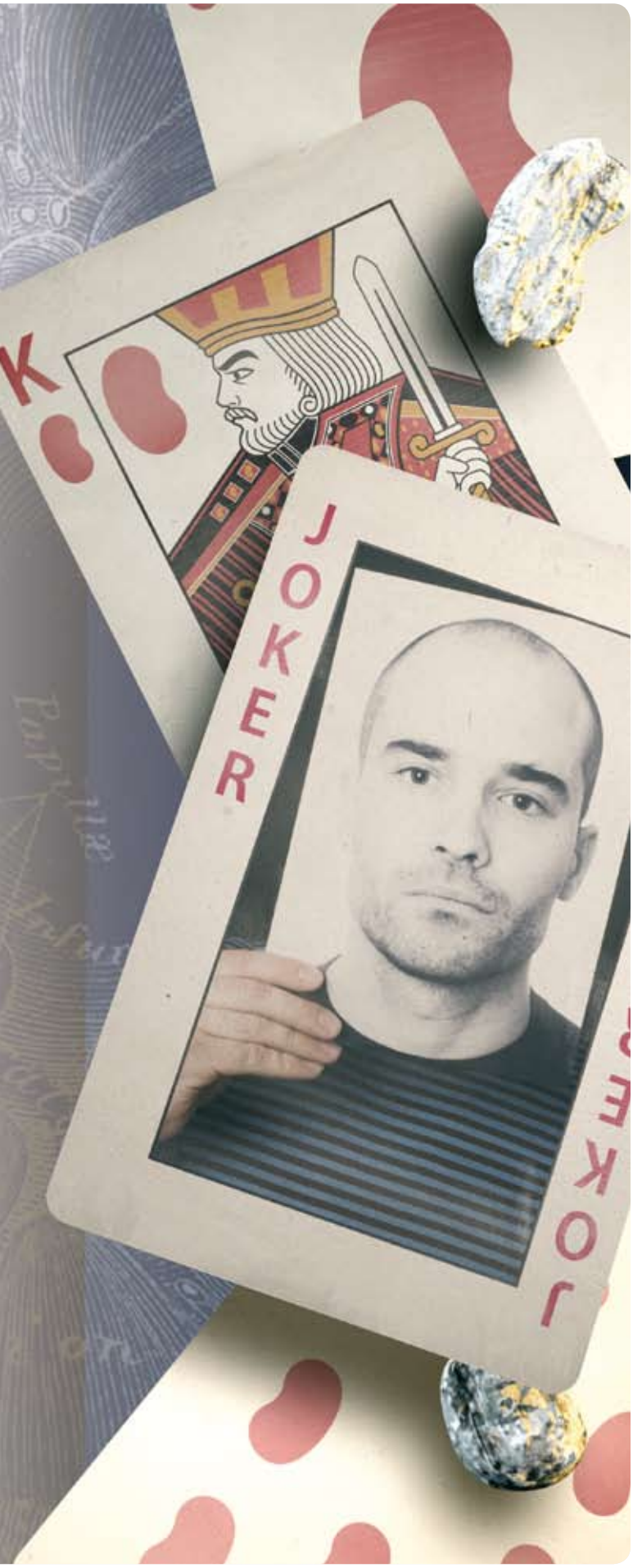
Clinicians who suspect that a patient is seeking an opioid for reasons other than legitimate pain relief should document the discussion and diagnosis. During the history and examination and before any treatment is prescribed consider:

- Asking unexpected questions when taking the patient's history to counteract any scripted responses the patient has prepared
- Including questions about substance-use, alcohol and previous prescription medicine use during the patient's history
- Assessing whether the symptoms are consistent with the natural history of the condition; in the case of renal colic pain will usually be spasmodic
- Using distraction techniques during the physical examination, e.g. firmly palpating a non-affected area while only gently palpating the affected area, when looking for consistency in the patient's posture, movement and examination findings. Asking non-medical questions while palpating the patient's abdomen is another distraction technique.
- Seeking a second opinion from a colleague

Patients who are fabricating their condition will be highly attuned to clinical indecisiveness and a firm and evidence-based clinical opinion is the best way to discourage drug-seekers.[10] When prescribing an analgesic consider:

- Refusing to prescribe an opioid by providing a calm and clear explanation why an opioid is not the most appropriate first-line treatment for acute pain in patients with renal colic
- Ask to see some identification, it is less likely a drug-seeker will be prepared to provide this and if they do this will be useful if they are reported to the police
- Write the exact amount of medicine prescribed until the next consultation in words if it is decided that an opioid is the appropriate treatment
- Prescribe for a limited time, e.g. for two or three days
- Provide supervised daily dosing

When there is a strong suspicion that a patient is a drug-seeker other practice members should be alerted in case the patient displays threatening behaviour. Other staff members may also be able to point out inconsistencies in the patient's behaviour, e.g. did they appear distressed or in pain on the phone or in the waiting room? Drug seekers will often use more than one doctor or be known by local Pharmacists and phone calls to colleagues once the patient has left the practice may confirm that a patient has a history of drug-seeking behaviour.

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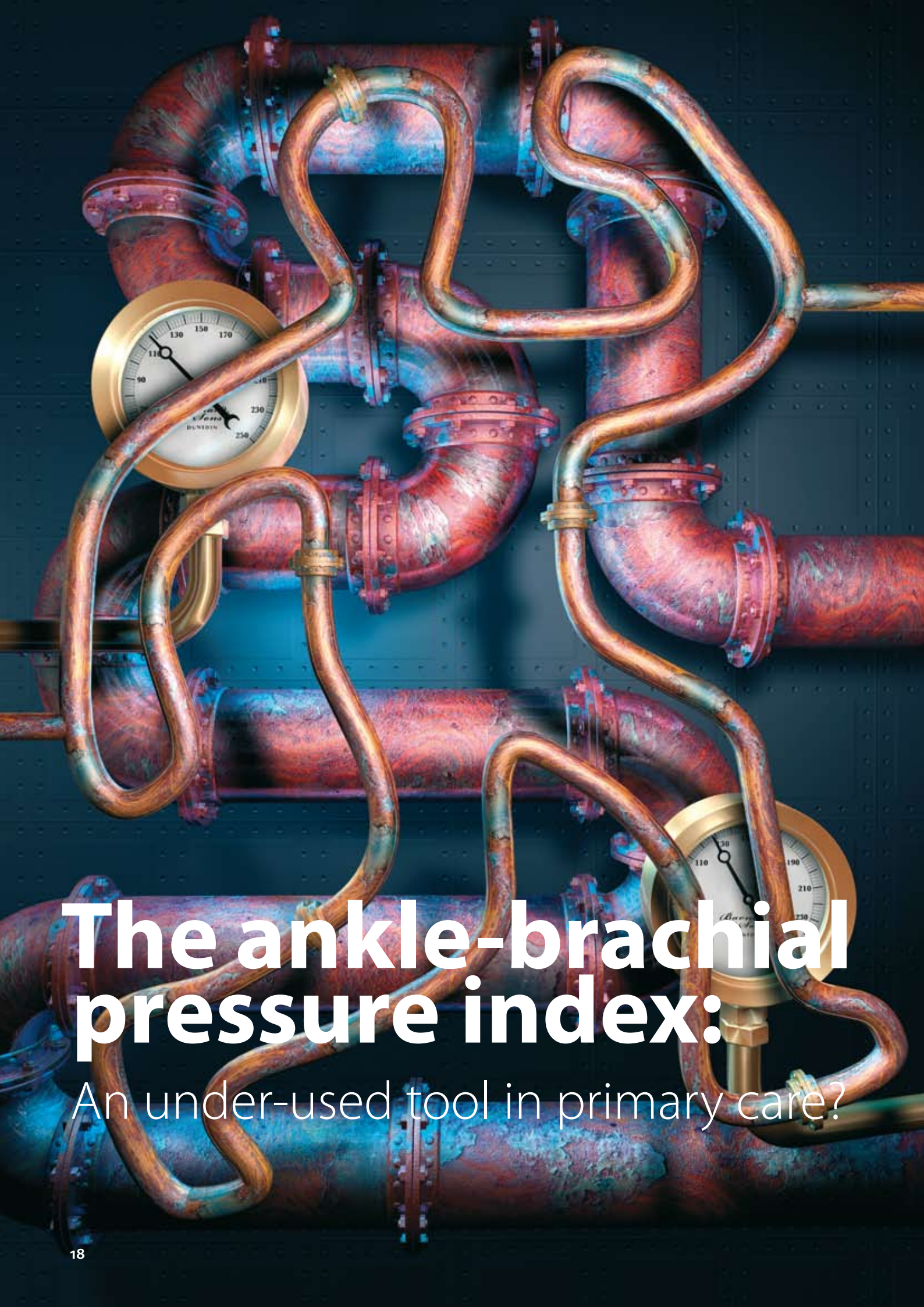

# The ankle-brachial pressure index:

## An under-used tool in primary care?

*Calculating a patient's ankle-brachial pressure index (ABPI) is a simple, low-cost and non-invasive way of detecting peripheral artery disease in the lower limbs. Atherosclerosis is the most frequent cause of peripheral artery disease and the patient's atherosclerotic burden is reflected by the degree to which their ABPI is reduced. Measuring ABPI therefore provides a useful window into what is happening in the cardiovascular system and an additional prognostic tool to that provided by more frequently used surrogate markers of cardiovascular risk. Targeted testing of ABPI for people most at risk of developing peripheral artery disease and its complications, in combination with routine cardiovascular risk assessments, will lead to earlier and more appropriate treatment of all types of atherosclerotic disease.*

## Is your Practice measuring ankle-brachial pressure indices?

Peripheral artery disease is a significant risk factor for cardiovascular events and lower limb amputation. The prevalence of peripheral artery disease is increased among older people, people who smoke and people who have diabetes. In New Zealand there is limited epidemiological data on peripheral artery disease. However, it is likely that Māori and Pacific peoples are more severely affected by peripheral artery disease compared with European New Zealanders, as they are known to have significantly higher rates of cardiovascular disease in general.

The ankle-brachial pressure index (ABPI) is a non-invasive method for detecting or ruling-out the presence of peripheral artery disease. ABPI is a calculation of the ratio of the patient's systolic blood pressure at their ankle to the systolic pressure in their arm. ABPI is generally between 1.0 – 1.4 in healthy people, i.e. the systolic pressure at the ankle is greater than the systolic pressure at the arm. An abnormally low ABPI value (i.e. < 0.9) has a sensitivity of 79 – 95% and a specificity of approximately 95% for peripheral artery disease.[1]

Between one-third and one-half of patients with peripheral artery disease will have some evidence of coronary artery or cerebrovascular disease.[1] A meta-analysis of 16 studies involving over 48 000 patients without a history of coronary artery disease, found that when ABPI indicated the presence of peripheral artery disease the risk of cardiovascular mortality increased by over four times for males and approximately 3.5 times for females, compared with people with an ABPI in the normal range.[2]

The majority of General Practitioners do not currently perform routine ABPI measurements – presumably because they do not have access to the necessary equipment. When combined with a focused vascular examination, the ABPI is a useful tool in primary care for stratifying a patient's cardiovascular risk, and improving their management.

### Ankle-brachial pressure index testing has multiple uses

A pedal pulse that is easily felt on examination effectively excludes peripheral artery disease. However, measuring ABPI to detect peripheral artery disease is a more sensitive and replicable test compared to palpation of a pedal pulse, especially in patients who are obese or who have significant oedema.[1] Measurement of the ABPI can also provide valuable clinical information without the need to refer the patient to a vascular laboratory.

**ABPI is recommended for all patients who present with signs and symptoms suggestive of peripheral artery disease.** The physical examination of a patient with peripheral artery disease

may reveal reduced or absent pedal pulses on palpation, skin that is cool, shiny, hairless or thin, thickening of the nails, abnormal capillary refill time, pallor of distal extremities on elevation, leg pain and tissue ulceration or necrosis.[3] The classical initial symptom of peripheral artery disease is intermittent claudication. This is a tight cramp-like pain in the muscles of the calf, thigh or buttock that is reproduced with exercise and relieved within ten minutes of rest.[3] However, only 10% of patients with peripheral artery disease present with classical claudication and approximately 50% have atypical leg pain; the remainder of patients are asymptomatic.[3] Venous claudication, neurogenic claudication (spinal stenosis), popliteal artery entrapment, Raynaud's phenomenon and other vasospastic problems are differential diagnoses that may need to be considered in patients with symptoms suggestive of claudication. Therefore ABPI testing is not only useful for detecting the presence of peripheral artery disease, it is also helpful for ruling-out peripheral artery disease as a cause of symptoms in the lower limbs, particularly in older patients.

**ABPI provides an indication of disease severity** and the urgency of referral. The presence of ischaemic rest pain suggests increased severity of peripheral artery disease and an increased risk to the limb. Patients with ischaemic rest pain often present with a burning pain in the arch or distal foot that occurs when their feet are elevated, e.g. in bed, and resolves when they place their feet on the floor. An ABPI < 0.4 indicates the patient has critical limb ischaemia.[4] This is a potentially life-threatening condition characterised by severely reduced circulation, ischaemic rest pain and tissue loss due to ulceration and/or gangrene.[5] Due to severely impaired circulation, 5 – 10% of patients with peripheral artery disease will require surgical revascularisation to reduce the risk of amputation.[5]

**ABPI is used to assess the safety of compression treatment** when considering compression hosiery and bandaging for patients with venous disease or ulceration. ABPI may still be performed as a confirmatory measure in patients with a palpable pedal pulse, before applying compression hosiery or compression bandages, because of the risk of complications developing in patients with undiagnosed peripheral artery disease.

**ABPI is used to exclude peripheral artery disease** in patients who are undergoing treatment that may result in vascular complications, e.g. patients undergoing leg or foot surgery.[5]

### Targeted use of ABPI in asymptomatic patients

There is currently insufficient evidence to recommend population screening for peripheral artery disease using ABPI.[3] However, international guidelines recommend that people who are at risk of developing artery disease (see below), be offered a clinical assessment that includes an ABPI measurement.[3, 5]

Risk factors for peripheral artery disease include:[3, 5]

- Older age
- Smoking, past and present
- Diabetes
- Hyperlipidaemia
- Hypertension
- Reduced renal function (eGFR < 60 mL/min/1.73 $m^2$)

In particular, international guidelines recommend targeted testing for peripheral artery disease for the following groups:[6]

- All people aged between 50 and 69 years who smoke or have diabetes
- All people from age 70 years regardless of risk-factor status
- All people with a Framingham risk score > 10%

Current smokers are estimated to be almost four times as likely to develop peripheral artery disease as non-smokers.[5] Over half of all amputations due to peripheral artery disease are reported to occur in patients with diabetes.[5]

## Performing ankle-brachial pressure index testing

The following equipment is recommended for measuring the ankle-brachial pressure index:[8]

- A hand-held portable Doppler device with a frequency of 8 – 10 MHz, although 5 MHz probes may be better for patients with significant ankle oedema. Devices can be purchased for under $700 and training is generally provided by the supplier. More expensive devices with LCD screen and printing options are also available.
- A sphygmomanometer
- Ultrasound transmission gel

### How to measure the ankle-brachial pressure index

For the purposes of excluding peripheral artery disease it is sufficient to perform only one ABPI measurement, i.e. by dividing the systolic pressure detected at a single posterior tibial artery by the systolic brachial pressure of one arm (see below). The diastolic pressure is not measured and is not required when measuring the ABPI.

With the patient in a supine position (Figure 1):

1. Place the blood pressure cuff approximately two to three centimetres above the antecubital fossa for the brachial pressure and approximately five centimetres above the medial malleolus for the ankle pressure
2. The Doppler probe should detect a clear arterial pulse before the cuff is inflated
3. Inflate the cuff slowly until the systolic pressure is indicated by the disappearance of the Doppler sound. N.B. This does not need to be highly precise as the ratio is calculated to a single decimal point.
4. Divide the ankle systolic pressure detected at the posterior tibial artery by the brachial pressure

If the patient's ABPI is < 0.9 then this indicates they have peripheral artery disease and additional measurements are recommended to increase the accuracy of the assessment of the disease severity:

5. Divide the highest ankle systolic pressure in each of the posterior tibial and dorsalis pedis arteries* in both feet by the highest brachial systolic pressure from each arm; the lowest resulting value is the patient's overall ABPI.

* This measurement may not be possible in all patients as 12% of the general population has a congenital absence of the dorsalis pedis pulse.[8]

The ABPI procedure may cause discomfort for patients with lower leg pain or cellulitis. If ulcers or wounds are present on the ankle then a protective barrier, e.g. a plastic wrap, should be placed over the affected area before the cuff is applied.[8]

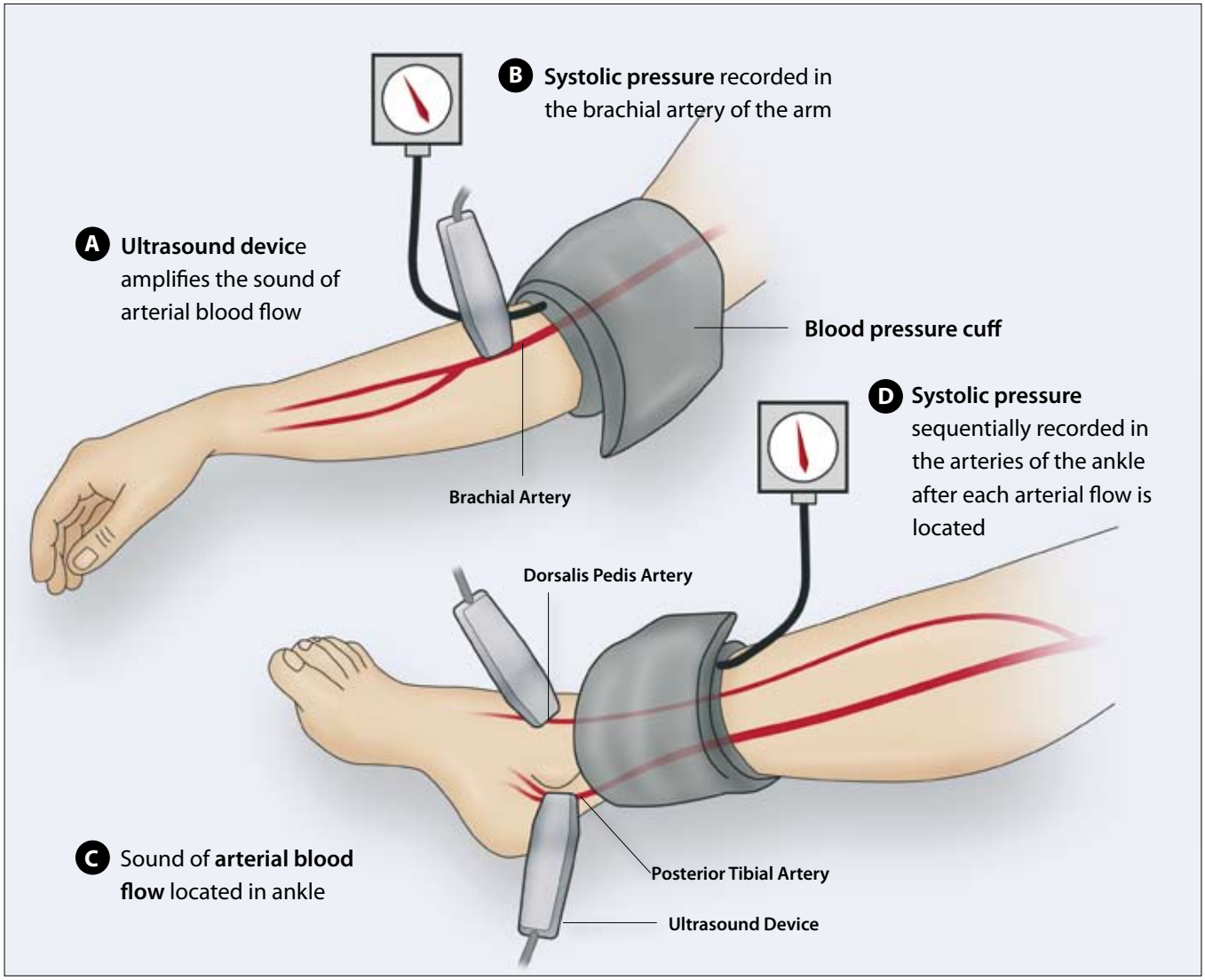


**Figure 1:** Sequentially measuring the brachial systolic pressure and ankle systolic pressure in the posterior tibial and dorsalis pedis arteries with a single hand-held Doppler ultrasound device

## ABPI can be used as a marker of cardiovascular risk

A low ABPI, i.e. < 0.9, is an independent predictor of cardiovascular risk and measuring ABPI has been widely suggested for the detection of subclinical disease in order to prevent cardiovascular mortality and stroke.[1, 2, 7] For some patients detection of a low ABPI may allow a more accurate estimation of cardiovascular risk than is provided solely by traditional risk assessment tools, e.g. patients with no other history of cardiovascular disease.[7] A meta-analysis involving over 48 000 patients found that an ABPI ≤ 0.9 approximately doubled the risk of total mortality, cardiovascular mortality and major coronary events across all Framingham risk categories assessed.[2] For example, the overall ten-year rate of cardiovascular mortality was 7.3% for males with an ABPI between 0.91 and 1.1, but 18.7% in males with an ABPI ≤ 0.9.[2]

### Interpreting the ankle-brachial index

An ABPI between 1.0 – 1.4 (Table 1) is sufficient to exclude peripheral artery disease in most patients (see: "Limitations of ankle-brachial pressure index" on opposite page). Referral to a vascular laboratory should be considered for patients with an ABPI > 1.4, as this result is clinically inconclusive. In a patient with a borderline APBI, i.e. 0.9, where there are additional reasons to suspect peripheral artery disease, e.g. symptoms and risk factors, consider discussing the result with a vascular surgeon as further investigations, such as exercise testing, may be recommended.

An ABPI of < 0.9 indicates significant occlusion in the arteries supplying the patient's lower extremities and is diagnostic for peripheral artery disease. The lower the patient's ABPI, the more severe the disease, with an ABPI < 0.4 indicating critical limb ischaemia.[4]

In patients with an ABPI > 0.8 compression hosiery is considered safe.[9] However, in patients with an ABPI < 0.8, high compression hosiery (i.e. 30 – 40 mmHg at the ankle) is not recommended when treating lower limbs, e.g. non-healing leg ulcers in patients with diabetes, due to the increased risk of skin necrosis.[8] If ABPI is < 0.5, compression hosiery should not be used.[8]

**Table 1:** Clinical interpretation of the ankle-brachial index (ABPI)[1, 4, 5]

| Ankle-brachial pressure index (ABPI) | Clinical interpretation |
|---|---|
| **> 1.4** | Inconclusive due to non-compressible blood vessels |
| **1.0 – 1.4** | Normal; peripheral artery disease can be excluded in most patients |
| **0.9** | Borderline; discussion with a vascular surgeon may be appropriate depending on the patients symptoms and risk factors |
| **< 0.9** | Abnormal and diagnostic of peripheral artery disease |
| **< 0.4** | Critical limb ischaemia |

## What to do when a patient is diagnosed with peripheral artery disease

After performing a vascular examination, criteria that would indicate an increased urgency of referral to a vascular surgeon include:

- An ABPI < 0.5
- Known peripheral artery disease presenting with a new ulcer or area of necrotic tissue
- An ulcer that is not responding to treatment
- Intermittent claudication when walking for less than 200 m
- Young and otherwise healthy patients with claudication to rule-out rare causes, e.g. popliteal artery entrapment

Discussion with a vascular surgeon should also be considered when:

- There is doubt concerning the patient's diagnosis
- There is uncertainty around the significance of an ABPI result
- There is doubt about the need for treatment or what treatment options are available

### Treatment of peripheral artery disease

The treatment of peripheral artery disease focuses on:

1. Improving quality of life in symptomatic patients
2. Reducing overall cardiovascular risk, which may have a small disease-modifying effect on peripheral artery disease

All patients with an ABPI < 0.9 have peripheral artery disease and are clinically assumed to have a 5-year cardiovascular risk > 20%.[10] Therefore the use of cardiovascular risk charts when performing routine cardiovascular risk assessments in these patients is not necessary and management of cardiovascular risk factors should be intensive.[10] The modifiable and non-modifiable risk factors for peripheral artery disease are the same as those for other forms of cardiovascular disease.[5]

Patients with peripheral artery disease will often have co-morbidities. An Australian study of patients in general practice from 2008 – 2012 found that the prevalence of managed, i.e. known, co-morbidities in patients with peripheral artery disease was: hypertension (10.7%), diabetes (8.0%), lipid disorders (3.9%) and ischaemic heart disease (3.7%).[11]

## The limitations of ankle-brachial pressure index testing

1. The Doppler device that is used in the measurement of ABPI indicates the velocity of blood flow and although this is related to blood volume, it is not a measure of the amount of blood that peripheral tissues are receiving.
2. The technique is unable to determine the exact location of a patient's arterial stenosis or occlusion.
3. ABPI can be falsely elevated in patients with calcification of the medial arteries, e.g. in some patients with diabetes, renal dysfunction or rheumatoid arthritis.[8]
4. Some patients with arterial stenosis may present with intermittent claudication and normal ankle pressures at rest.[8] Referral for vascular testing may be required for patients where there is reason to suspect the presence of peripheral artery disease despite a normal or elevated ABPI being recorded.

## Lifestyle advice is the first-line treatment for peripheral artery disease

Some patients with peripheral artery disease may not associate their symptoms with their lifestyle, e.g. smoking or a lack of exercise. Give patients lifestyle advice to address modifiable risk factors, which in turn is likely to improve the symptoms of peripheral artery disease:[5]

- Smoking cessation
- Regular exercise
- Weight loss
- Eating a healthy and balanced diet

**Smoking cessation advice and support should be given to all patients with peripheral artery disease who smoke.**[5] There are relatively few robust studies investigating the direct benefits of smoking cessation on peripheral artery disease. There is observational evidence suggesting that smoking cessation will improve mobility in patients with peripheral artery disease.[5] However, the strongest evidence for the benefits of smoking cessation in patients with peripheral artery disease comes from cardiovascular outcomes. The excess cardiovascular risk of people who smoke is reported to be halved within one year of cessation and be the same as non-smokers within five years.[5] It can also be explained to patients that continued smoking will decrease the effectiveness of other interventions such as exercise programmes or surgery.

**Patients are recommended to walk for twenty minutes per day** and encouraged to exercise to the point of maximal pain.[5] Improvement, e.g. towards the goal of pain-free walking in patients with intermittent claudication, should be assessed after three months and regularly thereafter.[5] Patients with peripheral artery disease require a structured programme of regular walking because people who participate in exercise programmes have been found to benefit from improved limb function and general health. This is likely to be due to improved distal blood flow following the creation of new collateral blood vessels stimulated by the production of growth factors, e.g. vascular endothelial growth factor, and the release of vasodilating compounds, e.g. nitric oxide.[12] Compliance with an exercise programme is likely to be improved by supervision. Supervised exercise programmes involving walking three times a week on a treadmill have been shown to provide greater benefit to patients with peripheral artery disease compared with unsupervised programmes.[13] Where supervised programmes are not accessible, suggesting that patients participate in group exercise programmes may improve compliance and replicate the benefits of supervised exercise programmes.

## Pharmacological treatment of peripheral artery disease itself is unproven

There is little evidence supporting the pharmacological treatment of peripheral artery disease itself. However, emerging evidence suggests that angiotensin converting enzyme (ACE) inhibitors may improve walking ability in patients with intermittent claudication. A meta-analysis of six studies comprising over 800 patients found that treatment with an ACE inhibitor improved the maximum walking distance of patients with intermittent claudication by approximately 120 metres and improved pain-free walking distance by approximately 75 metres.[14] However, the ACE inhibitor with the greatest evidence of benefit is ramipril, which is not currently available in New Zealand. It is unknown if the improvement in walking distance associated with ramipril is due to a class effect of ACE inhibitors or whether it is specific to this medicine. The use of ACE inhibitors has not been shown to have a significant effect on ABPI, although this may be due to the limitations of ABPI testing.[14] Additional guidance on this issue will be published when more evidence is available.

Pentoxifylline (oxypentifylline) is a vasoactive medicine that has been used to improve blood flow in patients with peripheral artery disease by decreasing blood viscosity. It is partially subsidised in New Zealand, but is rarely used. In the United Kingdom the use of pentoxifylline is not recommended for the treatment of intermittent claudication in patients with peripheral artery disease, on the basis of lack of evidence of clinical and cost-effectiveness.[15]

## Pharmacological reduction of cardiovascular risk is recommended for all patients

Patients with peripheral artery disease require pharmacological treatments to reduce their cardiovascular risk:

- **Antiplatelet treatment** with either aspirin or clopidogrel (depending on the patient's cardiovascular history and presence of co-morbidities) is recommended for prevention of vascular ischaemic events. Antiplatelet treatment reduces the risk of serious vascular events by approximately one-quarter in patients with peripheral artery disease.[16]

- **Statins** are recommended for all patients with peripheral artery disease, unless contraindicated. NICE guidelines report a 17.6% reduction in cardiovascular events for patients with peripheral artery disease taking simvastatin with a total cholesterol > 3.5 mmol/L.[5] Statin use may also result in atherosclerotic plaque stabilisation and even plaque regression independently of their lipid-lowering ability.

- **Hypertension** should be treated to a target of 130/80 mmHg.[10] Dietary salt intake should be restricted.
- **$HbA_{1c}$ target** for patients with diabetes and peripheral artery disease should be ≤ 50 – 55 mmol/L (or as individually agreed, depending on other clinical factors).[10]
- **Renal function** should be monitored regularly, e.g. annually, in patients with peripheral artery disease. Microalbuminuria is the earliest sign of diabetic kidney disease.[10]

**Beta-blockers** may be cautiously continued in patients with peripheral artery disease where they are clinically indicated. Contrary to historical concern, a Cochrane review of six studies with a small sample of 119 patients found no evidence that the use of beta-blockers adversely affected walking distance, calf blood flow or vascular resistance in patients with peripheral artery disease.[17]

For further information on pharmacological treatment recommendations for hypertension and diabetes, see: "Hypertension in adults: the silent killer", BPJ 54 (Aug, 2013) and "Improving glycaemic control in people with type 2 diabetes", BPJ 53 (Jun, 2013).

## Referral may be required if interventions are unsuccessful

Vascular surgeons can provide advice and suggestions of additional treatment options at any stage during the patient's management. If smoking cessation, exercise, weight loss and pharmacological reduction of CVD risk have not been effective in improving the patient's symptoms within six months, then patients with peripheral artery disease should be referred to a vascular surgeon to discuss ongoing management of their condition, including a tailored exercise programme. Surgical procedures are performed on relatively few patients compared to the number of people diagnosed with peripheral artery disease. Vascular imaging, functional testing and surveillance programmes may be considered before more invasive procedures such as angioplasty, stent placement or revascularisation are considered.

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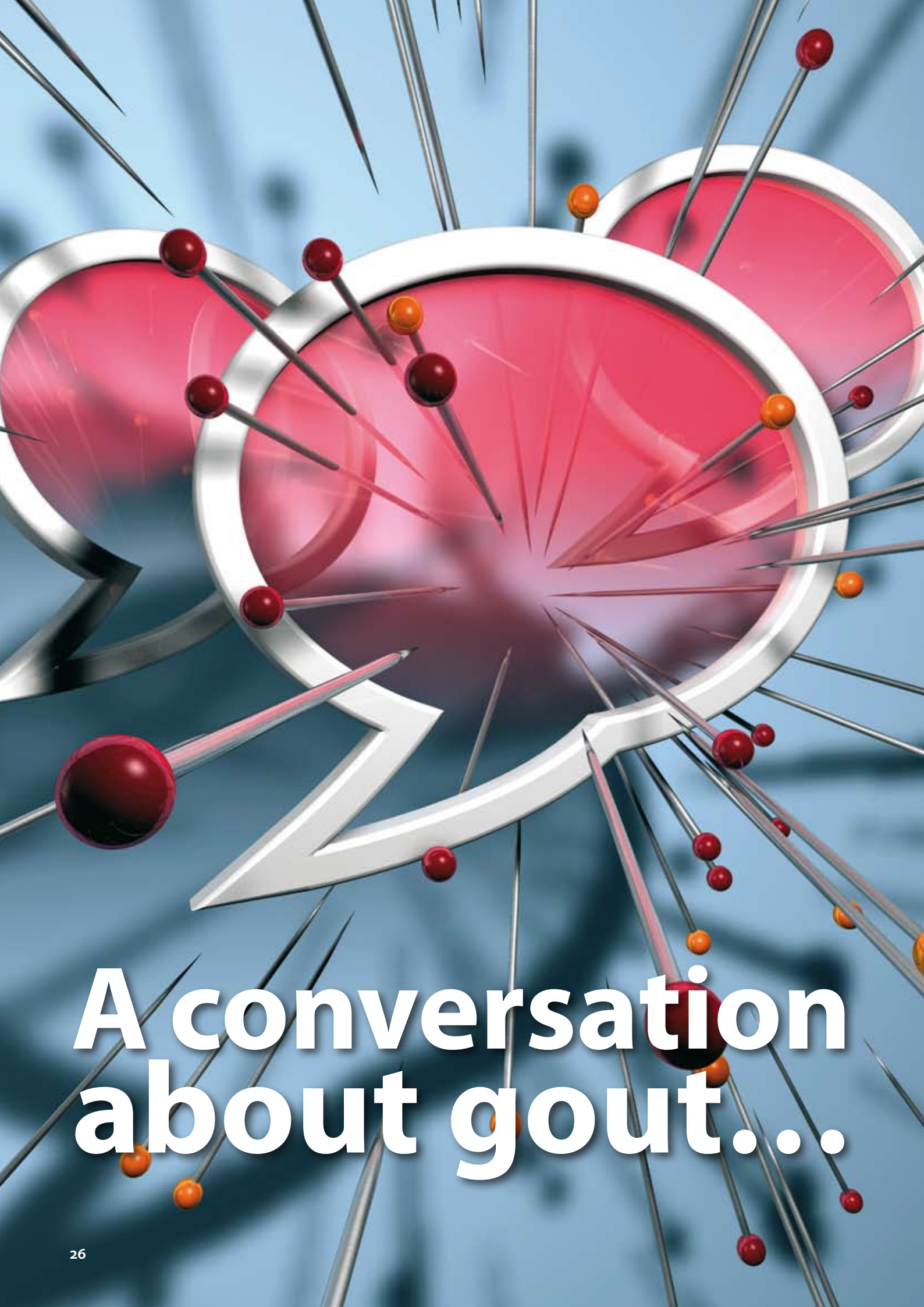


# A conversation about gout...

*In New Zealand, the majority of people with gout have higher than optimal serum urate levels. A primary reason for this is a lack of understanding of what gout is and of the need for ongoing treatment. Effective communication and educating patients about their condition improves their long-term outcomes. We interviewed Leanne Te Karu, a Pharmacist Prescriber from Taupo with a special interest in managing patients with gout, about why she thinks the message is not getting through. We discuss her approach to helping increase people's knowledge of gout, and include simple strategies to improve communication, enhance understanding and improve the health and quality of life of people with gout.*

## The challenges of managing gout

> *"It's such a bizarre thing that gout is something that, on the whole, is so easily treatable, so easily preventable and yet we as health professionals do so poorly."* — Leanne Te Karu

In New Zealand, surveys of health data sets estimate that at least 4% of adults aged over 20 years have gout, with higher rates in Māori (at least 6%) and Pacific peoples (at least 8%).[1, 2] Prevalence also increases with age, and is higher in males and in people living in lower socioeconomic areas; it is estimated that one-third of Māori and Pacific males aged over 65 years have gout.[1] It is likely that a significant number of people with gout are currently not identified, which would make estimates of prevalence even higher.[3]

A significant proportion of people with gout in New Zealand are poorly managed; it has been reported that studies in New Zealand have found that only approximately 50% of patients with gout had received a serum urate test in the previous year.[4]

A study involving patients with gout in South Auckland found that only 20% of those who were tested regularly had a serum urate level at or below target at any time in the previous year.[5]

One of the main barriers to managing gout is that patients often have a limited understanding of their condition and the medicines they take to control it, which can negatively affect self-management and medicine adherence.[6, 7]

Stoicism, embarrassment, a belief that gout is self-inflicted, fear that they will be "told off" by the clinician and that gout is a normal part of ageing are all commonly cited as reasons for poorer long-term outcomes.[6, 8] In contrast, increased knowledge (as perceived by the patient) about gout is positively correlated with improved management.[9]

However, the process of educating and engaging people with gout, as with many long-term conditions, is challenging.

This article is based on an interview with gout and clinical pharmacy researcher **Leanne Te Karu**. Leanne has worked across many facets of the health sector including hospital, community pharmacy, academia, marae and primary care. She is a Pharmacist Prescriber based in Taupo and runs a clinic in Turangi. She was a founder of the Māori Pharmacists' Association and has had a long-standing involvement in increasing health equality, particularly in Māori and lower socioeconomic communities.

## Three steps to improving communication

Most people with gout will benefit from improved education about their condition and their treatments. However, this process is complicated by the differences in the level of patient's knowledge, literacy, education and interest. Because of this, information and material provided to patients must be individualised and appropriate for them. The following three-step approach may be helpful when discussing complex information with a patient:

- Assess the patient's current understanding of the topic
- Build on that knowledge
- Check that the patient has understood the information you intended to convey

This then creates a loop, with gaps in understanding forming the basis of the further education, after an attempt to convey information.

### Assess the patient's current knowledge

*"We need to ascertain what people know first. It starts with checking what people know, so that you have a platform to go forward from."* — Leanne Te Karu

Start by asking the patient what they have been told about gout or how they would normally manage an acute attack. This can create an opportunity to ascertain what the patient knows and their level of understanding without the patient feeling like they are being tested.

### Build on that knowledge

*"It is essential that we deal to those fallacies about gout: that it's purely about food; that it's all your fault... and the myths about allopurinol being ineffective or 'bad'"* — Leanne Te Karu

Once the clinician understands the level of knowledge the patient has, they can fill in any gaps, discuss incorrect beliefs and suggest practical approaches to self-management. Education should cover what gout is, the difference between acute and preventative treatments and the lifestyle aspects of gout management.

### Check that the patient has understood

*"Before the end of the consultation we need to do a final check to ensure we have imparted the messages we intended. The important part is that we take ownership of any potential gaps in knowledge i.e. the responsibility is ours as health professionals. You can try various approaches, e.g. saying 'Ok, so I've done a lot of talking today. I just need to make sure that I'm doing my job correctly and that I've explained it clearly and what you got out of it?'"*

— Leanne Te Karu

As Leanne states, the final part of the conversation is ensuring that the patient has understood. This could be done by asking the patient what they will say if their partner or a family member asks them about gout and how it is treated. This forms an important part of the conversation, as information that sounds clear to a health professional will not always be clear to a patient.

### Health professionals have a responsibility for the health literacy of their patients

*"We don't often talk about the health literacy skills of the health professional. The onus has invariably and historically sat with the patient in front us. More emphasis needs to be placed on ensuring we are providing understandable messages and checking for that understanding."*

— Leanne Te Karu

Helping patients to understand what gout is requires a certain level of communication skill on the part of the clinician. While this is seemingly obvious, the current level of poor management, outcomes and medicine adherence clearly indicates that there is a gap in what patients should know about gout, and what they do know.

Given the wide range in levels of comprehension and literacy in patients, being able to adapt language to the individual patient is important. When talking about any health issue, patients will respond better when they perceive their healthcare professional to be understanding and understandable. A good strategy is to relate information to the patient's background and past experiences, provide practical information and avoid jargon.

## Cultural competency facilitates building health literacy

*"Health literacy needs to be thought of as a component of cultural competency. The overarching umbrella must be that people feel safe enough to share all that is relevant. In terms of gout, whanau often have stories, perceptions and experiences that are intergenerational. Again, at the heart of our practice is our responsibility to be culturally competent to ensure people feel safe to approach you, to share with you and to feel they have been understood."*

— Leanne Te Karu

The Medical Council of New Zealand states that: "Cultural competence requires an awareness of cultural diversity and the ability to function effectively, and respectfully, when working with and treating people of different cultural backgrounds. Cultural competence means a doctor has the attitudes, skills and knowledge needed to achieve this."[10]

Leanne stresses that cultural competency is an essential part of any attempt to improve a patient's understanding of their health and is fundamental to the entire interaction.

Gout can be easily diagnosed, prevented and treated. Clear clinical pathways have been developed that are built on robust best practice evidence. Yet there are still people with poorly controlled and managed gout. Leanne believes that engagement is the missing link.

## Dissolving the myths about gout

There is significant misinformation about gout in the community and many "myths" surrounding its pathogenesis, treatment and prognosis.

### Myth 1 – It's all about diet

*"[We need to be really clear] that it's not all about food. I think that's a huge myth out there that we have to dispel, because that prevents people coming forward; they think they're going to be judged about their diet – both food and drink intake. People often try to avoid all known triggers and still they experience flares. This can lead to blame both from self and whānau. It also reinforces a stereotype with younger ones who then delay seeking treatment. "*

— Leanne Te Karu

Many people hold the belief that gout is primarily a lifestyle disease. As Leanne states, this is not the full story. Genetic predisposition, usually due to inefficient renal urate clearance, is thought to account for a significant proportion of the prevalence of gout; it is reported that up to 60% of gout may be attributed to genetics.[11] One-in-four people with gout have a known family history of gout.[11] Māori and Pacific peoples in particular appear to be genetically predisposed to developing gout.[8, 12]

It is accepted that alcohol (particularly beer), purine-rich meats (e.g. red meat and offal), seafood (particularly shellfish and oily fish) and fructose and sucrose-sweetened drinks contribute to increased serum urate levels. Dietary and lifestyle changes are important and can achieve a lowering of serum urate levels,

but for most patients, pharmacological treatment of gout will play a more significant role in controlling hyperuricaemia.[13]

Dietary and lifestyle changes can be difficult for patients to adhere to and understand. As Leanne states, often the known triggers of gout are relatively healthy foods, e.g. tomatoes, kaimoana (seafood) and oranges which can still be enjoyed in moderation once target serum urate has been achieved. Sometimes this can be motivation for maintaining treatment when people realise they can enjoy such foods again.

## Myth 2 – You cannot exercise if you have gout

*"I agree there are conflicting messages out there, because we know that in an acute stage if you exercise your serum urate levels are going to go up, so we don't want that to happen, but we do want you to have an active lifestyle overall."*
— Leanne Te Karu

In the short-term, aerobic exercise may temporarily increase serum urate levels.[14] This should be carefully explained to patients to avoid discouraging them from exercising. Of course, exercise will be physically difficult or impossible for many patients during an attack due to pain and limited mobility.

Explain that increased exercise between acute exacerbations will be beneficial in the long-term, particularly for those who are overweight or obese. Exercise is also beneficial in reducing the risk of developing many of the co-morbidities associated with gout, such as cardiovascular disease (CVD).

Once the patient's acute symptoms have resolved, if necessary, help them to develop an exercise plan. Ask the patient to suggest a level of activity they feel they can commit to on a daily basis and use this as a starting point. Over time, the patient's level of activity should ideally be at least thirty minutes per day, the minimum amount recommended for New Zealand adults.[16]

Leanne has found that many patients are open to participating in organised exercise programmes, e.g. a walking or swimming group. A large number of whānau are now involved in events such as "Iron Māori".

Leanne also cautions against stereotyping as some of the people she sees are very fit young men, with low body fat percentages, playing sport at representative levels. This is another reason that we need to de-stigmatise gout so all people feel able to seek health assistance.

## Myth 3 – Allopurinol is a bad drug

*"I believe that because historically we have not prescribed allopurinol as recommended we have perpetuated the myth that allopurinol is a 'bad drug'. By this I mean sometimes allopurinol is initiated at an increased dose with or without concurrent NSAIDs cover (more often than not – without) and people end up having a flare. We then do poorly at titrating dosage to reach target and people again get flares – they begin to wonder at the point of it all. I also find that sometimes people are not clear on the function of allopurinol and take it only while they have a flare. Again whose fault is it if they are not clear – certainly not theirs I would advocate."* — Leanne Te Karu

Ensure patients understand that allopurinol is the mainstay of gout prevention, and the majority will need urate-lowering treatment for long-term control.[17] It can be explained (in an appropriate way) that allopurinol inhibits the activity of an enzyme (xanthine oxidase) needed to create urate.[13] If this enzyme is blocked, serum urate levels will fall and urate crystals will slowly dissolve over time.[13]

Many patients are hesitant to take allopurinol, as there is significant misinformation about the medicine in the community. One of the more widespread objections to allopurinol is that it will worsen the symptoms of gout. This belief has likely arisen due to the increased risk of gout exacerbations in the first six months of treatment when allopurinol is dosed or titrated sub-optimally, e.g. using a starting dose of 300 mg instead of titrating up from a lower dose.

Explain to the patient that allopurinol is a safe and highly effective medicine if taken consistently. It may cause flares when treatment begins, but as cover, most colchicine or NSAIDs (e.g. naproxen) is given concurrently, these should be manageable.[17] This can be used as an opportunity to explain to the patient the need for titration and the necessity of taking the medicine every day, including during gout flares. Other strategies, such as using blister packs during the titration phase, can be considered to aid patients and to reduce medication errors.

If, despite optimal use of allopurinol, gout is still unable to be managed (or if allopurinol is not tolerated), further treatment options may be considered, e.g. probenicid, benzbromarone, febuxostat.

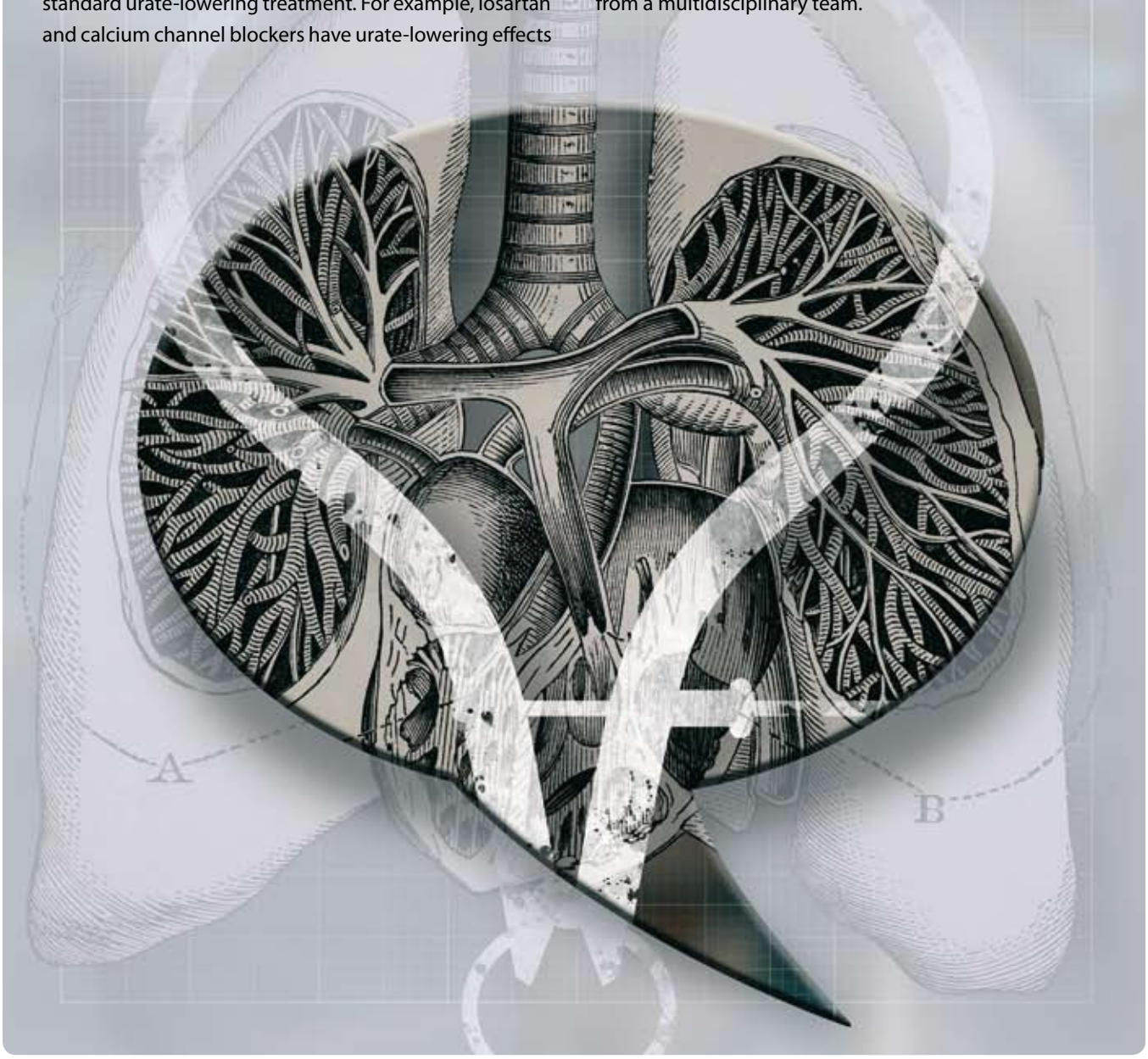
## Presentations for gout can be used as an opportunity to address co-morbidity

In New Zealand, it is estimated that 40% of people with gout have cardiovascular disease and/or diabetes.[15] The European League Against Rheumatism (EULAR) recommendations state that associated co-morbidities, such as hyperlipidaemia, hypertension, hyperglycaemia, obesity and smoking, should be addressed in people with gout as part of their routine management.[17]

Apart from the obvious benefit of detecting and managing these conditions in their own right, there is evidence that the management of co-morbidities has a positive effect on serum urate levels, independent of standard urate-lowering treatment. For example, losartan and calcium channel blockers have urate-lowering effects which may be useful in the treatment of hypertension in patients with gout.[15] Atorvastatin also has urate-lowering properties and may be useful in patients with gout who require a statin.[15]

Conversely, several medicines that are used to treat associated co-morbidity can increase serum urate levels, such as diuretics and low dose aspirin.[15]

Management of patients with gout with multiple co-morbidities, such as heart failure, severe hypertension or renal damage, may require discussion with and input from a multidisciplinary team.

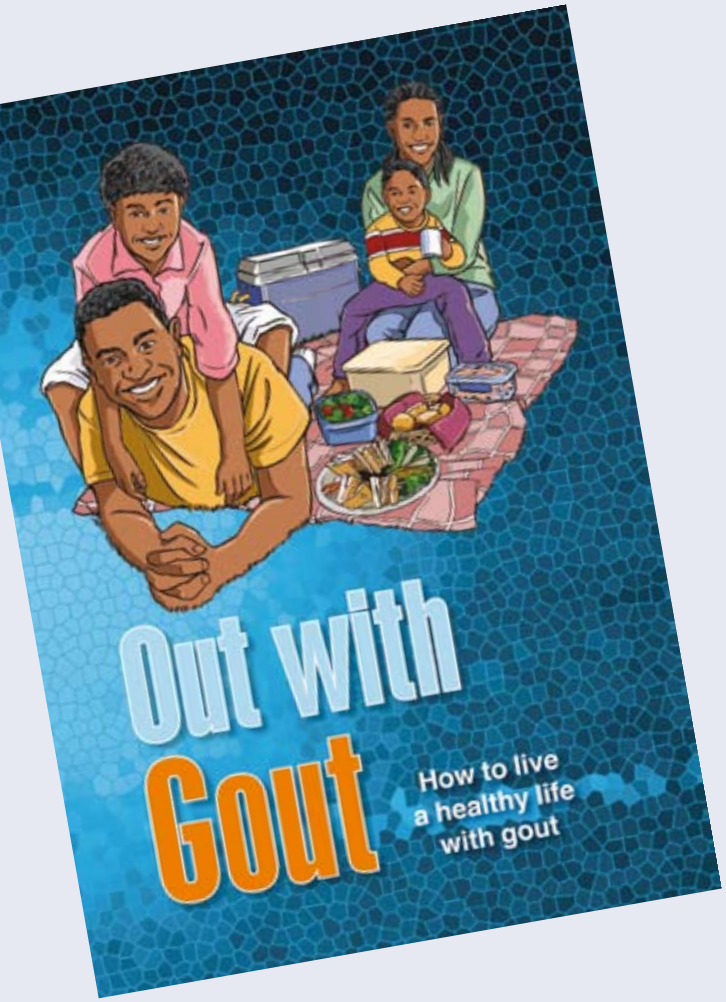


## Resources for patients

The "Out with Gout" booklet, produced by PHARMAC can be recommended, or provided, to patients as a take-home resource. The booklet is culturally relevant to New Zealanders and is available in English and Te Reo Māori and can be ordered in other languages.

The booklet is available from **www.pharmac.health.nz/medicines/your-health/gout** and alternate language translations can be ordered from: **www.pharmaconline.co.nz**

For further patient resources, see: **www.gouthappyfeet.com/gout-how-it-effects-you**




### Myth 4 – Gout is an acute joint disease

*"It's about [the patient] understanding that it's not just about joint pain … that gout is a chronic condition… that it's actually about their kidneys, and about cardiovascular disease."* — Leanne Te Karu

For many patients, the pain and disability present during attacks will be the primary motivator for seeking treatment. However, this motivator is absent between exacerbations and in people who have reached their target urate level, which can then lead to them stopping their medicines. As Leanne phrased the problem: *"[NSAIDs or prednisone] work during a flare… so why do I want to take a medicine everyday forever?"*

This problem can be likened to an issue commonly encountered in people with asthma; regular use of a reliever medicine, but often suboptimal use of preventer medicine. As with asthma, understanding the role of each medicine is the key.

Helping patients understand what urate is, that NSAIDs only cover the symptoms and attempting to get patients actively involved in trying to lower their serum urate levels is crucial. Annual urate testing, which is necessary to monitor urate-lowering treatment efficacy and dosage, can be used to illustrate ongoing improvements in urate level and give justification for continuing allopurinol treatment.

Patients will benefit from knowing that gout is a chronic condition that requires long-term management to prevent joint erosion and permanent disability. Along with the long-term damage to the joints, gout is associated with other significant risks (see: "Presentations of gout should be used as an opportunity to address co-morbidity"). Hyperuricaemia, the primary risk factor for gout, is associated with an increased risk of:[13]

- Hypertension
- Renal damage
- Diabetes and insulin resistance syndrome
- Hyperlipidaemia
- Cardiovascular disease (CVD)
- Obesity

*"It's a little bit like diabetes… you are not always hypo or hyperglycaemic when you have diabetes, but you always have diabetes. [With gout], you always have this underlying tendency to have a gout flare if your urate level is too high."*

— Leanne Te Karu

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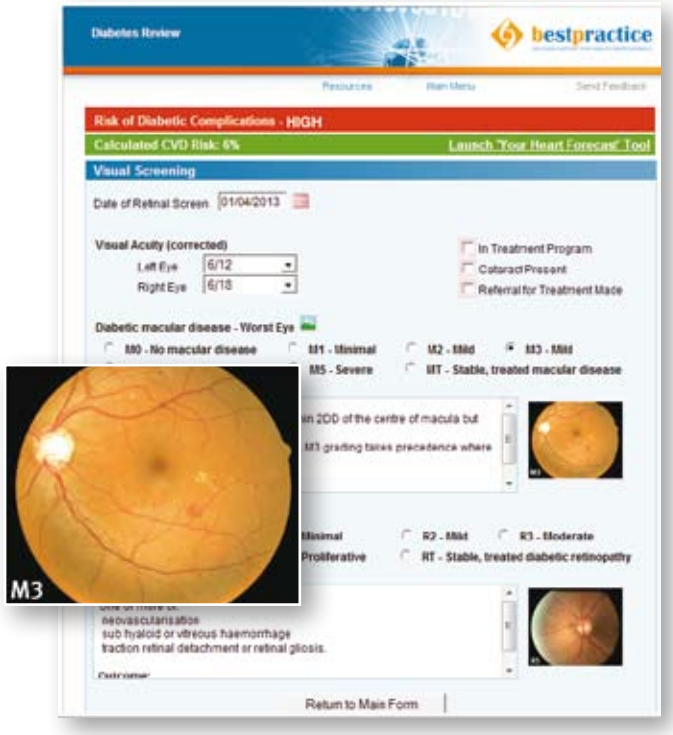


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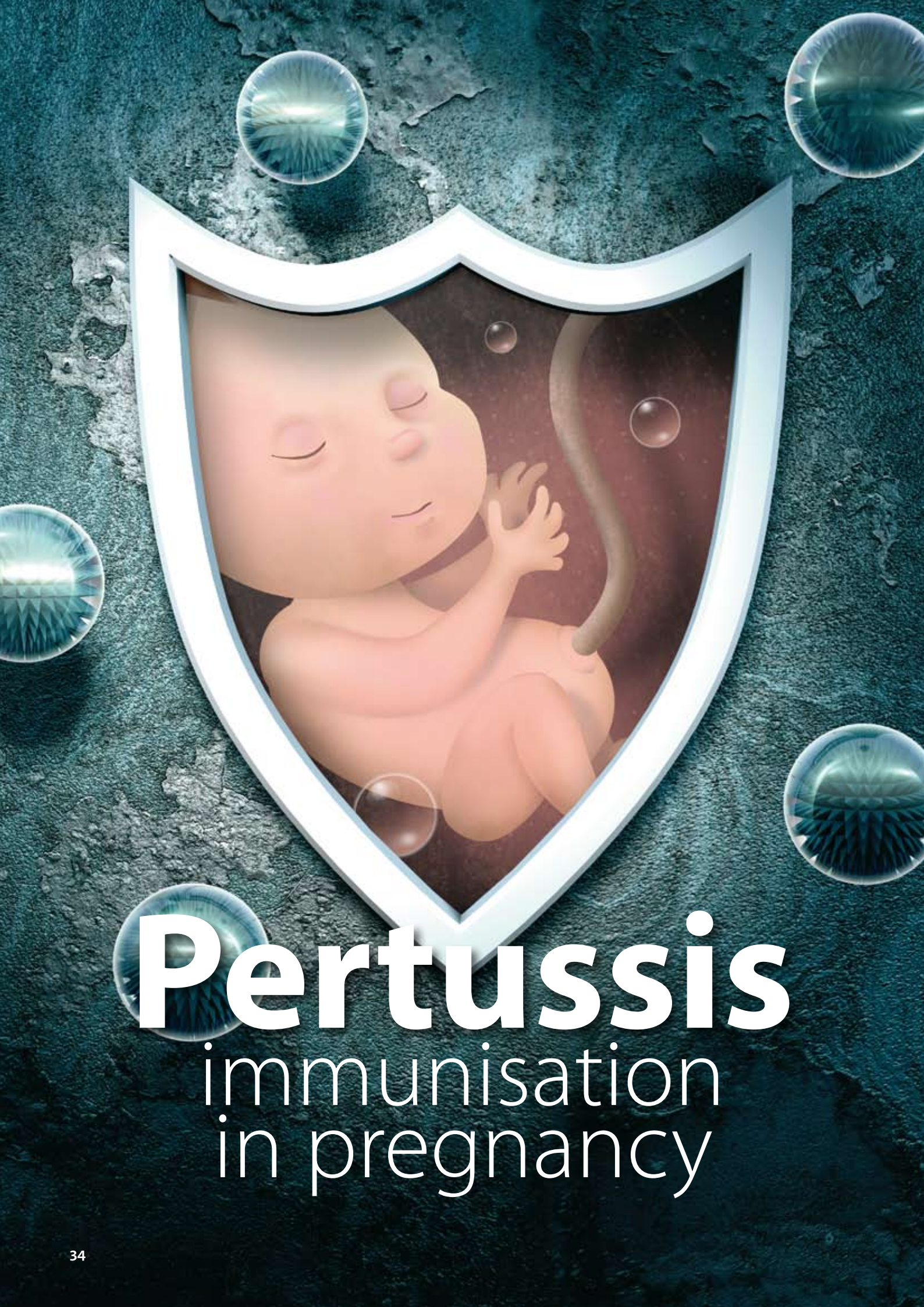


# Pertussis immunisation in pregnancy

*New Zealand is slowly emerging from its most recent outbreak of pertussis. The highest-risk period for pertussis in infants is in the first six months of life, prior to the completion of their full course of infant immunisation. Almost all deaths due to pertussis occur in infants aged six months or under. Improving total immunisation coverage remains the best means of protecting young children from pertussis. However, pertussis immunisation of the mother while pregnant provides some passive immunity to the infant during their first six months of life, so is strongly recommended.*

## The pertussis epidemic is waning, but immunisation is still important

New Zealand is slowly emerging from its most recent outbreak of pertussis. At present, the number of notifications for pertussis is still high, but is declining. There were 169 notified cases in January, 2014, compared with 566 in January, 2013, and 444 in January, 2012*.[1] Since the outbreak began in August, 2011, there have been a total of 10,060 pertussis notifications, resulting in 560 hospitalisations and three deaths.[1]

Pertussis in infants is almost always severe. Infants aged under one year account for less than 10% of notifications, but approximately 60% of hospitalisations.[1] Approximately 90% of pertussis fatalities occur in infants.[2] There are three stages to pertussis infection: the catarrhal stage, the paroxysmal stage and the convalescent stage. Classically, pertussis in infants will cause a clinical illness of six to twelve weeks or longer.[2] The paroxysmal stage, which generally occurs in the second to third week of clinical illness, is associated with severe, forceful coughing followed by massive inspiratory effort (this is the archetypal "whoop" of whooping cough).[2] Severe coughing may cause vomiting and cyanosis. Common complications include pneumonia and otitis media. Seizures and encephalopathy can occur due to cerebral hypoxia occurring with severe paroxysms.[2] Rarer complications include pulmonary haemorrhage, subdural and spinal epidural hematoma, epistaxis, gastrointestinal haemorrhage, subconjuctival haemorrhage, rupture of the diaphragm, umbilical and inguinal hernia, rectal prolapse, apnoea, rib fracture and severe alkalosis with associated tetanic seizures.[2] Bronchopneumonia is present in most fatal cases of pertussis; pulmonary hypertension, pulmonary or cerebral haemorrhage and atrophy are also reported.[2]

Pertussis outbreaks continue to occur in New Zealand, and most other developed nations, every three to five years. This is primarily because immunity to pertussis declines over time following either infection or immunisation, but is also compounded by inadequate levels of immunisation.[3]

Improving total immunisation coverage remains the best means of protecting young children from pertussis. All infants should receive three doses of the pertussis vaccine by age six months (DTaP-IPV-HepB/HiB), with booster doses at ages four (DTaP-IPV) and eleven years (Tdap).[4] Delay in receiving any of the three infant doses of pertussis vaccine is associated with a significantly increased risk of hospital admission for pertussis.[3, 5] In addition, delay in receiving the first vaccination is a strong predictor of subsequent incomplete vaccination.[3]

The highest-risk period for pertussis in infants is in the first six months of life, prior to the completion of their full course of infant immunisation. Almost all deaths due to pertussis occur in infants aged six months or under.[6] Pertussis immunisation of a mother while pregnant provides some passive immunity to the infant during these first six months,[6] so is recommended.[7]

For further information on pertussis and the recent epidemic, see "Pertussis: halting the epidemic by protecting infants", BPJ 51 (Mar, 2013).

* Figures for 2012 represent 7 January, to 3 February, rather than the whole of the month, as data was recorded differently in 2012.

## The pertussis vaccine in women who are pregnant

### The pertussis vaccine remains subsidised for women who are pregnant

The pertussis vaccine is subsidised during times of epidemics for women who are pregnant; pertussis vaccination is currently still subsidised. Women who are pregnant are eligible for the subsidy if given the Tdap vaccine (Boostrix) between weeks 28 – 38 of pregnancy.

### Evidence for the efficacy of immunisation of pregnant women

The uptake of the pertussis vaccine in New Zealand in women who are pregnant is reported to be low (estimated around 13%). There is evidence for the efficacy of pertussis vaccination in women who are pregnant, in providing immunity to both the mother and the infant, and it is considered safe. In one large United States study analysing a birth cohort of 131 019 infants, vaccination during pregnancy (between 28 – 38 weeks) reduced infant pertussis cases by 33%, hospitalisations by 38% and deaths by 49%.[8]

Maternal pertussis antibodies are readily transferred to infants across the placenta, and antibody concentration in infants at birth are approximately equal to that of the mother.[6, 9] However, pertussis antibodies gradually decline following infection (antibodies decline over four to 20 years) or immunisation (antibodies decline over four to 12 years).[9] As a result, the majority of infants are born to mothers with pertussis antibody titres below the level that is considered necessary to provide functional protection against pertussis infection.[6] In addition, after birth the infant's antibody level falls rapidly, and by age four to six months, most infants who have not been immunised will have no measurable antibody to pertussis.[6, 9] Even when infants are immunised at age six weeks, antibody levels will be too low to reliably prevent infection for the first weeks and months of life.

With maternal immunisation during pregnancy, the level of antibody in infants is significantly increased,[6, 9] and there is a strong likelihood that newborn infants whose mothers are immunised will have some protection against pertussis.[6] The infant's pertussis antibody levels will still decline following birth, but sufficient immunity is thought to persist until the active immunisation of infants begins at age six weeks.[6] The primary series of vaccinations does not provide optimal protection until all three vaccinations have been received,[3] although it is likely that maternal antibodies still provide some increased protection beyond the initial vaccination.

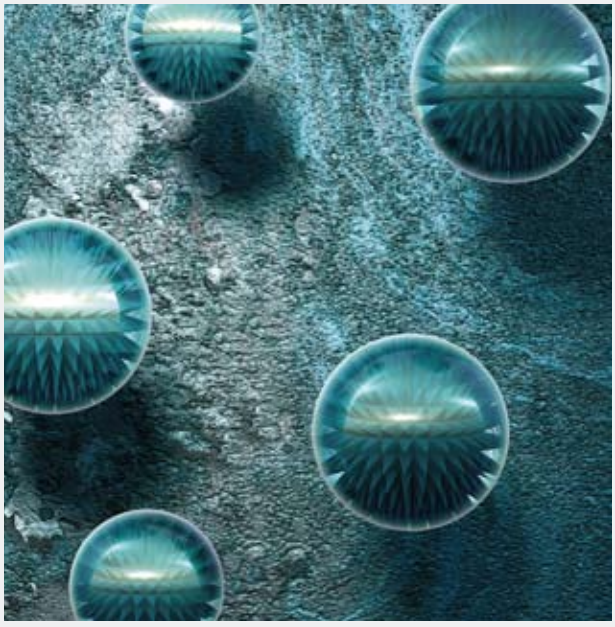
### Timing the vaccine

The timing of pertussis vaccination is important. Adult antibody levels peak approximately two weeks following vaccination, and have then been shown to decrease rapidly. Antibody levels in women vaccinated prior to pregnancy or early in pregnancy may be insufficient to provide effective

## Treating pertussis in women who are pregnant

If women who are pregnant contract pertussis late in their pregnancy, there is a significant increase in the risk of passing the infection to the infant at or soon after birth.[12] Because of this, women who are pregnant who present with pertussis should be prescribed antibiotics regardless of when symptoms started. While antibiotic treatment is unlikely to alter the course of the patients illness or reduce their symptoms, it has been shown to reduce transmission rates.[13]

Erythromycin, 400 mg, four times daily, for 14 days, is the recommended first-line antibiotic in women who are pregnant.



passive immunity to the infant after birth.[10] The vaccine should be given between 28 – 38 weeks gestation, as it allows enough time for passive transfer of immunity from the mother to the infant to occur.[11] The vaccine is subsidised from 28 weeks gestation to facilitate the best timing.

## The safety of the vaccine in pregnancy

Vaccination in pregnancy with the Tdap vaccine, which contains acellular pertussis (inactivated), is considered safe.[4] No elevation or unusual patterns of serious adverse effects have been identified in women who are pregnant receiving the vaccine.[8] In addition, the tetanus and diphtheria components, as Td vaccine, have been safely used in women who are pregnant for several decades.[8]

The only contraindication to use of the pertussis vaccine is an anaphylactic reaction to a prior dose or any component of the vaccine.[4]

## Cocooning can also be used to protect infants from pertussis

In the United States, in 76 – 83% of fatal cases of pertussis in infants since 2004 (90% of whom were aged under three months), the infection was transmitted by a family member, most often the mother.[9] Immunising adults and older children, that have regular contact with infants, such as fathers, siblings, grandparents and other caregivers, can be used to provide a "cocoon of immunity" to help prevent infection until the infant's pertussis immunisations are completed.[4] One dose of Tdap vaccine (Boostrix) is sufficient in this group.[4] This will usually be unsubsidised.

If a woman does not get vaccinated during pregnancy or declines vaccination during pregnancy, and has never received Tdap before, vaccination immediately following birth is recommended (but not funded).[11] While this will not have the same benefit in providing maternal antibodies to the infant, it may help to limit the infant's exposure to pertussis. The vaccine can safely be given if the mother is breast feeding; there is limited evidence as to whether maternal antibodies can be passed on via breast feeding.

It is recommended that other adults with significant contact with infants, such as healthcare workers and early childhood service workers, are also immunised against pertussis (one dose, repeated at ten-yearly intervals).[4] Outbreaks of pertussis have been linked to healthcare organisations and childcare facilities, and infant fatalities due to nosocomial spread have been reported.[3] As a result, some New Zealand DHBs have begun implementing pertussis immunisation programmes for staff who have frequent contact with infants.[3]

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# Update on the **Adverse Drug Reaction reporting tool**

*Reporting suspected adverse drug reactions enables the collection of information on the safety and quality of medicines and vaccines after they have been approved. An electronic adverse reaction reporting tool was launched in New Zealand in 2009. The reporting tool was designed to make the process of reporting events easier by pre-populating patient details, allowing more data to be included and enabling more timely advice to be provided to prescribers. In the five years since it's launch, electronic notifications using the ADR tool have doubled.*

## Adverse drug reactions reporting in New Zealand

Adverse drug reaction reporting is one of the most important sources of data for assessing the safety and quality of a medicine. Prior to marketing, all of the information on a medicine's safety and efficacy is based on clinical trial data. While vital, clinical trials rarely reflect the actual use of a medicine or the typical population for whom a medicine is prescribed.

Adverse drug reaction reporting forms the core of post-marketing surveillance, and the identification of unusual patterns of adverse effects has lead to the withdrawal or restriction of many medicines since the World Health Organisation began the international drug monitoring programme in 1971.

Adverse reactions reporting in New Zealand is managed by Medsafe and the Centre for Adverse Reactions (CARM). CARM receives, on average, 4000 spontaneous adverse reaction reports each year. Approximately half of these adverse reaction reports are submitted from general practice.

When CARM receives a report, it is processed, coded and then assessed by relevant specialist clinicians. The person submitting a report will then receive a reply from CARM that includes information on the likely cause of the reaction and how frequently the reaction is reported.

Although New Zealand's adverse reactions reporting system is highly regarded internationally, it is thought that, at most, one-in-ten adverse reactions are reported. For example, analysis of the data stored in the Patient Management Systems of 30 general practices found that of the 725 entries in the medical warnings files that recorded an adverse reaction or allergy to at least one medicine, only 21 were reported to CARM.

There are a number of reasons why an adverse reaction might not be reported. These include the absence of a prompt to initiate reporting, failing to realise that an adverse reaction has occurred, assuming that a reaction is already well known and the time required to manually fill in reaction forms.

## The launch of an electronic adverse reaction reporting tool

On 1 April, 2009, the Minister of Health launched a new electronic adverse drug reaction (eADR) reporting tool in New Zealand.

The tool was designed to make the reporting of adverse reactions to CARM easier. To do this, it uses an online reporting form pre-populated with patient details from the Practice Management software.

### Simpler reporting should mean more reporting

The adverse reaction tool was developed to help decrease the time involved in reporting. Pre-populating the reporting form with patient data reduces manual entry of information. Electronic reporting means less paperwork and removes the need to post or fax reports to CARM.

The ability to extract data from Patient Management software makes it easier to include results from laboratory tests and other investigations. This has improved the ability of CARM's advisory clinicians to review the data and to determine whether the medicine is responsible for the reaction.

As well as making the process simpler, electronic reporting reduces the time it takes for advice to be provided. In addition, CARM now adds patient-specific alerts through the medical warning module of the NZHIS system. Alerts are attached to the patient's NHI number so, for example, when a patient is admitted to hospital, the patient does not receive a medicine they have already reacted to.

### Electronic reporting is gaining traction

As of February, 2014, 594 general practices have transmitted information to CARM via the eADR tool which launched in 2009.

In 2009 there were 378 individual reports submitted through the eADR tool. In 2013 this had doubled to 616 reports. As a percentage of total reports to CARM, this represents an increase from 8% in 2009 to 15% in 2013.

While the total number of adverse reactions reported to CARM via any method has remained stable from 2009 to 2013, the percentage of reports received from general practice has increased from 46% in 2009 to 55% in 2013. This suggests that the eADR tool may be encouraging reporting from the general practice sector especially among nurses; 20% of reporters in 2009 were nurses compared to 33% in 2013.

## How do I use the eADR?

To access the eADR, look for "Adverse Drug Reactions Reporting" on the modules list on your BPAC Dashboard.

Once opened the tool automatically pre-populates the patient's medical history, medicine use and gives the option of including laboratory test results.

As vaccines make up approximately one-third of the adverse reaction reports received every year, the tool has been designed with a specific vaccine tab. If the suspected medicine is a vaccine, the tool pre-populates the batch number, the date of administration and how the vaccine was given.

Once a description of the reaction and other pertinent information is entered, a report can be electronically sent to CARM. The details of the patient and reporter are encrypted in the electronic reporting tool, and as with the paper-based form, the information provided in the report is only viewed and used by CARM.

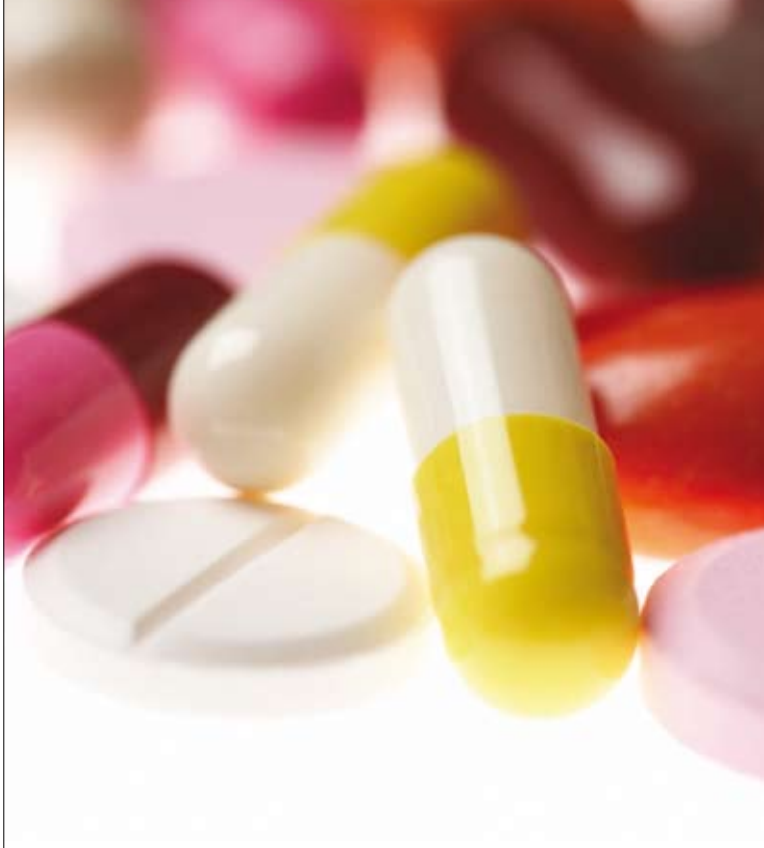
In general, it appears that the reports generated by the eADR tool reflect a standard set of subsidised medicines being prescribed, e.g. smoking cessation medicines, antibiotics, antihypertensives, antidepressants and NSAIDs were all among the most commonly reported medicines. The reports generated through the electronic form are similar to the overall make-up of the reports, e.g. vaccines make up 39% of e-reports compared to 35% of reports overall.

Health professionals are encouraged to make use of the eADR tool and ensure that all potential adverse drug reactions are reported to CARM.

**A request from CARM:** ensure that the dates of prescriptions for each of the medicines are included in the report to enable clear identification of the concomitant medicines at the time of the adverse reaction occurring.

**ACKNOWLEDGEMENT** Thank you to **Janelle Ashton,** Manager Information Systems, New Zealand Pharmacovigilance Centre, University of Otago, Dunedin for providing data for this article.





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# Adverse Drug Reaction

## Adverse Drug Reaction Reporting Tool

GPs in all regions of New Zealand have access to an online tool to report Adverse Drug Reactions directly to the Centre for Adverse Reactions Monitoring (CARM).

The reporting form pre-populates with patient demographic and relevant clinical data from the GP practice software. This facilitates completion of a detailed report while encrypted electronic submission ensures confidentiality of information. Every report submitted receives a personal reply from CARM.

Look for 'Adverse Drug Reaction Reporting' on the Module list of your BPAC Dashboard.

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# Ethics In General Practice

**GENX 824, Semester 2 – 2014**

POSTGRADUATE STUDIES

UNIVERSITY of OTAGO
Te Whare Wānanga o Otāgo
NEW ZEALAND

YOUR PLACE IN THE WORLD

| | |
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| **Venue:** | Department of General; Practice and Rural Health, 55 Hanover Street, Dunedin |
| **Faculty Convenors:** | Associate Professor Chrys Jaye, Professor Susan Dovey & Dr Katharine Wallis |
| **Residential date:** | Saturday July 5th and Sunday July 6th, 2014<br>NB there is only one residential for this paper |

**GENX 824 is a 15 point paper** which is offered by distance learning over one semester and can be credited towards the Postgraduate Diploma in General Practice (PGDipGP).

This paper is an introduction to health care ethics as applied to general practice. Its aim is to examine the different philosophical approaches to ethics and to view their applications in the contemporary health care setting on a range of topical issues. It provides a safe and confidential platform for in-depth discussion with colleagues about ethical challenges arising in general practice, and for reflection on practitioners' own values.

There is one residential at the start of the course and 6 modules:

- Money and medicine
- Ethics and screening
- Beginning of life
- Dying
- Patient choices
- Environmental and global issues
- Open topic

Each participant brings a unique perspective and case-based experience and will have the opportunity to focus on an issue of personal interest. Common outcomes of this paper are a greater clarity when dealing with ethical issues in complex health care situations, and an improved ability of ethical reasoning.


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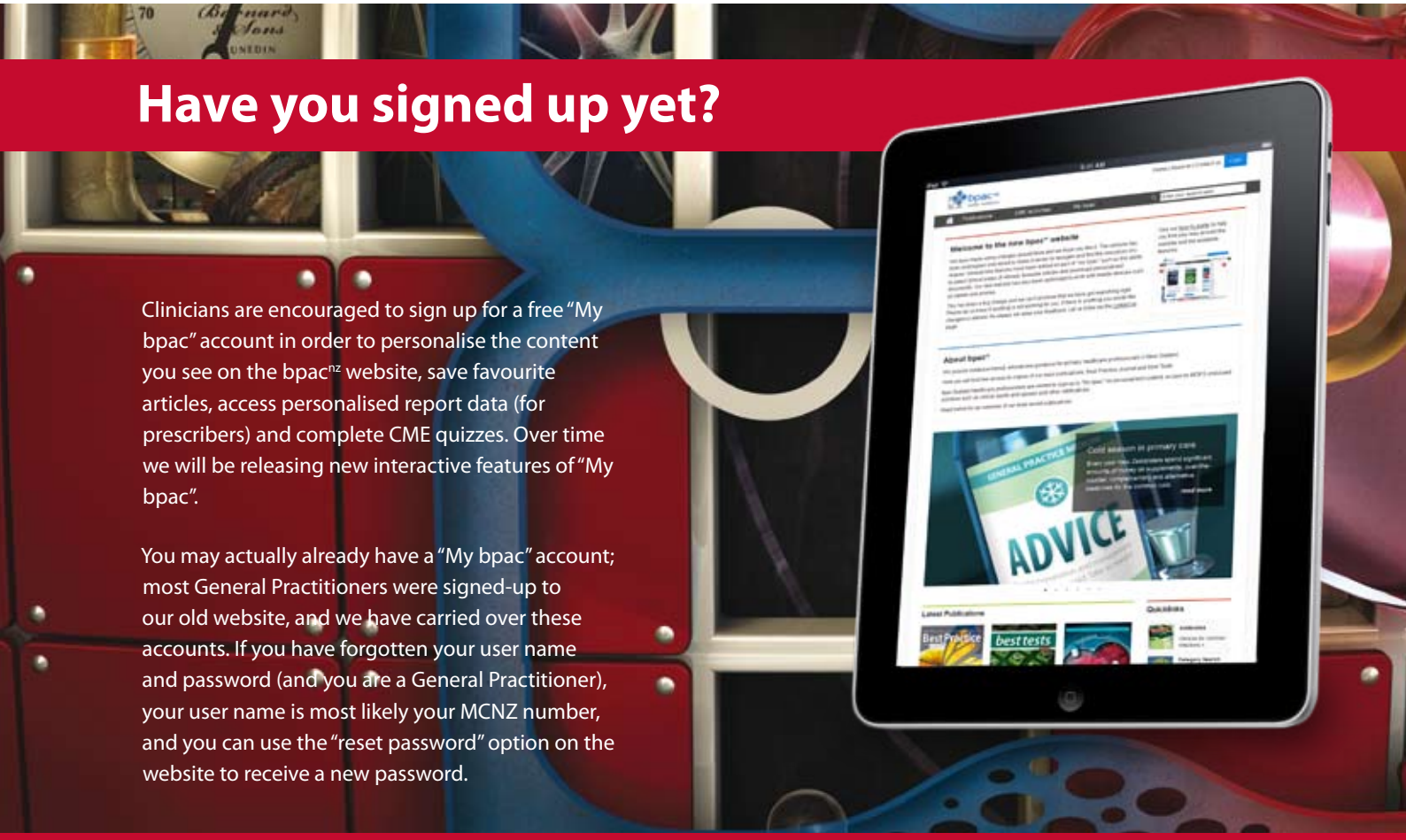


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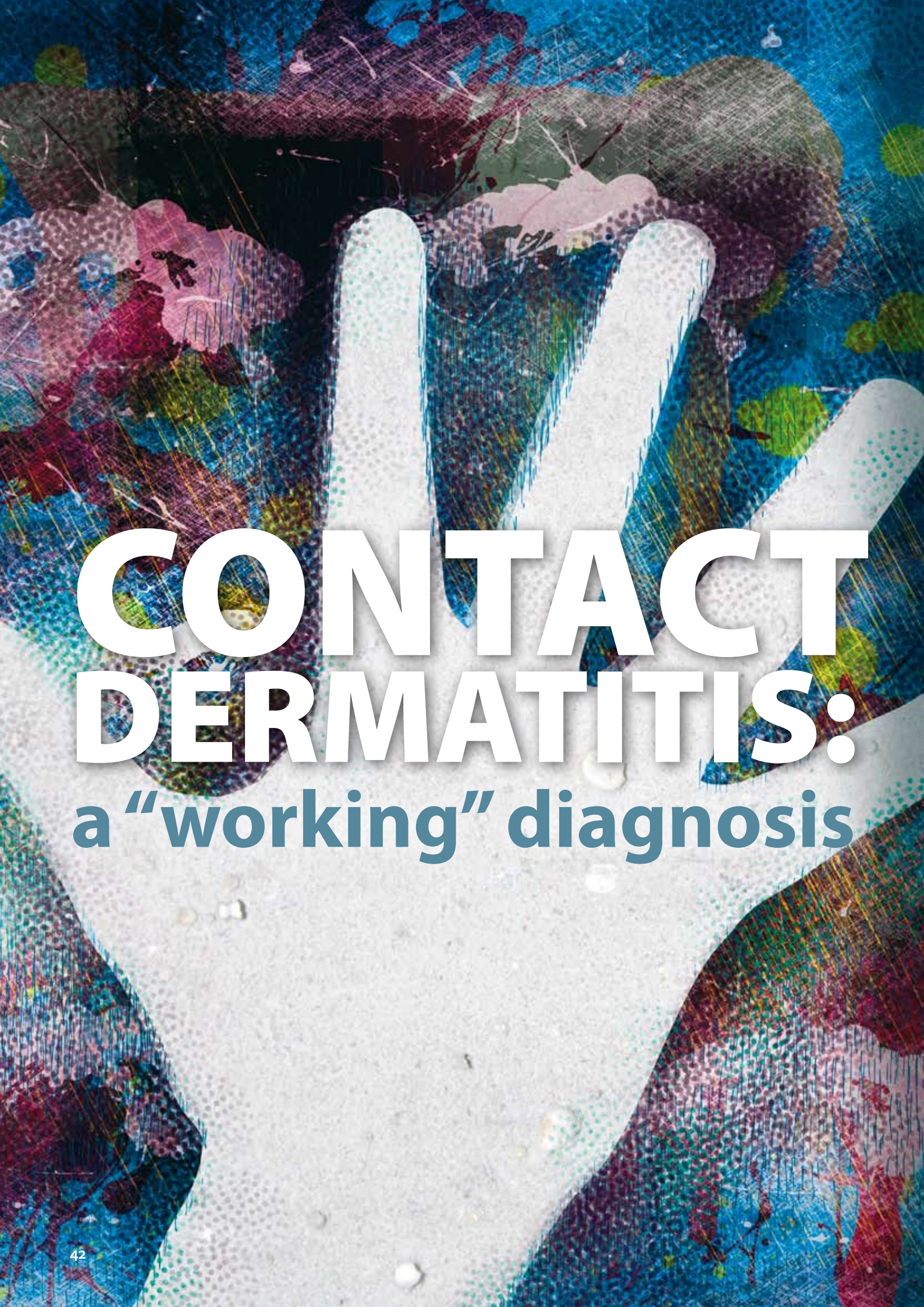

# CONTACT DERMATITIS:
## a "working" diagnosis

**Contributed by: Dr Lissa Judd, Occupational Dermatologist, Wellington**

Up to 20% of the general population suffer from contact allergy,[1] and it is estimated that there are 5 – 19 cases of occupational contact dermatitis per 10 000 full time workers per year.[2]

People working in the following industries are most affected by occupational dermatitis:[3]

- Food handler/chef
- Hairdresser/beautician
- Medical/dental/nurse/vet
- Agriculture/florist/gardener
- Cleaning/laundry
- Painting
- Mechanical/engineer
- Printing/lithography
- Construction

## Clinical features of contact dermatitis

Contact dermatitis encompasses:

- Contact irritant dermatitis
- Contact allergic dermatitis
- Contact urticaria
- Photocontact dermatitis
- Systemic contact dermatitis.

Different forms of dermatitis may co-exist, e.g. an individual may have atopic dermatitis, contact irritant dermatitis and contact urticaria. In general, morphology does not differentiate contact from endogenous dermatitis; the diagnosis is suggested by the distribution, severity, temporal association with certain activities and allergy testing as appropriate.

**Contact irritant dermatitis** can be subdivided into subjective irritancy (stinging within minutes of contact, without objective findings), acute contact irritant dermatitis (a chemical burn) and chronic contact irritant dermatitis (when physical or chemical damage overwhelms the skin's repair mechanisms). Irritants include over- and under-hydration, soaps and detergents, solvents, abrasives, acids and alkalis. The likelihood that contact irritant dermatitis will develop depends on the potency of the irritant(s), occlusion, temperature, anatomical site and innate susceptibility; anything which impairs the skin's barrier function will potentiate the damaging effects of exposure to irritants. Contact irritant dermatitis is normally the cumulative effect of multiple irritants, and most commonly it affects the hands.

**Contact allergic dermatitis** affects only a small percentage of individuals exposed to an allergen. Many years of uneventful exposure may precede sensitisation, but once sensitised even tiny exposures can induce dermatitis. A cell-mediated immune reaction results in dermatitis one to four days after contact with the allergen. Contact allergic dermatitis most commonly affects the hands and face, but may also involve sites of secondary contact where small amounts of allergen have been transferred accidentally by contaminated fingers. Although there are thousands of potential allergens, a relatively small number account for the majority of cases of contact allergic dermatitis. Common allergens include rubber additives, chromate, epoxies, nickel, hair dyes, fragrances, biocides and plant derivatives including colophony (resin).

**Contact urticaria** may be IgE-mediated, or (more commonly) may occur through non-immunological mechanisms. It results in immediate itching, welts or aggravation of eczema at the site of exposure, and occasionally generalised urticaria (in the case of immune-mediated contact urticaria). It is most commonly caused by raw meat, fish or vegetables in food handlers, fish processors and abattoir workers; it can also be caused by rubber latex.

**Photocontact dermatitis** affects sun-exposed sites when a chemical in contact with the skin is altered by ultraviolet to produce either a photoallergen (causing dermatitis through immunologic mechanisms) or a phototoxin (causing dermatitis through non immunologic mechanisms). In New Zealand most photoallergic contact dermatitis is due to sunscreen chemicals, and most phototoxic reactions are due to furocoumarins in plants such as parsnip and celery.

**Systemic contact dermatitis** occurs when a person with a contact allergy to a substance (usually a medicine) is exposed to that substance systemically.

## Investigation of contact dermatitis

**Contact irritant dermatitis** is diagnosed based on the patients history: the affected sites are exposed to irritants with sufficient frequency, duration or concentration to be a plausible cause of the dermatitis; the dermatitis improves or resolves following reduction or cessation of the irritant exposure; and there are no alternative explanations that might better account for the signs and symptoms.

**Contact allergic dermatitis** is diagnosed by patch testing: haptens are applied under occlusion to intact skin for up to 48 hours, and then the sites are checked for signs of reaction (erythema, papules, and vesicles). The sites are checked again on day four, and ideally again on day six or seven. The tests include a standard series of haptens (which is designed to pick up approximately 80% of the relevant positive reactions in that country), and any additional haptens as determined by the patient's history of exposure. Photopatch testing for the diagnosis of allergic photocontact dermatitis is the same, except the haptens are photoexposed on day two.

**Contact urticaria** is diagnosed by scratch-patch testing (test substances are applied over a superficial scratch, occluded, and left for 20 minutes), or occasionally prick tests or RAST tests.

A recent editorial in Archives of Dermatology commented that "most dermatologists use patch testing infrequently, and a significant minority of dermatologists do not patch test at all."[4] Of those that do patch testing, many limit their test to a routine screen, which adequately evaluates only 15.7% of patients with contact allergy.[4] Any patient with persistent dermatitis, which requires aggressive treatment for its control, should be considered for patch testing. The 2008 guidelines prepared for the British Association of Dermatologists suggest that the rate of patch testing should be around 143 patients per 100 000 population per year.[5] This would be equivalent to testing 600 – 700 individuals in the Wellington region per year, however, the actual amount of patch testing carried out is far lower than this. The scarcity of facilities for patch testing, photopatch testing and scratch patch testing is a major impediment to the adequate investigation (and therefore management) of contact dermatitis.

## Management of contact dermatitis

Anti-inflammatory creams or systemic agents (the choice of which depends on the anatomical site, extent and severity of the dermatitis) form the basis of treatment for contact dermatitis, however, there are specific recommendations for irritant and allergic forms of contact dermatitis.

**Contact irritant dermatitis** can be prevented and managed by reduced exposure to irritants and the use of moisturising creams. While this sounds simple enough, in practice this is a complex area. Wearing gloves for prolonged periods may prove to be more irritating than the exposure the person was trying to avoid by wearing gloves. There is a paucity of data on barrier creams and moisturisers, particularly in respect of their benefit in the management or prevention of dermatitis in specific occupations.

**Contact allergic dermatitis** management usually requires complete avoidance of the relevant allergen(s), since even tiny exposures may cause a flare. Determining the relevance of positive reactions on the allergy test, and counselling the patient, are not always straightforward tasks. The patient needs to be educated regarding the substances which need to be avoided in a way which is comprehensive enough to avoid accidental exposure to the allergen(s) in future, but simple and concise enough that the patient is not confused and overwhelmed. The difficulty is that some chemicals have multiple names. For example, the sunscreen filter 2-hydroxy-4-methoxy benzophenone is also called Oxybenzone, Benzophenone 3, Eusolex 4360 and Escalol 567. A patient with an allergy to amine hair dyes might unwittingly use a "natural" hair dye, or they may think that black henna is safe, without reading the small print to discover that the product contains small amounts of p-phenylenediamine to boost the colour. The person who reacted to colophony used as a soldering flux needs to know that they may react to pine wood, the waterproofing agent on cardboard boxes, some adhesives, and so on.

### Implications for work

While short periods away from work may be necessary for people with occupational contact dermatitis, recommendations to change career should not be given lightly. Most workers with contact dermatitis can continue in their jobs with appropriate treatment and work modifications; people who are atopic may still have symptoms, whether they stay or leave their jobs.

## Notifying the Medical Officer of Health

Many medical practitioners are unaware that disease and injury caused by exposure to hazardous substances requires notification to the local Medical Officer of Health. This includes skin disease. A hazardous substance is defined as anything that can explode, catch fire, oxidise, corrode or be toxic to humans (Hazardous Substances and New Organisms Act 1996). To notify a case, a short electronic notification form is located on the *bestpractice* dashboard (log in at **www.bestpractice.org.nz** or go directly through MedTech) – look for "Hazardous Substances & Lead Notifications". Primary care practices that do not use *bestpractice* Decision Support software should still inform their Public Health Unit of any notifications.


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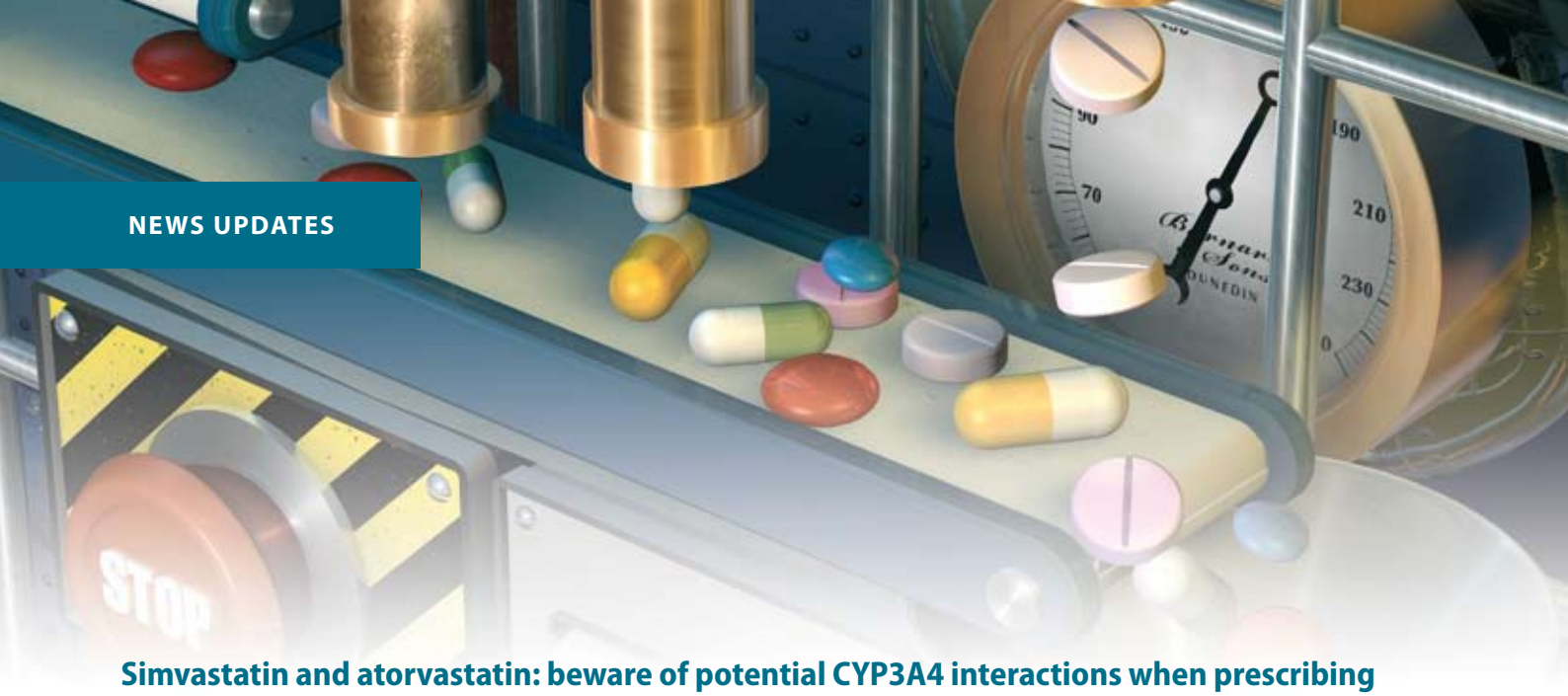
## Case study: a surgeon with contact dermatitis

A 55-year-old surgeon, with a history of atopic eczema since childhood, had suffered from severe hand dermatitis for the last six months – it was seriously impairing his ability to work, despite treatment with potent steroid creams and systemic steroids (which only controlled it briefly). In his occupation he is at risk of contact irritant dermatitis on account of frequent hand washing and prolonged glove wearing, however, patch testing demonstrated that he was also allergic to six of the nine brands of glove available in his workplace (four of which produced very vigorous reactions), and two of the three surgical scrubs that were tested. Following patch testing we were able to give advice on appropriate gloves and scrubs which allowed him to continue his normal work.




## Simvastatin and atorvastatin: beware of potential CYP3A4 interactions when prescribing other medicines

Simvastatin and atorvastatin are the most frequently prescribed statins in New Zealand. Simvastatin, and to a lesser extent, atorvastatin, are metabolised by the hepatic isoenzyme CYP3A4. Medicines that inhibit or induce this enzyme (Table 1) are likely to affect the plasma concentration of these statins, resulting in either an increased risk of adverse effects (e.g. myopathy and rhabdomyolysis) or a reduction in the effectiveness of treatment.[2] For example, one study which investigated the effect of erythromycin (a potent CYP3A4 inhibitor) on serum simvastatin concentrations found that combined use resulted in a 6.2-fold increase in simvastatin exposure.[1]

Other statins, e.g. pravastatin, are not significantly metabolised by CYP3A4 and are therefore less likely to have significant CYP enzyme interactions. However, caution is still required if prescribing any medicine that alters CYP3A4 with any statin as there have been case reports of interactions.[1, 3]

If a patient is using a combination of a CYP3A4 inhibitor and a statin, advise them to report any symptoms of myopathy and possible rhabdomyolysis, i.e. unexplained muscle pain, tenderness or weakness, especially in combination with dark coloured urine. If myopathy does occur, the statin should be stopped immediately.[1]

**Potent CYP3A4 inhibitors** are contraindicated in people using simvastatin (Table 1). These include the macrolide antibiotics erythromycin and clarithromycin, azole antifungals and protease inhibitors used for HIV and hepatitis C. It is appropriate to stop using simvastatin or atorvastatin for a short time if the use of a potent inhibitor is required. For example, a patient can be advised to omit their simvastatin doses while completing a course of erythromycin, if there is no alternative.

**Moderate CYP3A4 inhibitors** include the calcium channel blockers, amlodipine, diltiazem and verapamil. When using simvastatin and moderate CYP3A4 inhibitors together, the dose of simvastatin should not exceed 20 mg per day (Table 1) and patients should be monitored for adverse effects. Atorvastatin may be used in conjunction with moderate CYP3A4 inhibitors with caution.

**Minor CYP3A4 inhibitors**, such as the macrolide antibiotics, azithromycin and roxithromycin, have only a minimal effect on simvastatin and atorvastatin levels. However, there have been isolated case reports of rhabdomyolysis when they have been used in combination with simvastatin.[1]

**CYP3A4 inducers** include carbamazepine, rifampicin and St John's wort. These reduce the plasma concentration of simvastatin and atorvastatin and may reduce their effectiveness. If these medicines are used in combination with simvastatin and atorvastatin, lipid profiles should be monitored and the statin dose increased if necessary.

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**Table 1: Examples of medicines that interact with simvastatin and atorvastatin** (adapted from Prescriber Update, Medsafe[2])

| Interacting medicine | Simvastatin | Atorvastatin |
|---|---|---|
| **Potent CYP3A4 inhibitors**<br>Erythromycin<br>Clarithromycin<br>Azole antifungals (e.g. itraconazole, posaconazole, voriconazole)<br>Protease inhibitors (e.g. ritonavir, telaprevir, boceprevir)<br>Gemfibrozil<br>Ciclosporin<br>Danazol | Combination contraindicated; use alternative or temporarily stop simvastatin for the duration of the treatment course | Avoid combination if possible but if required then use with caution and monitor for adverse effects, e.g. unexplained muscle pain, tenderness or weakness, especially in combination with dark coloured urine |
| **Moderate CYP3A4 inhibitors**<br>Amiodarone<br>Amlodipine<br>Verapamil<br>Diltiazem<br>Nicotinic acid (> 1 g/day) | Do not exceed 20 mg/day | Use with caution and monitor for adverse effects (as above) |
| **Minor CYP3A4 inhibitors**<br>Azithromycin<br>Roxithromycin | Case reports of rhabdomyolysis. Use with caution and monitor for adverse effects (as above). | No clinically significant interactions |
| **CYP3A4 inducers**<br>Carbamazepine<br>Phenytoin<br>Rifampicin<br>St John's Wort | Probable reduction in plasma concentration of statin. Monitor lipid profile more regularly than usual for the patient. | Possible reduction in plasma concentration of statin. Consider monitoring lipid profile more regularly than usual for the patient. |


## Treatment duration of metronidazole for giardiasis

*Dear Editor*

*[Re: "Appropriate use of metronidazole", BPJ 43, Apr, 2012]. For the treatment of giardiasis, this article recommends a daily 2 g dose of metronidazole x 3 days because it "is as effective as longer courses," citing Gardner and Hill (2001). However, Gardner and Hill (2001) state: "Although the efficacy of three days of 2 to 2.4 g in a single daily dose APPROACHES that of longer regimens, this regimen is NOT recommended" [emphasis correspondents own]. That seems like a big misreading.*

***Remy Okazaki***
*(Online comment)*

In the metronidazole article (BPJ 43), the Gardner and Hill reference was used for the following sentence: "The single daily dose, shorter course regimen (three days) is recommended as it improves compliance, and is as effective as longer courses". The reference is referring to the latter half of the sentence only, regarding the effectiveness rather than the reccomendation. The correspondent is correct that Gardner and Hill did not recommend this treatment and in retrospect this was poorly referenced.

In the review article, Gardner and Hill (2001) discussed a range of treatments for giardiasis. They found that for giardiasis, the efficacy of a three day, higher dose treatment course of metronidazole (93 – 100% efficacy) was comparable to that of the more conventional five to ten day, lower dose treatment course (60 – 100% efficacy).[1] They, however, did not recommend the shorter course of treatment because at the time, giardiasis was not an approved treatment indication for metronidazole and there was concern that the higher doses may be associated with increased adverse effects.[1] These include headache, nausea, vertigo and a metallic taste in the mouth.

However, since 2001, in the context of more recent medicine approvals and further experience in regards to adverse effects, the three day course of metronidazole has become more standard within medicine formularies. For example:

- New Zealand Formulary: Metronidazole for giardiasis; oral Adult 2 g, daily, for 3 days, or 400 mg, 3 times daily, for 5 days [unapproved dose], or 500 mg, twice daily for 7–10 days [unapproved dose]
- New Zealand Formulary for children: Metronidazole for giardiasis; oral child 1 – 3 years 500 mg, once daily, for 3 days, child 3 – 7 years 600 – 800 mg, once daily for 3 days, child 7 – 10 years 1 g, once daily, for 3 days, child 10 – 18 years (see adult dose)
- British National Formulary: Metronidazole for giardiasis; 2 g daily, for 3 days, or 400 mg, 3 times daily, for 5 days, or 500 mg, twice daily, for 7–10 days; child 1–3 years 500 mg, daily, for 3 days; 3–7 years 600–800 mg, daily, for 3 days; 7–10 years 1 g, daily, for 3 days
- AHFS drug information (United States): For the treatment of giardiasis, the the usual dosage of oral metronidazole for adults is 250 mg 3 times daily for 5–7 days. Adults have been treated successfully with a single daily dose of 2 g for 3 days. For adults with coexistent amebiasis, the usual dosage is 750 mg 3 times daily for 5 – 10 days.

Ornidazole for one to two days is an alternative first-line treatment for giardiasis.

**Best Practice Tip:** Check the latest version of the bpac$^{nz}$ antibiotic guide for the most up to date advice about antibiotic treatments for common infections managed in general practice.

**Reference:**

1. Gardner TB, Hill DR. Treatment of giardiasis. Clin Microbiol Rev 2001;14(1):114-28.

## Formula for home-made oral rehydration solution

*What is the current recommendation for a home-made oral rehydration solution if pre-prepared products are not available?*

*(online comment)*

A quick internet search, and indeed a search of our own articles on the bpac$^{nz}$ website, will result in several slightly different recommendations for a recipe for home-made oral rehydration formula to treat dehydration, e.g. in people with diarrhoea managed at home. The reason for this is that the recommended formula has changed over recent years to include less salt and glucose.

The currently recommended formula for oral rehydration solution from the World Health Organisation is:

- 6 teaspoons of sugar
- ½ teaspoon of salt
- 1 litre of drinking water

See: **http://rehydrate.org/solutions/homemade.htm**

Patients/caregivers should be advised to measure these amounts carefully, and not to make the solution more concentrated – too much sugar can worsen diarrhoea and too much salt can cause adverse effects such as water retention and increased blood volume. Making a more diluted solution (i.e. a little more than 1 L of water) is not harmful. The solution can be stored in a cool place, or refrigerated. It should not be stored for longer than 24 hours.

Commercial rehydration products (which come in various flavours) that are available in New Zealand include:

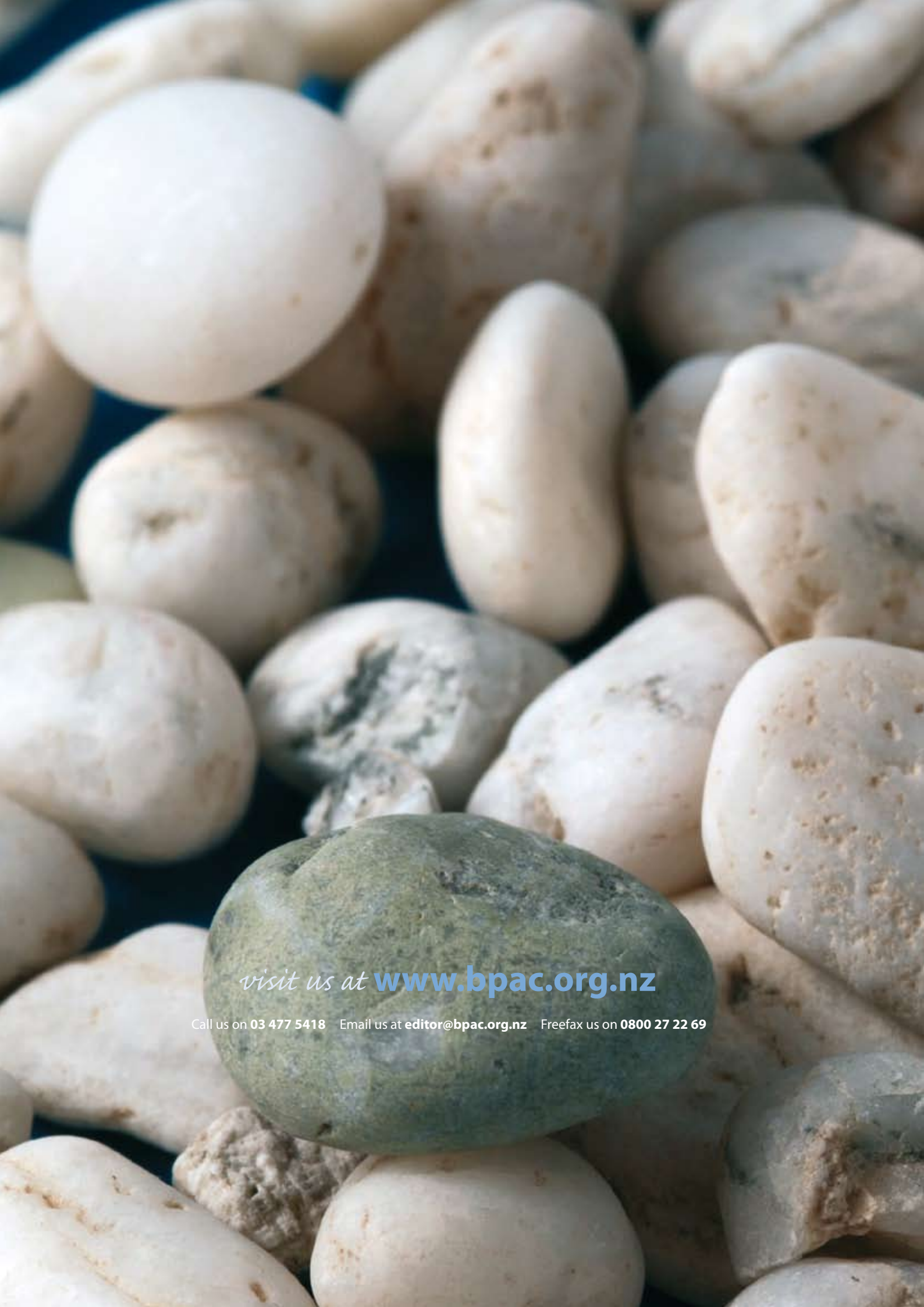
- Enerlyte, Gastrolyte, Hydralyte and Pedialyte sachets for solution
- Gastrolyte, Hydralyte and Pedialyte tablets for solution
- Hydralyte oral liquid and ice block sachets, and Pedialyte oral liquid

Pedialyte oral liquid and Enerlyte sachets are fully subsidised for patients on prescription, with 10 Enerlyte sachets subsidised on a PSO. Products may also be purchased from pharmacies and supermarkets.

For children who are dehydrated, oral rehydration solution should be encouraged frequently, in small amounts. As a general guide, give 50 mL/kg over four hours. Oral rehydration solutions are not usually required for adults with dehydration being managed at home, however, the same formula as for children can be used. Adults with dehydration should increase oral fluid intake to 2 L per day.

See: National Institute for Health and Care Excellence (NICE). Diarrhoea and vomiting in children. Available from: **http://publications.nice.org.uk/diarrhoea-and-vomiting-in-children-cg84/guidance**

**We value your feedback. Write to us at: Correspondence, PO Box 6032, Dunedin or email: editor@bpac.org.nz**



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