GOUT | ACNE | INFLUENZA | PERTUSSIS | UNAPPROVED MEDICINES

Best Practice

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An update on the management of gout

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better medicine

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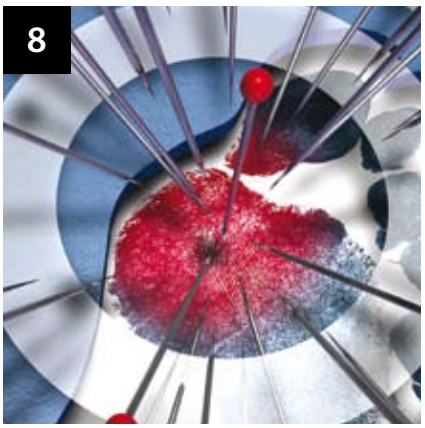

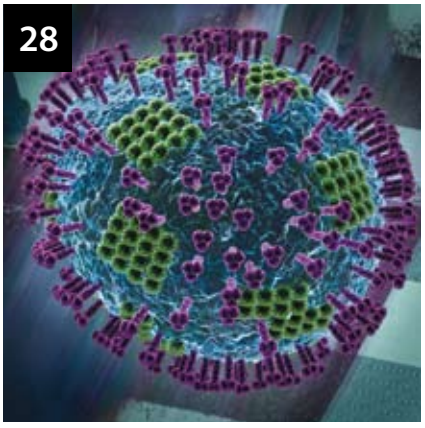

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The management of gout involves treatment of an acute attack, lifestyle modification and urate lowering treatment to achieve a target serum urate level. Recent evidence shows that a starting dose of allopurinol based on eGFR provides a safe, practical and effective treatment regimen. Benzbromarone, a uricosuric medicine which is currently unapproved in New Zealand, is to become available, fully subsidised, under Special Authority criteria from 1 April, 2013. Although benzbromarone has been associated with rare cases of serious liver toxicity, there is evidence that supports its use as a further therapeutic option for patients if optimal use of allopurinol and/or probenecid has failed to achieve target urate levels or if these medicines are unable to be tolerated.

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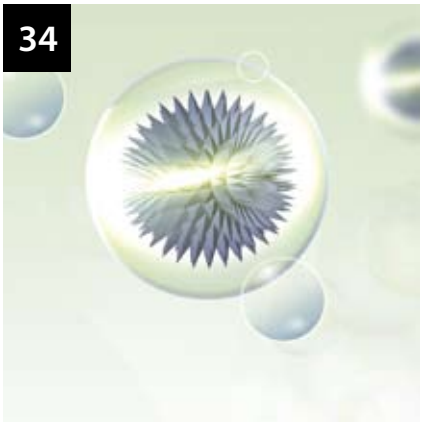

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Infants who have not yet completed the National Immunisation Schedule and children who are not immunised, or only partially immunised, are most at risk from pertussis. The best way to protect at-risk individuals is on-time vaccination, as it protects against infection and reduces the number of people in the community that can transmit the bacteria. Pertussis booster vaccinations in the combination Tdap vaccine are fully-subsidised as of January 2013 for pregnant women between 28 – 38 weeks gestation.

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In late 2012, there was a global increase in norovirus notifications, due to the spread of a novel norovirus, referred to as Sydney 2012. A worldwide warning for a severe norovirus season in 2013 has been issued, and outbreaks of Sydney 2012 have already been reported in New Zealand. Treating dehydration and reporting of suspected outbreaks are key aspects of management.

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Unapproved medicines and unapproved uses of medicines: keeping prescribers and patients safe

Firstly, what is an approved medicine?

An approved medicine is a medicine which has been through a regulatory process in New Zealand and can be considered safe to prescribe, under the conditions set out in the Medicine Data Sheet. The prescriber must still consider both the benefits and risks of using the medicine, before it is prescribed.

In New Zealand, medicines are approved by the Minister of Health, under advisement from the Medicines and Medical Devices Safety Authority (Medsafe). Medsafe's regulatory approval process ensures that both prescribers and patients have access to safe, quality medicines and medical devices. For a medicine to be approved for sale, distribution and marketing in New Zealand, the company that markets the medicine must apply for consent in accordance with the Medicines Act 1981. When a medicine is approved, it is only approved for the specific indications, doses and routes of administration that were applied for. If the medicine is a prescription medicine or a restricted medicine the company must submit a Medicine Data Sheet that outlines the use of the medicine for prescribers. Any changes to the datasheet, such as a new indication or dose, must be applied for and approved.

The Medicines Adverse Reaction Committee (MARC) works with Medsafe to advise the Minister of Health on the safety of approved medicines, specifically the risk-benefit profile of new medicines. The Centre for Adverse Reactions Monitoring (CARM) collects reports of suspected adverse reactions to medicines and informs Medsafe of potential safety issues with approved medicines.

If a significant safety or quality issue is identified, a warning or recall is requested by Medsafe, and in extreme cases, the Minister of Health can withdraw consent for the approval of the medicine.

Australia New Zealand Therapeutic Products Agency

In 2011 it was announced that regulatory agencies Medsafe and the Australian Therapeutic Goods Administration (TGA) were to be superseded by the Australia New Zealand Therapeutic Products Agency (ANZTPA), by mid-2016. Medicines and medical devices in Australia and New Zealand will then be regulated and monitored through a single approval and reporting process.

During the lead-in period, Medsafe and the TGA will be publishing recalls and warnings for therapeutic products in a joint database, and establishing a joint protocol for approval of medicines. An online database for patients to search for information on adverse medicine reactions is already available.

For further information see: **www.anztpa.org**

Commonly used medicines which are unapproved in New Zealand

- Melatonin is used for various sleep disturbances such as insomnia and some parasomnias. It is only approved for short-term treatment of insomnia in people aged over 55 years (Circadin 2 mg tablets). Other melatonin products in New Zealand, e.g. 3 mg capsules and 1 mg and 3 mg tablets, are not approved.
- Indometacin (indomethacin) is a NSAID used for pain in inflammatory conditions such as rheumatic disease. This medicine was previously approved in New Zealand, but is now no longer approved because the approved product is no longer available and the product supplied is different.
- Ethambutol is used in the long-term management of tuberculosis, which is prevalent in some parts of New Zealand. This medicine is fully subsidised on the Pharmaceutical Schedule, but is not an approved medicine.
- Liothyronine is a synthetic thyroid hormone, unapproved in New Zealand, which is sometimes used in patients with hypothyroidism.
- Thiamine injection is used for the management of Wernicke's encephalopathy in patients going through acute alcohol withdrawal. It is an unapproved medicine in New Zealand, although oral thiamine is approved.

What is an unapproved medicine?

An unapproved medicine is a medicine for which consent, or provisional consent, has not been given by the Minister of Health for sale, distribution or marketing in New Zealand, i.e. it has not been through the Medsafe regulatory process, approval has lapsed, the application was withdrawn or the product available is different in some way to the product that was approved. Unapproved medicines may still be prescribed to patients.

Section 25 of the Medicines Act allows an authorised prescriber to "procure the sale or supply of any medicine" for a patient in their care. This means that prescribers may prescribe any medicine to a patient (within their scope of practice), regardless of whether it is approved or unapproved in New Zealand. However, the prescriber must always provide an adequate professional and ethical standard of care, which includes gaining informed consent from the patient for use of the unapproved medicine.

Section 29 of the Medicines Act allows the sale or supply of unapproved medicines. The person or company who supplies the medicine must notify the Director-General of Health of the supply (via Medsafe), and record the name of the prescribing medical practitioner, the patient for whom the medicine was prescribed and the name and place of supply.

There are many medicines which are commonly used, and approved for use, in other countries, but which are not currently approved in New Zealand. This does not necessarily mean that they are unsafe to use. It is more likely that no application has been made for approval in New Zealand. Medsafe cannot vouch for the quality, safety and efficacy of unapproved medicines and may not be in a position to monitor and advise on their safety. Responsibility lies with the practitioner who prescribes an unapproved medicine. The practitioner must consider the evidence and clinical experience of the use of the unapproved medicine and weigh up the risks and benefits.

N.B. The original source, quality, safety and efficacy of medicines purchased online cannot be verified or guaranteed. When obtaining "unapproved medicines" it is recommended that a New Zealand supply chain be used.

For further information see: "Medsafe warns of dangers of purchasing medicines online", Medsafe, 2011. Available from: **www.medsafe.govt.nz/hot/media/2011/DangersOfPurchasingMedicinesOnline.asp**

What is an unapproved use of a medicine?

If an approved medicine is prescribed outside of the approved indications, dose range or route of administration, this is an unapproved use of a medicine, also known as "off-label" use.

The Medicines Act allows the practitioner to determine the dose and route of a medicine which is prescribed and the indication for which is it prescribed for, but the prescriber must take responsibility for the safety of this if it is an unapproved use.

Approved medicines which are prescribed for an unapproved indication, dose or route can be supplied as usual, i.e. it is not necessary for Section 29 notification to occur if a practitioner prescribes "off-label".

Why consider prescribing a medicine in an unapproved way?

There are many reasons why a prescriber may consider an unapproved use of a medicine, ranging from following established treatment guidance to implementing new evidence that has emerged from the literature. In some cases, the prescriber may not even be aware that a medicine is being prescribed in an unapproved way, as it is used so commonly, e.g, the use of tricyclic antidepressants for neuropathic pain, omeprazole for reflux in infants (unapproved in children aged < 1 year) or nifedipine for the treatment of Raynaud's phenomenon.

Prescribing medicines in children

Many of the medicines administered to children are used off-label. This is because trials have not usually been conducted in this patient group and, therefore, the company marketing the medicine has not applied for use to be approved for this age-group. This is also why it is common for a medicine to be contraindicated for use in pregnant women.

An example of off-label prescribing in children is azithromycin, which is recommended for prophylaxis and treatment of pertussis in children. Although azithromycin is an approved medicine, pertussis is currently an unapproved indication for use

It can be difficult for a practitioner to weigh up the risks and benefits of using a particular medicine in a child, when there is limited or conflicting evidence of effectiveness or safety. For example, selective serotonin reuptake inhibitors (SSRIs) are considered the first-line pharmacological treatment for depression, and the only pharmacological option considered for younger people. However, SSRIs are unapproved for use in people aged under 18 years, and are associated with potentially serious adverse effects.

Check the Medicine Data Sheet or New Zealand Formulary before prescribing

Indications for medicines may differ with new formulations or generic versions, and for different agents within the same class of medicine. For example, the indications for SSRIs vary. Depression is the only consistent indication for all members of the group, while indications for obsessive compulsive, panic, social anxiety and post traumatic stress disorders are specific to individual types of SSRI. Paroxetine has the longest list of indications, ranging from depression to social phobia. All SSRI data sheets caution against the use of these medicines in children aged under 18 years.

There are also some anomalies between similar medicines, e.g. metoprolol succinate is indicated as an adjunct treatment in heart failure, but metoprolol tartrate is not.

Indication creep

Once a medicine has been approved in New Zealand, its use is often expanded across a broader range of conditions. However, the efficacy and safety of such use may not always be established. For example, quetiapine is indicated for the treatment of schizophrenia and related psychoses, but it is increasingly being prescribed for unapproved indications such as sedation in people with dementia, and for anxiety and insomnia. This is a worrying trend given that a larger population is being exposed to the potential serious adverse effects associated with quetiapine and other atypical antipsychotics, e.g. type 2 diabetes, sudden cardiac death and increased mortality in older people.*

Another concerning example of indication creep is oxycodone, which is approved for moderate to severe pain, including cancer pain, but appears to be frequently prescribed inappropriately in place of a weaker opioid.

Data sheets not updated

Sometimes medicines are prescribed off-label because

* McKean A, Monasterio E. Off-label use of atypical antipsychotics: cause for concern? CNS Drugs 2012;26(5):383-90.

evidence suggests that a non-indicated dose or route of administration is recommended, but the medicine supplier has, for whatever reason, not sought regulatory approval to update the data sheet. For example, low dose bendrofluazide has only recently been officially incorporated into the product datasheet despite guidelines for hypertension recommending low doses for many years.

How do you prescribe an unapproved medicine or an approved medicine for an unapproved indication?

The decision to prescribe an unapproved medicine, or to prescribe off-label, is at the discretion of the practitioner, based on their clinical experience and judgement, and in consultation with the patient.

The Health and Disability Commissioner's Code of Consumer Rights covers the obligation for a practitioner to obtain informed consent from the patient, before prescribing an unapproved medicine.

Increased professional responsibility and liability

If a patient experiences an adverse event while taking an unapproved medicine, or a medicine prescribed for an unapproved use, the responsibility, and liability, rests with the prescriber. Therefore, it is recommended that a decision to prescribe an unapproved medicine is documented in the patient's notes, including the rationale for the prescription, and that the decision was discussed with the patient. In general, it is recommended that prescribers obtain written consent from the patient when prescribing an unapproved medicine. It is acknowledged, however, that when off-label use of a medicine is so common that it is regarded as usual practice, obtaining consent may not be considered necessary, and this is at the clinician's discretion.

What should you tell the patient?

The patient should be fully informed that the medicine they are being prescribed is unapproved, or that the medicine is approved, but is being prescribed for a condition, at a dose, or via a route, that is unapproved.

The expected benefits, risks, adverse effects and cost should be discussed, along with other treatment options. Any warnings or contraindications associated with the medicine should be explained.

If the medicine is considered to be experimental, e.g. there is minimal or conflicting evidence to support its use, it is rarely used or it is part of a clinical trial, the prescriber must obtain written consent from the patient. A plan for monitoring treatment and adverse effects should be put in place.

If a patient is prescribed an unapproved medicine, the prescriber must advise them that the details about the supply of medicine (Section 29), including their name, will be recorded by the supplier and may also be sent to Medsafe.

What if the patient asks for a medicine they used overseas?

Patients who have immigrated to New Zealand or have spent time overseas may request that their doctor prescribes them a medicine that they have been using, which is not approved in New Zealand. Such medicines can be imported for use, but it is the obligation of the practitioner to consider approved, and subsidised, alternatives and be adequately informed about the medicine, e.g. researching the literature, consulting with colleagues, before assisting the patient to obtain it. Practitioners should have a plan in place to monitor the effect of the medicine.

N.B. Section 29 notification is not required if a medical practitioner imports a medicine to treat a patient. If the medicine is supplied from one medical practitioner to another, the supplying practitioner is encouraged to notify Medsafe. If a Pharmacist imports the medicine for the medical practitioner, they must notify Medsafe of the supply using the Section 29 reporting mechanism.

Are only approved medicines subsidised?

In New Zealand, the Pharmaceutical Management Agency (PHARMAC) is responsible for deciding which medicines are subsidised for use in New Zealand. The New Zealand Pharmaceutical Schedule indicates to prescribers which medicines are subsidised (either fully or partly), including any criteria for subsidy, e.g. Special Authority.

Although most medicines on the Pharmaceutical Schedule are approved medicines, and it is PHARMAC's preference to subsidise approved medicines where possible, this is not a criterion for subsidy. The decision to subsidise a medicine is based on the pharmaceutical needs of patients in New Zealand, and is dependent on the available funding. All patients who meet the criteria for subsidy (as per the Schedule), have equal access to the funding for a medicine, should a practitioner decide to prescribe it. PHARMAC is not responsible for the safety or quality of the medicines listed on the Pharmaceutical Schedule, nor for the supply or use of the medicine in accordance with the Medicines Act.

Unapproved medicines are identified in the Pharmaceutical Schedule with this symbol: S29 Where an approved medicine is subsidised for an unapproved use, this is also clearly indicated in the Schedule.

The New Zealand Formulary also contains information about the approval and subsidy status of medicines.

Resources

For further information about regulatory processes, refer to Medsafe: **www.medsafe.govt.nz**

For information on unapproved medicines, see: **www.medsafe.govt.nz/profs/unapp.asp**

For Medicine data sheets see: **www.medsafe.govt.nz/profs/Datasheet/dsform.asp**

Comprehensive information on both approved and unapproved medicines is available from the New Zealand Formulary: **www.nzf.org.nz**

To review the Medicines Act 1981, see: **www.legislation.govt.nz/act/public/1981/0118/latest/DLM53790.html**

ACKNOWLEDGEMENT: Thank you to **Chris James**, Manager, Clinical Risk Management, Medsafe and the team of the Compliance Management Branch, Medsafe for expert guidance in developing this article.

A cautionary tale

Dabigatran is a recently approved medicine in New Zealand. The indications for dabigatran are for prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation and for venous thromboembolism prophylaxis after major orthopaedic surgery. Some practitioners in New Zealand have been prescribing dabigatran for unapproved indications, such as in patients with mechanical heart valves, despite there being no evidence supporting this use. Medsafe, the United States Food and Drug Administration and the European Medicines Agency and have now stated that dabigatran is contraindicated in people with mechanical heart valves. So far several cases have been reported to CARM of patients with mechanical valves experiencing adverse reactions to dabigatran, such as developing thrombosis on the prosthetic valve. This is a clear example of an inappropriate use of a medicine for an unapproved indication.

For further information see: "Dabigatran revisited", BPJ 50 (Feb, 2013).

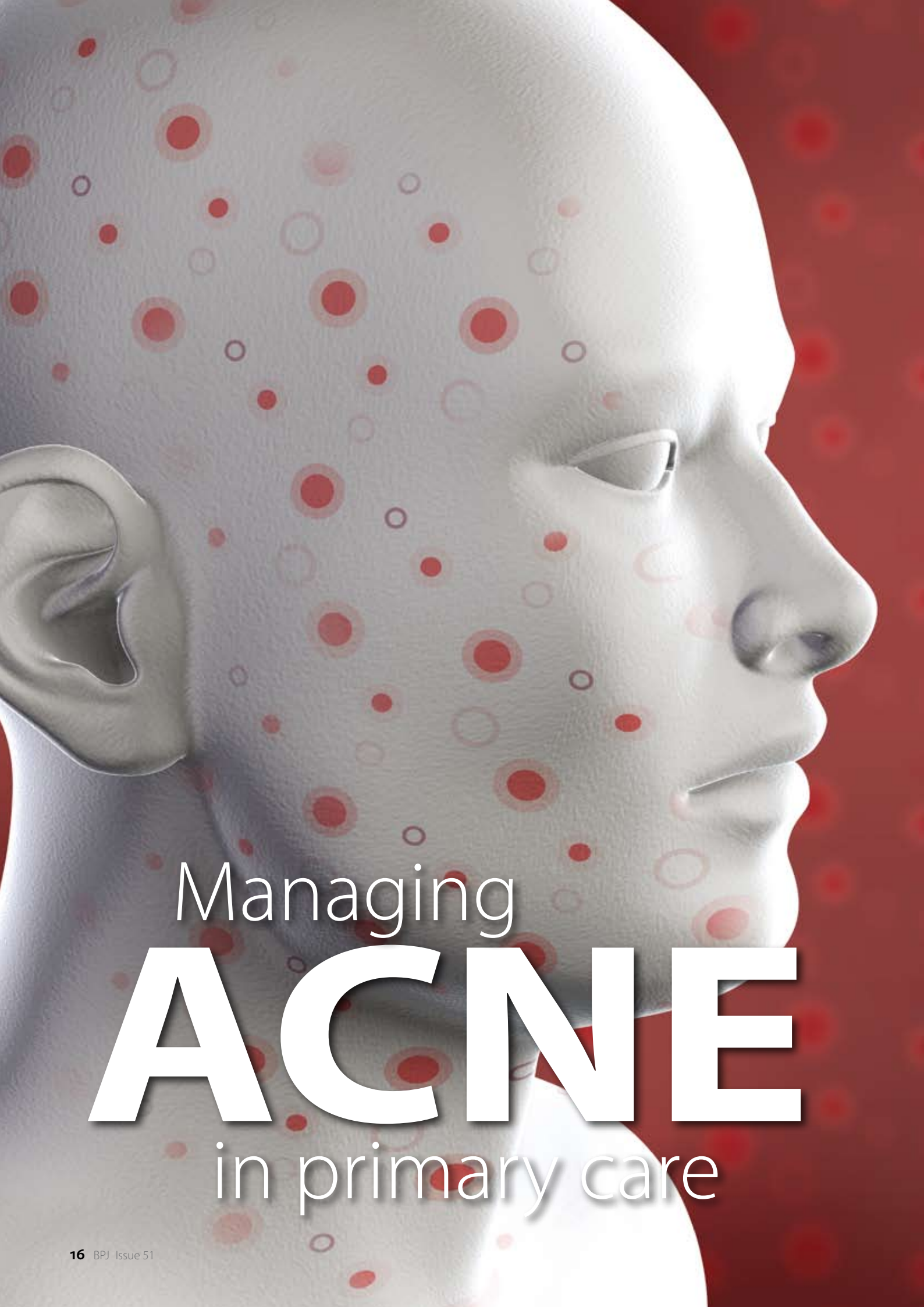
Benzbromarone is an unapproved, but subsidised medicine

Benzbromarone has been used for the treatment of gout in other countries for many years, but drug companies have not currently applied for this medicine to be approved for sale, distribution or marketing in New Zealand. However, patients with gout in New Zealand have already been using this medicine, based on adequate evidence of effectiveness and safety from international studies, experience of clinical use and expert clinical opinion.

Benzbromarone was initially funded by PHARMAC for some patients under one or more of its exceptions schemes, which allow funding of a medicine for named patients in specified circumstances. However, following positive reviews of benzbromarone by PHARMAC's advisory committees, and in the absence of availability of an approved version, PHARMAC has decided to fund an unapproved version of benzbromarone for the treatment of gout. Benzbromarone is to be listed on the Pharmaceutical Schedule from 1 April, 2013, fully subsidised, for all patients who meet the Special Authority criteria.

For further information see Page 12

An update on the management of gout



Managing ACNE in primary care

Acne is a common dermatological condition that affects most people at some stage in their life. Because acne is regarded as "normal" and over-the-counter products are readily available, most people will not seek treatment from their General Practitioner. However, for some, acne will become significant enough to require medical management. Pharmacological treatment for acne is based on the severity of the symptoms and the impact of the condition on the patient. Treatment ranges from topical medicines for mild acne to oral isotretinoin for severe acne.

History and examination help determine the severity of acne

More than 80% of people will develop some degree of acne between age 11 – 30 years.[1] Acne is usually mild and transitory, however, it can lead to complications including scarring, dyspigmentation and psychological issues such as anxiety, depression and, rarely, suicide.[2, 3]

The patient should be asked questions about:

- The duration of acne symptoms, sites affected and the typical appearance (i.e. their acne may be unusually severe or mild on the day they present)
- Possible aggravating factors, such as use of cosmetics, skin products or sunscreens
- Use of medicines that may cause acne, e.g. antipsychotics or lithium. Anabolic steroids are associated with acne (particularly on the trunk), and should be enquired about if there is other evidence for this suspicion.
- Menstrual history and oral contraception in females
- Treatments that have been trialled, including over-the-counter medicines, and how long they were trialled for
- Psychological and sociological effects of their acne

The skin should be examined to assess the physical severity of the acne in order to classify it for treatment.[4]

Mild acne is predominately indicated by the presence of non-inflammatory lesions (i.e. comedones – see "The vocabulary of acne", over page). Some inflammatory lesions (pustules or papules) may be present, but generally less than 10 – 15.

Moderate acne consists of multiple comedones (10 – 40) and inflammatory lesions (10 – 40). Nodules may occasionally be present, and there may be some limited scarring. Lesions may also be present on the trunk.

Severe acne is indicated by the widespread presence of nodules and cysts, and/or a large number of inflamed pustules and papules. Scarring is likely to be present. Nodulocystic acne is a particularly severe form of acne characterised by multiple inflamed nodules and scarring, usually including the trunk. It most often affects young males.

 For further information, including photographs of each stage of acne, see: "How to treat acne", BPJ 20 (Apr, 2009).

Discuss the severity of the patient's acne with them. Many people will perceive their acne to be worse than the clinical appearance suggests, and this should be taken into account in the treatment approach. The converse may also be true, e.g. a parent may perceive the acne to be worse than the patient believes or the physical findings suggest.

In some people, acne is a contributing or aggravating factor for psychological issues. A psychological assessment, such as HEADSSS, may be appropriate.

Taking baseline photographs of acne severity and lesion distribution is useful for assessing response to treatment, and encouraging medicine adherence.[3] Most electronic patient management systems allow images to be added to the patient record.

Pharmacological treatment of acne

The treatment of acne is based on the severity of the patient's symptoms, following a step-wise approach. General skin care advice should be recommended throughout all steps.

General treatment advice for all levels of acne severity

Patients should be advised to wash their face gently with warm water and mild soap or cleanser, twice daily. An un-medicated face-wash is sufficient, although products containing benzoyl peroxide or salicylic acid can be effective. Rough scrubbing should be avoided as it causes follicular rupture, increasing the inflammatory response. Patients with sensitive skin, e.g. atopic dermatitis, should avoid soap, and anti-acne cleansers may cause irritation and contact dermatitis.

Acne products should be applied to all areas usually affected by acne, rather than just applied to individual lesions.[5] Patients should also be informed that when using topical products, including prescription products, it may take several months before significant results are seen.[4]

Patients should ensure that their facial products, including cosmetics and sunscreens, are not contributing to their acne.

Best Practice Tip: Tell patients to look for cosmetics and skin care products that are labelled as "non-comedogenic".

Mild acne – Topical treatments

First-line treatment for mild acne is a combination of topical benzoyl peroxide and a topical retinoid or a topical antibiotic.

Benzoyl peroxide is not subsidised and can be purchased over-the-counter.

The topical retinoids adapalene and tretinoin are prescription only and fully subsidised (one tube at a time) for use in patients with acne. Topical isotretinoin gel is available by prescription, but is not subsidised.

Topical erythromycin and clindamycin, and combination products with benzoyl peroxide and adapalene, and benzoyl peroxide and clindamycin are available by prescription, but are not subsidised.

Benzoyl peroxide

Benzoyl peroxide is topical antimicrobial and keratolytic (i.e. softens and removes outer layers of skin).

Benzoyl peroxide is available as a gel, cream or cleanser, and ranges in strength from 2.5% – 10%. The 2.5% strength is sufficient for most people, and higher concentrations are associated with greater adverse effects. The choice between gel, cream and wash should be based on patient preference

The vocabulary of acne

Sebum	Oil produced by sebaceous glands, within a hair follicle, most noticeably on the face
Comedone	Small elevations on the skin surface caused by occlusion of the follicle by sebum and keratin. Comedones can be open or closed and are the primary form of non-inflammatory acne.
Open comedone	Commonly called blackheads. A "plug" of melaninised keratin blocks the opening of the follicle.
Closed comedone	Commonly called whiteheads. Occur when the follicle becomes completely blocked.
Papule	A solid elevation of skin with no visible fluid, usually < 5 mm and usually erythematous (in acne)
Pustule	An elevation of skin which contains cloudy or purulent material consisting of necrotic cells and neutrophils
Nodule	A firm dome-shaped elevation, > 5 mm in diameter, usually erythematous and painful
Acne cyst	A fluctuant lesion > 5 mm in diameter, which may or may not be inflamed

and skin-type, with gels being more suited to oily skin. A rinse-off cleanser is more suitable if irritation occurs and is more convenient for treating acne affecting the trunk.

Washes can be used once or twice daily, and should be applied for thirty seconds before rinsing thoroughly. Topical benzoyl peroxide gels and creams should be applied once daily, removing after two hours, for three days, and then, if tolerated, applied once daily, at night, and left on overnight. Some patients may tolerate twice daily applications.

The adverse effects of benzoyl peroxide include skin irritation, dryness and redness. Direct contact with eyes or other mucous membranes will cause severe irritation. Most of the adverse effects can be minimised by reducing the time the product is on the skin before being washed off, or by reducing the concentration used. Advise the patient that if their skin peels or becomes very dry, an oil-free moisturiser can be used. Benzoyl peroxide will bleach linen, clothing and towels.

Salicylic acid 0.1 – 2% cream is an alternative to benzoyl peroxide, but is generally less effective and may also cause skin dryness.[6] It works by softening and descaling the skin, thereby reducing comedones.

Topical retinoids

Topical retinoids inhibit keratinocyte differentiation and proliferation. They reduce comedones and have significant anti-inflammatory effects.[7] They are not suitable for patients with very inflammatory acne and they may not be tolerated by patients with sensitive skin. Topical retinoids must be applied at night, as UV radiation degrades retinoids.

Adapalene is available as a 0.1% cream and gel. It should be applied thinly, once daily.[8] Adapalene is usually better tolerated than tretinoin.[7] The gel is suitable for most people, although those with dry skin may prefer the cream.

Tretinoin is available as a 0.05% cream, and should be applied thinly, once daily. Application should be "built up" to avoid adverse effects: on the first night, apply for five minutes before washing off; on the second night, apply for ten minutes; on subsequent nights, increase the application time by 30 minutes until a two-hour application is achieved, at which point the cream can be left on overnight.[7,8]

Topical retinoids should be trialled for at least two months before considering another treatment. The initial phase of treatment may cause a mild acne flare, followed by significantly declining acne severity over one to two months.[7] Continued, long-term use of retinoids appears to be safe and effective.[7]

Acne: complex pathophysiology

There are four primary pathogenic factors that lead to an acne lesion:[2,5]

1. Sebum production
2. Increased follicular keratinisation
3. *Propionibacterium acnes* follicular colonisation
4. Release of inflammatory mediators

Hormonal changes during puberty increase sebum production.[5] Predisposition to hyperkeratinisation leads to occlusion of hair follicles and sebaceous ducts, forming open or closed comedones.[5] *P. acnes* bacteria in the follicle breaks down sebum into fatty acids and peptides and may rupture the follicle wall.[5] This causes an inflammatory response and the formation of papules and pustules. Deeper inflammation leads to nodules and cysts.[2] Scarring may then occur as deeper lesions heal.

Advise patients to continue using the topical retinoid even if acne initially appears slightly worse, but to arrange a review if severe flares develop.

Adverse effects include skin irritation, dryness and erythema. If adverse effects are intolerable, advise patients to reduce the time that the product is on the skin before being washed off, and to apply a mild, oil-free moisturiser if there is obvious peeling. Topical retinoids are not associated with the same adverse effects as oral retinoids, such as isotretinoin. However, there is consensus among experts that they should not be used in females that are pregnant or planning pregnancy.

Topical antibiotics

Topical antibiotics work by reducing the number of *P. acnes* on the surface of the skin and in hair follicles and sebum ducts. They may also have anti-inflammatory effects.

Topical erythromycin 4% gel or clindamycin 1% solution or lotion should be applied twice daily, with treatment reviewed after eight to twelve weeks. To limit the development of bacterial resistance they should only be used alongside benzoyl peroxide or a topical retinoid.[2, 4]

Adverse effects of topical antibiotics include skin irritation, contact dermatitis and, rarely, gastrointestinal disturbance.

Moderate acne – oral antibiotics or hormonal contraception

Oral antibiotics may be considered for patients with moderate acne, or mild acne that has not responded to topical treatments after two months. N.B. topical treatment with benzoyl peroxide or retinoid should be continued.

Doxycycline 50 – 100 mg, daily, for four to six months, is the first-line antibiotic choice (N.B. 50 mg tablets are not fully subsidised).[6] If effective, the dose can be tapered after four months to alternate day treatment. If the standard dose of doxycycline is ineffective, increase to 100 mg, twice daily, provided it is tolerated. Doxycycline is contraindicated in children aged under 12 years and women who are pregnant.

Although minocycline is as effective for acne as other tetracyclines, it is associated with a greater risk of lupus erythematosus-like syndrome, hepatitis and pigmentation, and is not fully subsidised.[9] Erythromycin 400 mg, twice daily, can be used as an alternative to a tetracycline, however, it may be less effective, possibly due to increasing *P. acnes* resistance.[6]

Adverse effects associated with tetracycline antibiotics include oesophageal irritation, photosensitivity, *Candida albicans* vulvovaginitis and nausea and vomiting. Oesophageal and gastrointestinal irritation can be reduced by taking doxycycline with a glass of water and food, and advising the patient to avoid lying down for one hour after the dose is taken.

Combined oral contraception is an effective treatment for mild to moderate acne in females.[10] In general, oral contraception has fewer adverse effects than long-term antibiotics, and should be considered first for females.

A standard combined oral contraceptive (levonorgestrel + ethinyloestradiol, such as Ava or Microgynon) should be tried initially.[10] These are fully subsidised and usually well tolerated.

Combined oral contraceptives containing cyproterone, e.g. Ginet (fully subsidised), may be more effective than other oral contraceptives and are suitable for women with polycystic ovary syndrome.[10] However, cyproterone-containing oral contraceptives slightly raise the risk of venous thromboembolism (approximately 40 cases per 100 000 women treated for one year, compared to 20 cases for levonorgestrel-containing contraceptives), and should be used with caution.[11, 12]

Combined oral contraceptives containing less androgenic progestogens, such as drospirenone + ethinyloestradiol (Yaz and Yasmin, not subsidised) or desogetrel + ethinyloestradiol (Mercilon and Marvelon, partly subsidised) may also be suitable.[10] However, these are more expensive to the patient than fully subsidised options, and have a similar risk of venous thromboembolism as cyproterone-containing contraceptives.

Progesterone-only oral contraceptives, depot progesterone and progesterone implants may worsen acne.[13]

Although a reduction in seborrhoea is usually apparent within two to three cycles, it may take up to six cycles after initiating the oral contraceptive before an improvement in acne is seen.[5]

Severe acne – isotretinoin

People with severe acne, treatment-resistant acne or older adults with persistent acne may require oral isotretinoin.[5] Isotretinoin is associated with many adverse effects, is a major teratogen and requires monitoring throughout treatment, therefore may not be a suitable option for everyone.[14] If isotretinoin is unsuitable or is not tolerated, a higher dose of

antibiotic, e.g. doxycycline 100 mg, twice daily, if tolerated and not already trialled, and discussion with, or referral to, a dermatologist is recommended.[2,4]

The efficacy of isotretinoin

Isotretinoin has been shown to affect all four pathogenic processes involved in acne formation and results in sebaceous gland apoptosis (cell death) and altered gene expression.[16–18] Isotretinoin is highly effective for clearing acne and reducing recurrence. A single course of isotretinoin will result in significant improvement or complete remission of acne in nearly all patients. Long-term efficacy depends on individual patient factors and the duration and dose of treatment.[18] If isotretinoin is ineffective, investigation of a potential endocrine cause for the acne, such as polycystic ovary syndrome, should be considered.[19]

Recurrent acne may be treated with a further course of isotretinoin, and in some cases long-term, low-dose treatment is appropriate, however, discussion with a Dermatologist is recommended if this is being considered.[18]

The adverse effects of isotretinoin

Isotretinoin is associated with a range of serious adverse effects (Table 1, over page). Some, particularly cheilitis, are so common that they can be considered indicators of adherence.[17] Isotretinoin may cause an initial worsening of acne, but severe flares are uncommon. It is important to discuss these adverse effects with patients prior to initiation, to optimise adherence. Most adverse effects are dose-related and starting with a low dose may reduce the incidence and severity.

Females should be aware that isotretinoin is teratogenic and that exposure to it, particularly in the first trimester, is very likely to lead to spontaneous abortion or severe birth deformities.

Both females and males should be advised not to donate blood during treatment with isotretinoin or for one month after treatment stops.[14]

Initiating isotretinoin

When initiating isotretinoin, it is recommended that an electronic decision support module is used.

Practitioners should discuss with the patient, and then provide in writing, the potential adverse effects, particularly teratogenicity in females. A suitable patient information brochure is provided with the medicine by the distributor. Baseline laboratory investigations should be requested (Page 23). Female patients will require advice on contraceptive options, and where necessary, be prescribed contraceptives (some will already be using oral contraceptives for managing acne symptoms). Patients (and parents/caregivers for those under age 16 years) should be asked to sign a consent form, to indicate that they understand the adverse effects that are possible while taking isotretinoin and, for female patients, the importance of not becoming pregnant during the course of their treatment and a further month after it has been discontinued.

Consent forms for patients are available in the *bestpractice* Decision Support isotretinoin module.

Dosing isotretinoin

The recommended starting dose of isotretinoin is 0.5 mg/kg/day. Daily doses can be titrated up or down, between 0.1 and 1 mg/kg/day, depending on response to treatment and presence of adverse effects. The total dose of isotretinoin over the course of treatment should be between 120 – 150 mg/kg of body weight.[14] The length of treatment is dictated

Special Authority requirements for isotretinoin

Isotretinoin is available, fully subsidised, for patients with acne vulgaris, who meet the Special Authority criteria.

The Special Authority criteria are:[15]

1. The patient must have had a trial of the other available treatments with an inadequate response, and;
2. The practitioner is a Dermatologist, vocationally registered General Practitioner or Nurse Practitioner working in a relevant scope of practice, and:
3. The practitioner is up to date on their knowledge of the available acne treatments, and:
4. The patient is either:
   a. A female and, if of reproductive age, pregnancy has been excluded prior to initiation of isotretinoin and that the patient understands the risk of teratogenicity and understands that she must not become pregnant during the course of treatment or one month after, or;
   b. A male.

Table 1: The prevalence of adverse effects with isotretinoin and recommended management[14, 16–18]

Adverse effect	Management
Cheilitis	Emollient lip balms and sunscreen application
Dry skin	More common in people prone to atopic dermatitis. Use non-soap cleansers, lip balms and moisturisers.
Acne flare	Mild acne flare will usually improve with continued isotretinoin treatment. Temporary cessation of treatment may be necessary if the flare is moderate. Lower doses may reduce the risk of flares. Significant flares, particularly with acne fulminans (a severe form of acne that can occur after unsuccessful treatment), are rare but require urgent referral to a dermatologist.
Eczema	Mild eczema may be managed with regular use of emollients, but patients with moderate or severe eczema may require a moderate-potency topical corticosteroid
Impetigo	Treat with topical or oral antibiotics, such as fusidic acid ointment or flucloxacillin
Nose bleeds	Treat symptomatically
Skin photosensitivity, fragility	Sun-protective measures including use of sunscreens. Avoidance of chemical peels, dermabrasion and waxing. Shaving may continue but encourage use of shaving cream. Avoid unnecessary sun exposure and tanning beds.
Dry, irritable eyes or photosensitivity	Use artificial tears. Reduce use of contact lenses if necessary. Use sunglasses where needed. If artificial tears fail to help or if discomfort is severe, temporary cessation or reduction in dose of isotretinoin may be required.
Elevated lipid levels	Lipid levels should be monitored, especially in patients with elevated pre-treatment levels, risk factors or prolonged courses of isotretinoin. Consider dose reduction or cessation of treatment if fasting triglycerides >6 mmol/L. Dietary advice should include avoidance of alcohol and sugary drinks. Lipid levels are likely to return to baseline one month after treatment finishes.
Abnormal liver function	Monitoring of LFTs is recommended during treatment. This is usually only necessary in patients with pre-existing liver disease, co-morbidities or those receiving high-dose treatment, however, guidelines recommend monitoring all patients prescribed isotretinoin. Cessation of treatment is not required in patients with mild increases in liver enzyme levels. If liver enzymes are > 2.5 times the upper limit of normal, it is recommended to cease isotretinoin and investigate further. Levels usually return to normal within two weeks of cessation.
Depression	There is no clear evidence that isotretinoin causes depression, but depressive symptoms may be seen in people undergoing isotretinoin treatment.[20] If significant depression arises during treatment, cessation of isotretinoin may be warranted; referral or discussion with a adolescent mental health specialist should be considered. Refer to a Dermatologist for further treatment of the acne.

by the daily dose. Courses usually last between three to four months but may continue for one year or longer. Total doses of >150 mg/kg are associated with increased adverse effects.[16] The dose and duration of the course may be adjusted on an individual basis; some patients will wish to reduce the dose or stop isotretinoin when the active acne has settled.

Isotretinoin should be taken, once daily, after the main meal, which should contain some fat (e.g. milk), to help increase absorption.

While isotretinoin is available in 5, 10, 20 and 30 mg capsules, only the 10 and 20 mg capsules are fully subsidised. Doses calculated by body weight may need to be rounded to suit the subsidised options.

Contraception is essential for females taking isotretinoin

Isotretinoin is a major teratogen, and will cause significant birth defects or spontaneous abortion in approximately half of all pregnant women taking the medicine.[21, 22] Practitioners should obtain an up-to-date and reliable sexual history from the patient and ensure that all females of reproductive age are:[17]

- Not pregnant prior to beginning treatment
- Given strong advice against becoming pregnant during or within one month of completion of a course of isotretinoin
- Using two forms of reliable contraception, ideally hormonal contraception* and a barrier method
- Prescribed, or know how to access, emergency contraception, and know how and when to use it

* Combined oral contraceptives are generally recommended as progesterone-only contraceptives may be less effective in a person taking isotretinoin and can worsen acne (Page 20).

Monitoring patients taking isotretinoin

Isotretinoin can have significant adverse effects, including liver enzyme abnormalities, hyperlipidaemia, hypertriglyceridaemia and cytopaenias (a reduction in one or more types of blood cell), and monitoring is recommended throughout the course of treatment.[17] Due to a long history of use in New Zealand and internationally, there has been a trend among Dermatologists toward reduced testing for patients taking low doses of isotretinoin, however, the recommendation for regular testing remains as best practice.

Triglyceride levels can be elevated due to isotretinoin treatment.[17] Several reasons for this have been proposed, including down-regulation of lipases and changes in gene expression leading to increased antagonism of triglyceride metabolism.[23] Trigylceride levels > 9 mmol/L are associated with pancreatitis. A reduction in dose or cessation of treatment should be considered if triglyceride levels rise above 6 mmol/L. Isotretinoin must be stopped if pancreatitis occurs.[17]

Transient increases in liver enzymes can occur in people taking isotretinoin.[17] These increases are usually mild and benign and will resolve upon cessation of isotretinoin. If liver transaminases are > 2.5 times the upper limit of normal, investigation of possible causes of liver dysfunction (e.g. viral hepatitis, alcoholism) is required and it is recommended that isotretinoin is stopped. Patients should be advised of the risk of drinking alcohol in excess while taking isotretinoin.

Rarely, isotretinoin causes reversible cytopaenias, therefore it is recommended to monitor full blood count.[17]

People with severe liver or kidney dysfunction, hyperlipidaemia, hypercholesterolaemia or diabetes may be at an increased risk of these adverse effects and discussion with or referral to a dermatologist should be considered before prescribing isotretinoin.

Adverse psychological issues have been associated with isotretinoin, particularly depression and suicidality, but causality has not been established. Depression may be present before treatment or can occur for unrelated reasons.[17] A brief psychological assessment for depression and suicidal tendency should be performed prior to prescribing isotretinoin, and then briefly whenever the patient is seen during and after treatment.

Baseline investigations should occur prior to prescribing isotretinoin and repeated at least once during the course of treatment, and should include:[6, 14, 21]

- Lipid levels
- Liver function tests
- Full blood count

Pregnancy testing with serum hCG is also required at baseline, monthly during treatment, and again five weeks post-treatment.

What has changed since March, 2009?

Access to subsidised oral isotretinoin for severe acne, was widened on 1 March, 2009, to allow vocationally registered General Practitioners and Nurse Practitioners working in an appropriate field to prescribe the medicine, fully subsidised, subject to Special Authority criteria.[15]

The widening of access created significant debate among Dermatologists and General Practitioners. Dermatologists were particularly concerned that:

- The medicine is difficult to use and General Practitioners would not have the training or experience to use it safely
- Widening access would increase prenatal exposure to teratogens and therefore increase pregnancy terminations and birth defects

For further information see: "The isotretinoin debate; should we be arguing about who is prescribing isotretinoin or is the real issue how it is being prescribed?", BPJ 20 (April, 2009).

Is general practice prescribing isotretinoin correctly?

General Practitioners are now significant prescribers of isotretinoin. From July, 2011 – June, 2012 there were a total of 46 531 dispensed prescriptions for isotretinoin, of which 58% originated from a General Practitioner.[24]

Since 2009 the number of prescriptions dispensed per patient prescribed isotretinoin has decreased by approximately 15%.[24] The reason for this is unclear, but may be due to larger doses per prescription, lower overall doses of isotretinoin or increased rates of medicine cessation.

There has also been an important methodological improvement in isotretinoin prescribing. Recording of patient NHI numbers on prescriptions has improved markedly since access to isotretinoin was widened to include General Practitioner prescribing. From July, 2011 – June, 2012 NHI numbers were recorded in 91% of all

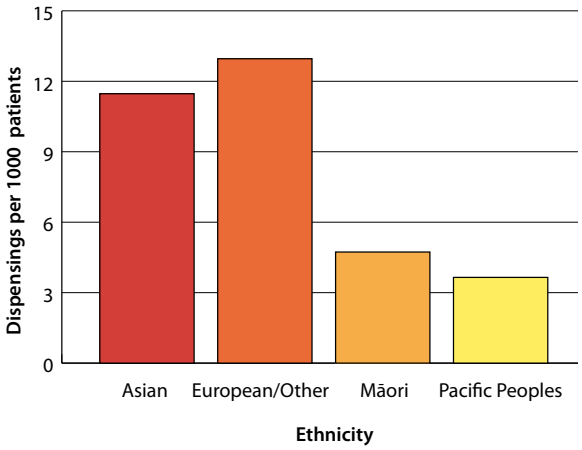


Figure 1: Isotretinoin dispensed, by ethnicity

Number of dispensings per 1000 enrolled patients, all prescribers, July, 2011 to June, 2012*

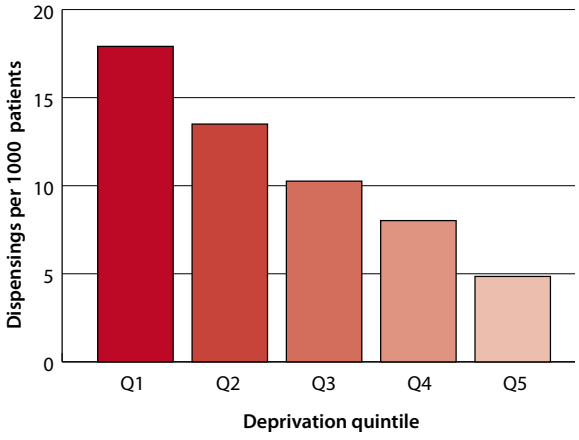


Figure 2: Isotretinoin dispensed, by deprivation quintile (Q1= least deprived, Q5 = most deprived)

Number of dispensings per 1000 enrolled patients, all prescribers, July, 2011 to June, 2012*

* only dispensings with an NHI number recorded for a primary care enrolled patient are included

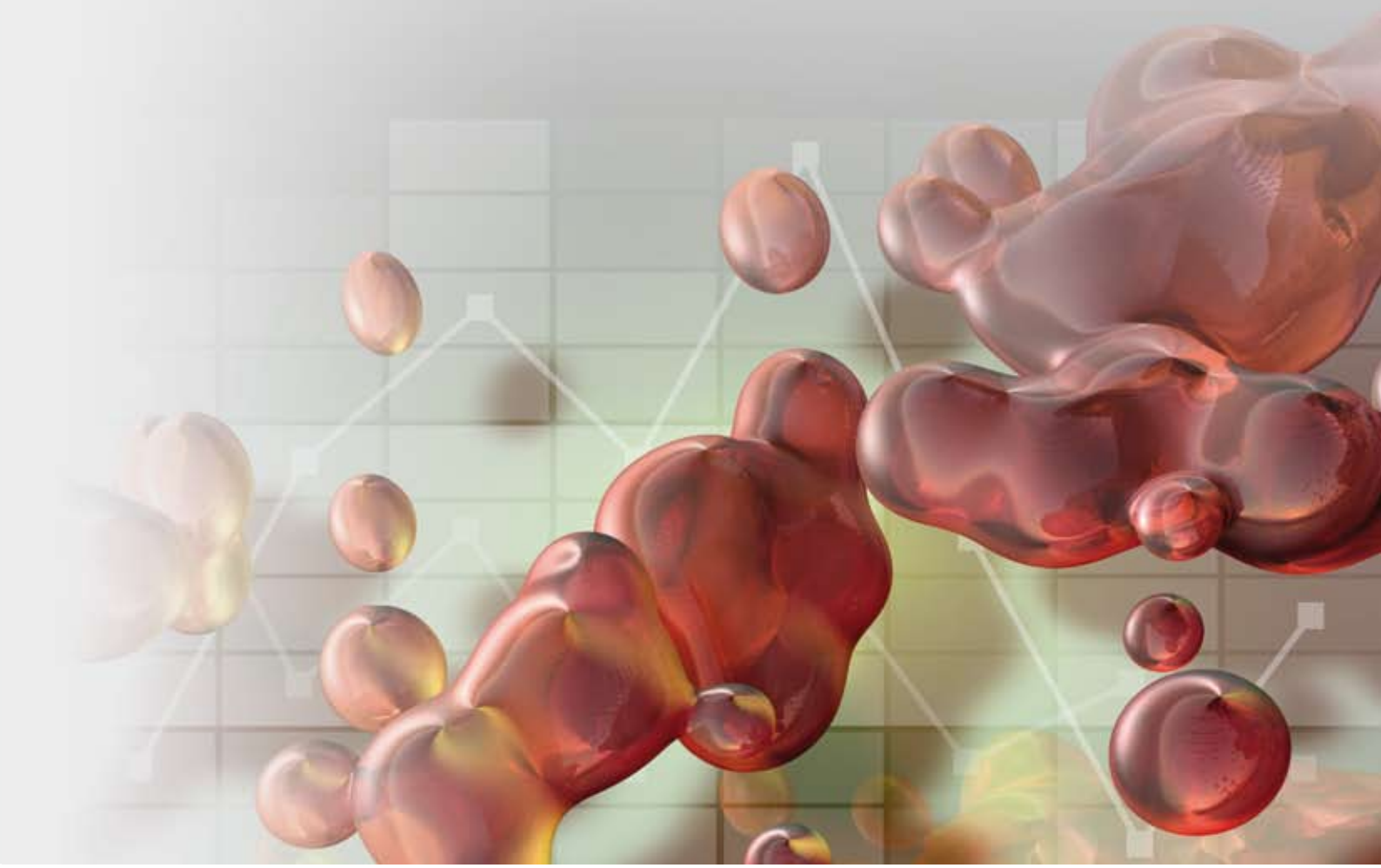
isotretinoin dispensings compared to only 60% prior.[25] Recording of NHI numbers allows analysis of medicine use to occur.

There has been no change in the number of serious adverse effects reported to Centre for Adverse Reactions Monitoring (CARM) since the widened access to prescribing. However, the impact of General Practitioner prescribing of isotretinoin on abortion rates due to teratogen exposure is not able to be monitored due to differences in the way that prescription medicines are coded between primary and secondary care.

Have the prescribing disparities of isotretinoin been reduced?

An unintended effect of limiting access to isotretinoin was an increase in health disparities due to the limited access to publicly funded and private Dermatologists in New Zealand.[25] The result was that a person living in the least deprived socioeconomic area was 2.5 times more likely to be prescribed isotretinoin than a person living in the most deprived area, and that Māori and Pacific peoples were five times less likely to be prescribed isotretinoin than people in other ethnic groups, largely New Zealand Europeans.[25] This is despite the fact that there is no significant evidence of an association between the incidence of acne and deprivation level or ethnicity.[25, 26] One of the primary reasons for widening access to isotretinoin was to reduce this disparity.

However, the most up-to-date data shows no obvious changes in prescribing behaviour between the highest and lowest decile socioeconomic areas, and between ethnicities (Figure 1 and 2).[25] This is despite increased access to isotretinoin via general practice. This may suggest that the actual or perceived severity of acne is lower in these groups, and therefore treatment is not sought.



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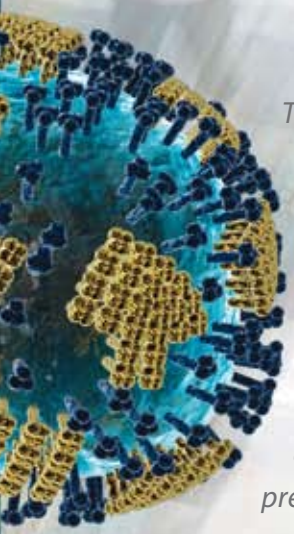
The 2013 influenza season: **New strains, new vaccines**



The dominant influenza virus to circulate in New Zealand this "flu season" is likely to be an A(H3N2) virus, similar to the virus that caused a severe outbreak in Canterbury in 2012. The 2013 vaccine contains new strains, including A(H3N2), therefore this is an important year for influenza vaccination in New Zealand. The immunisation of people aged 65 years and over is a particular focus, as vaccination rates among this group have been trending downwards over the past five years. Older people have been reported to have more severe outcomes with the H3N2 strain that has been circulating in North America this winter. Emerging evidence suggests that annual influenza vaccination can also reduce cardiovascular risk in older people. Immunisation of pregnant women is safe and can be encouraged at any stage of pregnancy.

This year's vaccine is different to previous years

It is too early to predict how severe the 2013 influenza season will be in New Zealand, however, a particularly severe outbreak was seen in Canterbury in 2012 with a similar virus to that expected to be the dominant strain in all centres this year. The Centres for Disease Control and Prevention (CDC) reported an earlier than normal start to the Northern Hemisphere season with rapid increases in the rates of influenza-associated hospitalisations and deaths among older people in the United States.[1]

Influenza vaccination during the New Zealand 2013 season is more important than in recent years because this year the vaccine contains two new strains that were not present in the 2010 – 2012 vaccines. A key message for health professionals to deliver to patients is, therefore, that: "there may be strains of the flu circulating this year that vaccinations from previous years are unlikely to provide protection against."

The decision to change the vaccine composition follows a World Health Organisation (WHO) recommendation, after laboratory testing showed changes in antibody reactions to circulating strains and also a change in the dominant viruses in circulation.[2]

The 2013 vaccine contains:[3]

1. A/California/7/2009 (H1N1)-like strain
2. A/Victoria/361/2011 (H3N2)-like strain (new)
3. B/Wisconsin/1/2010-like strain (new)

Two vaccines are funded for 2013:

- **Fluvarix** is approved for use in adults and children aged over six months
- **Fluvax** is approved for use in adults and children aged over five years, however, Public Health experts recommend that Fluvax should not be given to children aged under nine years and should not be given to children who have a history of febrile convulsions. This follows research showing increased rates of febrile reactions, including febrile convulsions in this age group.[4]

Neither vaccine should be administered to people who have had anaphylactic reactions to any of the vaccine's components.[3] Fluarix contains traces of gentamicin sulphate and Fluvax contains traces of neomycin and polymyxin.[3] Both influenza vaccinations are derived from hen eggs and may contain residual egg protein. People who have had a confirmed anaphylactic reaction to egg protein should only be administered the vaccine under specialist supervision.[3] People who have a non-anaphylactic allergy to eggs can be administered the vaccine as normal. People who are acutely unwell or have a fever over 38°C should delay having the vaccine until they are well.

How many doses of the vaccine are needed?

One dose is required for adults, children aged over nine years, or children aged between six months and nine years who have already received an influenza vaccination in any previous year. Children aged between six months and nine years who are receiving their first influenza vaccination should have two

doses, at least four weeks apart.[7] This is because they may not have had contact with viruses with antigenic properties similar to the strains present in the vaccine and are likely to require an additional dose to establish immunity.

Who is eligible for subsidised vaccinations?

The following eligible groups will receive a fully subsidised seasonal influenza vaccination if they visit their General Practice clinic before 31 July, 2013:

- Anyone aged 65 years and over
- Anyone with cardiovascular, cerebrovascular or chronic respiratory disease, cancer, Type 1 or 2 diabetes or a specified condition
- Pregnant women at any stage of gestation

A complete list of conditions that qualify a person for free vaccination is available from: **www.influenza.org.nz/?t=887**

N.B. People with asthma who do not require regular preventive medicines, those in remission from cancer, and people with hypertension and/or dyslipidaemia without evidence of end-organ disease are not eligible for subsidised influenza vaccination.

Who else should be encouraged to get vaccinated?

People with risk factors for exposure to influenza and its complications should also be encouraged to be vaccinated, in particular children aged between six months and five years. Risk factors for influenza complications include:

- Pacific or Māori ethnicity

PHO Performance Programme – Influenza vaccination rates are decreasing

Influenza vaccination is a PHO Performance Programme (PPP) Indicator that accounts for 9% of the Performance funding; 3% for the total population and 6% for the high need population.[5] High need populations include Māori and Pacific Peoples and people living in Quintile 5 (most deprived) socioeconomic areas. The target is assessed by counting the enrolled patients aged 65 years and over who have received an influenza vaccination during the most recent campaign (the numerator). This number is then divided by the number of enrolled patients aged 65 years and over at the beginning of the most recent campaign period (the denominator). Only vaccinations received by people aged 65 years and over are included in the PPP results. PHOs that have a large number of people who decline offers of vaccination will therefore find it difficult to meet the target.

The programme goal is for at least 75% of people aged 65 years and over at the end of the annual influenza vaccination season to have received the influenza vaccine during the most recent campaign.[5]

The rate of influenza vaccinations has trended downwards over the past five years (Figure 1) for people aged 65 years and over. The most recent data captured from July – September 2012 suggests that in 2013 rates may have stabilised, with the national rate of vaccination dropping only slightly from 64.4% to 63.7%.[6] However, this is more than 10% below the programme goal of 75% coverage. It is important that the trend of declining influenza vaccination rates in New Zealand is reversed. In 2012, no PHO achieved the target rate of 75%.

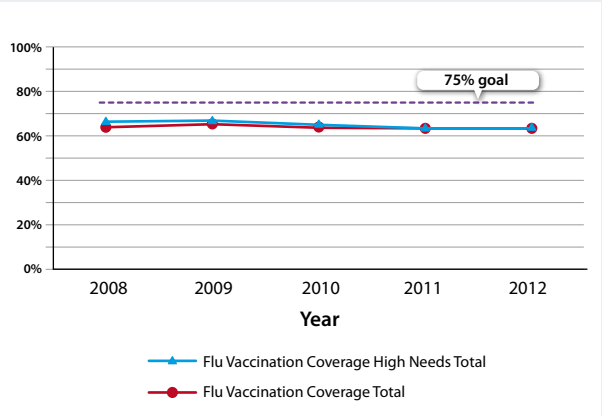


Figure 1: Influenza vaccination rates from 2008 to September 2012 for all people aged 65 years and over in New Zealand[5]

- Living in a low socioeconomic area or a crowded household
- Exposure to second-hand cigarette smoke
- Frequent illness

Women who intend to become pregnant during the influenza season and people travelling overseas, especially to the Northern Hemisphere from October to May should also be encouraged to be vaccinated.

Healthcare workers are strongly recommended to be vaccinated because they have high exposure rates to influenza virus and immunisation of healthcare workers may reduce patient morbidity.[8] Endorsement of vaccination by healthcare professionals can influence an individual's decision to be vaccinated, even if they did not initially want to be.[9] Influenza vaccination is free to all staff employed by District Health Boards in New Zealand. In 2012, almost half of all employees received an influenza vaccination. Rates were highest among doctors (57%) and lowest among midwives (37%).[10]

Influenza vaccination is important for older people and women who are pregnant

Annual influenza vaccinations are important for people at increased risk of influenza-related complications. This is not only because different strains of influenza may be in circulation each year, but also because antibody titre begins to decline from one to two months post-vaccination.[3] This is more pronounced in older people. Immunity levels in people aged over 65 years have been shown to be significantly reduced at six months post-vaccination and may not be sufficient to provide protection after this time.[3, 11]

Annual influenza vaccination may reduce cardiovascular risk. Mortality rates due to stroke and myocardial infarction increase by 10 – 15% during winter.[12] Recently, several studies have suggested that annual influenza vaccination may have a cardio-protective effect. A meta-analysis, including over 290 000 patients, found that receiving an annual influenza vaccination was associated with significant reductions in myocardial infarction (odds ratio 0.73), all-cause mortality (odds ratio 0.61), and major adverse cardiac events (odds ratio 0.47).[13] Another meta-analysis which included over 30 000 participants aged over 55 years with known vascular disease, found that vaccination was associated with a reduced risk of major vascular events when the virus in circulation was well matched to the vaccine.[12]

The pathophysiology of the possible effect of influenza on cardiovascular risk is not clear. Suggested mechanisms include increased risk of plaque rupture, endothelial dysfunction, fever-associated tachycardia, impaired breathing, modulation of blood clotting and immune and inflammatory processes.[12, 13]

Administering influenza vaccination during all trimesters of pregnancy is considered safe,[14] and can be done at the same time as pertussis vaccination occurs. Women who are pregnant and newborn infants are at increased risk of influenza-related complications. Women with asthma or diabetes who are pregnant are three to four times more likely to contract influenza and develop an influenza-associated illness.[3] Neither Fluvax or Fluarix are approved for use in infants aged younger than six months, however, young infants have high rates of hospitalisation from influenza. Vaccination during pregnancy is therefore the best way to decrease a newborn infant's influenza risk because it increases antibody delivery, giving temporary protection to the infant via the placenta. Ideally all siblings and carers of infants will also be vaccinated to provide a "cocoon of immunity" around the infant. Studies on the effectiveness of pertussis vaccination have shown that immunisation of family members can provide protection to infants where there is a high prevalence of disease within the community.[15, 16] It is likely that these findings apply to other vaccine preventable illnesses such as seasonal influenza.

Reducing the number of patients who decline influenza vaccination

When discussing influenza vaccination with patients who may be reluctant to be immunised, it is important to emphasise the following points:

- There are two new strains of "the flu" in the vaccine this year, in recognition of changing circulating strains internationally
- Annual immunisation is likely to help to reduce the risk of an older person having a stroke or heart attack in the future
- Immunisation helps to protect the families and friends of people who are immunised who may be more vulnerable to the complications of influenza

Best Practice Tip: A standardised statement can be prepared for the practice to use when offering influenza vaccination to patients. This may be of particular use when phoning patients who are unlikely to present for vaccination without encouragement. The "Don't let the flu get you!" website has template patient recall letters which may be useful when contacting patients who have previously declined vaccination. Available from: **www.influenza.org.nz**

Pneumococcal vaccination

Pneumococcal infection by the bacterium *Streptococcus pneumoniae* is a frequent cause of respiratory illnesses, e.g. otitis media, bronchitis and sinusitis. Many people in New Zealand carry these bacteria without developing invasive disease. However, serious complications such as pneumonia, meningitis and septicaemia can develop when *S. pneumoniae* invades normally sterile tissue. Young children, older adults and people who are immunodeficient are most at risk of this occurring.

Four pneumococcal vaccines are licensed in New Zealand. Synflorix (10-valent) and Prevenar13 (13-valent) are conjugate vaccines. Pneumovax23 and Pneumo23 (both 23-valent) are polysaccharide vaccines. Conjugate vaccines generate better quality, more longer-lasting antibodies and have immune memory unlike polysaccharides. Conjugate vaccines are also more effective when used as boosters.

The 10-valent Synflorix vaccine at age six weeks and age three, five and 15 months is funded for all infants as part of the National Immunisation Schedule.[17] Prevenar13 vaccine is used for children at high risk of complications, followed by Pneumovax23 vaccine after age two years.[17] High-risk children aged under five years (Table 1) and all people with functional or anatomical splenectomy are eligible for fully subsidised vaccination with both Prevenar13 and Pneumovax23.

Pneumovax23 vaccination is recommended by the Ministry of Health, but not subsidised, for all people aged 65 years or over and adults and children aged over five years at increased risk of invasive pneumococcal disease due to co-morbidity or immunodeficiency (Table 1), who have not been previously immunised.[17] The Immunisation Advisory Centre also recommends that Prevenar13 be given eight weeks before Pneumovax23 in high-risk patients, to produce better immune

Table 1: Children and adults considered to be at high risk of pneumococcal disease[17]

Children with these conditions/treatments are considered high risk*	Adults with these conditions/treatments are considered high risk
■ Receiving immunosuppressive or radiation therapy ■ Primary immune deficiencies or HIV ■ Renal failure or nephritic syndrome ■ Diabetes ■ Down syndrome ■ Organ transplants ■ Cochlear implants or intracranial shunts ■ Cerebrospinal fluid leaks ■ Receiving long-term corticosteroid treatment and daily prednisone, or taking ≥ 20 mg prednisone per day ■ Pre-term infants born prior to 28 weeks gestation ■ Chronic pulmonary disease, including asthma treated with high-dose corticosteroids ■ Cardiac disease with cyanosis or failure	■ Aged over 65 years ■ People with a history of invasive pneumococcal disease ■ Functional or anatomical asplenia, e.g. sickle cell disease or splenectomy ■ Chronic illness, e.g. chronic cardiac, renal or pulmonary disease, diabetes or alcoholism ■ Immunocompromised, e.g. nephritic syndrome, lymphoma and Hodgkin's disease, HIV ■ Cerebrospinal fluid leak ■ Cochlear implants

* Eligible for funded pneumococcal vaccination if aged under five years

response.[18] This is an ideal, but potentially expensive strategy for the patient.

Healthy people aged over 65 years generally require only a single dose of Pneumovax23, but those at high risk should receive a second dose three to five years after their first dose.

There are no contraindications to pneumococcal vaccination other than a previous severe reaction to the vaccine or any of its components. The safety of the vaccine has not been confirmed in pregnant women, therefore it is recommended that immunisation occur following pregnancy, unless the risk of infection is substantial.[17]

 For further information see: "The management of community-acquired pneumonia", BPJ 45 (Aug, 2012).

ACKNOWLEDGEMENT: Thank you to **Dr Nikki Turner**, Director, CONECTUS and The Immunisation Advisory Centre, University of Auckland and **Associate Professor Lance Jennings**, Virologist, University of Otago, Christchurch and Canterbury Health Laboratories, Canterbury DHB for expert guidance in developing this article.

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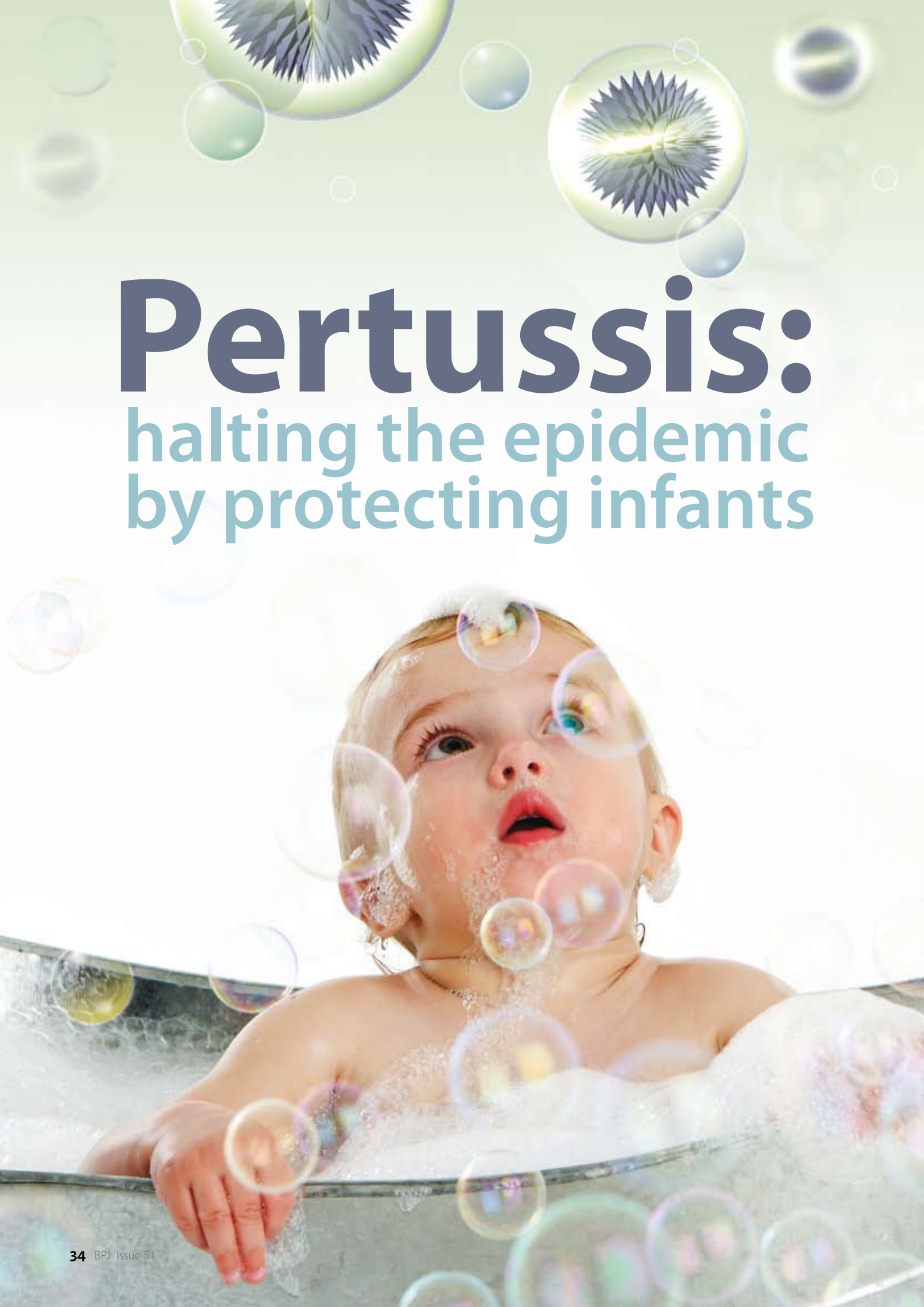
Pertussis:
halting the epidemic by protecting infants



Infants who have not yet completed the National Immunisation Schedule and children who are not immunised, or only partially immunised are most at risk from pertussis. The best way to protect at-risk individuals is on-time vaccination, as it protects against infection for infants who are at highest risk and reduces the number of people in the community that can transmit the bacteria. Pertussis booster vaccinations in the combination Tdap vaccine are fully-subsidised as of January, 2013 for pregnant women between 28 – 38 weeks gestation

The New Zealand pertussis epidemic

Bordetella pertussis infection, also known as pertussis or whooping cough, is currently at epidemic levels in New Zealand. In 2012 there were 5793 reported cases and two deaths.[1] Canterbury (1209), Capital and Coast (680) and Nelson Marlborough (670) DHBs reported the highest numbers.[2] Figure 1 shows pertussis hospitalisations by calendar month since 1998.

Infants aged under one year are at the greatest risk of severe disease and account for over 60% of the hospitalisations that have occurred since the latest outbreak began in August 2011.[2] Health professionals can reduce severe pertussis infection rates by recommending on-time vaccination for all infants and children, and booster vaccinations for women who are pregnant and adults with regular contact with infants.

Pertussis immunisation recommendations

There are three acellular pertussis-containing vaccines (i.e. vaccines containing only antigenic fragments of the pertussis bacteria) funded under the New Zealand Immunisation Schedule:[3]

1. INFANRIX-hexa provides protection against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and disease caused by Haemophilis influenza type b. This vaccine is used for primary vaccinations in infants and children aged up to seven years.
2. INFANRIX-IPV provides protection against diphtheria, tetanus, pertussis and poliomyelitis. This vaccine is used for primary vaccinations of infants and children aged up to seven years.
3. BOOSTRIX or ADACEL is used to provide booster vaccinations against diphtheria, tetanus and pertussis. It is licensed for use in children aged over ten years, adults and women who are pregnant.

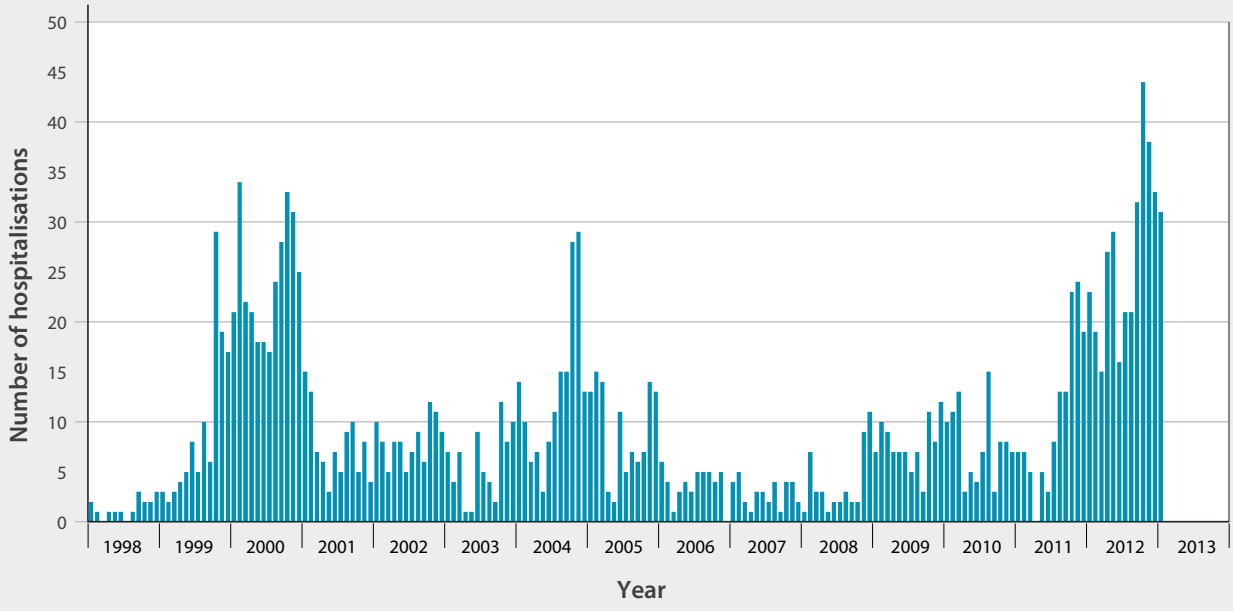
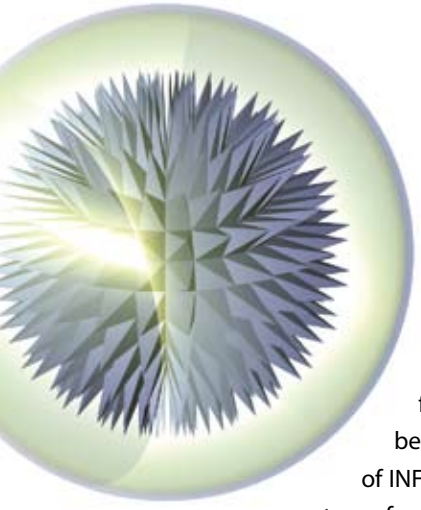


Figure 1: Pertussis hospitalisations in New Zealand by calendar month, from January, 1998 to January, 2013[1]

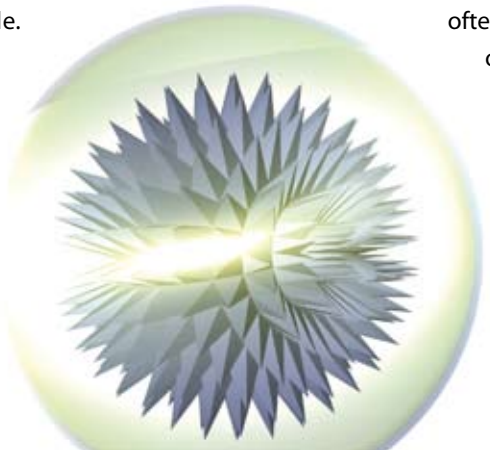


In infants a primary course of INFANRIX-hexa is recommended at ages six weeks, three months and five months.[3] The minimum dose-interval is four weeks and the first dose is not recommended before age six weeks. A single dose of INFANRIX-IPV is then recommended at age four years, followed by a booster at age 11 years with BOOSTRIX.[3] The ideal coverage target is for 95% of infants to be fully-vaccinated at ages six weeks and 16 months.[3]

Immunity to pertussis develops within 10 – 14 days of immunisation.[3] However, the effectiveness of the pertussis vaccination declines with time and protection can be expected to last between five to ten years in children.[4] If pertussis vaccination is administered after contracting a pertussis infection, the vaccination will be ineffective in preventing acute illness.

The Ministry of Health recommends that adults with regular contact with infants be offered booster vaccinations to form a "cocoon of immunity" to protect infants in the first year of life. The effectiveness of this approach is likely to be influenced by disease prevalence.[5] During outbreaks, "cocooning" infants is more likely to reduce the number of infants who become infected.[5] The exact duration of protection from pertussis immunisation in adults is unknown,[3] but it can be presumed that vaccinations received in childhood are no longer providing adequate protection from pertussis. All people with occupational (e.g. midwives, healthcare workers and carers) or household (e.g. parents, grandparents and older siblings) contact with infants should receive a booster vaccination (BOOSTRIX or ADACEL). The dose should be repeated every ten years for healthcare workers and people who work with children.[3] Vaccination is not subsidised in these groups.

Parents and grandparents may be more motivated to ensure they are immune to pertussis if it is explained that vaccination will reduce the likelihood that they infect infants who have yet to complete the immunisation schedule. An international study of 95 infants with pertussis found that 76 – 83% contracted pertussis from household members.[6]



Pertussis vaccination for pregnant women between 28 – 38 weeks gestation is now fully-subsidised (as of 1 January, 2013). This BOOSTRIX vaccination will be subsidised until the current pertussis epidemic is over and can be administered at the same time as the influenza vaccination.

Maternal antibody levels have been shown to decrease quickly following pertussis immunisation, and levels in women vaccinated during pre-conception or early in pregnancy may be insufficient to provide passive immunity to the newborn infant.[7] Therefore, immunisation later in pregnancy is more likely to provide some protection for the infant while they are still vulnerable prior to completing their primary immunisation course.[8] The vaccine can be safely given to pregnant women from 20 weeks, and after 38 weeks gestation, but receiving the vaccine too early or too late may mean that the infant is still exposed to pertussis during delivery and as a newborn. It takes approximately two weeks after the booster vaccination for immunity to pertussis to develop. In addition, women 20 – 27 weeks or > 38 weeks gestation would have to meet the costs of vaccination themselves.

The only contraindication for pertussis vaccination is an anaphylactic reaction to a previous dose, or any component of the vaccine. Pertussis vaccination is not known to be associated with any significant adverse effects, other than pain or redness at the injection site. Mild fever has been reported to occur in up to 20% of infants receiving the vaccination.[3] Vaccination of children with an evolving neurological disorder, e.g. uncontrolled epilepsy, should be discussed with a paediatrician first.

Management of pertussis

The presentation of patients with pertussis is influenced by age and immunisation status. Young infants may deteriorate rapidly and display apnoea and cyanosis, rather than cough. In older patients the illness often begins with a seven to ten day period where symptoms are clinically indistinguishable from a minor respiratory infection. This is referred to as the catarrhal stage, during which individuals are most infectious.[3] Following the catarrhal stage, paroxysmal bouts of coughing begin to develop, during which the characteristic "whoop" noise can often be heard on inspiration in younger children. Gasping or gagging may be noticed instead of whooping in older children and adults. Vomiting can follow bouts of coughing. Coughing lasts two to eight weeks and is often worst at night.

A diagnosis of pertussis during the catarrhal stage of the disease is difficult to confirm. A

diagnosis becomes more likely where a patient has an acute cough for 14 days or more and has either: an inspiratory whoop, paroxysmal bouts of coughing, post-cough vomiting or apnoea, for which there is no other known cause.[9]

Laboratory testing is not required to confirm pertussis in an outbreak situation, where a patient is linked to a confirmed case, for notification purposes or to confirm a patient is no longer infectious.[9] Testing should be considered where confirmation is needed to manage vulnerable contacts, e.g. where a family member is aged under one year, or where a diagnosis is uncertain.[9]

Treatment and prophylaxis of pertussis

Antibiotic treatment for pertussis is recommended to reduce transmission of the disease. Treatment should be initiated if the patient presents within three weeks of onset of cough, after which time people are generally no longer infectious.[9] Treatment is unlikely to alter the clinical course of the illness, unless it is begun in the catarrhal stage.[10] Antibiotics should be given if the duration of cough is unknown. Women who are in the last trimester of pregnancy are considered high-risk and should be prescribed antibiotics, regardless of the timing of onset.[3] Young children can deteriorate rapidly and may require hospitalisation.

Azithromycin is first-line for treatment and prophylaxis of pertussis in infants and children, erythromycin is first-line for adults:

- Infants and children < 45 kg – azithromycin 10 mg/kg in a single dose on day one, followed by 5 mg/kg, once daily, for days two to five (five days total). Erythromycin 10 mg/kg, four times daily for 14 days is an alternative.
- Children > 45 kg and adults – erythromycin 400 mg, four times daily for 14 days.* Azithromycin 500 mg on day one, followed by 250 mg, once daily, on days two to five, is an alternative.

* Erythromycin ethyl succinate is currently the only subsidised form of oral erythromycin available in New Zealand. Treatment and prophylaxis is recommended for 14 days with erythromycin ethyl succinate. There is evidence that seven days of treatment with erythromycin estolate (which has superior tissue and serum concentrations compared with the other erythromycin salts), is as effective as 14 days. However, erythromycin estolate is not currently available in New Zealand.[11]

Parents should be informed that the use of all macrolides (e.g. azithromycin or erythromycin) in infants aged under three months is associated with an increased risk of hypertrophic pyloric stenosis and monitoring for complications, e.g. forceful vomiting, should occur during treatment and for one month following completion.

Azithromycin subsidy and dosing changes

Azithromycin liquid (as of 1 November 2012) and tablets (as of 1 December 2012) are now fully subsidised, without restriction, for a maximum of five days treatment. There is currently a lack of published consensus on the dosing regimen for azithromycin in children for pertussis. United States, United Kingdom and Australian guidelines differ in their advice, with some advising different regimens depending on age. The consensus in New Zealand, among infectious disease specialists, is now to use the same regimen in children < 45 kg, regardless of age: 10 mg/kg on day one, followed by 5 mg/kg on days two to five. Due to concerns about resistance to azithromycin, it is not recommended as a first-line treatment in adults for pertussis.

Prophylactic antibiotics are recommended for people who have spent more than one hour in the close proximity of an infectious person if they:[9, 11]

- Are aged less than one year
- Have an infant aged less than one year in the same household, or they spend significant time with infants aged less than one year
- Are pregnant, particularly in the last weeks of pregnancy
- Are at risk of severe complications, e.g. people who are immunocompromised or have severe asthma

For further information see: "Pertussis: an avoidable epidemic", BPJ 45 (Aug, 2012).

ACKNOWLEDGEMENT: Thank you to **Dr Nikki Turner,** Director, CONECTUS and The Immunisation Advisory Centre, University of Auckland for expert guidance in developing this article.

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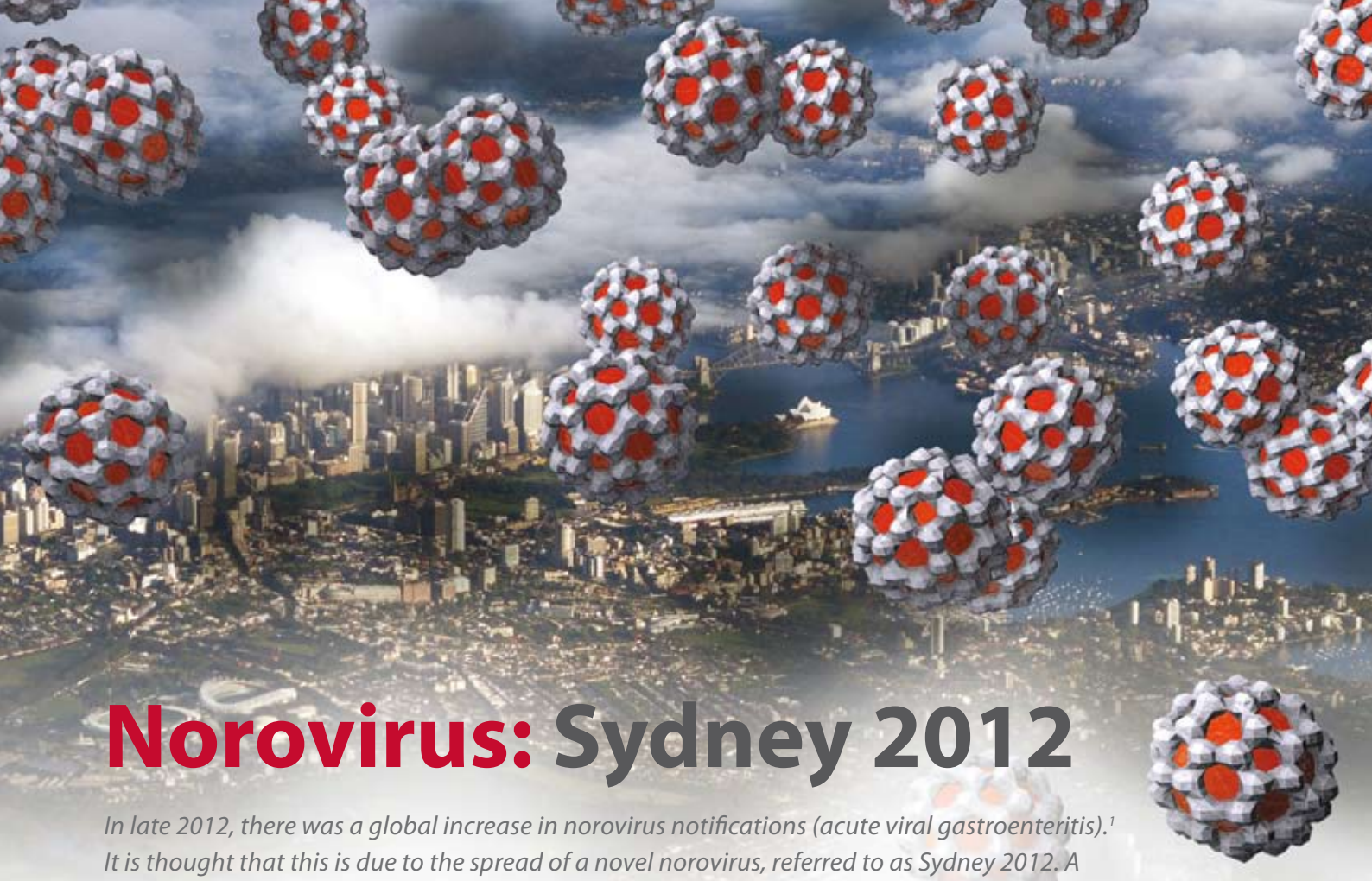


Norovirus: Sydney 2012

In late 2012, there was a global increase in norovirus notifications (acute viral gastroenteritis).[1] It is thought that this is due to the spread of a novel norovirus, referred to as Sydney 2012. A worldwide warning for a severe norovirus season in 2013 has been issued, and outbreaks of Sydney 2012 have already been reported in New Zealand. Treating dehydration and reporting of suspected outbreaks are key aspects of management.

Diagnosis and management of suspected norovirus

The typical incubation period for norovirus is 24 – 48 hours. Acute onset of nausea is often the first symptom, accompanied by abdominal cramps and watery diarrhoea. Vomiting can occur, and may be more common in young people, while diarrhoea may be more common in adults.[2] Patients can also experience a mild fever, headache, fatigue and myalgia. Norovirus infections are self-limiting and symptoms typically resolve in one to two days. Dehydration is the most common complication of the illness.

The purpose of the clinical examination is to assess the degree of dehydration and to exclude other possible causes. Details of stool and vomitus frequency and consistency should be noted. The patient's recent history of fluid intake, urine output, and the use of medicines that may cause diarrhoea, as well as any recent overseas travel, should also be enquired about. Routine examination should include an assessment of the patient's general appearance, temperature, heart rate and blood pressure, respiratory rate and character, skin turgor and capillary refill time.

Diarrhoea and vomiting are non-specific symptoms in younger children. Red flags which may indicate a condition other than viral gastroenteritis, include high fever, symptoms related to other systems, prolonged symptoms and severe abdominal pain or bilious vomiting.[3]

Most patients with norovirus can be managed at home, however, referral to hospital may be considered for patients with severe dehydration, older patients who are unable to manage at home by themselves or younger infants whose condition may deteriorate more rapidly. Patients with gastroenteritis, who have impaired kidney function or who have had a previous episode of acute renal decline, should discontinue non-essential, nephrotoxic medicines, e.g. NSAIDs. Consider withholding ACE inhibitors, ARBs and diuretics in older patients with gastroenteritis if dehydration does occur.

For further information see: "Assessment and management of infectious gastroenteritis" : BPJ 25 (Dec, 2009).

Laboratory investigations are not routinely required for patients with suspected norovirus.

Anti-diarrhoea or anti-emetic medicines are not generally recommended as they may deter the use of appropriate fluid treatment, can prolong symptoms and are associated with other adverse effects.[3] In adults with severe vomiting, a single dose of an antiemetic (IM or buccally) may give symptomatic relief, and enable oral rehydration to occur.

Reporting norovirus outbreaks

Acute gastroenteritis is a notifiable infectious disease when there are two or more people with a suspected common source, or a single person in a high risk area, e.g. a food-handler.

Best Practice Tip: If your practice sees, or hears of, an unusual number of patients with gastroenteritis in a week, even if no common source or high risk area is identified, contact your local Medical Officer of Health. They will then determine if further investigation and outbreak reporting is needed.

Infection control of norovirus

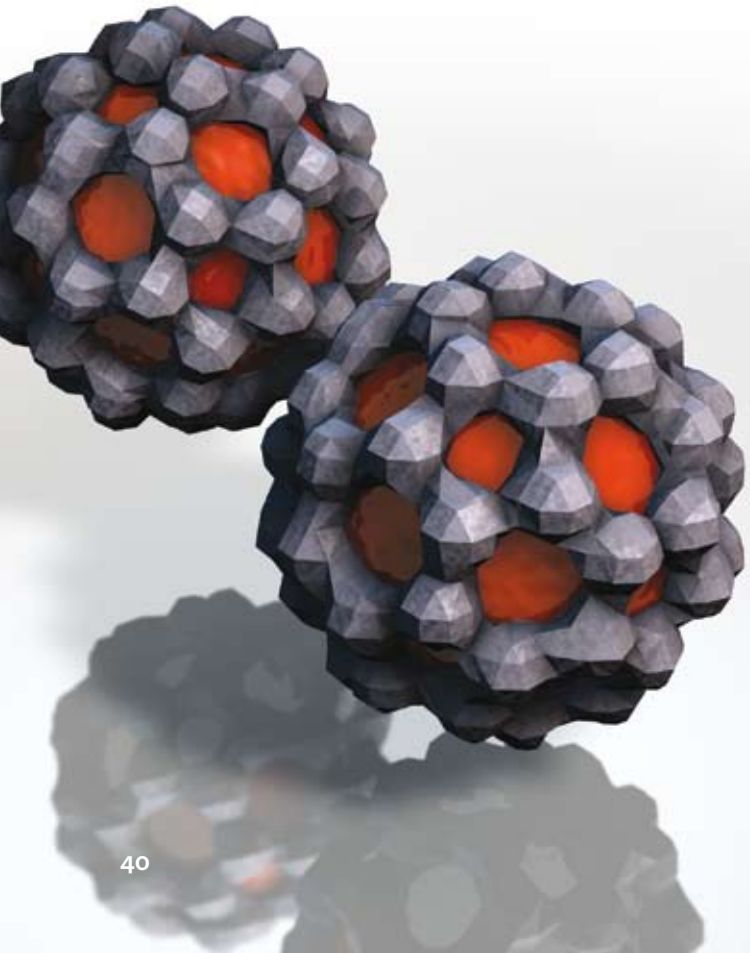
Patients with suspected norovirus should be advised to stay at home until they have been symptom-free for at least 48 hours. Food handlers are a particularly common vector for norovirus transmission and one infected person can result in an outbreak infecting thousands of people.[4]

Effective hand hygiene is the most important measure for preventing the spread of norovirus.[2] All people who may have come into contact with an infected person should be instructed to regularly wash their hands under running water and vigorously rub with soap for a minimum of 20 seconds. Hands should be thoroughly dried with a hand drier or disposable towel to minimise the transfer of pathogens.[2] Alcohol-based gels can be used where the use of soap and water is impractical, but should not be routinely used as a replacement for thorough hand washing.[3]

For infection control in the general practice surgery after seeing a patient with suspected norovirus, use a bleach solution (0.1% sodium hypochlorite) to disinfect contaminated surfaces, after regular cleaning.[2] Quaternary ammonium and phenolic disinfectants do not have sufficient activity against norovirus due to its structure.[2]

For further information see: Ministry of Health guidelines for the management of norovirus outbreaks, available from: **www.health.govt.nz** (key word = norovirus).

ACKNOWLEDGEMENT: Thank you to **Dr Fran McGrath**, Deputy Director of Public Health & Acting Manager Communicable Diseases, Ministry of Health, and team for expert guidance in developing this article.



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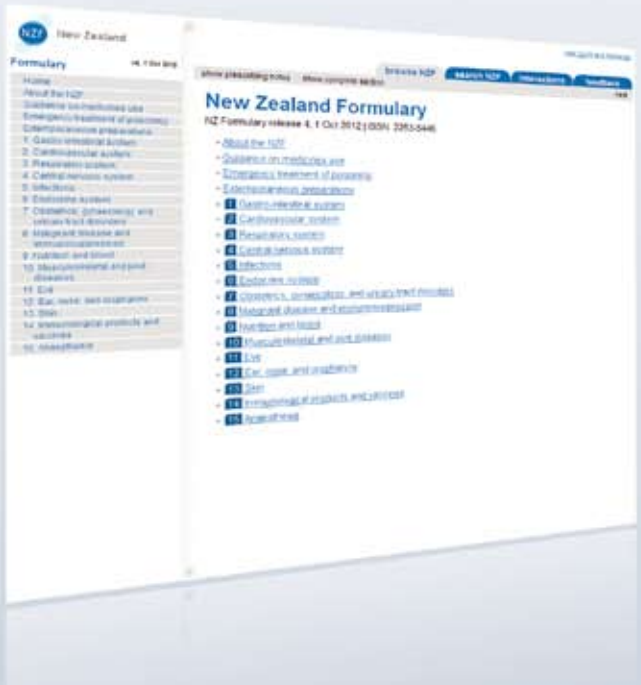

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Why can't we use quinine for night cramps?

Dear Editor,
As a continuing prescriber of quinine for leg cramps, I wonder if the Medsafe guideline should really still be regarded as the last word on it for leg cramps in New Zealand. The Medsafe advice on prescribing comes over as an all or nothing risk, when the reality is that it is about estimated risks versus benefit to the patient. Responsible, informed prescribing should address these.

The Cochrane systematic review describes this quite succinctly: "There is moderate quality evidence that there is a significant increase in minor adverse events with quinine compared to placebo but not in major adverse events. Overdosage, however, is well documented to cause serious harm including death."

Dr Mick Tarry, *General Practitioner*
Ashburton

In the article "Nocturnal leg cramps", BPJ 49 (Dec, 2012), we agree that quinine is an effective treatment for reducing the frequency and severity of cramps, however, the unpredictable and serious nature of its potential adverse effects mean that it is no longer recommended for this indication. After reviewing the safety of quinine, Medsafe informed prescribers in 2007 that muscle cramps had been removed as an approved indication,[1] with a reminder again in 2010.[2] Many other international medicine regulatory agencies, e.g. the United States Food and Drug Administration (FDA) and the Australian Therapeutic Goods Administration (TGA), have issued similar statements.[3, 4] We acknowledge the correspondent's point of view, but believe that the risk of prescribing quinine outweighs the benefit gained, for a condition, which although unpleasant, is not life-threatening.

The adverse effects associated with quinine can be grouped into three categories:[5]

1. Dose-dependent reactions (occur with normal therapeutic use, but more common with higher doses): gastrointestinal disturbance, tinnitus, vertigo, visual disturbance
2. Overdose reactions (occur at doses higher than therapeutic level): cardiac arrhythmias, blindness, seizures
3. Hypersensitivity reactions (occur at any time, and with any dose): thrombocytopenia, disseminated intravascular coagulation, acute renal failure, haemolytic uraemic syndrome

Other risk factors for using quinine, particularly in elderly people, include renal impairment, medicine interactions (e.g. digoxin, anticoagulants, phenothiazines) and memory loss which increases the potential for medicine administration errors and overdose.[5]

The Cochrane review in 2010 included 23 trials with 1586 participants (of which 58% were from five unpublished studies). It was concluded that compared to placebo, quinine reduced the number of muscle cramps over two weeks by 28%, reduced intensity by 10% and reduced the days on which cramp occurred by 20%. Cramp duration was not significantly reduced.[5] The review also found that although more minor adverse effects occurred with quinine compared to placebo, there was no significant difference in risk of major adverse reactions between quinine and placebo.[5] However, the occurrence of major, life-threatening adverse effects with quinine is rare – one patient had an event (thrombocytopenia) out of the 1103 participants for which data was available.[5] Had there been more participants able to be studied, and the power of the study greater, a different conclusion may have been reached.

The authors of the Cochrane review summed this up with the following: *"On the basis of these* [number of adverse events]*, quinine appears to be reasonably safe, but it is not possible to accurately calculate the true incidence of serious or life-threatening side effects which are rare…It is however on the basis of these serious adverse effects that the FDA has banned the marketing of quinine for muscle cramps and that the American Academy of Neurology has recommended in their report that it only be used as a last resort in intractable cramps and with close monitoring…Major adverse events are rare but can be serious or fatal so that in some countries prescription of quinine is severely restricted."*[5]

The main problem when weighing up the risks and benefits of using quinine is that the most serious adverse effects are due to hypersensitivity reactions, which are not dose-dependent, and may occur rapidly, after taking quinine for the first time, or after years of use. There is no current evidence which enables clinicians to predict which patients will experience serious adverse effects.[5]

Since January, 2008 (i.e. after the Medsafe warning), the Centre for Adverse Reactions Monitoring (CARM) in New Zealand has received 12 reports on quinine, six of which were for patients who had developed thrombocytopenia. Two of these patients experienced life-threatening effects, and in one, haemorrhage occurred within 12 hours of their first dose of quinine. The indication for prescribing quinine in all six reports was for muscle cramp.

When managing a patient with leg cramps, first rule-out underlying causes of the cramp or associated conditions such as medicine use (e.g. diuretics, naproxen, statins, long-acting beta-2 agonists), chronic dehydration, structural disorders, peripheral vascular disease, oesteoarthritis, diabetes or neurological disorder. There is limited evidence that exercise and muscle stretching is effective in reducing symptoms.[6, 7] A 2012 Cochrane review of non-pharmacological treatments for leg cramps concluded that there is an urgent need for quality data on emerging treatments.[8]

Nortriptyline, diltiazem, orphenadrine citrate, verapamil or gabapentin may be considered for patients with severe, intolerable symptoms, used at the lowest effective dose and discontinued if no benefit is observed.[9, 10] However, the treatment of leg cramps is an unapproved indication for the use of these medicines (with the exception of orphenadrine citrate), and patients should be informed of the risks and consent to treatment (see: "Use of unapproved medicines", Page 3).

For further information see: "Nocturnal leg cramps: is there any relief?" BPJ 49 (Dec, 2012).

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Metabolic monitoring with atypical antipsychotics

Dear Editor,

I have been using BPJ 40 (Nov, 2011) and BPJ 3 (Feb, 2007) articles on atypical antipsychotic use, for discussion in peer groups. As the BPJ 40 article suggests, there is significant off-label prescribing of atypical antipsychotics in non-schizophrenic or dementia patients (risperidone), and that generally patients are started on this in secondary care. The question has been raised whether non-schizophrenics and those on lower off-label doses (generally) require the same level of monitoring. Additionally, with the HbA_{1c} test for diabetes now being the standard, has this replaced glucose monitoring in this cohort?

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The short answer is yes, all people prescribed atypical antipsychotics, regardless of dose or indication, require the same level of monitoring for metabolic effects.

People with schizophrenia or bipolar disorder have an increased risk of cardiovascular morbidity and mortality compared to the general population, due to both disease and treatment factors.[1] However, it appears that the adverse metabolic effects of atypical antipsychotics occur regardless of dose of medicine or indication for treatment.[2] Although older age is a cardiovascular risk factor, young people are particularly susceptible to the cumulative effects over time of antipsychotic-induced weight gain and insulin resistance.[1] This is a growing concern in light of recent trends of increased off-label prescribing to young people for anxiety, insomnia and post-traumatic stress disorder.[2]

Adverse metabolic effects of atypical antipsychotics include:[1]

- Impaired glycaemic control, and therefore increased risk of type 2 diabetes
- Hyperlipidaemia, particularly decreased high density lipoprotein (HDL) and increased triglycerides
- High blood pressure, particularly in males

Clozapine is associated with the greatest risk of weight gain, followed by olanzapine and quetiapine, although all atypical antipsychotics are associated with metabolic adverse effects.1 Other medicines which are commonly co-prescribed with antipsychotics can contribute to weight gain, e.g. selective serotonin re-uptake inhibitors (SSRIs), tricyclic antidepressants, sodium valproate and lithium.[1]

Monitoring for metabolic adverse effects should occur in any patient prescribed an atypical antipsychotic medicine, regardless of dose or indication (Table 1).

Table 1: Recommended monitoring for patients taking atypical antipsychotics

Factor	Frequency of monitoring
Lifestyle interventions	Regularly encourage and support exercise, weight loss, smoking cessation, healthy eating and reduced alcohol consumption
Hyperlipidaemia	Fasting lipids test at baseline, then every three months for year one, and annually for subsequent years
Type 2 diabetes	HbA_{1c} at baseline, then every three months in year one (or fasting glucose monthly for first three months in patients at high risk)*, and annually for subsequent years
Blood pressure	Baseline, then every three months in year one, and annually for subsequent years
Weight/BMI	Baseline, then monthly. Offer dietary intervention if significant weight gain (≥ 7% of baseline weight)

* HbA_{1c} is now the preferred test for detecting diabetes, and should be used in preference to a fasting glucose test in most clinical situations. However, HbA_{1c} is not reliable when blood glucose levels rise too rapidly to affect HbA_{1c}, such as in some patients newly initiated on atypical antipsychotics. Therefore, in patients with other risk factors for diabetes, fasting blood glucose is recommended at baseline, and monthly for the first three months. HbA_{1c} can be used for long-term monitoring.

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