

URTICARIA | COPD | INFLUENZA VACCINE | HPV VACCINE

# Best Practice

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Issue 43 April 2012



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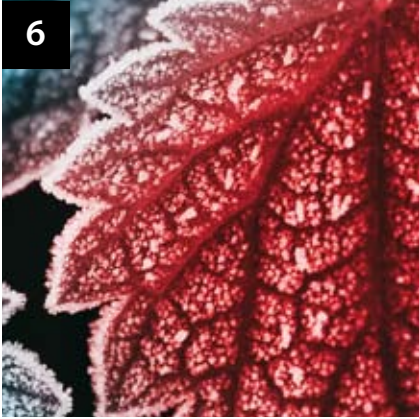
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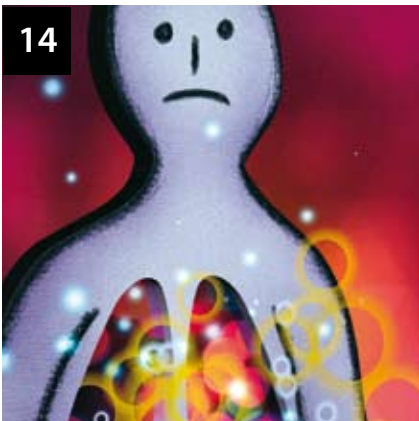
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6 **Diagnosis and treatment of urticaria**

Urticaria is a common condition, which is usually non-allergenic, but in the majority of patients a specific cause will not be found. Extensive diagnostic testing is not recommended unless there is strong evidence to suspect a specific trigger. Treatment is aimed at symptom relief, using oral non-sedating antihistamines first-line. Additional medicines can be added, depending on the severity and duration of symptoms. Most cases of urticaria are acute, however, in some cases, episodes may occur over several months or even years.



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14 **Diagnosis and management of COPD in Māori and Pacific peoples**

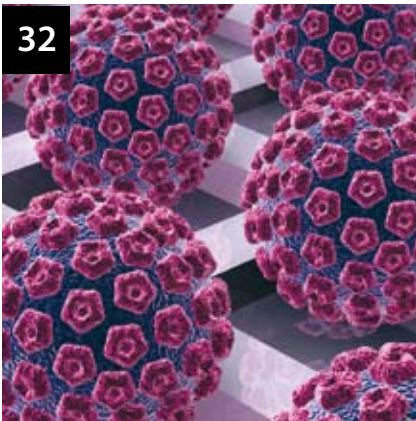
COPD disproportionately affects Māori and Pacific peoples in New Zealand. It is essential that people most at risk of COPD receive support and education about smoking cessation, the impact of COPD and the importance of early detection. Spirometry is the “gold standard” test for diagnosing COPD. Management focuses on smoking cessation, pharmacological treatment, pulmonary rehabilitation and psychosocial support.



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26 **Seasonal influenza vaccinations: the 2012 edition**

The 2012 seasonal influenza vaccine contains the same strains as in previous years, however, annual vaccination is still necessary. It is important that people most at risk of complications of influenza, such as people aged over 65 years and pregnant women, receive the influenza vaccine. Although not funded, vaccination is encouraged for children aged between six months and five years as this age group is also vulnerable to complications of influenza.



- 32 **The HPV vaccination programme: addressing low uptake**  
The human papillomavirus (HPV) vaccine was added to the national immunisation schedule in 2008 for females aged 12 years. The vaccine is funded for females aged between 12 and 20 years. So far, uptake of the school-based vaccination programme has been lower than expected, therefore primary health care providers are encouraged to offer information, address any fears or concerns and promote uptake of the vaccine. Although not funded, the vaccine can also be given to males and older females.
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Use of the term “screening”; bpac<sup>nz</sup> recertification programme; Testing for allergy in general practice

All web links in this journal can be accessed via the online version:  
[www.bpac.org.nz](http://www.bpac.org.nz)

“ Learn from the mistakes of others. You can't live long enough to make them all yourself.

– ELEANOR ROOSEVELT



The bpac<sup>nz</sup> Patient Safety Incident Reporting system is an online resource for people working in community health care to report and review patient safety incidents.

Reports are submitted anonymously, to identify factors which have contributed to patient safety incidents and to share solutions to prevent these incidents from occurring again.

Incidents can be reported and cases reviewed at:

[www.bpac.org.nz/safety](http://www.bpac.org.nz/safety)

# The New Zealand Formulary

COMING SOON



NZF

Finding information about medicines can often be an arduous process – there is no shortage of information both in hard copy and online, but how do you know which source to trust and how do you go about finding information that is New Zealand specific? What about subsidy information? What about medicines information that will help in the management of patients with more complex or long-term illnesses? What about interactions?

In September 2011, after a “request for proposal” process, the Ministry of Health announced that the New Zealand Medicines Formulary Limited Partnership (NZMF LP) was the preferred provider of a medicines formulary for New Zealand. The NZMF LP is a partnership between Dunedin-based bpac<sup>nz</sup> and BPAC Inc, in conjunction with the Royal Pharmaceutical Society (United Kingdom).

**The development of the NZF is on track for full public release on 19 July 2012.**

## About the NZF

The NZF is a resource that will be available free of charge for all healthcare professionals prescribing, dispensing and administering medicines across community and hospital care. A true “one stop shop”, the NZF addresses the need for general purpose, point-of-care information about the use of medicines in New Zealand. It will aid in decision making and contribute to best practice through standardised and evidence-based information about medicines. Over time the NZF will be fully integrated into the e-health environment, including prescribing and dispensing systems across primary and secondary care.

The NZF builds on the New Zealand Universal List of Medicines, and incorporates information from the British National

Formulary (BNF). It is adapted for the New Zealand context and covers medicines used in New Zealand, including Section 29 medicines where appropriate.

Initially, the NZF will cover information such as:

- Medicine indications, dosage, cautions, contraindications, side effects, warnings, patient advice and cautionary and advisory labelling
- The use of medicines in renal and hepatic impairment, pregnancy, lactation and sport
- Subsidy information
- Medicine interactions
- Concise disease management advice
- Adverse event reporting

Further enhancements are planned over time such as the development of the New Zealand Formulary for Children, tools to allow integration of preferred medicines lists and local protocols in hospital care, and other extensions according to user feedback.

When publically released on 19 July 2012, the NZF will be available:

- In a format ready for integration into clinical IT systems used by general practices, hospitals and community pharmacy. The NZF team are currently working with IT vendors to ensure that integration of the NZF into clinical IT systems occurs as soon as possible.
- As an application for installation on individual computers
- As an eBook
- To third parties for the development of added value applications, e.g. smart phones and tablet computers
- Online at: [www.nzformulary.org](http://www.nzformulary.org)

## Governance

The NZMF LP Board has representation from each of the three partners. The Chief Executive Officer is Professor Murray Tilyard. There are two advisory groups that assist the clinical editorial team – the New Zealand Formulary Advisory Board (NZFAB) and the Editorial Advisory Board (EAB).

The NZFAB is the representative body that advises on the NZF product from a sector/clinical user perspective. It is chaired by Dr Don Mackie, Chief Medical Officer, Ministry of Health. Each member of the NZFAB has a responsibility to liaise with their representatives to gain a thorough understanding of sector needs and ensure that the NZF continues to meet these needs.

The EAB is responsible for reviewing the clinical content of the NZF. It is chaired by Professor John Campbell, Professor of Geriatric Medicine, University of Otago and consultant physician, Dunedin Hospital, Southern DHB. The responsibility of the EAB is to ensure that the content is clinically sound, of high standard and relevant to New Zealand practice. The EAB

receives advice and guidance on policy and scope of content, but is independent of the NZFAB with respect to editorial and clinical processes.

## The clinical editorial team

The clinical editorial team is comprised of managing Editor and clinical pharmacist, Dave Woods, and his Dunedin-based team of five clinical pharmacists, supported by advice from external medical specialists and associate editors.

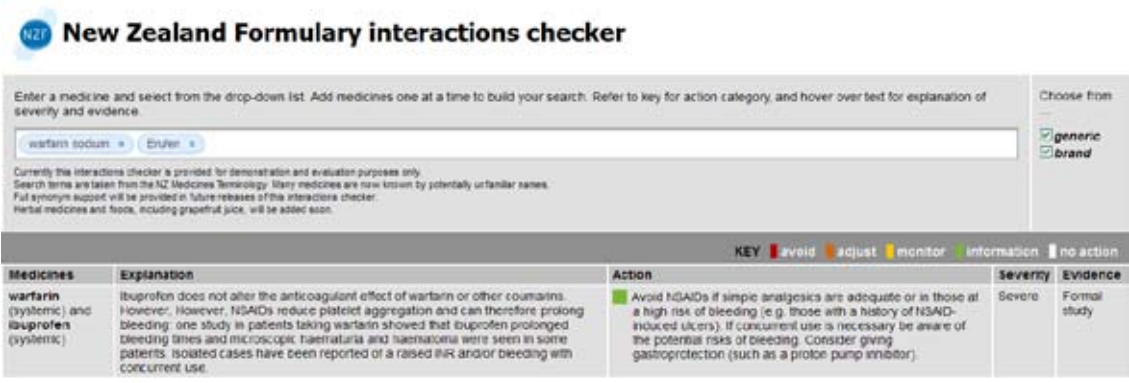
The clinical editorial team has made excellent progress in reviewing, and customising to the New Zealand context, 19 chapters of the BNF, containing more than 1000 medicine monographs and associated prescribing notes. The team is on track to complete this significant piece of work by the end of May 2012, in time for the formal release of the NZF on 19 July 2012.

 For further information, email: [contact@nzformulary.org](mailto:contact@nzformulary.org)

One of the early deliverables for the NZF is an online interactions checker.

**For a sneak preview, visit: [www.nzformulary.org](http://www.nzformulary.org)**

Have a go and tell us what you think!



**NZF New Zealand Formulary interactions checker**

Enter a medicine and select from the drop-down list. Add medicines one at a time to build your search. Refer to key for action category, and hover over text for explanation of severity and evidence.

Choose from:  
 generic  
 brand

Currently this interactions checker is provided for demonstration and evaluation purposes only. Search terms are taken from the NZ Medicines Terminology. Many medicines are now known by potentially unfamiliar names. Full synonym support will be provided in future releases of this interactions checker. Herbal medicines and foods, including grapefruit juice, will be added soon.

KEY ■ avoid ■ adjust ■ monitor ■ information ■ no action

Medicines	Explanation	Action	Severity	Evidence
warfarin (systemic) and ibuprofen (systemic)	Ibuprofen does not alter the anticoagulant effect of warfarin or other coumarins. However, NSAIDs reduce platelet aggregation and can therefore prolong bleeding. One study in patients taking warfarin showed that ibuprofen prolonged bleeding times and microscopic haematuria and haematomas were seen in some patients. Isolated cases have been reported of a raised INR and/or bleeding with concurrent use.	<span style="color:green">■</span> Avoid NSAIDs if simple analgesics are adequate or in those at a high risk of bleeding (e.g. those with a history of NSAID-induced ulcers). If concurrent use is necessary be aware of the potential risks of bleeding. Consider giving gastroprotection (such as a proton pump inhibitor).	Severe	Formal study

The background of the entire page is a close-up photograph of stinging nettle leaves. The leaves are serrated and have a fine, hair-like texture. Most of the leaves are in shades of cyan and blue, but one leaf in the center-right is highlighted in a vibrant red color. The lighting is dramatic, with strong highlights and deep shadows, giving the leaves a three-dimensional appearance.

# The diagnosis and treatment of **URTICARIA**

*Urticaria is a common condition, in which the majority of cases are non-allergenic. A focused clinical history and physical examination are the most useful tools when diagnosing and treating urticaria. Specific triggers are often not found, therefore extensive diagnostic testing is not recommended, unless there is strong evidence to suspect a specific trigger. In some cases, urticaria may be a symptom of an underlying systemic disease and it is important to be aware of this possibility and to refer for further investigation when necessary.*



## Classification and aetiology of urticaria

Urticaria is the term used to describe a group of skin conditions, characterised by the presence of wheals. Approximately one in five people experience urticaria (commonly referred to as hives) at some stage in their life.<sup>1,2</sup> In many cases, a specific trigger for the urticaria is not found. In rare cases, urticaria may be a sign of systemic disease, such as an autoimmune condition.

The two main classifications of urticaria are:

- Ordinary (spontaneous) urticaria – which can be acute or chronic
- Physical urticaria

**Acute urticaria** describes “one-off” outbreaks and recurrent episodes occurring over a period of less than six weeks. It is the most common type of urticaria, and is more frequently seen in children and young adults.<sup>1,3</sup> It is estimated that 20 – 30% of cases of acute urticaria in infants and young children develop into chronic urticaria.<sup>4</sup> Approximately 50% of cases of acute urticaria are idiopathic, i.e. a specific trigger is not identified.<sup>3</sup>

**Chronic urticaria** describes episodes of urticaria which occur over a period longer than six weeks. In rare cases urticaria may persist for a lifetime, but this is more common in cases of physical urticaria.<sup>5</sup> Approximately 30% of patients presenting

in primary care with urticaria will have chronic urticaria.<sup>6</sup> Chronic urticaria occurs more frequently in adults, and in women (approximately 60% of cases).<sup>1</sup> It is estimated that in 40% of people with chronic urticaria, there is evidence of an autoimmune process, and in 20% there is evidence of a physical stimulus,<sup>1</sup> although a specific cause is often not found.

**Physical urticaria** occurs in a localised area after contact with a physical stimulus. Individual episodes usually resolve within a two hour period, but physical urticaria often persists as a chronic, recurring condition.<sup>3</sup> Dermatographism (skin writing) is the most common form of physical urticaria, triggered by firm stroking or scratching of the skin, or contact with clothes or other objects (Figure 1).<sup>3</sup>

Other types of physical urticaria include;

- Contact urticaria – absorption of substances through the skin or mucous membranes
- Cholinergic urticaria – sweating, e.g. after exercise or exposure to heat
- Delayed pressure urticaria – sustained pressure to a site on the body, e.g. on the buttocks after sitting
- Cold urticaria – most frequently caused by swimming in cold water or exposure to cold wind (Figure 2)
- Solar urticaria
- Vibratory urticaria



**Figure 1: Dermatographism**

Images provided by DermnetNZ



**Figure 2: Cold urticaria**

## Most cases of urticaria are non-allergenic

Most cases of urticaria are **not** caused by allergy but are the result of histamine being released by direct mast cell degranulation (i.e non-IgE mediated).

Examples of causes of non-allergenic urticaria include:<sup>2</sup>

- Infection – bacterial (e.g. *Helicobacter pylori*, *Mycoplasma pneumoniae*), viral (e.g. infectious mononucleosis, viral hepatitis), parasitic (e.g. Giardia) or fungal (e.g. Candida)
- Medicines – especially opiates, aspirin and non-steroidal anti-inflammatory drugs (NSAIDs)
- Non-allergenic contact with topical compounds, food preservatives, raw meat or vegetables
- Non-allergenic food reactions to compounds such as alcohol, salicylates in fruit or from bacterial decomposition (food poisoning)
- Hypersensitivity to physical stimuli such as scratching, friction from clothing or other objects, light, heat, cold, water or vibration
- Autoimmune conditions such as systemic lupus erythematosus and autoimmune thyroid disease

## Allergy-induced urticaria

Allergy induced urticaria is most common in people with a history of atopy.

Examples of causes of allergenic urticaria include:<sup>2</sup>

- Medicines, e.g. antibiotics
- Food allergy, e.g. fish, eggs or nuts
- Insect stings, e.g. wasp, bee
- Contact allergens, e.g. latex or cosmetics

## Clinical history and examination

Clinical history and physical examination are usually sufficient to diagnose urticaria. A specific cause is identified in approximately one-half of patients with acute urticaria and one-quarter of patients with chronic urticaria.<sup>3,7</sup>

### Clinical history

The clinical history should cover:

- Frequency, size, distribution and duration of the lesions – to determine type of urticaria
- Recent consumption of new or unusual food or medicines, recent infections, or participation in or

exposure to new activities, locations or products or chemicals – to determine potential triggers

- Occupational exposure to chemicals or inhalants – to determine potential long-term triggers
- History of similar episodes and response to treatment
- Personal and family history of atopy – more likely to be allergy-induced urticaria

### Physical examination: clinical features of urticaria

An episode of urticaria is identified by highly pruritic, well-defined, pink-to-red wheals, often with a pale centre (Figure 3), which usually last no more than 48 hours and leave no remaining marks. The lesions may occur anywhere on the skin and can range in size, from a few millimetres to centimetres, and vary in shape, forming round, oval, annular (ring) (Figure 4), serpiginous (wavy), gyrate (circular, coiled) or targetoid (target pattern) plaques. The lesions may also merge to form large geographic or giant patches (Figure 5). The surface skin remains smooth. The presentation of urticaria is similar in both children and adults.

Approximately 40% of people with urticaria also have signs of angioedema.<sup>1</sup> Angioedema involves the deeper epidermis and subcutaneous tissues and most frequently affects the eyes, mouth, throat, tongue, hands and feet. Angioedema without urticaria is rare and can be life-threatening if the larynx is involved. Further discussion of this condition is outside the scope of this article.

Further examination should be guided by the clinical history. Dermatographism can be tested for by stroking the skin firmly and looking for linear wheals occurring within a five minute period. The application for several minutes of an ice cube, heat, pressure or water may rule out other forms of physical urticaria.

In some cases, examination may be necessary for underlying conditions that may precipitate urticaria, such as:

- Bacterial or fungal infections of the skin
- Autoimmune thyroid disease – may be indicated by an enlarged thyroid
- Connective tissue diseases – may be indicated by joint swelling or tenderness or oral ulceration, e.g. rheumatoid arthritis, systemic lupus erythematosus
- Liver disease/dysfunction – may be indicated by tenderness on palpation of the liver or jaundice, e.g. cholestasis can cause pruritus and acute urticaria can be an early sign of hepatitis A, B and rarely C<sup>8</sup>

## Differential diagnosis

There are a large number of conditions (some of them rare) which may cause symptoms similar to urticaria. The transient and pruritic nature of lesions is one of the most distinctive aspects of urticaria, but pruritus is sometimes absent. Angioedema is also more likely to be associated with urticaria than other skin conditions.

If the signs and symptoms are not typical of urticaria, other diagnoses that may be considered include:

- **Atopic dermatitis** – usually highly pruritic, but can be distinguished from urticaria by the lack of transitory wheals, excessively dry skin and other skin surface abnormalities, strongly associated with personal or family history of atopy
- **Contact dermatitis** – can be distinguished from urticaria by a lack of transitory wheals and the presence of skin surface changes such as blisters, dryness and peeling
- **Fixed drug eruptions** – tender, well defined, round or oval patches, often with central blistering that generally occur in the same place on the body each time a specific medicine is taken
- **Erythema multiforme** – an acute, and at times recurring, hypersensitivity to a variety of causes including infections and medicines. Lesions are usually present on the face and distal limbs and can last for up to seven days.
- **Bullous pemphigoid** – a chronic, autoimmune condition, which usually affects elderly people. Characterised by erosions and tense bullae filled with clear, cloudy or blood-stained fluid, most frequently occurring in body folds.
- **Urticarial vasculitis** – characterised by wheals that resemble urticaria, but last longer than 48 hours and often leave bruising and areas of increased pigmentation as they resolve
- **Papular urticaria** – urticated pruritic papules at the site of insect bites, common in young children and in people who have travelled.

## Laboratory investigation of urticaria

Laboratory testing is not indicated for patients with acute urticaria as the diagnosis is usually clinical.

In patients with chronic urticaria, testing does not usually help to establish a cause, direct management or improve patient outcomes.<sup>9</sup> In a study of 356 patients with urticaria referred for allergy and immunology evaluation, only one patient benefited from a change in management due to testing



Figure 3: Classical whealing

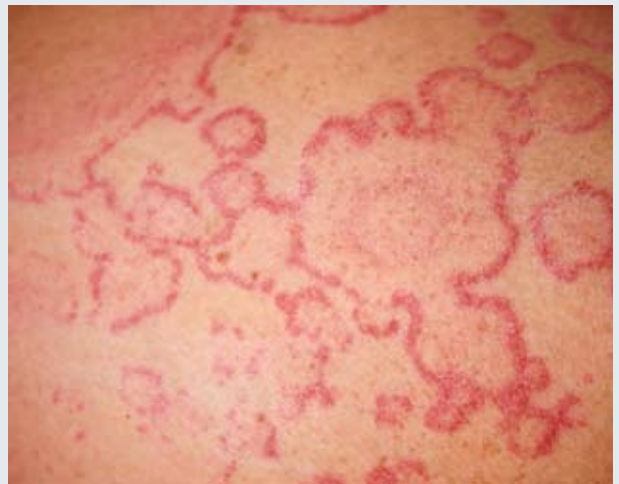


Figure 4: Annular pattern



Figure 5: Giant urticaria

Images provided by DermnetNZ


and only 319 (17%) of the 1872 tests ordered had abnormal findings.<sup>10</sup>

Laboratory testing may be useful in selected patients with chronic urticaria, e.g. if an underlying condition is suspected, they have failed to respond to treatment, or if the condition is severe.<sup>9</sup> The choice of investigations should be guided by positive findings from the clinical history and physical examination. Discussion with a dermatologist may also be helpful.

The following investigations may be appropriate for specific clinical circumstances:

**Skin prick testing** may be considered when an allergic cause for the urticaria is suspected and confirmation would be useful for management, e.g. if avoidance measures are being considered. Skin prick testing should not be performed routinely. Skin prick testing may not be reliable in older adults and children aged under two years should be referred to an allergy clinic for testing as the results may be difficult to interpret. Skin prick testing in pregnant women should only be requested if the benefits outweigh the risks, as in rare cases it can cause uterine contractions.<sup>11</sup>


**Serum allergen-specific IgE testing** is second-line to skin prick testing when skin prick testing is unsuitable or unavailable.

 For further information see: "Appropriate use of allergy testing in primary care", Best Tests (Dec, 2011)

**Full blood count** may indicate an allergy or an intestinal infection if the eosinophil count is elevated. Neutropenia may suggest an autoimmune or viral cause, while neutrophilia may be caused by a bacterial infection. Acute viral infections, e.g. Epstein-Barr virus, or autoimmune thyroiditis may cause a high lymphocyte count.

**Thyroid antibody** testing may be useful following discussion with an appropriate specialist, if a thyroid autoimmune disorder is suspected. Chronic autoimmune urticaria is associated with antithyroid antibodies in approximately one-quarter of cases.<sup>3</sup>

**Skin biopsy (3 mm punch biopsy)** is only rarely required, if urticarial vasculitis is suspected or when the diagnosis is uncertain. Atypical features of urticaria include pain or burning rather than pruritis, complete non-response to antihistamines, wheals persisting for longer than 48 hours, or not fully resolving, with remaining hyperpigmentation.

 **Best Practice tip:** Before contacting a dermatologist, take anatomic views and close-up digital images of the patient's skin lesions. Emailing good quality clinical images may assist the discussion, particularly if the patient's clinical signs are intermittent.

## Treatment for urticaria

Acute urticaria generally resolves over a short period of time, however, chronic urticaria can persist for months or even years (particularly physical urticaria). This can be frustrating for both patient and doctor, especially when there is no known cause.

In a study of 220 patients with chronic idiopathic urticaria, it was found that after one year:<sup>6</sup>

- 47% were symptom-free
- 60% with ordinary urticaria and angioedema were symptom free
- 39% with ordinary urticaria only were symptom free
- 16% with physical urticaria were symptom free

Management is focused on avoiding triggers where known, and using medicines for symptom relief.

## Avoidance strategies

When the clinical history does not reveal an obvious cause for the urticaria, an avoidance strategy for potential triggers may be considered.

Patients can be advised to stop any non-essential medicines, herbal supplements or topical preparations. In particular, aspirin, codeine and non-steroidal anti-inflammatory drugs (NSAIDs) may contribute to wheal formation, even when they are not the primary cause of the eruption. If symptoms resolve (or do not recur), medicines/products can be reintroduced sequentially, if necessary, and the patient should report any return of symptoms.

Dietary investigations rarely identify a specific trigger for chronic urticaria, and are not necessary in cases where symptoms can be easily controlled with oral antihistamines. However, if the patient wishes to, a food diary may be used to record and eliminate suspected triggers. Particularly motivated people may try a narrow diet of rice and a single source of protein for two weeks, while discontinuing all antihistamines. Foods can then be slowly reintroduced and reactions noted in the food diary.<sup>1</sup>

## Pharmacological treatment

Introduction of medicines for the treatment of urticaria should be considered in the following order:

1. Commence non-sedating oral antihistamines
2. Add conventional sedating oral antihistamines and/or H2 receptor antagonists
3. Add tricyclic antidepressants
4. Add oral corticosteroids - only for patients with severe acute urticaria

**Non-sedating oral antihistamines** are the first-line pharmacological treatment for both acute and chronic urticaria due to their effectiveness and relative lack of anticholinergic and central nervous system effects. Although referred to as “non-sedating”, these medicines may still cause sedation at usual doses in some patients. In New Zealand cetirizine and loratadine are fully-funded (see Table 1 for recommended doses). Individual response to antihistamines may be variable, however, cetirizine is thought to be the quickest acting, therefore may be trialed first.<sup>2</sup>

Oral antihistamines may be taken on an “as-required” basis, due to their rapid onset of action, but may be more effective when taken daily. The recommended maximum adult dose of cetirizine and loratadine is 10 mg per day, however, European guidelines recommend non-sedating antihistamines be prescribed at up to four times the standard dose (i.e. cetirizine or loratadine 40 mg daily) before second-line medicines are considered as adjunctive treatment.<sup>12</sup>

**Sedating oral antihistamines** are rarely used as a monotherapy for urticaria, but can be used in combination with non-sedating antihistamines. These medicines may be useful for patients with nocturnal symptoms that prevent sleep. Promethazine (fully funded) is a suitable choice and can be prescribed at the following doses:<sup>13,14</sup>

- Adults; 25 – 75 mg, at night
- Children aged five to ten years; 10 – 25 mg, at night
- Children aged two to five years; 5 – 15 mg, at night

**H2 receptor antagonists** such as ranitidine or famotidine, when used in combination with antihistamines, may be of benefit to some people with chronic urticaria as 15% of histamine receptors in the skin are H2-type.<sup>3</sup> These medicines are not recommended as monotherapy because their ability to reduce pruritus is limited and there is little clinical evidence of their effectiveness.

**Tricyclic antidepressants** have histamine receptor antagonist activity and may be especially useful in treating chronic urticaria, in combination with non-sedating antihistamines. Due to its sedating properties doxepin (30 – 50 mg) is an appropriate treatment for nocturnal symptoms. Amitriptyline (10 – 50 mg) may also be effective.

**Oral corticosteroids** may be added for people with severe acute urticaria. The recommended dose for adults is 20 – 40 mg daily, or for children 1 mg/kg daily, maximum 40 mg, tapering to the lowest effective dose over the course of two to five days.<sup>13</sup> Corticosteroids are nearly always inappropriate in people with chronic urticaria as long-term use should be avoided.

**Table 1:** Recommended doses for fully-funded, non-sedating antihistamines available in New Zealand<sup>13,14,15</sup>

Antihistamine	Adult dose	Child dose (6 – 12 years)	Child dose (2 – 6 years)
<b>Cetirizine</b>	10 mg, once or twice daily*	10 mg, once daily or in divided doses	5 mg, once daily or in divided doses
<b>Loratadine</b>	10 mg, once or twice daily*	> 30 kg: 10 mg, once daily < 30 kg: 5 mg, once daily	5 mg, once daily

\* Although the maximum dose in the New Zealand medicine datasheet is 10 mg, this medicine is often used (and required) in higher doses, without any reports of adverse effects, in order to successfully manage urticaria<sup>12, 16</sup>

## Antihistamines during pregnancy

Ordinary urticaria is uncommon in pregnant women and little is known about the safety of antihistamines in women who are pregnant or breastfeeding. The majority of information that is available concerns the older, first-generation sedating antihistamines. Generally, all antihistamines should be avoided by women who are pregnant, especially during the first and third trimester.<sup>17</sup> However, there have been no reports of major birth abnormalities in women who have used newer, non-sedating antihistamines during pregnancy.<sup>12</sup> Loratadine (pregnancy category B1)<sup>19</sup> may be considered for the treatment of urticaria in women who are pregnant when the benefits of treatment are thought to outweigh the risks.<sup>12</sup> Sedating antihistamines may be considered in severe cases of urticaria occurring during pregnancy, if the patient has not responded to non-sedating antihistamines. However, these medicines should be avoided around the time of delivery to reduce the chance of causing sedation in the infant.


It is recommended that antihistamines are avoided during breastfeeding as most are present in breast milk, however, a similar consideration of risk vs. benefit may occur.



N.B. Topical corticosteroids are not useful in the treatment of urticaria and may cause adverse effects with longer-term or higher-potency use, e.g. skin atrophy. Topical antihistamines are also not effective for treating urticaria and are not recommended due to the risk of sensitisation and resulting contact dermatitis.<sup>17</sup>

**Cooling preparations** containing 0.5 – 1% menthol in a cream or lotion base, e.g. cetomacrogol cream, may provide symptom relief. The use of cool damp cloths, reduction of night-time heating and tepid showers may also be useful.

**Referral for specialist treatment** may be considered if the diagnosis is uncertain or where symptoms are severe and poorly controlled. A number of further treatment options are available including immunosuppressants, e.g. cyclosporin, and leukotriene receptor agonists, e.g. montelukast. If a complex drug or food trigger is suspected then consider referral to an immunologist. **Phototherapy** using ultraviolet B radiation reduces the number of mast cells in the upper dermis,<sup>12</sup> and may be effective in reducing symptoms in cases of physical urticaria that are resistant to antihistamines.<sup>18</sup> Patients can be referred to a dermatologist for this treatment.

 **Best Practice tip:** A standard treatment regimen for urticaria – begin with cetirizine, if symptoms are not controlled, add promethazine 25 mg at night and ranitidine 300 mg during the day. This will settle symptoms for most people. If symptoms still persist, add in a tricyclic antidepressant.

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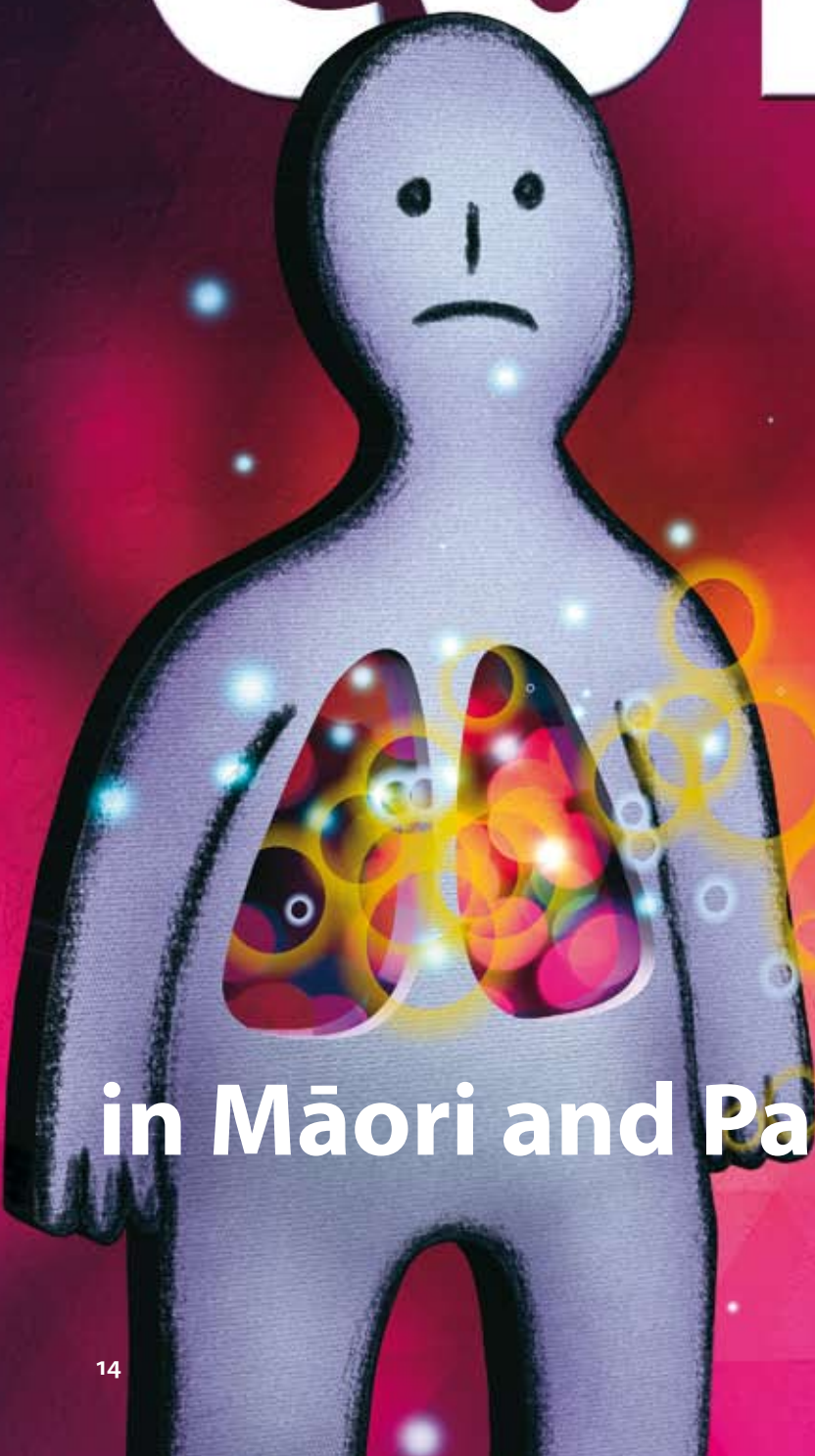
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Diagnosis and management of

# COPD



**in Māori and Pacific peoples**



The health burden of Chronic Obstructive Pulmonary Disease (COPD) for Māori and Pacific peoples represents one of the most significant healthcare disparities in New Zealand. To reduce this gap it is recommended that practices adopt a tailored approach towards COPD management in Māori and Pacific peoples that focuses on community awareness, early diagnosis, smoking cessation and education for patients and their families.

## The burden of COPD

Chronic Obstructive Pulmonary Disease (COPD) is estimated to affect 15% of all New Zealanders aged over 45 years.<sup>1</sup> It is the fourth leading cause of death in New Zealand behind cancer, heart disease and stroke.<sup>1</sup> COPD is permanent, disabling and frequently progressive. Over 85% of cases of COPD are caused by inhalation of tobacco smoke.<sup>1</sup>

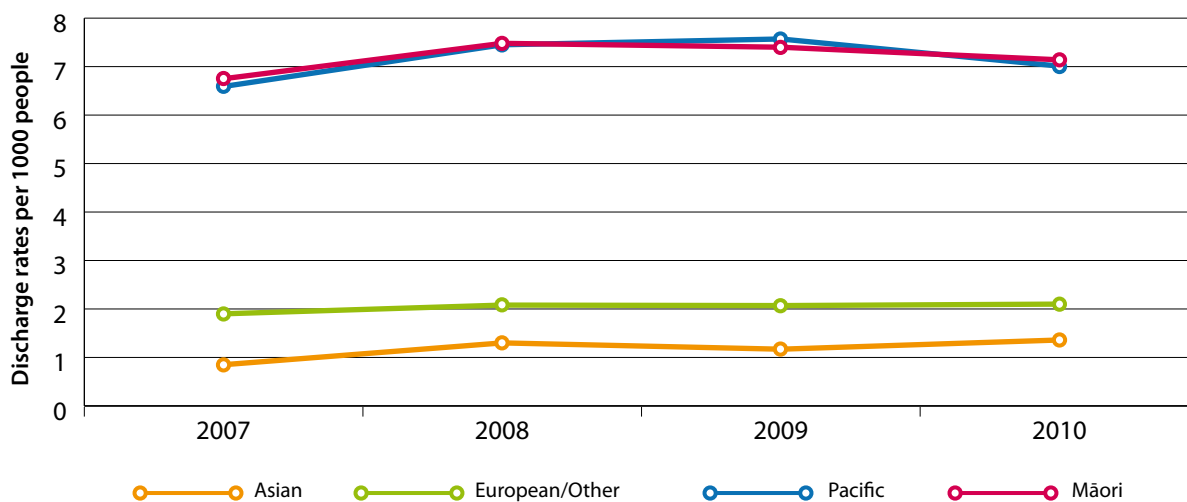
### COPD in Māori and Pacific peoples

Amongst New Zealanders aged 50 – 64 years, Māori are approximately five times more likely to die from COPD-related causes than non-Māori and are affected by COPD up to 20

years earlier.<sup>2,3</sup> COPD is ranked as the third highest health priority for Pacific peoples in the Auckland DHB region.<sup>4</sup>

There is also evidence that COPD may be under-diagnosed in New Zealand, especially among Māori. In a study of 3500 randomly selected people aged over 25 years in the greater Wellington area, 736 people were referred for pulmonary testing. Overall, 16% of those tested had COPD, and 23% of Māori in the group had COPD.<sup>5</sup>

Hospital discharge rates (Figure 1) show that Māori and Pacific peoples are three to four times more likely to be admitted to hospital for COPD than people in other ethnic groups in New Zealand.<sup>6</sup>



**Figure 1:** Age-standardised hospital discharge rates in New Zealand with a primary diagnosis of COPD, per 1000 enrolled patients by ethnicity\*

\* Data source: Ministry of Health, National Minimum Data Set (NMDS). Hospital Discharges Population source: DHB Estimated Resident Population 1996-2006 (Prioritised)

## Communicating risk

Understanding COPD is an important part of management. Visual aids, such as the airway diagrams in the Asthma Foundation's "Breathe easier with COPD" booklet, are useful tools to demonstrate what COPD is and show its damaging effects on the lungs. Encouraging people to take educational material home is an effective way to involve families and increase understanding.


Another approach is to use examples that relate to everyday life. Focusing on the importance of kaumātua (elders) on the marae and within whānau may be a good way to emphasise the potential impact that COPD can have if kaumātua were absent.

When finishing a consultation, a good approach to see if the patient has understood a message is to ask; "When your whānau asks what advice I gave you, what will you say?"

 The Asthma Foundation provides downloadable booklets on its website, including "Breathe easier with COPD". Available from: [www.asthmafoundation.org.nz/resources.php](http://www.asthmafoundation.org.nz/resources.php)

## Spirometry devices

Equipment of a high standard is required to take accurate spirometry measurements. Software should display a real-time flow volume graph adjusted for body temperature. Results should be able to be printed and the equipment easily dismantled for cleaning and disinfection. Flow-based spirometers need to be regularly checked with a calibrated syringe. Training in the use of a spirometry device is recommended.

 The Asthma Foundation provides information on spirometry courses for health professionals. A list of recommended portable spirometers is available from: [www.asthmafoundation.org.nz/spirometry.php](http://www.asthmafoundation.org.nz/spirometry.php)

**Promoting awareness** may encourage Māori and Pacific peoples with COPD to contact their general practice earlier. Some patients may delay visiting their doctor due to the slowly progressive nature of the disease, while others may be dismissive of their symptoms, e.g. just a "smoker's cough" or "just being older and unfit". Financial barriers to accessing services are also likely to contribute.<sup>7</sup>

Every Māori or Pacific person who is a current, or ex-smoker, or has household members that smoke should be made aware of the:

- Support that is available to help them stop smoking
- Symptoms of COPD and the need to visit a health professional if a family member displays symptoms
- High impact COPD has on Māori and Pacific communities

Once a person has symptoms of COPD, lung damage has already occurred. This damage cannot be reversed, but can be substantially slowed through smoking cessation and prevention of exacerbations.

**"Support not blame"** is an important approach for health professionals engaging with people who have COPD. A feeling of judgement or blame, because of the association between smoking and COPD, may cause people to present to their general practice later than they otherwise would have. General practice staff need to be seen as welcoming and supportive.

## Testing for COPD

### Spirometry

Spirometry is the recommended method for diagnosing COPD.<sup>8</sup> Ideally this should be performed with a device that allows electronic analysis of results (see "Spirometry devices"). International guidelines recommend that spirometry should be offered to any person aged over 40 years with any of the following characteristics:<sup>2</sup>

- Chronic cough (may be sporadic and unproductive)
- Chronic sputum production (phlegm)
- Dyspnoea that is persistent or progressive and worse with exercise
- History of exposure to tobacco, occupational smoke, dust or chemicals
- Family history of COPD


Due to the earlier age of onset and increased burden of COPD in Māori and Pacific peoples, testing for COPD in selected people who are at increased risk should begin at a younger

## Rates of smoking in Māori and Pacific peoples are unacceptable

In 2009, 21% of New Zealanders aged 15 – 64 years were current smokers.<sup>11</sup> Smoking rates were higher for Māori (males 40.2%, females 49.3%) and Pacific peoples (males 32.3%, females 28.5%) in the same age group.<sup>11</sup> This is the primary reason Māori and Pacific peoples are disproportionately affected by COPD. Encouragingly, survey results show that smoking rates among younger Māori and Pacific peoples may be decreasing. The 2011 ASH smoking survey found that Māori secondary school students had the greatest decline in daily smoking rates, with a change from 14.1% in 2010 to 10.3% in 2011. Rates among Pacific students reduced from 7.0% to 5.9%.<sup>12</sup>

**Aukati Kaiapaipa** is a face-to-face smoking cessation service that is accessible in most communities. The programme

provides Māori access to NRT, motivational counselling and other activities. A list of providers is available on the Aukati KaiPaipa website: [www.aukatikaipaipa.co.nz/contact-us](http://www.aukatikaipaipa.co.nz/contact-us)

 For further information see: “Smoking cessation for Māori”, BPJ 22 (Jul, 2009)

**Training to provide smoking cessation support for Pacific peoples** is provided by the Heart Foundation. This consists of one day of theory training and one day of follow-up support. For further information see: [www.heartfoundation.org.nz/programmes-resources](http://www.heartfoundation.org.nz/programmes-resources)

## A new approach to smoking cessation using a “buddy” system

People with COPD who continue to smoke often feel judged. This perception may prevent people attending consultations, accessing treatment or even leaving their home. A recent small trial in a deprived area of the United Kingdom has shown some success in overcoming this.<sup>13</sup>

People with COPD who have successfully stopped smoking are assigned as “buddies” to other motivated people with COPD who are current smokers. The “buddies” are given brief training in smoking cessation and then provide support and encouragement for their “buddy” during the cessation attempt. Results from the programme in 2011


showed that of 30 people who had used this support service, the four-week abstinence rate was over 80% and abstinence at 12 months was 50%. This compares to abstinence rates of 44% and 23% respectively for other smokers using varenicline and psychosocial support to aid their cessation attempt.<sup>14</sup>

This experience from the United Kingdom is an example of whānaungatanga (togetherness and support) being applied to smoking cessation and may be directly transferable to Māori and Pacific communities in New Zealand.




age, e.g. Māori or Pacific peoples who are heavy smokers and have a family history of COPD may benefit from being offered testing from age 30 years.

It is important that normal spirometry results are not interpreted by the patient as a disincentive to stop smoking. Conversely, early detection and the “shock” of a diagnosis of COPD often helps to motivate people to stop smoking.<sup>9</sup>

 Asthma Societies throughout New Zealand provide spirometry and support services for people with COPD. A list of local branches of Asthma Societies is available from: [www.asthmafoundation.org.nz/asthma\\_societies.php](http://www.asthmafoundation.org.nz/asthma_societies.php)

If spirometry is unavailable, questionnaires, such as the clinical COPD questionnaire (CCQ), may be used as an indication of the likelihood of COPD.

 The clinical COPD questionnaire is available from: <http://ccq.nl/>

**Spirometry testing** should be performed when the patient is clinically stable and without infection. Patients should be advised not to use a short-acting bronchodilator in the six hours prior to testing, or a long-acting bronchodilator in the 12 hours prior to testing.

Values should be measured:

- Before and 10 – 15 minutes after administering a short-acting beta-2 agonist, e.g. salbutamol 400 micrograms (four puffs) via a spacer

or

- Before and 30 – 45 minutes after administering a short-acting anticholinergic, e.g. ipratropium 160 micrograms (eight puffs) via a spacer

A diagnosis of COPD is defined as a post-bronchodilator forced expiratory volume (in one second) to forced vital capacity ratio (FEV1/FVC) of < 0.7.<sup>10</sup>

The peak expiratory flow rate (PEFR) should not be used in the diagnosis or management of COPD as it is a measure of airflow in large airways.


### Assessing the severity of COPD

Assessment of COPD severity should take into account the following:<sup>2</sup>

- Level of breathlessness (Table 1)
- Spirometry results (Table 2)
- Exacerbation risk – calculated from the number of exacerbations experienced in the previous 12 months: less than two exacerbations is low risk, two or more is high risk
- Presence of co-morbidities – influences risk of hospitalisation and overall mortality risk


### Management of COPD

Once a diagnosis of COPD has been made, there is strong evidence that smoking cessation reduces the rate of lung function decline.<sup>10</sup> People with COPD who smoke, typically smoke more cigarettes per day than other smokers and have a comparatively higher physical dependence to nicotine.<sup>15</sup> Motivating a person with COPD to stop smoking (i.e. using “ABC” – ask, brief advice, cessation support) should be the primary management focus, followed by pharmacological treatment, pulmonary rehabilitation and management of exacerbations.

 For further information on smoking cessation see: “Update on smoking cessation”, BPJ 33 (Dec, 2010).

## Pharmacological treatment of COPD

Medicines for COPD are used to improve patient comfort and exercise tolerance while reducing the frequency of exacerbations. No medicine currently available has been conclusively shown to modify the long-term decline in lung function associated with COPD.<sup>2</sup> Medicine choice should be based upon severity of symptoms and patient-specific response (Table 3, over page). It is important that patients and their whānau monitor symptoms in order to discuss management with their healthcare team. If inhaled medicines are used, training in inhaler technique is essential and inhaler technique should be regularly assessed.

 The Asthma Foundation website has printable booklets which provide instructions on correct inhaler use, storage and cleaning. Available from: [www.asthmafoundation.org.nz/resources.php](http://www.asthmafoundation.org.nz/resources.php)

## Choosing a treatment regimen

The following points are generally applicable when selecting medicines for the management of stable COPD:<sup>2</sup>

- Inhaled bronchodilators are preferable to oral bronchodilators
- When symptoms are mild, short-acting bronchodilators are preferable to long-acting formulations
- When symptoms are more severe, long-acting bronchodilators are superior due to increased duration of action and a reduction in the risk of exacerbations. There is no strong evidence to recommend one long-acting formulation over another and treatment choice should be based on patient perception of symptom relief
- When COPD is severe and the risk of exacerbations is high, the addition of inhaled corticosteroids is indicated
- Suggested starting doses of medicines are listed in Table 4 (over page)

**Short-acting beta-2 agonists (SABA)**, e.g. salbutamol, terbutaline, are usually prescribed as “rescue” medicine (as required) for the relief of breathlessness.

**Short-acting anticholinergics**, e.g. ipratropium, have been shown to improve quality of life and decrease the need for oral corticosteroid treatment, while decreasing the risk of adverse effects compared to SABA.<sup>10</sup>

**Short-acting combinations**, e.g. salbutamol and ipratropium, have been shown to improve spirometry results and reduce the need for oral corticosteroids, compared to ipratropium alone.<sup>10</sup>

**Table 1:** Modified Medical Research Council questionnaire for assessing breathlessness.<sup>2</sup>

Grade	Description of breathlessness
0	Only gets breathless after strenuous exercise
1	Gets short of breath when hurrying on the level or walking up a slight hill
2	Walks slower than people of the same age due to breathlessness, or has to stop for breath when walking at own pace on the level
3	Stops for breath after walking for 100 m or after a few minutes on the level
4	Too breathless to leave the house, or breathless when dressing

A symptom grade of 0 or 1 indicates few symptoms, a grade  $\geq 2$  indicates a high level of symptoms

**Table 2:** Classification of airflow limitation severity in patients with FEV1/FVC  $< 0.7$ .<sup>2</sup>

Classification	Post-bronchodilator FEV1*
Mild	$\geq 80\%$ Predicted
Moderate	$\geq 50\%$ to $< 80\%$ Predicted
Severe	$\geq 30\%$ to $< 50\%$ Predicted
Very severe	$< 30\%$ Predicted

\* Most spirometers provide predicted values from healthy population studies that account for height, age and gender

**Table 3:** Recommended initial pharmacological treatment of COPD.<sup>2</sup>

Severity	First-line	Second-line
Few symptoms and low risk of exacerbations	Short-acting anticholinergic or SABA	Combined short-acting bronchodilators or Long-acting bronchodilator
Many symptoms and low risk of exacerbations	Long-acting anticholinergic or LABA	Long-acting anticholinergic + LABA
Few symptoms and high risk of exacerbations	ICS + LABA or Long-acting anticholinergic	Long-acting anticholinergic + LABA
Many symptoms and high risk of exacerbations	ICS + LABA or Long-acting anticholinergic	ICS + LABA + long-acting anticholinergic

**Table 4:** Suggested starting doses of inhaled medicines for COPD<sup>10, 16</sup>

Medicine	Dose per puff	Number of puffs	Frequency	Delivery device
<b>Beta-2 agonist</b>				
Salbutamol	100 micrograms	2	Four times daily as required	MDI
Terbutaline	250 micrograms	2	Four times daily as required	DPI
Salmeterol	25 micrograms	2	Twice daily	MDI
	50 micrograms	1	Twice daily	DPI
<b>Anticholinergic</b>				
Ipratropium	20 micrograms	2	Four times daily	MDI
Titropium	18 micrograms	1	Once daily	DPI
<b>Combination inhalers</b>				
Salbutamol and ipratropium	100/20 micrograms	2	Four times daily	MDI
Budesonide and eformoterol	200/6 micrograms	2	Twice daily	DPI (dose different for MDI)
Fluticasone and salmeterol	125/25 micrograms	2	Twice daily	MDI (dose different for DPI)
<b>Corticosteroid</b>				
Budesonide	400 micrograms	1	Twice daily	DPI
Fluticasone	250 micrograms	2	Twice daily	MDI or DPI

MDI = metered dose inhaler, DPI = dry powder inhaler

**Long-acting beta-2 agonists (LABA)**, e.g. salmeterol, reduce exacerbations and improve symptoms, and are more effective at maintaining symptom relief than SABAs. They are effective for at least 12 hours and can be administered twice daily.

**Long-acting anticholinergics**, e.g. tiotropium, reduce exacerbations and have an effect over 24 hours and are therefore administered once daily. There is an increased risk of dry mouth and urinary retention. Tiotropium is fully subsidised under Special Authority.

**Inhaled corticosteroids (ICS)**, e.g. budesonide, fluticasone, decrease the exacerbation rate compared to placebo, and increase quality of life,<sup>2</sup> but do not appear to prevent lung function deterioration and may increase the risk of pneumonia.<sup>12</sup> Systemic absorption does occur and long-term use must be balanced against the risk of adverse effects. Beclomethasone is also available but there is less evidence for its use in COPD.

**Combination inhaled corticosteroids with long-acting beta-2 agonists**, e.g. budesonide with formoterol and fluticasone with salmeterol (fully subsidised under Special Authority), can be taken twice daily.

**Theophylline**, available in long-acting tablets or oral liquid, is used as a third-line treatment for people with COPD when other bronchodilators are either ineffective or unavailable for long-term treatment.

**Long-term continuous oxygen therapy** (16 – 24 hours per day) may be of benefit in selected patients with COPD who have a PaO<sub>2</sub> consistently less than 55 mm Hg. Home oxygen is usually initiated by a respiratory physician. The patient must be clinically stable and have stopped smoking for at least one month.

### Managing exacerbations

A COPD exacerbation is an acute event where symptoms deteriorate beyond normal day-to-day variation to the point where a change in the medicine regimen is required.<sup>2</sup> This is characterised by an increase in dyspnoea, cough or sputum production, most commonly caused by a respiratory tract infection. COPD exacerbations are known to increase the rate of lung function decline and are associated with increased rates of mortality.<sup>17</sup> The higher rate of hospitalisation amongst Māori and Pacific peoples due to COPD suggests that COPD exacerbations affect these groups more significantly than other groups. People with COPD need to be able to identify exacerbations and seek treatment early.

### Inhaled anticholinergics and cardiovascular risk

A 2008 meta analysis assessing 17 trials found that inhaled anticholinergics were associated with a significantly increased risk of cardiovascular death, myocardial infarction or stroke in people with COPD.<sup>18</sup> However, a 2010 study of almost 20 000 people with COPD found that tiotropium was associated with a reduction in cardiovascular events and cardiovascular mortality.<sup>19</sup> But another study, published in the same journal, showed an increased risk of cardiovascular events associated with the use of ipratropium in a large population with COPD.<sup>20</sup> There is ongoing controversy regarding the interpretation of these results. There is currently no biological explanation why the two anticholinergics would have different cardiovascular effects and a dose-response relationship for the effect has not been demonstrated. Both medicines have low systemic absorption. Until the evidence is understood better, the potential adverse effects of ipratropium and tiotropium need to be balanced against the known benefits of these medicines.



Strategies to reduce the risk of exacerbations include:

- Improving exercise capacity
- Influenza vaccination (annually – funded for people with COPD) and pneumococcal vaccination (five-yearly) for people with COPD and their families
- Reducing the risk of infection by avoiding people who have symptoms of an upper respiratory tract infection, e.g. cough, rhinitis, nasal congestion, sneezing
- Avoiding smoke and other environmental pollutants, e.g. smog
- Optimised control of co-morbidities
- Warm and well ventilated homes


**Treatment options for exacerbations** include bronchodilation with SABA, either alone or in combination with short-acting anticholinergics; doubling the dose or increasing the frequency of use, e.g. from four times to six times per day, if necessary. If the patient is using a long-acting bronchodilator then this should also be continued during the exacerbation. A short course of oral corticosteroids, e.g. 20 – 40 mg, once daily, for 7 – 14 days, may also reduce recovery time, improve lung function and reduce the risk of a relapse.<sup>10</sup>

Antibiotics should only be used to treat exacerbations when there is an increase in cough, dyspnoea, sputum volume or purulence. First-line treatment choice is amoxicillin 500 mg, three times a day, for five days. Second-line is doxycycline 100 mg, twice daily, for five days if the patient is penicillin allergic or has had a recent course of amoxicillin.

When a patient has a history of exacerbations, or may have difficulty accessing a general practice, a step-wise self-management plan, including optimising bronchodilator use, oral corticosteroids and indications for antibiotic use may be useful.<sup>10</sup>

**Referral** to secondary care should be considered when:


- A previously mobile patient can no longer walk short distances
- Dyspnoea prevents eating or sleeping
- There is an inability to manage at home due to exhaustion
- A high-risk co-morbidity is present, e.g. heart failure or ischaemic heart disease
- There are sign of hypercapnia (CO<sub>2</sub> retention) present, such as altered mental state
- There is an inadequate response to treatment or uncertain diagnosis

 For further information see: “Management of acute exacerbations of COPD in Primary Care”, BPJ 23 (Sept, 2009)


### **Pulmonary rehabilitation may improve symptoms of COPD**

Pulmonary rehabilitation refers to programmes which combine multiple approaches to attempt to break the cycle of COPD, where decreased physical activity due to dyspnoea leads to further loss of fitness and eventual immobility. There is strong evidence that rehabilitation programmes improve the symptoms of COPD and reduce hospitalisations.<sup>10</sup> Pulmonary rehabilitation also reduces muscle wasting and weight loss, and programmes that include psychosocial support have been associated with significant reductions in anxiety and depression.<sup>10,21</sup> The minimum time-frame for a rehabilitation programme to be beneficial appears to be six weeks,<sup>10</sup> and the longer the programme lasts, the greater its effectiveness.<sup>2</sup> Family members play an important role in motivating a person with COPD to remain compliant with their rehabilitation programme.

**Weight loss** is common in people with COPD as the added effort to breathe can increase energy requirements by 15–20%.<sup>22</sup> People with COPD who are underweight have increased mortality rates.<sup>22</sup> Pulmocare is a high fat, low carbohydrate dietary supplement, designed to minimise CO<sub>2</sub> production. It is available under Special Authority for people with hypercapnia as a result of COPD.

 For further information see: “The nutritional management of unintentional weight loss in people with COPD”, BPJ Special Edition; Prescription Foods (May, 2011).

**Psychosocial support** is particularly important for Māori and Pacific peoples with COPD. People with COPD have an increased risk of developing symptoms of anxiety and depression, both of which are linked to poor health outcomes.<sup>10,23</sup> In addition, Māori and Pacific adults have a higher prevalence of mental health disorders in general than other ethnic groups.<sup>24</sup> Cognitive behavioural approaches have been shown to significantly reduce depression and improve the health status of people with severe COPD.<sup>25</sup> Strategies include relaxation, breathing techniques, positioning and chest clearing techniques and modification of negative thoughts.<sup>25</sup>

 For further information on pulmonary rehabilitation programmes contact the respiratory department at your local DHB. The Asthma Foundation’s “Breathe easier with COPD” booklets provide a list of suggested exercises that can be performed at home and practical ways of dealing with the stress and limitations of COPD.



## Are Māori and Pacific peoples receiving optimal treatment for COPD?

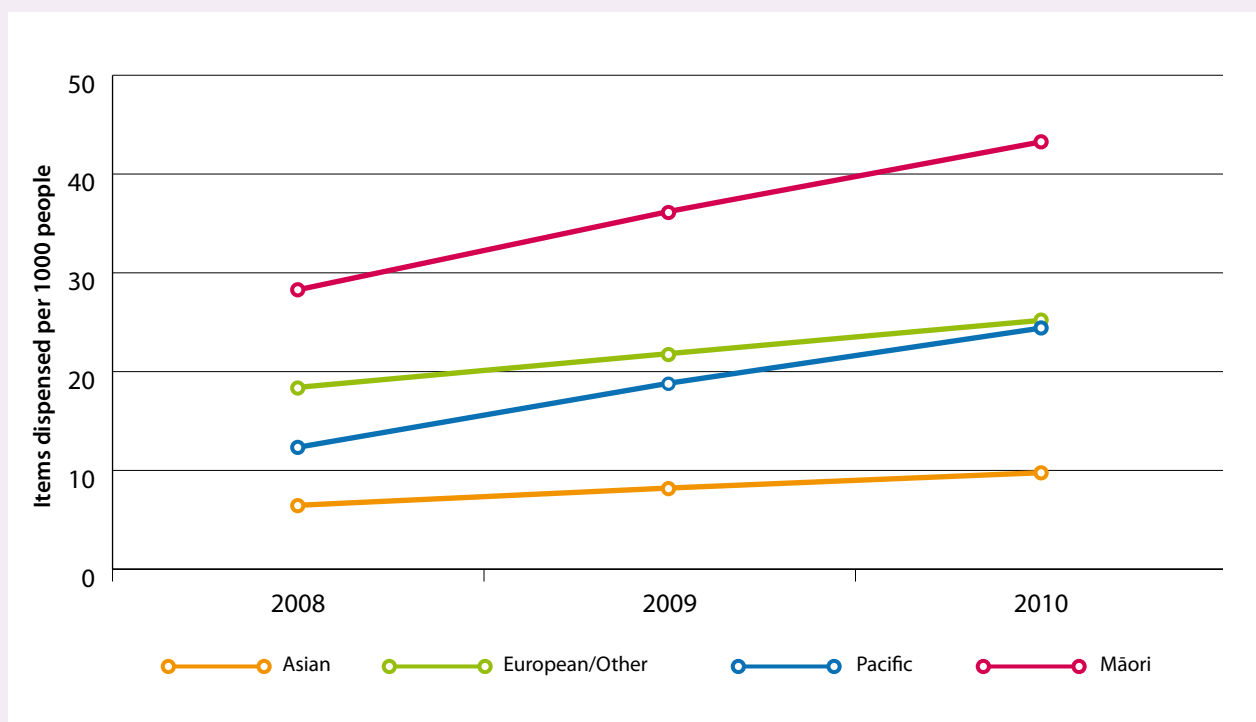
Māori and Pacific peoples are three to four times more likely than people of other ethnicities to be hospitalised due to COPD (Figure 1, page 15). Tiotropium is known to reduce COPD exacerbations and related hospitalisations.<sup>26</sup> It is available in New Zealand under Special Authority for patients with moderate or severe COPD.

Tiotropium dispensing rates in New Zealand by ethnicity (Figure 2) show that:

- Māori have a higher rate of tiotropium dispensing than other ethnicities, but are prescribed only one-third to one-half more tiotropium despite hospitalisation rates being three to four times greater

- Pacific peoples have the same rate of hospitalisations for COPD as Māori, yet are prescribed less tiotropium than Māori or European/Other people

It is unknown if these disparities are due to tiotropium not being prescribed to these patient groups, or if the prescriptions are not being collected. In addition, there is no available data on medicine compliance for people with COPD in New Zealand.



**Figure 2:** Age-standardised rates of tiotropium dispensing (items dispensed) in New Zealand per 1000 enrolled patients by ethnicity, 2008 to 2010\*

\* Discharges source: As per Figure 1 Population source: As per Figure 1

## The Tu Kotahi Asthma Trust

Formed in the Hutt Valley in 1995, the Tu Kotahi Trust provides a Marae-based “by Māori, for Māori” support programme for people with COPD. The goal of the group is to promote COPD education and a sense of togetherness and support (whānaungatanga) throughout the whānau.

A research programme is currently underway to quantify the programme’s outcomes. Anecdotal evidence from participants indicates that the Trust is achieving success in providing timely access to health care for Māori affected by COPD. The use of Te Reo Māori and understanding of culture (tikanga) and hospitality (manaakitanga) have created a non-threatening and supportive environment for Māori. One participant described this by saying:

“...at the hospital they’re speaking a language I could never understand, but you come here and sit down and use language that I understand...that’s a big barrier that got broken down...just getting to know on my level, instead of me climbing up to theirs.”

The group encourages participation in a regular exercise programme. Medicine compliance and management of exacerbations have improved through the delivery of simple demonstrations and visual explanations. Members are also encouraged to consider issues such as housing and co-morbidities when supporting people with COPD.

Through encouraging early engagement with individuals and their whānau, the Trust has identified a number of people in their early 30s and 40s who are in the early phase of COPD. This is likely to provide significantly better outcomes for these people, while simultaneously achieving financial savings through early disease management.

Raising community awareness and providing community-based resources for the diagnosis and management are important strategies in combating COPD.

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# Childhood Asthma

The *bestpractice* Childhood Asthma module assists clinicians in providing the most appropriate course of action for a patient depending on their symptoms and history. Individualised advice about what treatment to consider and when referral is appropriate is offered, as well as a personalised asthma action plan for each patient.

**Progression through an initial consultation** for a patient presenting with symptoms/risk factors for asthma. The probability of asthma is determined from this information and then management recommendations are provided.

**Control and treatment of previously diagnosed asthma** using a stepwise approach. This section includes information about appropriate choice of devices, dose, possible non-pharmacological management and when to refer.

**Use the module to create a personalised Action Plan** which clearly illustrates to the patient and caregivers:

- What inhaler to take
- When to take it
- How much to take
- What to do in the event of an emergency
- What might trigger the patient's asthma



This PHARMAC funded module is  
FREE to General Practice



[www.bestpractice.net.nz](http://www.bestpractice.net.nz)

An aerial, high-angle photograph of a busy city street with a zebra crossing. The scene is slightly blurred, suggesting movement. Several large, stylized virus particles are overlaid on the image, appearing as if they are floating or attached to the ground. The virus particles are spherical with a blue and yellow color scheme and a complex, multi-layered structure. The text "Seasonal influenza vaccinations:" is overlaid in a large, white, sans-serif font across the upper portion of the image.

# Seasonal influenza vaccinations:

**the 2012 edition**



*The seasonal influenza vaccine for 2012 contains the same virus strains that have been included in the vaccines for the previous two years. PHO Performance Programme data has shown a small decline in uptake in 2011 amongst elderly people, possibly due to duplication of the influenza strains in the vaccine from 2010. It is important that uptake of regular annual influenza vaccination does not decline further this year, as annual vaccination is required even when the strains are repeated. Clinicians should be prepared to address patient concerns and ensure that people in high risk groups receive the vaccine in time for the “influenza season”.*

## What’s in the vaccine this year?

The 2012 seasonal influenza vaccine contains the following virus strains:

- A/California/7/2009(H1N1)pdm09-like strain (“Swine flu”)
- A/Perth/16/2009 (H3N2)-like strain
- B/Brisbane/60/2008-like strain

The choice of these strains is based on the recommendation of the World Health Organisation which is endorsed by the Australian Influenza Vaccine Committee.<sup>1</sup> They are the influenza strains that are expected to circulate during the 2012 Southern Hemisphere influenza season. They are the same virus strains that were in the 2010 and 2011 vaccinations.

## Two vaccines brands

There are two funded vaccine brands in 2012: Fluvax and Fluarix.

**Fluarix** is approved for children aged over six months and adults.

**Fluvax** is approved for children aged over nine years and adults, but should not be given to any child with a history of febrile convulsions.<sup>2</sup>

## How many doses are needed this year?

Adults and children aged over nine years require only one dose of the vaccine.

Doses for children aged between six months and nine years vary depending on whether they have previously been vaccinated for influenza:

- Children who are receiving their first ever influenza vaccination should have two doses, at least four weeks apart. This is because they are likely to be immunologically naïve to influenza of any strain and require an initial priming dose.<sup>2</sup>
- Children who have received a dose at any stage in the past, need only a single dose

## PHO Performance Programme – Influenza vaccination

Influenza vaccination in people aged 65 years and over is a PHO Performance Programme Indicator and accounts for 9% of the Performance funding; 3% for the total population and 6% for the high need population.<sup>4</sup> High need populations include Māori and Pacific Peoples and people living in lower socioeconomic areas (i.e. New Zealand deprivations deciles 9 and 10).

The programme goal for influenza vaccination is: *for at least 75% of the enrolled patient population aged 65 years or over to have received the influenza vaccine during the most recent influenza campaign.*

Performance is calculated by the number of people aged 65 years or over who have received their immunisation in the most recent campaign, divided by the total number of people aged 65 years or over enrolled at that practice.

The number of vaccine claims for this age group was 65% in 2011, down from 67% in 2010. While this decline is relatively small, it is important that this trend is reversed as the programme has not yet reached its goal.



## Who is eligible for free influenza vaccinations this year?

Fluarix and Fluvax are subsidised for eligible people if administered prior to 31 July, 2012.

Eligible people include:

- All people aged 65 years and over
- Women who are pregnant
- People with the following medical conditions:
  - Cardiovascular disease, e.g. ischaemic, congestive, rheumatic or congenital heart disease – excluding hypertension or dyslipidaemia
  - Cerebrovascular disease, e.g. stroke
  - Chronic respiratory disease, e.g. asthma, COPD
  - Diabetes
  - Chronic kidney disease
  - Current cancer, excluding basal or squamous skin cancer if non-invasive
  - Immunocompromised people, including those with autoimmune disease, immune suppression, human immunodeficiency virus (HIV) and transplant recipients
  - Children on long-term aspirin treatment
  - Other – neuromuscular disease, central nervous system diseases and haemoglobinopathies

In addition, Canterbury District Health Board will fund influenza vaccination in 2012 for all people aged 6 – 18 years (due to earthquake-damaged housing).

A comprehensive list of eligible conditions can be found at: [www.influenza.org.nz](http://www.influenza.org.nz).

## Who else should be encouraged to get vaccinated?

Although the vaccination will not be subsidised, consider encouraging parents to have children aged between six months and five years vaccinated. This is particularly important if any risk factors are present, which can increase the chance of exposure or complications from influenza. Risk factors for influenza complications include:

- Māori or Pacific ethnicity
- Living in a low socioeconomic area or a crowded household
- Being exposed to second-hand cigarette smoke
- Frequent illness

It should, however, be acknowledged that many of the people that are at an increased risk from influenza complications may also have some of the greatest barriers to vaccination, such as cost and access to community care.

Women who intend to become pregnant during the influenza season should be vaccinated.

People who are travelling to the Northern Hemisphere during its influenza season (approximately October to May) should also be encouraged to be vaccinated.

#### **Healthcare providers should be vaccinated**

Healthcare providers have one of the highest exposure rates for influenza in the community. Immunisation is the most effective way to minimise exposure to the influenza virus, including the risk of transmission to patients and their families.<sup>3</sup>

#### **Who should not get the vaccine**

People with an acute illness or fever over 38°C should delay having the vaccine until they are well.

People who have a confirmed anaphylactic reaction to egg protein should not be given the vaccine, unless the benefit of vaccination outweighs the risk.<sup>2</sup>

### **Concerns and common myths about influenza vaccination**

Research shows that the strongest single factor influencing patient uptake of the influenza vaccine is a recommendation from a doctor or nurse.<sup>5</sup> Any consultation leading up to the influenza season presents an opportunity to discuss the vaccine, address any concerns and provide unbiased, evidence-based information about immunisation. In a recent study of vaccine uptake, the two most common reasons patients cited for not getting vaccinated were fear that the vaccine is not safe and the belief that they were not at risk from influenza.<sup>6</sup>

The following evidence may be helpful in addressing specific patient concerns.

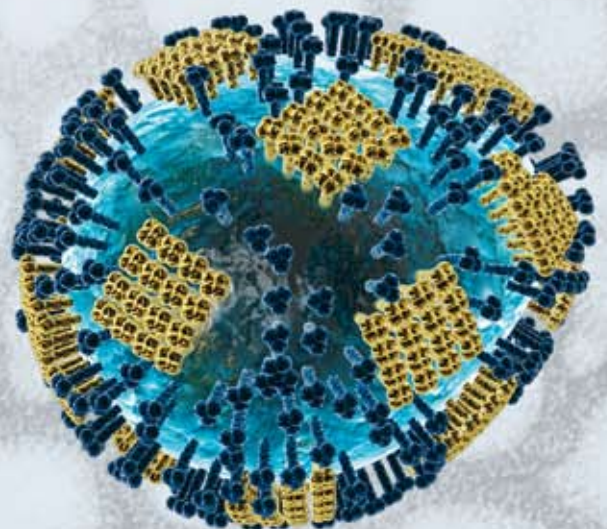
#### **Common concerns about influenza vaccination during pregnancy**

Women who are pregnant and newborn infants have an increased risk of contracting influenza and of influenza complications.<sup>7, 8</sup> During the 2009/2010 influenza season, pregnant women were four times as likely to be hospitalised,

### **Pharmacists can now administer the influenza vaccination**

As of August 2011, the Ministry of Health has allowed pharmacies in New Zealand to apply for permission to administer influenza vaccinations to adults aged 18 – 59 years who are not eligible for funding. Pharmacists must undergo vaccination training and can administer the unfunded vaccine, Intanza®.

People eligible for fully funded vaccines and all people aged under 18 or over 59 years who wish to be vaccinated, should be referred to their general practice.



seven times as likely to be admitted to intensive care and had a higher mortality rate from influenza than the rest of the population.<sup>7,9</sup>

**Timing of the vaccination** – Influenza vaccination is recommended for women who are pregnant or who are planning a pregnancy. The vaccine is safe to administer during all stages of pregnancy.

**Safety of vaccination for the foetus** – The influenza vaccine does not increase the likelihood of miscarriage or birth defects (but influenza may do).<sup>8</sup> Research suggests that maternal influenza immunisation reduces the likelihood of premature and low birth-weight infants.<sup>10</sup>

**Concerns about the use of mercury** – The influenza vaccines do not contain preservatives such as thiomersal (mercury).<sup>9</sup>

**Protecting newborn infants** – Mothers who are immunised during, or prior to, pregnancy are likely to pass on some resistance to their infant. A randomised, controlled trial found that vaccination of pregnant women reduced laboratory confirmed influenza cases by 43 – 63% in infants aged less than six months.<sup>11</sup> As neither influenza vaccine is approved for children aged under six months, this is a significant advantage. Parents may also wish to encourage siblings, carers and regular visitors to be vaccinated, in order to build an “immunity cocoon” around infants aged under six months.<sup>12</sup>

**Women who are breast feeding** – The influenza vaccine is safe for women who are breast feeding and infants who are breast fed may gain some resistance to the influenza virus.<sup>7</sup>

### “Why do I need it if it’s just the same as last time?”

It is recommended that people receive the influenza vaccine yearly even when the strains remain unchanged. Research has shown that some people will retain functional, cross protective immunity over long periods of time,<sup>13</sup> however, this immune retention cannot be predicted and testing for antibodies is not feasible.

Peak immunity is seen shortly after vaccination, even in patients who have received the vaccine previously, and then begins to slowly decline.<sup>2</sup> Those at the highest risk from influenza have the lowest levels of persisting immunity.<sup>14</sup> Therefore, healthcare providers should encourage regular vaccination even when strains do not change, particularly in high-risk groups such as those aged over 65 years and women who are pregnant.

### “It will give me the flu”

It is not possible to contract the influenza virus, or the common cold, from the influenza vaccine.

The vaccine does not contain live or whole viruses. The manufacturing process concentrates, inactivates and breaks the viruses up into protein subunits.<sup>2</sup>

The body’s immune response to vaccination, however, can result in symptoms such as fever, soreness and general malaise which may be perceived as “the flu” by the patient. These symptoms are usually mild and brief.

### “The vaccine is unsafe”

In a study of vaccine acceptance, the two most common fears about getting immunised were Guillain-Barré syndrome and anaphylactic reactions.<sup>6</sup>

Guillain-Barré syndrome is a rare, but potentially severe neurological condition, where the immune system, often triggered by a previous infection, attacks the peripheral nervous system, leading to weakness or paralysis. A Cochrane review of influenza vaccination found that the syndrome occurred in one person per million vaccinations given, indicating either an extremely rare adverse reaction or a reaction with no causal link.<sup>15</sup>

Anaphylaxis following vaccination is also rare. One study reported that anaphylaxis occurred in approximately 0.65 people per million vaccinations.<sup>16</sup>

### “I’m healthy and strong so I don’t need the vaccine”

The seasonal influenza vaccination enhances a healthy immune system and can still provide protection regardless of how robust that person’s immunity is. Despite this, healthy people who rarely contract viruses may be less motivated to be vaccinated. It may be helpful to explain that being vaccinated increases herd immunity, thereby protecting those who are less healthy or who cannot be vaccinated themselves.

### “It doesn’t work”

It is still possible to contract influenza after being vaccinated, particularly if the strains in the vaccine do not match the actual strains that arise during the influenza season. Elderly people, those with chronic conditions that may impair immune responses, pregnant women and infants aged under two years



are more likely to contract influenza. However, the severity of the illness and risk of hospitalisation is likely to be reduced in those who have been vaccinated.<sup>17, 18, 19</sup> In some cases a person may have been exposed to the influenza virus prior to being vaccinated.

### “I prefer natural remedies like vitamin C”

There is no consistent evidence to suggest that natural remedies such as garlic or vitamin C are clinically effective in reducing the prevalence or severity of influenza viruses.<sup>20</sup>

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# The HPV vaccination programme: addressing low uptake

*Approximately 200 women develop cervical cancer in New Zealand each year. High-risk strains of human papillomavirus (HPV) is linked to more than 99% of the abnormalities that lead to cervical cancer.<sup>1,2</sup> To help prevent these cancers the HPV vaccine (known as the cervical cancer vaccine) was added to the National Immunisation Schedule on 1 September, 2008 for girls aged 12 years. The cervical cancer vaccine used in New Zealand (Gardasil) protects against the two strains of HPV most commonly associated with cervical cancer (types 16 and 18) and two strains commonly associated with genital warts (types 6 and 11). Despite this, there has been a low uptake of the vaccine both in New Zealand and overseas.<sup>3,4</sup> Primary health care providers are encouraged to offer information, address any fears and concerns, and promote uptake of the vaccine amongst young females in New Zealand.*



## The human papillomavirus

Human papillomavirus (HPV) is a common infection that is spread through skin and sexual contact. Epidemiological studies in the United States have shown that four out of five people will be infected with HPV between age 15 – 50 years.<sup>5</sup>

Risk factors for contracting HPV include:<sup>6-8</sup>

- Age < 25 years
- Multiple sexual partners
- Younger age at first sexual activity
- Long-term oral contraceptive use

The majority of HPV infections are transient and asymptomatic with an average duration of six months.<sup>4, 9</sup> However, approximately 10% of infections in females become persistent and can lead to atypical cell growth, resulting in pre-malignant lesions in the genital tract, particularly the cervix.<sup>7</sup> The likelihood of an infection becoming persistent increases with age, due to increased exposure time, reduced level of cells returning to normal and reduced immune response to HPV.<sup>7, 8</sup>

Of the more than 100 strains of HPV, approximately one-third affect the genital tract – 15 of which are referred to as high-risk strains.<sup>10</sup> HPV types 16 and 18 are high-risk strains that are associated with approximately 70% of cervical cancer cases.<sup>8</sup> Low-risk HPV strains are either asymptomatic or cause benign abnormalities; such as HPV types 6 and 11, which cause 90% of genital warts.

### The role of HPV in cervical cancer

HPV DNA is detected in 95 – 100% of all cervical cancers (HPV types 16 and 18 account for 70%), as well as in 50% of anal cancers and in some rarer penile, vaginal and oropharyngeal cancers.<sup>11</sup>

Cervical cancer develops from HPV infection, via the following pathway:<sup>10</sup>

1. Exposure to a high-risk strain of HPV
2. HPV infection occurs
3. HPV infection is not cleared and becomes persistent
4. Detectable, pre-malignant changes occur in cells on or around the cervix
5. Cervical cancer develops from these pre-malignant lesions

Squamous epithelial cell abnormalities are predominantly found in younger females, while cancers are more prevalent in older females, suggesting a slow development from HPV infection through to cancer.<sup>9, 12, 13</sup>

## The New Zealand cervical cancer vaccine programme

The cervical cancer vaccination programme, using the HPV vaccine, began in New Zealand in September, 2008 with the aim of reducing the incidence of cervical cancer.

HPV vaccination is currently funded for females aged 12 – 20 years:

- Females born between 1 January and 31 December, 1992 have until 31 December, 2012 to receive their first vaccination dose
- Females born after 1 January 1993 have until their 20th birthday (not the end of their twentieth year) to receive their first vaccine dose

School-based vaccination programmes for females in Year Eight (age 12 years) are available nationwide, with the exception of the Canterbury DHB region, where the vaccine is only available through primary care providers.

Girls who decline (or if aged under 16 years, girl's parents who decline) to participate in the school programme can still have the funded vaccine through primary care.

### The vaccine

Gardasil is the funded vaccine for cervical cancer in New Zealand. It is made from protein sub-units and contains no live or whole viruses. It protects against four strains of the HPV virus: high-risk strains 16 and 18, and low-risk strains 6 and 11.

The vaccine is given in three doses over six months, at months zero, two and six. This schedule is designed to provide maximum immune response, however, people who have missed a scheduled dose should still be strongly encouraged to continue the vaccination programme. Previous doses do not need to be repeated and immunity is still likely to be achieved as long as the course is completed.

HPV testing should not be requested prior to, or post, vaccination.

Gardasil is approved for males aged 9 – 26 years and females aged 9 – 45 years. If females outside the funded age range or males wish to be vaccinated they can, at a cost of approximately \$450.00 for the three doses (see Page 36 for further discussion of vaccination in men and in women aged over 20 years).

### Safety

The HPV vaccine has a strong safety profile.<sup>14</sup> A report of the most recent adverse event data in New Zealand, to the end of 2009, indicated that 236, 299 doses had been given, resulting in 236 adverse reactions.<sup>15</sup> The majority of these were common immunisation adverse reactions (see below). Ten reports were categorised as serious, including one death, however, there is no evidence that this was related to the vaccine. The Centre for Adverse Reactions Monitoring (CARM) noted that the pattern of events was typical of post-immunisation symptoms and does not raise any particular safety concerns.<sup>15</sup> The World

Health Organisation has reported few significant adverse effects linked with the vaccination, after over 54 million doses administered in the previous six years.<sup>9</sup>

The most common adverse effects associated with HPV vaccination include:

- Mild pain at the injection site
- Mild swelling/redness at the injection site
- Nausea or headaches
- Dizziness/fainting

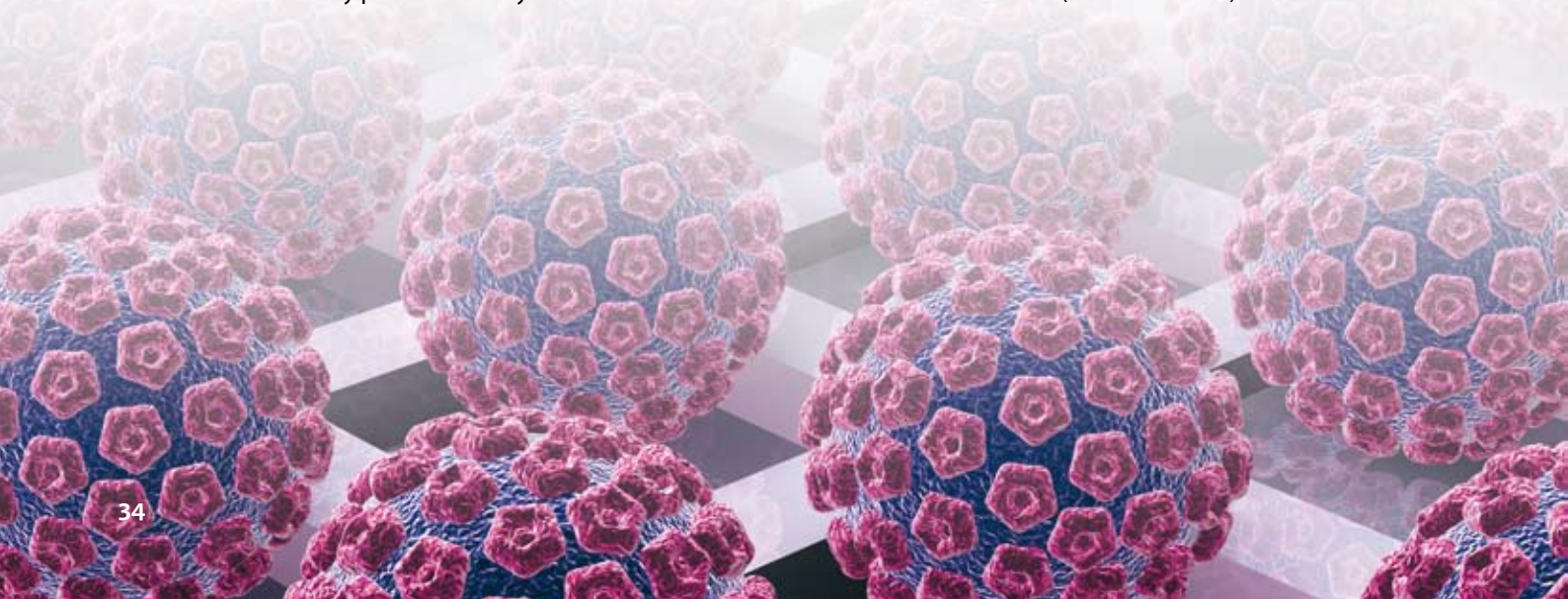
A 20 minute post-vaccination observation period is recommended to monitor for fainting or anaphylactic reactions.

### Efficacy

Gardasil is effective at creating antibody-resistance against the four HPV strains.<sup>9</sup> Randomised, post-marketing trials have found a seropositive response (i.e. antibodies to HPV were at detectable levels) in 100% of females aged 15 – 55 years who received the vaccine.<sup>16</sup>

There are early signs that the vaccine has begun to have an effect on the incidence of genital warts in New Zealand, which has dropped among sexually active females aged under 20 years by approximately 63% since the vaccination programme began.<sup>17</sup> A similar decline in genital warts is being seen for males aged under 20 years.<sup>17</sup> Large-scale studies in Australia have shown that the incidence of genital warts has declined almost completely in young, heterosexual males and females, four years after the HPV vaccine was introduced.<sup>18</sup>

It is yet unclear how effective the vaccine will be at protecting against cervical cancer, as the first trial populations vaccinated have not reached an age where they are at an increased risk of cervical cancer. The significant increase in antibodies following immunisation is strongly suggestive of protection.<sup>19</sup> Analysis of international studies (FUTURE I and II) has shown that the



HPV vaccine has significantly reduced the incidence of high grade disease of the cervix by 65%.<sup>20</sup> This is expected to be indicative of a lower rate of progression to cervical cancer.

HPV immunisation is still beneficial in people who are sexually active. Sexually active people may not have been exposed to all four types of HPV and in addition, immunisation has been shown to significantly increase antibodies, which may help to prevent re-infection.<sup>21</sup>

### Duration

Immunity gained from the HPV vaccine is predicted to be long-term. Ongoing studies indicate that the vaccine provides at least six years protection with limited antibody decline.<sup>19</sup> Protection against the four HPV types included in the vaccine remains at 100% at six years post-vaccination.<sup>16</sup> These studies will continue to monitor both the duration of immunity and safety of the vaccine.

### The continuing role of cervical screening

Regular cervical screening, as part of the national screening programme, is still required for females who have received the HPV vaccine.

The vaccine protects against the two HPV strains that cause approximately 70% of cervical cancers. The remaining 30% of cancers are caused by other HPV strains and cervical screening will still be required to detect abnormalities arising from them.

### Current coverage of the vaccination programme in New Zealand

The current immunisation goal, set out initially by the World Health Organisation, was for a minimum of 70% of young females to receive the HPV vaccine.<sup>14</sup> This level was recommended as it was thought to be the most cost-effective way in which to reach herd immunity and reduce cervical cancer. International debate is ongoing as to the advantage of now including young males in vaccination programmes, to improve herd immunity.

In 2010, the national uptake of the first dose of HPV vaccine for all females born between 1992 and 1997 was 52%.<sup>3, 4</sup> Vaccination was highest amongst Pacific females (70%), followed by Māori females (57%).<sup>3</sup> Almost all went on to complete the course, with national uptake of the third dose at 50%.<sup>22</sup>

Although overall figures are well below the immunisation


target, uptake and completion of doses is higher in New Zealand than in many other countries. In the United States uptake of the vaccine was 44% for the first dose, but decreased to 27% for the final dose.<sup>23</sup>

### Addressing low uptake of the school-based vaccination programme

With current uptake of school-based vaccination low, general practice can help to ensure that target levels of immunisation are reached.

All females aged 12 to 20 should be asked whether they have received the cervical cancer vaccine (and completed the course), whenever they present for a consultation. The National Immunisation Register will contain this information for some people, but only if they have agreed for the information to be collected and have provided contact details of their General Practitioner.

Those that have not received the HPV vaccine should be given information about the vaccine and vaccination should be offered. Providing education about the vaccine may help to increase uptake. If girls or their parents feel that they are still not ready or do not wish to receive the vaccine, a reminder can be set in the patient management system to ask again at a subsequent consultation.

 Patient leaflets are available from:  
[www.cervicalcancervaccine.govt.nz](http://www.cervicalcancervaccine.govt.nz)

### Barriers to vaccination – concerns, fears and misconceptions

The role of the health-care provider should be to offer unbiased, evidence-based information about the HPV vaccine and to address any fears or concerns. Research shows that the strongest indicator for acceptance and uptake of the HPV vaccine is a recommendation from a general practitioner.<sup>24</sup>

#### “My daughter is too young”

Evidence indicates that many parents prefer to have their child vaccinated later than the recommended age 12 years.<sup>25</sup> However, this age-based recommendation has been formed for two reasons; firstly, females in this age group have a stronger antibody response to the vaccine than older females and secondly, it allows for the majority of females to be vaccinated prior to commencing sexual activity.<sup>9</sup> The period with the highest risk of HPV infection is within two to three years after commencing sexual activity.<sup>2</sup> If sexual activity does not commence until adulthood there is unlikely to be

any disadvantage in early vaccination as immunity does not appear to decline over time.<sup>19</sup>

#### **“Why bother with the vaccine if I’m already sexually active”**

There is still benefit in immunising young people who are sexually active. Even after sexual activity has begun most people are very unlikely to have contracted all four of the strains in the vaccine and, even if they have, the vaccine increases antibody levels, which may prevent re-infection.<sup>21</sup>

#### **“Vaccines are unsafe /I don’t believe in them”**

The HPV vaccine has a strong safety profile and has been extensively used world-wide without serious complications.<sup>10, 16</sup>


Patient education has been shown to increase acceptance and uptake of vaccines in people who are “anti-vaccine” or concerned about the consequences of vaccination.<sup>24, 25</sup> The considerable benefit of an effective vaccine against cervical cancer should be carefully weighed against the small risk of adverse effects.

#### **“The vaccine will promote unsafe sex/promiscuity”**

The HPV vaccine is an important part of practicing “safe sex”. There is no evidence to suggest that immunisation against HPV leads to unsafe sex, lower rates of condom usage, a younger age of commencing sexual activity or an increased number of partners.<sup>26, 27</sup> Having the HPV vaccine has been shown to lead to increased communication about sex between mothers and daughters.<sup>27</sup>

#### **“Why bother, that’s what condoms are for”**

Being vaccinated is not a reason to stop using condoms, nor is the regular use of condoms a reason not to be vaccinated. Condoms provide modest protection against most genital HPV strains, however, skin-to-skin contact is sufficient to spread the virus so protection is not guaranteed.<sup>28</sup> Co-infection with chlamydia or gonorrhoea significantly increases HPV infection rate and condoms reduce the infection rate of these sexually transmitted infections (STIs).<sup>28</sup> Condoms also reduce the likelihood of persistent HPV infection in women due to reduced viral load and reduced co-infection with other STIs.<sup>28</sup>

 **Best Practice tip:** using the term “cervical cancer vaccine” rather than “HPV vaccine” may increase acceptance of the vaccine among younger females and their parents. Anecdotal evidence suggests that some people mistake “HPV” for “HIV”.

## **The potential benefit of immunising males and older females**

### **What about males?**

Gardasil is approved for males aged 9 – 26 years.<sup>29</sup> In males the vaccine will directly protect against genital warts, some anal and penile cancers, and provide indirect protection to future female partners against cervical cancer.

There is currently no recommendation to routinely vaccinate males in New Zealand, however, those who wish to be vaccinated can be encouraged to do so. Vaccination is not funded for males.


In response to the low uptake of the HPV vaccine in the United States, the Centre for Disease Control and the American Academy of Paediatrics have recently issued a recommendation that all males aged 11 – 12 years be routinely offered the vaccine, and that all males age 13 – 21 be included in a catch-up programme.<sup>30</sup>

### **HPV vaccine can be beneficial in females aged over 20 years**

Gardasil is approved for females aged 9 – 45 years,<sup>29</sup> but only funded for those aged 12 – 20 years. There is no recommendation to routinely vaccinate females aged over 20 years, however, it may provide protection for people in this age group, particularly those with risk factors for HPV infection, e.g. multiple partners.

The prevalence of HPV has two peaks in females: one between age 15 – 24 years and a second between aged 45 – 50 years.<sup>16</sup> The reason for this second peak is not well understood, but is likely to be due to either an age-related reduction in resistance to HPV, or an increase in sexual activity with new partners at that age. Vaccination may offer benefit in preventing this second peak.

Initially it was thought that immunising females after the commencement of sexual activity would not be beneficial due to the increasing likelihood that they will already have been exposed to the HPV strains in the vaccine. However, a study of females aged 26 years found that while many had some form of HPV infection very few had both strains 16 and 18.<sup>16</sup> In addition, those who had HPV prior to vaccination had a greater antibody response to the vaccine, suggesting that even if a person is already infected, or was infected in the past, they may still benefit from vaccination.<sup>16</sup>

 More information on the HPV vaccine can be found at [www.cervicalcancervaccine.govt.nz](http://www.cervicalcancervaccine.govt.nz) and [www.immune.org.nz](http://www.immune.org.nz)



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# Appropriate use of **metronidazole**



## How does metronidazole work?

Metronidazole is a core antibiotic for the treatment of anaerobic infections. Its mechanism of action is not entirely clear, but it is thought that the active metabolite interferes with DNA synthesis.<sup>1</sup>

Metronidazole is active against most anaerobic protozoa including *Giardia lamblia*, *Trichomonas vaginalis*, *Entamoeba histolytica* and *Blastocystis hominis*. Gram-negative anaerobic bacteria, such as those belonging to the *Bacteroides fragilis* group and Gram-positive anaerobic bacteria such as *Peptostreptococcus* and *Clostridium* species, are also usually sensitive to metronidazole.<sup>2</sup>

Despite extensive use worldwide, acquired resistance to metronidazole among anaerobic bacteria is rare.<sup>3</sup>

However, *Propionibacterium propionica* and approximately 70 – 75% of *Actinomyces* species are resistant to metronidazole.

Anaerobic infections are usually treated empirically, without susceptibility testing. Studies carried out in New Zealand have shown that anaerobic bacteria are still mostly susceptible to metronidazole and it remains a good empirical choice for suspected anaerobic infections.<sup>4,5</sup>


## Which infections should metronidazole be used for?

Indications for the use of metronidazole include; bacterial vaginosis, trichomoniasis, pelvic inflammatory disease (PID), giardiasis and *Clostridium difficile* infection. Metronidazole is an alternative to amoxicillin for the treatment of some oral infections. Table 1 lists first and second-line indications for metronidazole.

**Table 1:** First and second line indications for metronidazole


Infection	First-line	Second-line
Bacterial vaginosis	Metronidazole	–
Trichomoniasis	Metronidazole	–
Pelvic inflammatory disease	Metronidazole + ceftriaxone + doxycycline	Azithromycin (instead of doxycycline)
Giardiasis	Metronidazole or ornidazole	–
<i>Clostridium difficile</i>	Metronidazole	Vancomycin (hospital treatment)
Tooth abscess	Metronidazole or amoxicillin	–
Bites	Amoxicillin clavulanate	Metronidazole + doxycycline or co-trimoxazole
Diabetic foot infection	Amoxicillin clavulanate	Cefaclor or metronidazole + co-trimoxazole
<i>H. pylori</i>	Amoxicillin + clarithromycin + omeprazole	Metronidazole + clarithromycin + omeprazole

NB. Use of amoxicillin clavulanate and metronidazole together is unnecessary

 For further information see “Antibiotic choices for common infections”, available from: [www.bpac.org.nz](http://www.bpac.org.nz)

## First line indications for metronidazole


### Bacterial vaginosis

-  Metronidazole 400 mg, twice daily, for seven days OR a single dose of metronidazole 2 g (5 x 400 mg tablets)

Bacterial vaginosis results from the replacement of normal vaginal flora by anaerobic bacteria such as *Gardnerella*, *Bacteroides* and *Mobilunculus* species. A seven day course of metronidazole is now favoured as it is more effective than the single dose regimen for resolving symptoms, although compliance may be an issue. One study found that symptoms had resolved in 62% of women three to four weeks after the single-dose course and in 82% after the seven day course.<sup>6</sup> The seven day course is more appropriate for pregnant women because single dose regimens may result in higher serum concentrations, which can reach the foetal circulation.<sup>7</sup> The seven day course of metronidazole is also recommended in women who are breast feeding to reduce the concentration in the breast milk. Treating the male sexual partner of a woman with bacterial vaginosis is unnecessary because there is no evidence that it reduces the risk of relapse.<sup>7</sup>

Ornidazole has similar antimicrobial activities to metronidazole and is an effective alternative in the treatment of bacterial vaginosis. It is administered as a single dose of 1.5 g or 500 mg, twice daily, for five days. Unlike metronidazole, ornidazole does not interact with alcohol (Page 42), but it does potentiate the effect of warfarin.<sup>8</sup>

### Trichomoniasis


-  Metronidazole 400 mg, twice daily, for seven days or a single dose of metronidazole 2 g (5 x 400 mg tablets)

Trichomoniasis is a sexually transmitted infection caused by *Trichomonas vaginalis*. Metronidazole is active against this pathogen. The seven day treatment course is preferable. Single high dose metronidazole may improve compliance but it is associated with a higher rate of treatment failure and an increased risk of adverse effects, such as nausea, vomiting and a metallic taste. One review found that the cure rate in women treated with a single dose of metronidazole 2 g was 88% compared to 92% in women treated with the metronidazole for five to seven days.<sup>9</sup>

Sexual partners of a person with confirmed trichomoniasis should also be treated, even if asymptomatic. Culture is not required in males as it is seldom positive, even if infection is present.


Ornidazole is an effective alternative to metronidazole (see above).

### Pelvic inflammatory disease

-  Ceftriaxone 250 mg IM, plus doxycycline 100 mg, twice daily and metronidazole 400 mg, twice daily, for two weeks


Sexually transmitted pathogens are frequently the initiating cause of pelvic inflammatory disease (PID), however, PID should be treated as a polymicrobial infection. Two studies found that 35% and 50% of women with gonococcal PID had a polymicrobial infection.<sup>10</sup> Treatment should include cover for the most likely pathogens, *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and anaerobes. For this reason, the recommended treatment is ceftriaxone plus doxycycline and metronidazole. Metronidazole is included in this regimen to improve coverage for anaerobic bacteria, however, United Kingdom guidelines suggest that anaerobic bacteria are of relatively greater importance in women with severe PID so metronidazole may be stopped in women with mild or moderate PID who cannot tolerate it.<sup>11</sup>

### Giardiasis

-  Metronidazole 2 g, once daily, for three days or ornidazole 1.5 g, once daily, for one to two days

Giardiasis is caused by infection with the parasite *Giardia lamblia* (also known as *Giardia intestinalis*). Metronidazole or ornidazole are the recommended first-line antibiotics for giardia. The single daily dose, shorter course regimen (three days) is recommended as it improves compliance, and is as effective as longer courses.<sup>12</sup> If treatment fails, after excluding re-infection from asymptomatic contacts, metronidazole 400 mg three times daily for seven days can be used. Isolates of *Giardia lamblia* have been found with reduced susceptibility to metronidazole.<sup>2</sup>

### *Clostridium difficile* infection

-  Metronidazole 400 mg, three times per day, for ten to fourteen days

*C. difficile* is an anaerobic Gram-positive organism that causes diarrhoea, which in some cases can be severe. *C. difficile* infection most commonly occurs after use of broad-spectrum antibiotics, but can also be associated with the use of cytotoxic medicines, e.g. methotrexate. The normal bowel flora is altered, causing overgrowth of *C. difficile* and the production of toxins.<sup>2</sup>

A new highly pathogenic strain has caused severe outbreaks of disease in the United States and United Kingdom. This has not yet been observed in New Zealand, but a surveillance system has been set up as an early warning system.

If *C. difficile* infection occurs, where possible, discontinue the antibiotics for the original indication, or use a narrower spectrum antibiotic. This may lead to resolution of symptoms. Antidiarrhoeals, e.g. loperamide, should be avoided because they slow the clearance of the *C. difficile* toxin and worsen colitis.

Metronidazole and vancomycin (hospital treatment) are effective in the treatment of *C. difficile* colitis. Metronidazole is first-line treatment for mild to moderate *C. difficile* infection.<sup>13</sup> A 10 – 14 day course is recommended because, although 70% of patients respond to metronidazole in five days, 91% respond with a 14 day course.<sup>7</sup> Metronidazole can be given by intravenous infusion if oral treatment is inappropriate.<sup>14</sup> Vancomycin is reserved for severe *C. difficile* infection, for those who do not tolerate or respond to metronidazole and for cases that recur more than twice.<sup>15</sup>

#### Dental infection or abscess

✔ Metronidazole 400 mg, three times daily, for five days (or amoxicillin)

While acute symptoms of dental infection or abscess can be managed in general practice, most people should be referred to a dentist, in case further dental treatment such as root canal treatment or extraction is required. When signs of severe infection are present or the patient is systemically unwell, it is appropriate to prescribe metronidazole or amoxicillin.<sup>16</sup> There is no clear guidance about which antibiotic is preferable first. It is also possible to use metronidazole and amoxicillin together for severe dental infections.<sup>17</sup>

## Second line indications for metronidazole

#### Bites – human and animal

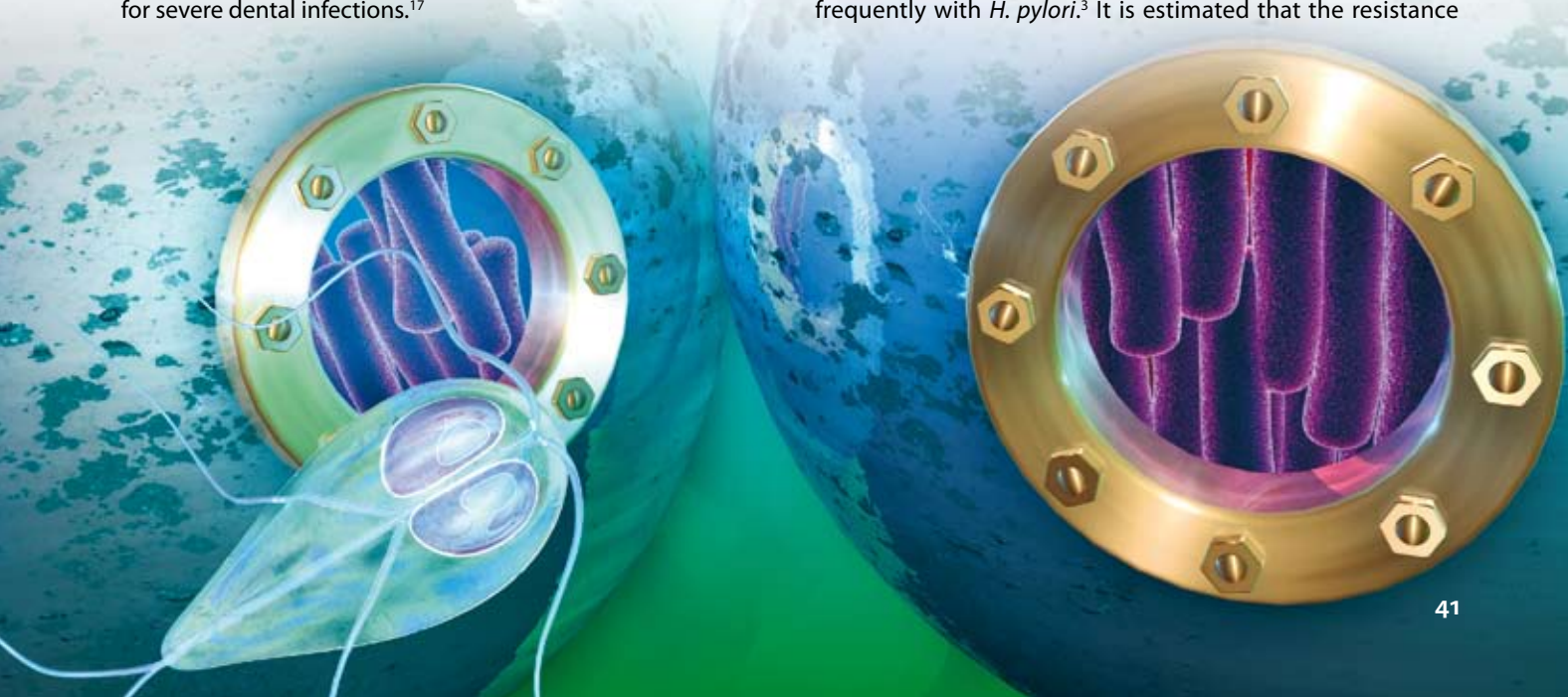
Metronidazole 200 mg to 400 mg, three times daily, plus doxycycline or cotrimoxazole is an alternative to amoxicillin clavulanate for the prophylaxis or treatment of human or animal bites in people who are allergic to penicillin. Most infections caused by bites are polymicrobial, with studies finding an average of three to four different species of bacteria per wound culture, including one anaerobe, from cat and dog bites and an average of five species of bacteria, including up to three anaerobes, for human bites.<sup>18</sup> Metronidazole is included in the regimen to cover beta-lactamase producing anaerobes. It is recommended that patients using the metronidazole plus doxycycline or cotrimoxazole regimen are reviewed after 24 and 48 hours because these antibiotics cover most but not all of the likely pathogens from a human or animal bite.<sup>7</sup>

#### Diabetic foot infection

Metronidazole 400 mg, three times daily in combination with cotrimoxazole is an alternative to amoxicillin clavulanate for the treatment of foot infection in a patient with diabetes who is allergic to penicillin. Cefaclor is also an alternative treatment. Diabetic foot infections are most likely to be polymicrobial. A wound swab is usually not necessary, but may be considered if the infection is not resolving.

#### *H. pylori* eradication

Metronidazole is an alternative to amoxicillin in triple therapy for the eradication of *H. pylori* for patients allergic to penicillin. Triple therapy consists of a seven day course of omeprazole 20 mg, clarithromycin 250 mg and amoxicillin 1 g (or metronidazole 400 mg) all taken twice daily. Metronidazole resistance in anaerobic bacteria is rare, but it has been reported more frequently with *H. pylori*.<sup>3</sup> It is estimated that the resistance



rate of *H. pylori* to metronidazole is 27%, however, there is considerable variation depending on location.<sup>19</sup> Failure rates of up to 20% have been reported for triple therapy including metronidazole.<sup>20</sup>

NICE guidelines suggest avoiding the use of clarithromycin or metronidazole if they have been used in the last year for any other infection because monotherapy with these antibiotics often leads to resistance.<sup>21</sup>

## Issues associated with metronidazole

### People taking metronidazole should avoid alcohol

Some people may experience adverse effects when alcohol is consumed while being treated with metronidazole. The existence of this interaction has been disputed, however, it is appropriate to advise people taking metronidazole to avoid alcohol (including products containing alcohol) during the course of treatment and for 48 hours afterwards.<sup>22</sup>

The mechanism of the interaction between alcohol and metronidazole is not well understood but it is thought that it is due to an accumulation of acetaldehyde (such as occurs in a disulfiram reaction) and the inhibition of other enzymes related to alcohol metabolism. This causes adverse symptoms such as nausea, vomiting, flushing, headache and palpitations.

### Metronidazole potentiates the effect of warfarin

Elevated INR and bleeding events have been reported with concurrent use of warfarin and metronidazole (and ornidazole). It is suggested that metronidazole inhibits the metabolism of S-warfarin, the more potent isomer of warfarin, resulting in increased serum levels of warfarin, potentially increasing its anticoagulant effects. INR should be monitored when warfarin and metronidazole are used together and the dose of warfarin adjusted if required.<sup>22</sup> N.B. Depending on the clinical circumstances, INR monitoring may be increased for patients taking warfarin who are unwell enough to require antibiotics, regardless of the type of antibiotic used.

**ACKNOWLEDGMENT:** Thank you to **Dr Rosemary Ikram**, Clinical Microbiologist, Christchurch for expert guidance in developing this article.

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Quiz feedback for

# BPJ 42

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## Depression in Young People

Depression in Young People is activated for patients under the age of 18 years when the Depression module is opened.

Structured clinical assessment is the key to identifying both problems and protective factors in young people.

It is desirable to offer opportunities for the young person to speak alone to the GP.

### Differentiating abnormal from normal behaviour

The following criteria can be used to help distinguish normal variations in behaviour from more serious mental health problems:

- **Safety:** there is a perceived risk
- **Duration:** problems last more than a few weeks
- **Intensity:** symptoms are severe and fixed, with a loss of normal fluctuations in mood and behaviour
- **Impact:** problems impact significantly on school work, interpersonal relations, home and leisure activities
- **Hypomanic episodes:** these may indicate bipolar disorder
- **Profound hopelessness**



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### Use of the term “screening”

Dear Editor,

I opened the latest Best Practice Journal (Feb, 2012) and read the article about HbA<sub>1c</sub> in the diagnosis of diabetes with interest – finally some common sense being applied to the diagnosis! So well done. However, you persist in using the term screening badly, and use the absolute nonsense term “opportunistic screening”.

There is no such thing as “opportunistic screening”. Either one screens – asymptomatic population, acceptable test (sensitive/specific) appropriate intervention, better outcome and all that – or one doesn’t. What you are actually referring to is the use of an investigation in a patient who presents in the context of their clinical care. It is not screening, it is a test, with a particular pre-test probability. It needs to be used appropriately, but it is not screening – it is an investigation.

What would be really useful is a rigorous critique of screening – I think you’ll find that virtually the only programmes for which there is evidence are cervical screening and the neonatal metabolic tests. The trouble with saying this out loud is that professing the lack of evidence for say, breast cancer screening, will incur the wrath of the politically correct.

**Dr Wayne Cunningham,**  
General Practitioner, Milton

We agree with Dr Cunningham that the use of the word “screening” has shifted over time, and that the appropriateness

of the word depends on the context. Screening is a method applied to populations, it is not a test applied to an individual. In future articles we will endeavour to use the term “screening” only in the context of formal population screening programmes such as cervical screening. Instead of “opportunistic screening”, we will refer to the practice of offering tests to patients who present for unrelated medical issues as “opportunistic testing”. For example, using HbA<sub>1c</sub> to opportunistically test high risk groups, such as Māori, for diabetes will reduce some of the barriers posed by traditional glucose testing, such as the need to fast.

### bpac<sup>nz</sup> recertification programme

Dear Editor,

A lot of General Practitioners are very upset about the new Medical Council of New Zealand levy to support BPAC and pay for us being (yet again) certified. There is a ground swell of opinion coming from my colleagues that this levy is a “rip off”.

The \$1200 levy applies to doctors who are not members of the Royal College, and that is a huge number of doctors. Maybe you can tell me how many?

To spring this unpleasant surprise on us without any warning was upsetting. Upset is probably an understatement, angry is more like it with a few of my mates. I really value BPAC but the constant money grabs (beyond just BPAC) is creating unhappy doctors – and I think maybe your PR needs to improve in order to “sell” the whole idea. Perhaps the MCNZ is more responsible here.

We already have over a half a dozen “professional bodies” looking after our “interests”, and to have to pay another one really sticks in the side.

**Dr Alex Luft**  
General Practitioner, Napier

Thank you for your comments. The new requirements for general registrants have been signalled by the Medical Council (MCNZ) for a number of years. Last year the council put out a “request for proposal” for organisations to provide this programme. Bpac<sup>nz</sup> was selected as the preferred provider for this service.

In New Zealand we have three categories of doctors:

1. Those who are vocationally registered in general practice or other specialities
2. Those in advanced training programmes
3. Those in the general registrant category

The MCNZ believe that there are 2000 to 2600 doctors in the general registrant category. One of the reasons for the uncertainty of this number is that not all doctors in advanced training programmes inform the medical council. I understand that there are approximately 800 general registrants working in General Practice.

As you point out, those of us in category 1, pay fees to college(s) and must meet the reaccreditation requirements. Those in category 3 have been required to have a named supervisor and meet requirements associated with this. When the recertification programme begins the requirements will be more rigorous, and as you point out, will cost registrants \$1200.

It is my personal wish (and one I know is shared by many in general practice) that this change will focus those in general practice working in the general registrant category, on attaining full vocational registration. I do however understand that for a variety of reasons not all will wish to.

**Professor Murray Tilyard**

CEO bpac<sup>nz</sup>

### Testing for allergy in general practice

Dear Editor,

I was pleased to see Allergy Testing reviewed in Best Tests (Dec, 2011), but have some concerns. The most important part in treating allergies is recognition and education, and general practice is ideally placed to provide this. Recognition is mainly based on clinical history, but testing can be useful, in particular if wheat, dairy or multiple food avoidance is being suggested for more than a few weeks test period. Dr Vincent St Aubyn Crump has written an excellent guide to diagnosing allergies in General practice which is available at: [www.allergy.org.nz/site/allergynz/files/GP%20diagnosis.pdf](http://www.allergy.org.nz/site/allergynz/files/GP%20diagnosis.pdf)

*My concern is that if the allergy is not accurately diagnosed the patient may not be receiving adequate education. Education should involve action plans, antihistamines (and occasionally adrenaline), avoidance advice and follow-up. Schools are required to have action plans for children with allergies and we will be increasingly asked to complete them, which is a good thing for best practice. The Australasian Society of Clinical Immunology and Allergy (ASCIA) action plans and the New Zealand School Guidelines, along with many other resources, are available at: [www.allergy.org.nz](http://www.allergy.org.nz)*

*In a recent large study in Melbourne,\* 10% of the 2,884 one-year-olds had food challenge proven IgE food allergy. Food allergies are increasing, more people have multiple allergies and they are lasting longer. So "containing" the budget as suggested may not be feasible, but aiming to have a balanced approach of judicious testing based on appropriate clinical history from an informed medical workforce is.*

#### Further resources:

*ASCIA provides excellent online training for health professionals, which takes about an hour and is endorsed for CME points: <http://etraininghp.ascia.org.au/>*

*There are also two excellent books I would recommend for anyone interested in finding out more, both are also available from Allergy New Zealand:*

*"Allergies. New Zealand's growing epidemic" by Dr Vincent St Aubyn Crump, 2009.*

*"The Allergy Epidemic. A Mystery of Modern Life" by Dr Susan Prescott, 2011.*

**Dr Kylie Morse**

General Practitioner Wellington, Allergy NZ board member

\* Osbourne N, Koplin J, Martin P, et al. Prevalence of challenge-proven IgE-mediated food allergy using population-based sampling and pre-determined challenge criteria in infants. *J Allergy Clin Immunol* 2011;127(3):668-76

**We value your feedback. Write to us at:  
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