# BEST PRACTICE

20

APRIL 2009

## Acne
## Sexual health
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# The isotretinoin debate

**Should we be arguing about who is prescribing isotretinoin or is the real issue how it is being prescribed?**

From March 1, 2009, general practitioners (GPs) and nurse practitioners have become eligible to prescribe funded isotretinoin, under special authority. The decision to widen access to this drug has resulted in considerable debate, especially among dermatologists who until now, were the sole prescribers of funded isotretinoin. Countries such as the UK and Australia debated the same issues, but the outcome was that specialist restriction of isotretinoin remained. Has PHARMAC made a questionable decision, or should it be commended for opening up access to a drug, that until now has been predominantly prescribed to those who have access to a dermatologist, and can afford the consultation fees?

There are two major safety concerns with isotretinoin :

- It is teratogenic at all therapeutic doses and durations of exposure
- It may be linked to depressive illness or suicidal ideation

It is, however, a highly effective treatment for severe acne that has not responded to any other therapy. Isotretinoin should be available, but prescribing must be closely aligned with extreme vigilance in providing concurrent contraception and counselling about its teratogenic effects, and monitoring for behavioural changes.

## The debate in Australia*

In 2008 concern was raised by Australian pharmacists that some prescribers of isotretinoin (predominantly dermatologists) were not warning patients about teratogenicity, did not prescribe concurrent contraception and had not documented any pregnancy tests. In Australia over the last five years there were 66 case reports of exposure to isotretinoin during pregnancy and an estimated four or five live births. There was also concern that despite isotretinoin being indicated for severe acne and only after other treatments fail, it is being increasingly prescribed as first-line therapy for mild cases.

Community Pharmacy in Australia suggested that GPs may be better placed to prescribe isotretinoin, as they are more familiar with a patient's overall clinical history. It was also proposed that a negative pregnancy test should be mandatory for a prescription, and patients should sign consent forms to indicate they understand the risks and precautions that need to be taken. An electronic data system could be used to regulate prescribing. The idea was that access could be broader but regulation more stringent.

* Australian National Drugs and Poisons Schedule Committee: Record of Reasons. 54th Meeting, 14-15th October 2008.

The following points were put forward to support GP prescribing:

- GPs have better awareness of overall clinical circumstances, gynaecological, sexual, social and psychological history
- Dermatologists may not have the experience or close rapport with the patient, to effectively address the potentially complex counselling issues and decide on appropriate contraception
- GPs are experienced prescribers of many complex medicines and the duty of care would not alter if the drug was isotretinoin
- Patients should not have to travel long distances or wait for a specialist appointment to access isotretinoin
- If access was to be widened training for GPs would be essential

In responding to the concerns raised by Community Pharmacy, Australian dermatologists said it was a valuable opportunity to reinforce the message of vigilance in providing contraception and pregnancy information to women who are prescribed isotretinoin. However they felt that dermatologists were still the most appropriate prescribers of isotretinoin. They made the following points:

- Dermatologists may only prescribe isotretinoin after completing a four year fellowship under a qualified dermatologist. GPs who lack this training may find it difficult to ascertain an individual dose requirement (which depends on the severity of the acne and weight of the patient) and to manage side effects.
- If prescribing was opened up to GPs, a larger number of pregnancies exposed to isotretinoin would occur and therefore a larger number of terminations and increased numbers of children born with significant disabilities
- Widening access would expose more people to potentially serious mental health related side effects
- GPs would be disadvantaged because they see acne patients only every month or two, whereas dermatologists see acne patients every day
- GPs would be under pressure to prescribe isotretinoin

After considering the evidence, the National Drugs and Poisons Schedule Committee ruled that the status quo should remain and that isotretinoin should only be prescribed by dermatologists and specialist physicians. The committee agreed that dose titration could be successfully carried out by medical practitioners other than dermatologists. However they did not believe that widening prescribing rights would alleviate the concerns about the reported failure of some prescribers to give contraceptive advice. They expected a commitment from relevant Colleges to remind prescribers about the need for vigilance. The committee also commented that a computer based system for tracking prescriptions was not warranted in Australia and that the 66 pregnancies in five years did not indicate that the current system was failing.

## The debate in New Zealand

In New Zealand, isotretinoin has been restricted by funding rather than by regulation. GPs could always prescribe isotretinoin, but until recently dermatologists were the only speciality that could prescribe the drug fully subsidised. However following a decision by PHARMAC, from March 1, 2009, vocationally registered GPs may also prescribe subsidised isotretinoin under special authority.

Dermatologists in New Zealand strongly opposed this decision. They had similar concerns to their Australian counterparts, including the lack of expertise by non-dermatologist prescribers in managing isotretinoin, the potential increase in pregnancy exposures and increase in the incidence of suicidal ideation, inappropriate pressure on GPs to prescribe isotretinoin, increased rate of reported adverse events and the bureaucracy involved with special authority.

In response to these concerns PHARMAC states that:

- GPs will receive training in prescribing and managing isotretinoin. It is anticipated that the RNZCGP will accredit and promote relevant training programmes
- If more people are taking isotretinoin, then there may be an absolute increase in the number of affected pregnancies, but the proportion of affected pregnancies will not necessarily be expected to increase. GPs will also be encouraged to be vigilant about giving contraception and pregnancy advice
- GPs are well placed to know a patient's medical history and be better positioned to detect symptoms of mental ill-health including depression and suicidal thoughts
- The pressure to prescribe is equally present for any type of doctor

PHARMAC says its decision was motivated by a desire to combat equity of access issues. Analysis of subsidised isotretinoin use showed that a person was 2.5 times more likely to be using this drug if they were living in the least deprived area (quintile 1) of New Zealand.**

PHARMAC is confident that GPs who prescribe the drug will be aware of the precautions with this medication and monitor patients closely. The special authority requirement for isotretinoin will ensure that all prescribers are reminded of the issues involved with prescribing this drug, it also allows for closer control and audit of prescribing activity.

** PHARMAC consultation letter, 30th October, 2008.

## Final word

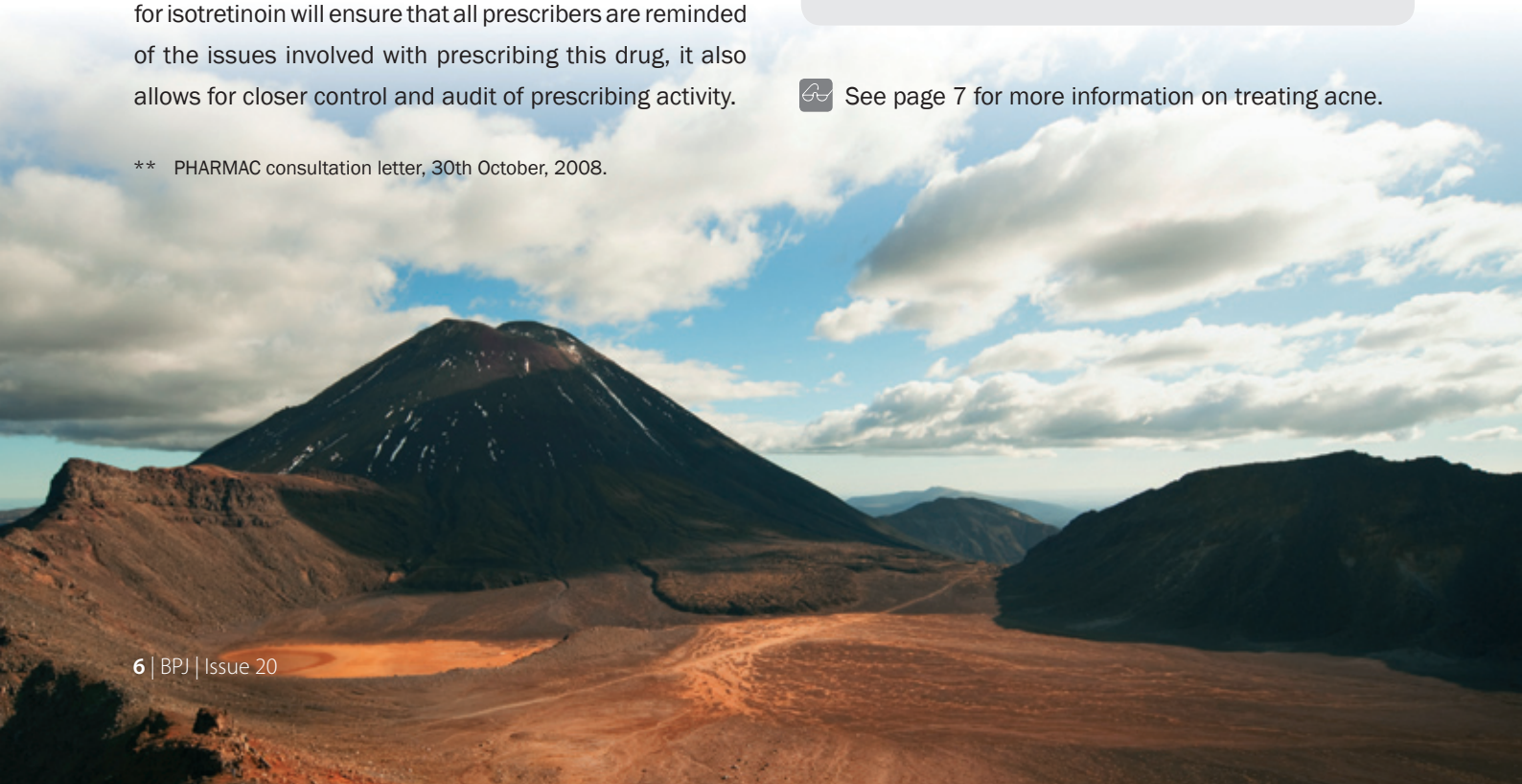
Concerns about increased exposure and adverse effects are valid regardless of who prescribes isotretinoin. Now that access has been widened, it is essential that all prescribers ensure that process is followed 100% of the time when isotretinoin is prescribed, and that it is reserved for severe cases of acne when all other treatment options have been tried and failed.

Rather than anticipating an increase in adverse effects and potential pregnancy exposures, prescribers should be aiming, through vigilance, to reduce these occurrences. If a GP does not feel confident in prescribing this drug, patients can still be referred to another GP or dermatologist.

It remains to be seen what the effect of widening access to isotretinoin will be. People who found difficulty in accessing a dermatologist, may finally receive a successful treatment for their acne, but this comes with the responsibility of protecting these people and their future children from potentially serious health risks. Only time will tell.

A *bestpractice* Decision Support module on acne was launched on 1st April 2009. This will be available to all GPs to assist and educate on managing and prescribing for acne.

See page 7 for more information on treating acne.



www.bpac.org.nz keyword: acne

# How to treat acne

Key reviewer: **Dr Amanda Oakley**, Specialist Dermatologist and Clinical Associate Professor, Tristram Clinic, Hamilton

## Key concepts:

- An inflammatory response to *P. acnes* results in papules, pustules and inflamed nodules
- Acne severity (mild, moderate or severe) may be based on the number, type and distribution of lesions
- Benzoyl peroxide, topical retinoids or topical antibiotics are suitable for mild acne
- Oral antibiotics may be suitable for moderate acne
- Combined oral contraceptives may be effective for moderate acne in women
- Isotretinoin may be suitable for severe acne, although it has many adverse effects and requires close monitoring and management - isotretinoin is a major teratogen, it is essential that women taking isotretinoin do not get pregnant

Acne is a common skin condition most prevalent in adolescents, affecting approximately 80% of people at some stage between the ages 11 to 30 years.[1, 2, 3] In a sample of New Zealand adolescents, 91% of males and 79% of females were affected by acne.[2, 3] Acne can also occur later in life and is present in approximately 5% of women and 1% of men over the age of 25 years.[1]

Acne can lead to dyspigmentation, scarring and psychological problems, especially anxiety and depression.[1] The aims of treatment are to reduce or clear skin lesions and prevent scarring and psychological sequelae.[1, 3]

## An inflammatory response to *P. acnes* results in papules, pustules and inflamed nodules

Increased sebum production occurs following the increase in androgen production at puberty. Hyperkeratinisation of the hair follicle prevents normal keratinocyte shedding, which then blocks the follicle resulting in open comedones (blackheads) and closed comedones (whiteheads).[5, 6] *Propionibacterium acnes* colonises the follicle and breaks down sebum into free fatty acids and peptides. Papules, pustules and inflamed nodules occur due to a variable inflammatory response to *P. acnes* and the chemicals it releases.[1]

## Acne diagnosis is based on history and examination

The diagnosis of acne is primarily based on history and examination.[5] Factors to consider when taking a history include:[2]

- Age of onset of acne and its duration
- Menstrual and oral contraceptive history in females
- Skin sensitivity and dryness (especially if atopic)
- Use of topically applied products such as cosmetics, cleansers, sunscreens, hair products and moisturisers that might be irritant or occlusive
- Use of other topical products, especially corticosteroid preparations
- Prescription and over-the-counter acne medicines used and their effect
- "Recreational" use of steroids e.g. gym use
- Presence of depression and/or poor self-esteem

## Examination and assessment of severity

Acne may present as non-inflammatory, inflammatory or a mixture of both.

### School students survey

In a survey of New Zealand secondary school students, 14.1% of students self-reported having "problem acne" with female, Pacific and older students reporting this most often. Those with more severe self-reported acne, females and Māori or Pacific students), were more likely to report difficulty in accessing medical treatment for acne (i.e. they reported that they wanted treatment but were unable to access or afford treatment from a doctor or specialist).[4]

### Hormonal investigations for acne in women

Acne in women may be due to a condition that causes excessive androgen production such as polycystic ovary disease (PCOS). If signs of hyperandrogenism (e.g. hirsutism or irregular periods) are present consider hormonal investigation or referral.[2, 7, 8] (see BPJ 12, April 2008)

**Non-inflammatory lesions include:**

**Closed comedones** – 1 to 5 mm white papules without perceptible follicular orifice

**Open comedones** – 1 to 3 mm dark papules with visible follicular opening

**Cysts** – non-tender larger fluctuant dermal or subcutaneous swellings

**Inflammatory lesions include:**

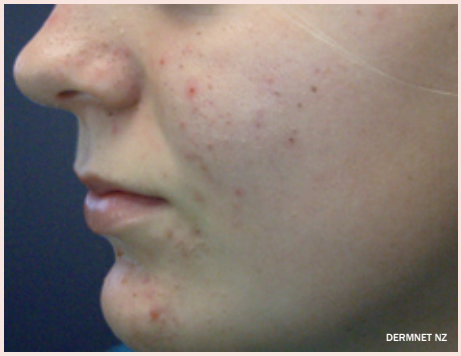
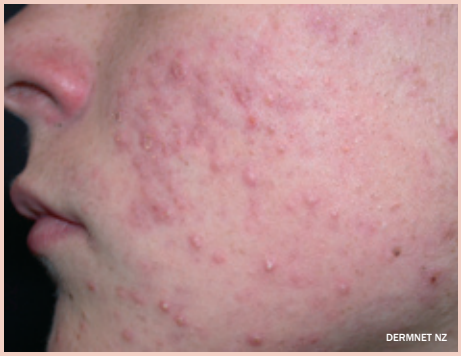
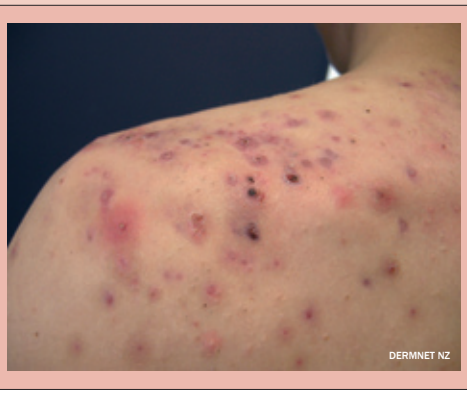
**Papules** – inflamed palpable lesions less than 5 mm in diameter

**Pustules** – similar to papules containing pus

**Nodules** – larger, well or poorly defined red lumps that are often very tender

The severity of acne may be based on the number, type and distribution of lesions (Table 1).

**Table 1:** Severity of acne[7]

| Severity | | Description |
|---|---|---|
| **Mild** |  | Non-inflammatory lesions (comedones) predominate. A few inflammatory lesions (papules and pustules) may be present (generally less than 10) |
| **Moderate** |  | More papules and pustules (10–40) and comedones (10–40) present. The trunk may be mildly affected. Occasional nodules and mild scarring may also be present |
| **Severe** |  | Widespread inflammatory lesions, nodules and scarring present. Usually involving the face, chest and back.<br><br>Moderate acne that has not settled after six months of treatment or acne of any severity that causes significant psychological distress is also classified as severe acne |

# Pharmacological treatment of acne – initial treatment depends on severity of acne

Initial treatment selection depends on the severity of acne. Initial management of mild acne is with topical therapies (benzoyl peroxide, topical retinoids and topical antibiotics). Oral antibiotics and/or hormonal treatments are added for moderate acne, and severe acne may require oral isotretinoin.

## Mild acne: benzoyl peroxide, topical retinoids or topical antibiotics are suitable

Benzoyl peroxide and the topical retinoids (adapalene, tretinoin and isotretinoin) are usually considered first line for mild acne. Topical antibiotics, which can be used in conjunction with benzoyl peroxide or a topical retinoid, may be useful for mild inflammatory acne.[1] Topical treatments for acne are not currently subsidised. Topical agents should be applied as a thin smear to all areas affected by acne as they are much less effective as spot treatment.

### Benzoyl peroxide

Benzoyl peroxide is an effective agent for comedonal and inflammatory acne. It is available over the counter in a range of formulations (e.g. washes, creams, gels) and strengths (2.5–10%).

The most common adverse effect of benzoyl peroxide is skin irritation, i.e., dryness and sometimes redness. This can be minimised by starting with a lower strength product and increasing.[8] Lower strength products (2.5–5%) are effective and cause less irritation than higher strength formulations (10%).[3] Patients should be advised that benzoyl peroxide can bleach clothes, towels, bedding and hair.

Azelaic acid may be used for mild comedonal acne. It causes less irritation than benzoyl peroxide but is generally believed to be less effective.[2, 7, 8]

### Topical retinoids: adapalene, tretinoin, isotretinoin

Topical retinoids inhibit comedone formation and therefore prevent the formation of new acne lesions. They are useful for treating inflammatory and non-inflammatory acne.[9] Topical retinoids available in New Zealand are adapalene, tretinoin and isotretinoin. While they all are similarly effective, adapalene may be better tolerated.[1, 8]

As with benzoyl peroxide, skin irritation is also common with topical retinoids and can limit their use for some people.[1] This can be minimised by slowly increasing the frequency of application over time, starting with application every second or third day and increasing as tolerance develops. Initially applying topical retinoids for shorter durations may also minimise skin irritation, for example, by washing the application off after a period of time (e.g. 20 minutes or more).[1, 9] Irritation may be exacerbated by applying excess amounts of topical retinoids and patients can be advised that a pea sized amount is sufficient for application to the whole face.[9]

Topical retinoids are applied at night because they are degraded by sun exposure. Sun protection during the day is also recommended because they can thin the stratum corneum.[2] There have been case reports of birth defects in infants born to mothers who used topical retinoids during pregnancy and for this reason they are not recommended for use in pregnancy.[9] However, there is thought to be no increase in circulating retinoid levels above normal, when used according to usual directions.

**Topical antibiotics: clindamycin and erythromycin**

Topical antibiotics are effective for mild inflammatory acne but have little effect on comedones. Monotherapy with topical antibiotics is not recommended because this can cause bacterial resistance.[1, 9] Combining treatment with benzoyl peroxide or topical retinoids prevents resistance and is more effective for clearing acne lesions.[7]

Clindamycin and erythromycin are the topical antibiotics available in New Zealand.

They usually cause less irritation than benzoyl peroxide and topical retinoids but may occasionally cause mild irritation and burning.[9]

One product that combines clindamycin and benzoyl peroxide (Duac Once daily) can be applied once daily at night. Otherwise separate products can be combined by using one in the morning and one at night. If treatment includes a topical retinoid, this should usually be used at night.[1]

Usually topical antibiotics should not be used for extended periods of time as bacterial resistance is more likely. Consider stopping topical antibiotics after approximately six to twelve weeks of treatment and continue the benzoyl peroxide or topical retinoid alone.[1]

Practice points for topical treatments:

- Apply to all areas of skin prone to acne – the main effect of topical treatments is preventing new comedones developing[7]
- Use for at least six weeks before deciding if treatment is effective – topical treatments prevent new lesions therefore adequate time is required to allow current lesions to resolve
- Continued improvement may occur for up to six months of continuous use
- Different formulations can be chosen depending on skin type – creams for dry sensitive skin, gels and topical solutions for oily skin[1]

## Glossary of topical acne medications

**Benzoyl peroxide**

2.5% – Benzac AC gel, PanOxyl Acne gel

4% – Brevoxyl cream

5% – Benzac AC gel, Benzac AC wash, Clean and Clear Continuous Control Acne Cleanser, Clearasil Ultra Acne Treatment cream, PanOxyl Acne gel

10% – Benzac AC gel, PanOxyl Acne gel

**Azelaic acid**

20% – Acnederm Lotion, Skinoren cream

**Topical retinoids:**

**Adapalene**

0.1% – Differin gel, Differin cream

**Isotretinoin**

0.05% – Isotrex gel

**Tretinoin**

0.05% – Retin-A cream, Retinova cream

**Topical antibiotics:**

**Erythromycin**

2% – Stiemycin topical solution

4% – Eryacne gel

**Clindamycin**

1% – Topicil solution

1%, with 5% benzoyl peroxide – Duac Once Daily gel

## Moderate acne: oral antibiotics are recommended

Oral antibiotics are appropriate for moderate acne and for acne that has not responded to topical therapy. They inhibit the growth of *P. acnes* and also have direct anti-inflammatory effect.[10] Tetracycline antibiotics such as doxycycline are usually the first line choice. Erythromycin-resistant *P. acnes* is common and for that reason erythromycin is usually reserved for treating acne in children, pregnant women and those with a hypersensitivity to tetracyclines.[9] Trimethoprim 300 mg daily may also be effective.

Oral antibiotics should be used in combination with a topical retinoid or benzoyl peroxide.[2, 6, 9] Short courses (however not usually less than three months) are now recommended over longer courses because of the risk of antibiotic resistance.[8] They may be prescribed for four to six months and may be tapered and discontinued once acne improves. Use of benzoyl peroxide or topical retinoids may help maintain improvements once oral antibiotics are stopped.[10] If acne relapses, treat with the same antibiotic as previously used.

Doxycycline and minocycline are usually taken at a dose of 100 mg to 200 mg daily. Photosensitivity and oesophagitis are common side effects of doxycycline. Vaginal thrush affects 5% of women treated with oral antibiotics. Minocycline is associated with other rare side effects such as blue-gray pigmentation, drug-induced lupus and hepatic dysfunction and for this reason is usually reserved for second line use.[2, 9] If minocycline is used for longer than six months, liver function tests will be required every three months.[11] Tetracyclines are not suitable for pregnant or breastfeeding women, or for children under 12 years old as they may harm bones and teeth of the unborn or developing child.[1]

When used for acne, erythromycin is taken at 400 mg twice daily. It may cause nausea and should be taken with food.[2]

### Interaction with combined oral contraceptives

It is thought that gut flora develop resistance to non-enzyme inducing antibacterials (all antibacterials apart from rifampicin and rifabutin) after three weeks of treatment. For this reason, women taking the combined oral contraceptive do not require additional precautions (e.g. condoms) after three weeks of treatment with an antibiotic.[12]

## Moderate acne: combined oral contraceptives may be effective for acne in women

Hormonal treatment of acne may be suitable for women who have premenstrual flares of acne, have acne that is resistant to conventional treatment, those with hormonal abnormalities, or women with acne that also require hormonal contraception.[1] Combined oral contraceptives containing cyproterone (e.g. Estelle) may be more effective than other oral contraceptives and are suitable for women with PCOS. However any oral contraceptive containing oestrogen is likely to have positive effects on acne.[7]

A therapeutic response may be seen after one cycle but usually takes up to six cycles to see a full response.[7]

## Isotretinoin for severe acne

Acne that has not responded to topical or oral therapy or acne that is severe on presentation may require treatment with isotretinoin. Isotretinoin can be a complex drug to use, as it has many adverse effects, requires monitoring and is a major teratogen. Isotretinoin should only be prescribed by doctors who have been educated in its safe and effective use. Patients may require referral to a dermatologist.

Patients should receive extensive verbal and written information regarding the medication, its risks, adverse effects and requirement for monitoring. They should be reviewed regularly during the course of treatment.

Isotretinoin is effective because it is active against all four contributing factors to acne.

Isotretinoin:[13]

- Reduces the size and secretions of sebaceous glands
- Prevents the formation of comedones
- Reduces colonisation of the skin by *P. acnes*
- Reduces associated inflammation

Results are unpredictable and highly variable. A single course of isotretinoin may result in prolonged remission of acne.[8] Acne is resolved in approximately 40% of patients after one course, 40% may have acne that recurs at low severity and usually responds to topical therapy or occasionally oral antibiotics are required and 20% of patients may need a further course of isotretinoin.[7]

### Contraindications to isotretinoin

Isotretinoin can not be used by women who are pregnant or breastfeeding, or by people who have severe hepatic impairment, hyperlipidaemia or hypervitaminoisis A.

Concomitant use of isotretinoin with tetracycline antibiotics should be avoided as it may increase the risk of raised intracranial pressure.

**Table 2**: Common adverse effects of isotretinoin and ways to minimise these[2, 15]

| Problem | Solution |
|---|---|
| Acne flare – sometimes very severe | Mild acne flare may occur initially and usually improves with continued treatment.<br><br>Severe flare may require a reduced dose or discontinuation of isotretinoin. Oral erythromycin and/or systemic steroids may be required. |
| Dry skin, lips and nostrils | Use non-soap cleansers, lip balm and thick emollients |
| Skin fragility, delayed wound healing and sun sensitivity | Use sunscreen and cover up in the sun (especially fair skinned people)<br><br>Avoid waxing but shaving can be continued with shaving cream |
| Dry, irritable eyes and contact lens intolerance | Use artificial tears and wear glasses or change to “dry eye” contact lenses if contact lens are not tolerated |
| Retinoid dermatitis – patchy or discoid-pattern dry red plaques often seen on the hands and forearms | Increase use of emollients. Moderate potency topical steroids are useful |
| Paronychia and staphylococcal infection of wounds, dermatitis and lip fissures | Treat with topical (fusidic acid) or oral antibiotics (flucloxacillin) |
| Tiredness, muscle and joint aches, headache | Paracetamol or a reduction in dose (especially if acne is improving)<br><br>Severe headache (especially if accompanied by visual changes) should be investigated for benign intracranial hypertension |

# Guidance on the **safe use of isotretinoin**

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## *bestpractice* acne including isotretinoin

The *bestpractice* acne module provides tools for the initial assessment of acne severity, context sensitive advice, treatment and management options.

Features guidance on the safe prescribing of isotretinoin.
Including:

- Contraindications, cautions and side effects
- Laboratory testing requirements and the timing
- Patient information
- Patient consent documents


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### Dosing

Patients may be initiated on 0.5 mg/kg/day for two to four weeks and then maintenance therapy can be continued at 0.1–1 mg/kg/day depending on response and tolerance.[14] A cumulative dose over the treatment course of between 120 mg/kg and 150 mg/kg is associated with an increased likelihood of prolonged remission.[7] Therefore a treatment course may last four to six months, depending on the daily dose. The maximum cumulative dose per course is 150mg/kg. If a further course is required, there should be a minimum of eight weeks between courses.

Adverse effects are often dose dependent and may be minimised with lower dose treatment for a longer time period.[7] See Table 2 for management of adverse effects associated with isotretinoin.

**Significant adverse effects include abnormal liver enzymes, hypertriglyceridaemia, cytopaenias and depression.[2]**

Transient increases in liver enzymes may occur but often return to normal with continued treatment. Liver function should be checked before and one month after the start of treatment and then three monthly.[16] If liver enzymes rise greater than two and a half times normal levels, investigation into other possible causes of liver dysfunction (e.g. viral hepatitis, alcohol) is required and the dose of isotretinoin may need to be reduced or the drug stopped altogether.[15]

Some patients may have a small increase in triglyceride or cholesterol levels. Levels may resolve on reduction of dose, discontinuation of therapy or modification of diet.[15, 16] Triglyceride levels in excess of 9 mmol/L have been associated with pancreatitis. Isotretinoin should be stopped if triglyceride levels are rising or if symptoms of pancreatitis develop.[16] Fasting lipids should be measured at baseline, one month after the start of therapy and at the end of therapy.[16]

Rarely isotretinoin causes reversible cytopaenias. A complete blood count is required at baseline and one month after commencing treatment. Further complete blood counts should be done if the patient presents with high fever, sore throat, petechiae or unusual bruising.[15]

There has been ongoing debate as to whether isotretinoin causes mood disorders. Studies so far have proved inconclusive as it has not been possible to accurately distinguish between mood change due to acne or due to isotretinoin.[17] Patients should be counselled about mood changes and closely monitored during treatment.[3]

## Isotretinoin is a teratogen

A major concern with isotretinoin use is its teratogenic effect. A single exposure during pregnancy can result in embryopathy and severe birth defects including ear abnormalities, central nervous and cardiovascular system defects.[6, 7] Long term cognitive and developmental effects may be present even if central nervous system abnormalities are not obvious.[15]

For this reason, every attempt to prevent pregnancy should be made, including: [17]

- Obtaining a current sexual history in ALL females of child bearing potential, whatever their age or likely behaviour
- A negative pregnancy test (preferably blood) is required in the two weeks before initiation and isotretinoin can be started on the second or third day of the next menstrual period
- Pregnancy tests are required monthly at each prescription
- Two forms of contraception are recommended for females (e.g. a hormonal contraceptive and a barrier method such as condoms) one month before, during and one month after treatment.

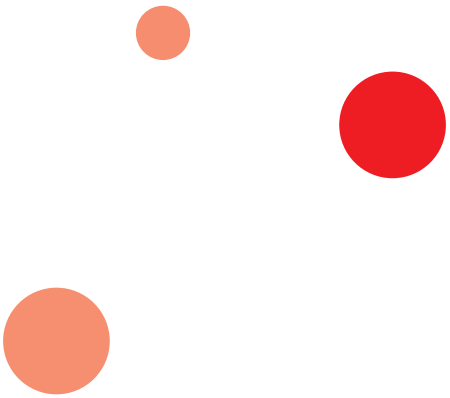
  NB: The progesterone-only pill may be less reliable during isotretinoin therapy and is not recommended

- Female patients should be advised to consult their GP, pharmacist or dermatologist if they have knowingly had unprotected sex during isotretinoin

therapy so that emergency contraception can be considered

- If a foetus is exposed to isotretinoin offer counselling regarding termination of pregnancy as early as possible
- Male and female patients should not donate blood during, and for one month after finishing isotretinoin treatment, because of this risk

It is recommended patients sign a consent form indicating they have understood potential adverse effects of isotretinoin and for females, the importance of not becoming pregnant while on therapy. A copy of this form is available in *bestpractice* Decision Support acne module or can be downloaded from the bpac website: **www.bpac.org.nz** keyword: isoconsent



Images contributed by NZ DermNet, the website of the New Zealand Dermatological Society: **dermnet.org.nz**

**References:**


1. Clinical Knowledge Summaries. Acne Vulgaris. Available from: http://cks.library.nhs.uk/acne_vulgaris (Accessed February 2009).
2. Oakley A. Acne. N Z Fam Physician 2005; 32(6): 400-3.
3. Purdy S, de Berker D. Acne. BMJ 2006; 333: 949-53.
4. Purvis D, Robinson E, Watson P. Acne prevalence in secondary school students and their perceived difficulty in accessing acne treatment. N Z Med J 2004; 117(1200).
5. Feldman S, Careccia RE, Barham KL, Hancox J. Diagnosis and treatment of acne. Am Fam Physician 2004; 69(9): 2123-30.
6. Tom WL, Fallon Friedlander S. Acne through the ages: case-based observations through childhood and adolescence. Clin Pediatr (Phila) 2008; 47: 639-51.
7. James WD. Acne. N Engl J Med 2005; 352: 1463-72.
8. In the Clinic. Acne. Ann Intern Med 2008; 149(1).
9. Zaenglein AL, Thiboutot DM. Expert committee recommendations for acne management. Pediatrics 2006; 118: 1188-99.
10. Wirth FA. Approach to acne vulgaris. UpToDate. Available from: www.uptodate.com (Accessed February 2009).
11. BNF 56. British National Formulary. 56th Ed. London: British Medical Association and the Royal Pharmaceutical Society of Great Britain; September 2008.
12. Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit. Drug interactions with hormonal contraception. Available from: www.ffprhc.org.uk (Accessed February 2008).
13. Katsambas A, Papakonstantinou A. Acne: systemic treatment. Clin Dermatol 2004; 22: 412-8.
14. MIMS New Ethicals Issue 10. Jan-Jun 2009. CMPMedica.
15. Sullivan JR. Oral isotretinoin. Aust Prescr 2005; 28: 59-61.
16. Pacific Pharmaceuticals. Isotane Data Sheet 2005. Available from: http://www.medsafe.govt.nz (Accessed February 2009).
17. British Association of Dermatologists. Isotretinoin for acne. Available from: http://www.bad.org.uk (Accessed February 2009).

# Let's talk about sex

www.bpac.org.nz keyword: sex

Key reviewer: **William Pearce**, RN, Christchurch Sexual Health Centre

## Why don't health professionals like talking about sex?

Sexual health is often not discussed during the course of a general practice consultation. Perhaps the most obvious reason is that doctors usually focus on the problem of the day and there is a lack of time to discuss general health issues. However there may be many other reasons for not talking to patients about sex, including embarrassment, fear of alienating the patient, lack of a trusting and comfortable professional relationship with the patient (although a close relationship can also act as a barrier), lack of confidence in speaking about sexual practices and lack of a reason to talk about sexual health.

Given that sexually transmitted infections (STIs) such as chlamydia and gonorrhoea are increasingly prevalent among young people in New Zealand, and patients are often asymptomatic, it is important that health professionals do take appropriate opportunities to talk about sex and don't wait until the patient raises the topic or presents with an STI.

## How to talk to patients about sex

A discussion about sexual health can take place with any patient, however, in particular consider talking to people who:

- Are in the age group at highest risk for STIs (15 – 25 years)
- Have had a recent change of sexual partner or relationship break-up
- Have multiple sexual partners
- Request a sexual health check
- Attend for a genitourinary complaint
- Attend for a cervical smear test
- Attend for contraception
- Are pregnant (which may include termination of pregnancy or antenatal advice)
- Have a condition or are on medication that may inhibit sexual function (e.g. diabetes, beta blockers, SSRIs)

### Barriers to talking about sex

In a study of primary care physicians in Belgium, only 44% regularly provided sexual health information to their patients (asking about sexual history, informing about safer sex and sexually transmitted infections). More than half would not give unsolicited information to an asymptomatic patient with an obvious STI risk. Just under one third of the doctors said that a large age difference between them and their patient was a barrier for speaking about sexual health and patients of the opposite sex were a barrier for 23% of female doctors and 13% of male doctors. Interestingly, a close professional relationship was seen as a barrier for talking about sex for 71% of the surveyed doctors.[1]

Many patients present at sexual health clinics because they feel unable to discuss their sexual behaviour or genital symptoms with their regular GP.

Health professionals may also wish to include a discussion about sexual health as part of a new patient appointment.

Patients often present with other concerns although the main reason for the consultation is a sexual health issue. Consultation skills are important in allowing the patient to discuss the sexual health issue (the "hidden agenda").

**Provide a welcoming and comfortable environment**

A consultation setting that is welcoming, comfortable and confidential is more likely to encourage openness when talking about sex. Practices should consider displaying literature in waiting rooms and consultation rooms that stresses the private and non-judgemental nature of their service.[2]

Explain that talking about sex is a routine aspect of healthcare and ensure that the patient does not feel that they have been singled out or suspected of being likely to have an STI. For example you could say "we ask all our patients about their sexual health…" or "most people are having sex, so we ask about it…".

Consider developing a practice policy on how to address sexual health issues with patients with communication difficulties e.g. English not first language, hearing impaired, learning difficulties.[1] Also consider cultural and ethnic differences and religious beliefs.

**Take a sexual history**

A sexual history should start with open questions, and then focus on areas of concern. Key skills for effective history-taking include knowing how to address attitudinal issues to sexual behaviour, knowledge about a range of sexual practices and understanding of the need to maintain confidentiality.[2]

Begin with questions about the patient's social background. This enables the patient to relax and any problems or risks can be assessed in context. Ask about marital status, duration of relationship with current partner, number of previous partners and their gender, home environment, family support, activities and interests.[3]

Discussion should also include questions about risk behaviours such as alcohol and illicit drug use, intravenous drug use, sharing of needles, syringes or drug preparation equipment, sexual partners from another country or commercial sex work.

Next, ask more specific questions about sexual practices depending on the patient's social history. Questions should not be prescriptive and should be tailored to the individual patient and circumstances. Issues that usually should be covered include:[2]

- Establish whether sexual activity is taking place
- Exposure history to determine specific risks and which sites need to be sampled; depending on the gender of partner(s), type of intercourse or sexual practices
- Use of condoms and other contraception (including correct use and consistency of use)
- History of previous STIs or STI testing
- STI history of partner(s) or presence of symptoms suggestive of STIs
- Assessment of HIV, hepatitis B and hepatitis C risk
- Discussion of other sexual health issues e.g. erectile dysfunction, premature ejaculation, vaginismus
- Discussion about sexual abuse and domestic violence

Generally, it is best to use medical terminology when discussing sexual health, however if appropriate, some colloquial language could be used for sexual practices, especially if the medical term may not be understood e.g. cunnilingus vs. oral sex.

## Contact tracing

Partner notification is an essential part of STI management. It is worth remembering there are many ways of contacting previous sexual partners. This may include email, texting, phone, face-to-face or letter. Patients should be offered the choice of:

- Patient referral, where patients themselves notify their sexual contacts to seek treatment
- Provide a referral, where the healthcare provider agrees to undertake the task of notifying sexual contacts to seek treatment.

If a patient attends as a contact of someone who has been infected, this person must not be identified. Conversely, the contacts attendance or non-attendance or clinical condition must not be revealed.[2]

In New Zealand conditions which must be reported to the Medical Officer of Health include hepatitis B and C and AIDS (but not HIV).

**Sexual orientation should be discussed as part of a sexual health check**

It is important that patients are asked about their sexual orientation or gender of sexual partners, so any specific health issues can be identified and testing targeted. This may include referral for counselling for younger patients who require assistance in exploring their feelings and telling their friends and family. Some younger lesbian, gay, bisexual or transgender people may be at increased risk of depression, suicide, substance abuse and violence.

In a study of 131 people aged 14 to 18 years, who openly identified themselves as lesbian, gay or bisexual, only 35% reported that their doctor knew about their sexual orientation. Almost two thirds (64%) said that their doctor should "just ask them". Of those who had disclosed their status to their GP, 57% thought that their healthcare had improved as a result.[4] Doctors should have some relevant information regarding support groups for young gay, bisexual or lesbian people if they disclose their sexual preference (see list of resources on page 23).

**Ask about symptoms**

As part of a sexual health discussion, patients should be asked about genitourinary symptoms, regardless of whether this was the reason for their consultation. This may reveal overlooked or ignored problems.[2]

Ask about:[2]

- A recent change in vaginal discharge or urethral discharge
- Vulval or genital skin problems
- Peri-anal/anal symptoms
- Lower abdominal pain
- Dysuria
- Changes in menstrual cycle, irregular bleeding or post-coital bleeding

If sexual history or symptom assessment results in laboratory testing, establish how results will be given and discuss any confidentiality issues.

**Give advice about safer sex**

Based on information gained from sexual history and symptom assessment, individualised advice should be given about practicing safer sex.

The only way to completely prevent STIs and other sexual health issues is to remain abstinent. However by modifying risky behaviours, sex can be made safer.

- Younger people could be encouraged to express sexual feelings in other ways e.g. massage, mutual masturbation
- If a person chooses to have sex, consistently and correctly using condoms (or other barrier contraception) is a key safer sex behaviour
- Even in a monogamous relationship, it may be appropriate to recommend condom use until both partners have had a sexual health check
- Condoms should always be used for anal sex to protect against STIs and other infections
- Older people may be less likely to have knowledge about STIs and safer sex methods, so could need extra advice and counselling

**Condoms provide protection against most but not all STIs**

Condoms should be used for vaginal, anal and oral sex. If used properly, they protect against STIs that are transferred through contact with genital secretions such as gonorrhoea, chlamydia, trichomonias, syphilis, HIV and hepatitis B and C. Protection against diseases such as human papilloma virus, herpes simplex virus, scabies and pubic lice depends on the site of the sore/ulcer or infection and whether this is covered by the condom.[5]

Condoms are provided free of charge from Sexual Health Centres and Youth Health Centres. They may also be prescribed or obtained by practitioner supply order (PSO). There are a variety of products available in sizes 49 – 60 mm, regular, extra strength or shaped. Choice of product is based on personal preference and self selection of size, however extra strength products are recommended for use during anal sex. It is not necessary to use spermicidal condoms – they are no more effective in preventing pregnancy and can cause vaginal irritation.

PHARMAC is currently consulting on listing a non-latex condom for those with a severe latex allergy.

Condoms should be stored in a cool, dry place and kept away from sunlight. Expiry dates should be checked before use. Only water based lubrication should be used (e.g. KY jelly). Do not use Vaseline, oils (e.g. baby oil) or body lotions.

Best Practice tip: Young people who are resistant to condom use seem to listen more when they are told that condoms protect against eight different infections and pregnancy.

**Other barrier methods**

Female condoms/femidoms/vaginal liners are available from family planning clinics and offer the same level of protection against STIs as a regular condom for vaginal sex. They are made from polyurethane, with an inner ring to aid insertion and an outer ring that rests on the female genital area. Female condoms can be disinfected after use with household bleach, washed in detergent, dried and re-used approximately five times.

An oral dam (also known as a dental dam) is a thin square of latex that is placed over the vagina or anal area during oral sex. These can be purchased from family planning clinics and some pharmacies or alternatively a cut open latex glove may be used.

## Special issues when talking about sex

**Same sex partners**

Some health professionals may feel uncomfortable or embarrassed asking about a patient's sexual preference and discussing same sex practices.

A common stereotype is that people with same sex partners have a much higher incidence of STIs due to

many sexual contacts and frequent casual or anonymous sex. However, the incidence of STIs is higher in people with multiple sexual partners, regardless of sexual orientation. STIs are transmitted similarly for vaginal and anal sex, although HIV is more easily transmitted through anal sex. Oro-anal sexual contact increases the risk for transmission of pathogens such as giardia and hepatitis A. Bacteria may also cause urethritis in both men and women. Hepatitis B is more common in men who have sex with other men but has not been shown to be spread by any specific sexual practices.[6]

- Avoid prejudice
- Do not presume that all people with same sex partners will engage in the same type of sexual behaviour. Up to one third of homosexual men choose not to practise penetrative anal sex[6]
- Anal sex is also practised by heterosexual couples (up to 10% regularly)[6]
- If a doctor has personal beliefs about homosexuality, which would compromise the level of care a patient receives, the patient should be referred to another doctor
- Ensure advice is accurate, it is better to ask for clarification of a certain term or practise rather than to offer misleading advice
- Sexual orientation is not always fixed – do not presume that a man who has sex with another man is homosexual or that a person who is married cannot be homosexual. Men or women may have a curiosity to experience same gender sex sometimes

**Sex in very young people**

A particular challenge facing health professionals is how to bring up the topic of sex with very young people, when it is suspected that they may be sexually active.

Young people usually find it difficult to confide to someone about their sexual behaviour. Building trust is extremely important. This is gained by maintaining privacy, confidentiality and a respectful, non-judgemental attitude at all times.

### Ideas for practice audits

- Patients asked about gender of sexual partner or if they have ever had a same sex partner
- Patients asked about condom use and offered condom prescription if appropriate
- Comprehensive sexual history noted
- HIV risk assessment performed
- Updated sexual history taken with new genitourinary complaints
- Patients asked if they have ever experienced sexual abuse or non-consensual sexual contact

Sometimes a parent or carer will accompany a young person to a consultation and be aware of the reason for the visit. But in most circumstances, accompanying adults should be asked to leave the room, before a discussion about sexual health takes place.

A social and sexual history should be taken and the patient encouraged to talk to a trusted adult. Anything that the young patient discloses must be kept private and confidential from their parent or carer, unless they have consented to discussion.

In some situations, a health professional may judge that further action is required, especially if there are concerns about the maturity and competency level of the young person. Questions which may aid in the decision whether to liaise with a senior colleague, a paediatrician or a child protection team include:[2]

- Do parents/carers know about the sexual activity?
- Do parents/carers know they are attending the doctor?
- Has the young person had sex against their will?

- Age of partner – are there any legal ramifications? (The legal age of consent to sexual intercourse is 16)
- Are there issues of vulnerability (self harm, psychiatric illness, drug or alcohol misuse, internet grooming)?
- Is the young person under 13?
- Is the young person being paid/rewarded for sexual activity?

As a general guide, any cases involving non-consensual sex or abuse should be referred immediately to a paediatrician or a doctor with special training (e.g. Doctors for Sexual Abuse Care - DSAC) as well as any relevant authorities (e.g. police).

Cases of people under 16 having consensual sex, should be reported to a public health officer or child protection service, if there is a significant age difference between the young person and their partner, or if there are issues of concern that may place the young person in physical or psychological danger.

**Further reading and resources**

Rainbow Youth – an organisation for gay, lesbian and bisexual youth, run by youth.

**www.rainbowyouth.org.nz**

Ministry of Health "Hubba Hubba" – Safer sex information aimed at youth

**www.hubba.co.nz**

The Word – Information on sex, life and relationships (Family Planning Association)

**www.theword.org.nz**

New Zealand Sexual Health Society – resources on safer sex and STIs

**www.nzshs.org**

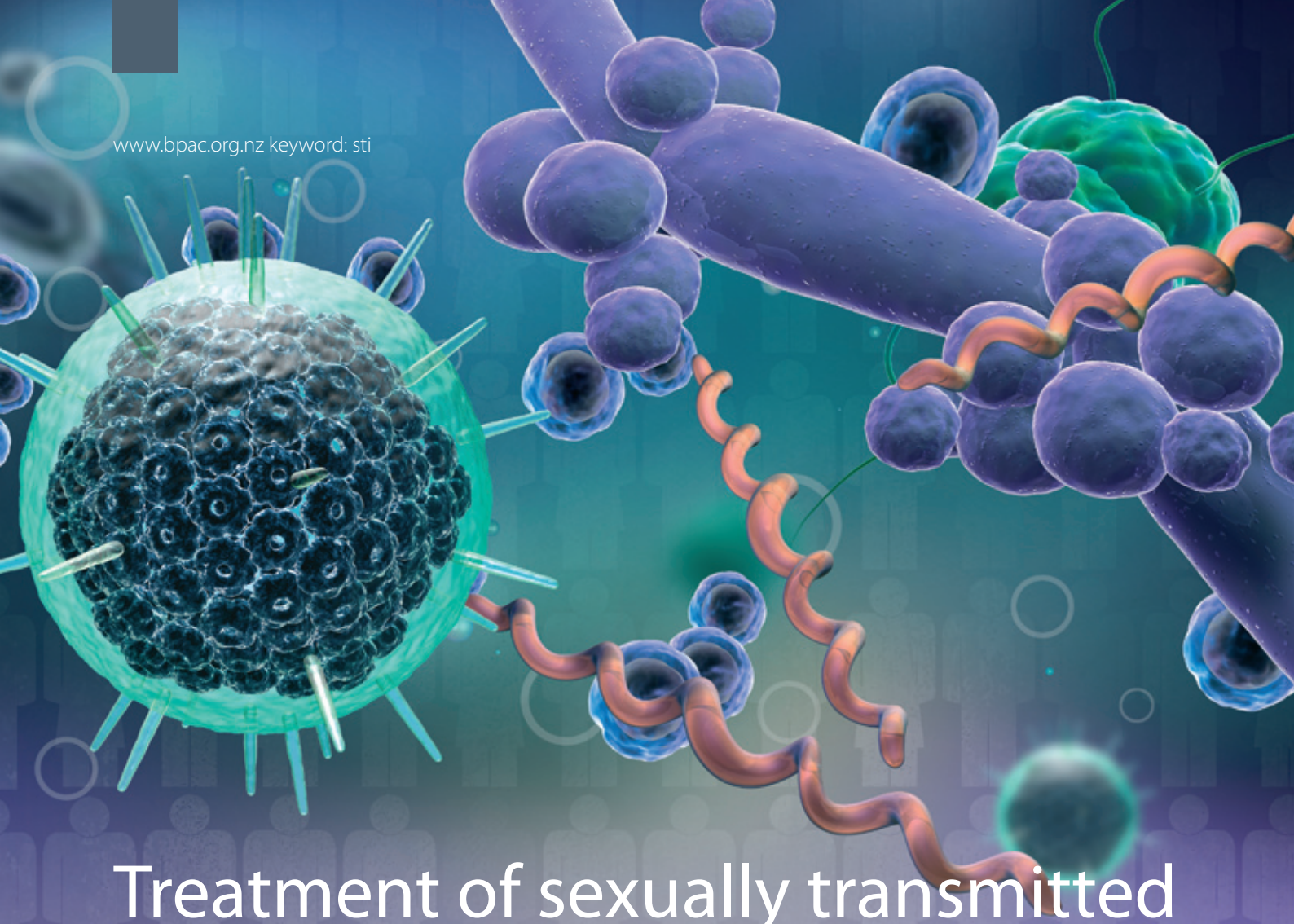
List of New Zealand sexual health clinics available from:

**www.nzshs.org**

**References:**


1. Verhoeven V, Bovijn K, Helder A, et al. Discussing STIs: doctors are from Mars, patients are from Venus. Fam Pract 2003;20(1):11-5.
2. French P. BASHH 2006 National Guidelines - consultations requiring sexual history-taking. Int J STD AIDS 2007;18:17-22.
3. Tomlinson J. ABC of sexual health: taking a sexual history. BMJ 1998;317:1573-6.
4. Meckler G, Elliott M, Kanouse D, et al. Nondisclosure of sexual orientation to a physician among a sample of gay, lesbian and bisexual youth. Arch Pediatr Adolesc Med 2006;160:1248-54.
5. Centres for Disease Control and Prevention (CDC). Male latex condoms and sexually transmitted diseases, 2009.
6. Bell R. ABC of sexual health: homosexual men and women. BMJ 1999;318:452-5.

www.bpac.org.nz keyword: sti



# Treatment of sexually transmitted and other genital infections

Key reviewer: **Dr Murray Reid**, Sexual Health Physician, Auckland Sexual Health Service

## General points:

- If one STI is present always consider testing for others
- Testing and treatment of partners should ideally be done simultaneously
- Give verbal information on safer sexual practices, contraception and offer written information to take away
- Advise sexual abstinence until course of treatment is completed (or for seven days after single dose treatment)

## Contact tracing

Testing and treatment of sexual partners is important. All sexual contacts within the past three months (or last contact if greater than three months ago) should be traced and advised to seek testing and/or treatment.

For more information on testing for genital infections, refer to Best Tests March 2009.

| Chlamydia | |
|---|---|
| **Best test:** | Men – First void urine (FVU); Women – endocervical swab if performing pelvic examination; Self collected vaginal swab acceptable for screening; Rectal swab in either sex if indicated by history |
| **Drug treatment:** | Azithromycin 1 g stat or<br>Doxycycline 100 mg bd for 7 days |
| **Drug treatment in pregnancy or breast feeding:** | Azithromycin 1 g stat (azithromycin not licensed for use in pregnancy in NZ but clinical experience and studies overseas suggest it is safe and effective[2] ) or<br>Amoxicillin 500 mg tid for 7 days or if allergic to penicillin use erythromycin<br>e.g. erythromycin ethyl succinate 800 mg qid for 7 days (14 day regimens are appropriate if GI intolerance is a concern) |
| **Other management:** | Contacts of a person who has tested positive for chlamydia should be treated.<br>For symptomatic rectal infection in men who have sex with men discuss treatment with a sexual health physician.<br>A test of cure should be done at 4 weeks post treatment in rectal infection, in pregnancy and when amoxicillin or erythromycin is used.<br>Repeat STI screen for those with positive results after 3 months. |

| Gonorrhoea | |
|---|---|
| **Best test:** | Men – urethral swab; Women – endocervical swab; If appropriate rectal and pharyngeal swabs. |
| **Drug treatment** | (including pregnancy and breastfeeding):<br>Ceftriaxone 250 mg* IM stat AND Azithromycin 1 g stat<br>Azithromycin is routinely given for treatment of chlamydia as co-infection is so common.<br>If the isolate is known to be ciprofloxacin sensitive, a 500 mg stat dose of ciprofloxacin can be used. Resistance rates vary by location. |
| **Other management:** | Test of cure is not usually required as standard treatment is >95% effective (provided compliant and asymptomatic after treatment) |

* Although most guidelines recommend ceftriaxone 250 mg for gonorrhoea, PID or epididymo-orchitis, currently the smallest unit amount available in New Zealand is a 500 mg ampoule. For the sake of simplicity some clinicians may choose to use a whole vial for one patient, i.e. 500 mg. Five ampoules are available on a PSO.

| Syphilis | |
|---|---|
| **Best test:** | Early – examination of chancre exudate by dark ground microscopy (NB this is often impractical because it needs to be examined within 10 –15 minutes).<br><br>After 6 – 12 weeks – serology |
| **Drug treatment:** | **Do not prescribe antibiotics or apply any solutions to ulcer prior to the patient being seen by a specialist** |
| **Other management:** | In the presence of a chancre or rash and/or positive serological finding, urgent referral to a sexual health or infectious disease physician is recommended.<br><br>Advise patient to abstain from sexual activity until seen by a specialist and the diagnosis is confirmed. |

| Genital Herpes (first episode) | |
|---|---|
| **Best test:** | Viral swabs. Type specific herpes serology is typically not indicated in an acute presentation as interpretation can be difficult. |
| **Drug treatment:** | Aciclovir 200 mg 5 x/day for 5 days or Aciclovir 400 mg tid for 7 days<br><br>Antiviral treatment may still be appropriate if patient presents >72 hours after development of symptoms if new lesions are developing or symptoms are severe.<br><br>Lignocaine gel 2% as required<br><br>Paracetamol 1 g qid |
| **Drug treatment in pregnancy or breast feeding:** | Aciclovir as above (note aciclovir not licensed for use in pregnancy although extensively used without significant adverse effects)<br><br>All pregnant women should be referred to a sexual health physician or obstetrician. Urgent referral if in the third trimester |
| **Other management:** | Advise increasing fluid intake so urine is dilute and less painful to pass and suggest urinating in the bath/shower to reduce stinging.<br><br>Written information is recommended for all patients. Useful resources can be found at **www.herpes.org.nz** |

| Trichomoniasis | |
|---|---|
| **Best test:** | Men – urethral swab; Women – high vaginal swab. |
| **Drug treatment:** | Metronidazole 400 mg bd for 7 days or Metronidazole 2 g stat. The single dose has the advantage of improved compliance but there is some evidence to suggest that the failure rate is higher. |
| **Drug treatment in pregnancy and breastfeeding:** | Metronidazole 400 mg bd for 7 days (NB single high dose regimens are avoided because they may result in higher serum concentrations which can reach foetal circulation). |

| Trichomoniasis continued | |
|---|---|
| **Other management:** | Avoid alcohol with metronidazole<br><br>Partner also requires treatment to prevent re-infection. A male partner of a woman with trichomoniasis should be treated even if asymptomatic as the culture is seldom positive even if infection present. |

| Bacterial vaginosis | |
|---|---|
| **Best test:** | High vaginal swab |
| **Drug treatment:** | Metronidazole 2 g stat or Metronidazole 400 mg bd for 7 days |
| **Drug treatment in pregnancy and breastfeeding:** | Metronidazole 400 mg bd for 7 days |
| **Other management:** | Avoid alcohol with metronidazole<br><br>Treatment of asymptomatic woman is unnecessary unless an invasive procedure is planned e.g. IUCD insertion, termination of pregnancy |

| Acute non-specific urethritis (NSU) | |
|---|---|
| **Best test:** | Diagnosis of exclusion. Urethral swab and FVU to exclude gonorrhoea and chlamydia |
| **Drug treatment:** | Azithromycin 1 g stat or<br><br>Doxycycline 100 mg bd for 7 days<br><br>If purulent discharge, treat as for gonorrhoea i.e. *ceftriaxone 250 mg IM stat and azithromycin 1g stat |
| **Other management:** | Treat contacts with azithromycin 1 g stat even if the contact's chlamydia test result is negative |

| Genital Warts | |
|---|---|
| **Best test:** | Clinical diagnosis |
| **Drug treatment:** | Patient applied: Podophyllotoxin 5 mg/ml bd for 3 consecutive days/week for 5 weeks or<br><br>Imiquimod 3 times a week (alternate days followed by 2 treatment free days) for up to 16 weeks<br><br>Clinician applied: Cryotherapy, laser, hyfrecation or surgical excision |
| **Drug treatment in pregnancy and breastfeeding:** | Cryotherapy only<br><br>Specialist referral may be required |
| **Other management:** | Barrier contraception may reduce transmission to partners<br><br>Treatment is cosmetic not curative<br><br>For patient resources see **www.hpv.org.nz** |

| Acute candidiasis | |
|---|---|
| **Best test:** | Women – vaginal swab; Men – subprepucial or glans penis swab |
| **Drug treatment:** | Women: Intravaginal antifungal (imidazole) or fluconazole 150 mg stat<br>Men: Topical antifungal (imidazole) |
| **Drug treatment in pregnancy and breastfeeding:** | Intravaginal antifungal (imidazole) |
| **Other management:** | Treatment of asymptomatic women is not generally necessary<br>Although candidiasis is not an STI it can be transferred with sexual contact. The partner should be treated if symptomatic or in some cases of recurrent candidiasis |

| Pelvic inflammatory disease | |
|---|---|
| **Best test:** | Pelvic exam, endocervical swabs for chlamydia and gonorrhoea, HVS for trichomonas, temperature, pregnancy test, consider FBC, CRP |
| **Drug treatment:** | Ceftriaxone 250 mg* IM stat AND Doxycycline 100 mg bd for 2 weeks<br>When symptoms are moderate/severe add metronidazole 400 mg bd for 2 weeks<br>Alternatively if compliance is likely to be poor:<br>Ceftriaxone 250 mg* IM stat AND azithromycin 1 g stat |
| **Drug treatment in pregnancy:** | Referral for specialist assessment is indicated. Admission may be required for IV antibiotics. |
| **Other management:** | Decision to remove IUCD should be made depending on the individual patient. Evidence suggests that treatment of PID can be successful in the presence of an IUCD. |

| Epididymo-orchitis | |
|---|---|
| **Best test:** | FVU for chlamydia, urethral swab for gonorrhoea, dipstick urine, MSU if suspect UTI |
| **Drug treatment:** | If STI pathogens suspected:<br>Ceftriaxone 250 mg* IM stat AND doxycycline 100 mg bd for at least 2 weeks<br>If UTI pathogens suspected:<br>Amoxycillin/clavulanic acid 500 mg tid for 2 to 3 weeks or<br>Ciprofloxacin 500 mg bd for 10–14 days |
| **Other management:** | Bed rest, analgesics and scrotal elevation are recommended |

| Molluscum Contagiosum | |
|---|---|
| **Best test:** | Clinical observation – look for firm flesh coloured bumps, often with waxy centres. |
| **Treatment options:** | Reassure and observe – in many cases no specific treatment is necessary.<br>Cryotherapy / curettage / diathermy.<br>Sterile sharp stick to remove contents (iodine or phenol may be applied).<br>Podophyllotoxin or imiquimod. |
| **Treatment in pregnancy:** | Podophyllotoxin is contraindicated and imiquimod should also be avoided. |
| **Other management:** | If infection occurs, topical antibiotics may be required |

* Although most guidelines recommend ceftriaxone 250 mg for gonorrhoea, PID or epididymo-orchitis, currently the smallest unit amount available in New Zealand is a 500 mg ampoule. For the sake of simplicity some clinicians may choose to use a whole vial for one patient, i.e. 500 mg. Five ampoules are available on a PSO.

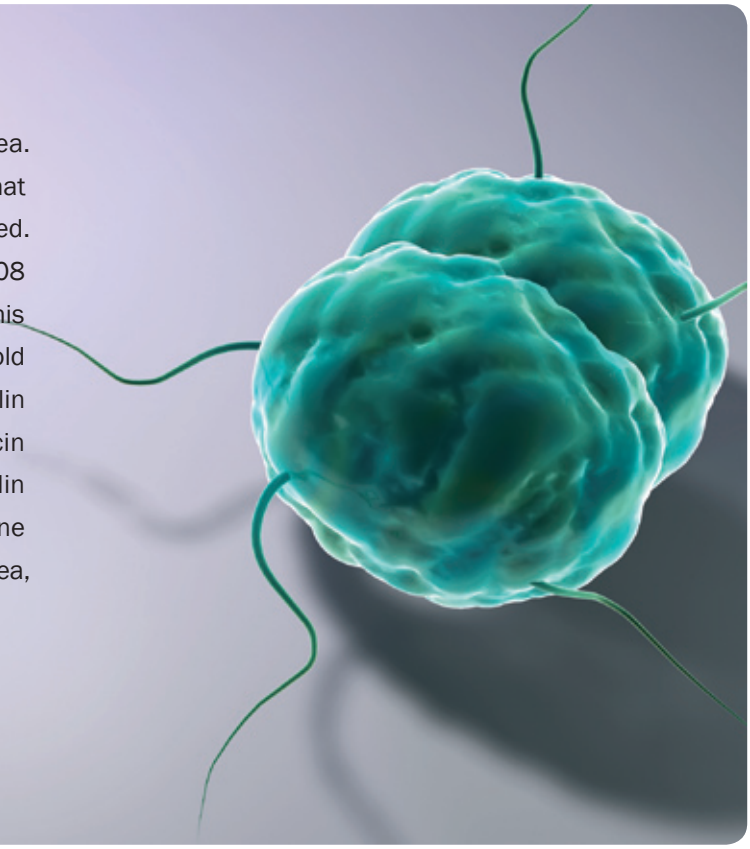
**Table adapted from the following references:**


1. Counties Manukau DHB. Primary Care Sexual Health Workstream. Available from www.healthpoint.co.nz. (Accessed March 2009).
2. Chlamydia Management Guidelines. Ministry of Health. July 2008. Available from http://www.moh.govt.nz/moh.nsf/pagesmh/8210/$File/chlamydia-management-guidelines.pdf (Accessed March 2009).
3. Kyle C. (ed). A Handbook for the Interpretation of Laboratory tests. 4th edition: Diagnostic Medlab; 2008.


## Ciprofloxacin resistance

Penicillin was originally used to treat gonorrhoea. However increasing penicillin resistance meant that empiric treatment with ciprofloxacin was favoured. But data collected by ESR between 2007 and 2008 shows that ciprofloxacin resistance is at 22%. This far exceeds the acceptable 5% resistance threshold for first-line therapy. The national rate of penicillin resistance for 2007/2008 was 6%. Ciprofloxacin resistance is now more prevalent than penicillin resistance in most areas of New Zealand. Ceftriaxone injection is advised for treating suspected gonorrhoea, unless susceptibility data is available.

Full report available from:
**http://www.surv.esr.cri.nz/PDF_surveillance/Antimicrobial/Gono/Gono2008Q1.pdf**



# The use of **insulin** in **Type 2 Diabetes**

Key reviewer: **Dr Rick Cutfield**, Diabetologist, Waitemata DHB

## Key points:

- Insulin is under used in people with type 2 diabetes
- There is evidence that early initiation of insulin is beneficial
- Initiation of insulin requires a team approach and close follow up
- Start with low doses of insulin and then slowly but steadily titrate until target $HbA_{1c}$ is reached
- Combined therapy with insulin and oral metformin can result in improved glycaemic control, less weight gain and fewer hypoglycaemic episodes

## Insulin often required for best management of type 2 diabetes

The challenge of achieving optimal blood glucose control in people with type 2 diabetes is something faced on a daily basis by many GPs. The progressive effects of diabetes on beta cell function and insulin resistance mean that oral anti-diabetic medications become less effective with time.[1] Best management of type 2 diabetes therefore inevitably results in consideration of the use of insulin.

The task of initiation of insulin therapy has traditionally been undertaken in a secondary care setting. Factors such as the increasing prevalence of diabetes, an aging population, financial constraints, the push for tighter control and the earlier need for insulin to achieve this mean that this role will increasingly fall to primary health care teams.[2,3]

## Insulin is under used in people with type 2 diabetes

There is evidence that insulin is under used in people with type 2 diabetes.[4,5] Studies show that for most people with type 2 diabetes, a target $HbA_{1c}$ level of 7% is not achieved, $HbA_{1c}$ levels are higher than recommended by most guidelines for extended periods of time (at least 12 months) and changes to treatment may not occur until mean $HbA_{1c}$ is 9% or more.[1, 5] Even after intensification of treatment, there is evidence that the $HbA_{1c}$ remains above the target level for at least another six months, because insulin doses are not titrated as frequently as required.[1]

## The benefits of adding insulin

Insulin can be the most effective drug for controlling hyperglycaemia in people with diabetes. It has more potential to lower blood glucose than oral medication and its use is limited only by hypoglycaemia.[10,11] There is increasing evidence that if insulin is initiated early then beta-cell damage and hence disease progression may be slowed.[12, 13] It is also now known that sulfonylureas, which stimulate the beta-cells to secrete insulin, may actually accelerate beta-cell failure.[14]

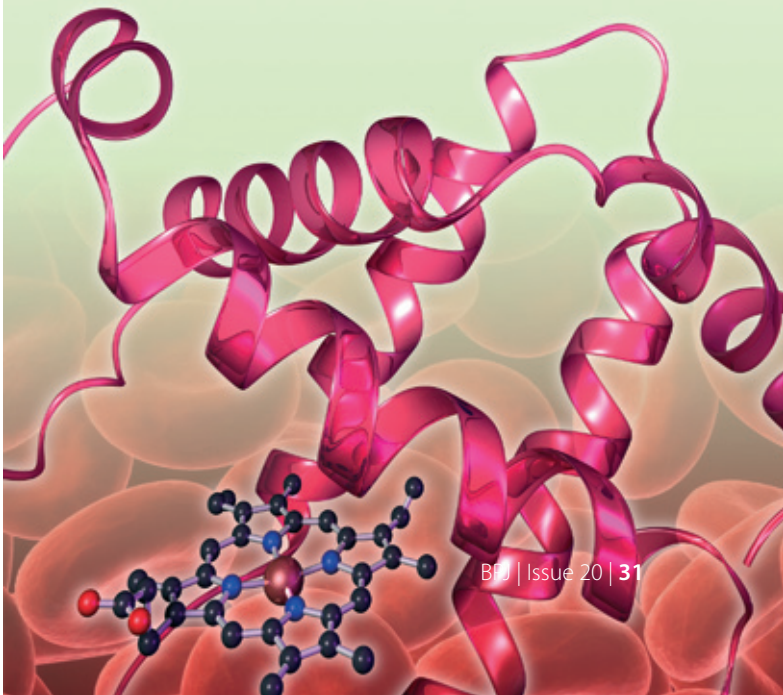
## What is an acceptable $HbA_{1c}$?

A target $HbA_{1c}$ of 7% remains the ideal for all diabetic patients. This may not be a realistic target for everyone but generally the lower the $HbA_{1c}$ the better and any reduction in level is beneficial.[6] A higher $HbA_{1c}$ may need to be negotiated in people who have frequent hypoglycaemic episodes or hypoglycaemic unawareness, in elderly people who are frail or have significant comorbidities and in people at risk of hypoglycaemia who may live alone.[6]

The current New Zealand guideline recommends that an individual target $HbA_{1c}$ is negotiated with each patient taking into account the following factors:[6]

- Risk factors (e.g. age, BMI, blood pressure, lipid status). The type and number of risk factors may influence treatment decisions particularly about insulin
- Presence of complications or comorbidities
- Adverse effects of therapy, particularly hypoglycaemia
- Patient choice
- Psychosocial circumstances e.g. frailty, age, living alone, mental illness, chaotic lifestyle

New evidence shows that reducing $HbA_{1c}$ below 7% is unlikely to be beneficial for older patients with long standing disease.[7] These patients with predominantly macrovascular complications, may not benefit from lowering $HbA_{1c}$ below 7%, if other vascular risk factors are controlled.[8, 9]



## Barriers to the use of insulin.[10, 11, 12, 15]

**Patient**

- The thought of injections
- Adverse effects including weight gain and hypoglycaemia
- The feeling they have failed
- Misconceptions about treatment with insulin – pre-existing ideas are often based on negative experiences from others
- Practical considerations (including the "hassle" factor)
- Technical skills and equipment required for self monitoring blood glucose (SMBG) and injections
- The possible impact on driving – this may impact on their job (e.g. taxi, passenger service vehicle, see page 36)
- Thoughts of discrimination or employment restrictions at work
- "Live for today" people – some people prefer to live with an increased risk of complications, particularly in situations where they currently have no symptoms that impact on day to day life

**Doctor**

- The complexity of the initiation process and of educating patients
- "Clinical inertia" [11]
- The need to change the view of insulin as a threat, punishment or last resort that is used only after patients have "failed"
- Adverse effects (e.g. weight gain, hypoglycaemia) including countering any patient anxiety about these
- Lack of resources, primarily time and personnel

**Most people with type 2 diabetes will eventually require insulin**

Endogenous insulin production will decrease over time for all people with type 2 diabetes. Most people with type 2 diabetes will eventually require insulin. Understanding this right from the time of diagnosis, is likely to reduce the shock, when it is decided that insulin is required. Starting insulin is likely to be a significant event for any patient – for many it will be overwhelming.[11] However if discussed early, it is less likely to be seen by patients as a failure or punishment.

Best practice tip: Tell patients they are not failing, only their beta cells are!

## When should insulin be initiated?

**Insulin is part of the normal progression in the management of people with type 2 diabetes**

Insulin should be considered in all people with type 2 diabetes who have unsatisfactory glycaemic control, despite lifestyle support and maximal oral hypoglycaemic agents. For a patient with significant hyperglycaemia who is already on maximal oral agents, the move to insulin should be immediate. The presence of diabetic complications and personal patient preference may also influence the decision to initiate insulin.

It is difficult to set an $HbA_{1c}$ level where insulin should always be initiated, as it will vary from patient to patient. One problem that GPs have, is knowing when to escalate treatment, and there is a tendency to leave people with type 2 diabetes with high $HbA_{1c}$ levels for long periods of time. This occurs both with initiation and titration of oral therapy and with initiation of insulin. Insulin should be viewed as just another step in the treatment ladder, and the most important thing is that action is taken, if the $HbA_{1c}$ level is unacceptable for a particular patient.

Occasionally insulin will need to be started in a person newly diagnosed with type 2 diabetes. Often these patients will be unwell with weight loss, hyperglycaemic symptoms

and significant ketonuria and require referral for hospital treatment.

**Are there patients who may not benefit from insulin?**

Early initiation of insulin is beneficial for younger patients who have a high lifetime risk of complications.[16] However in some older patients with no complications, the risks of insulin treatment may outweigh the benefits particularly if there is a short history of diabetes, no symptoms and less likelihood of complications developing in the patient's lifetime.

Initiation of insulin may not be a suitable option for the following groups of people:

- Some patients who are morbidly obese – treatment with insulin alone can increase weight which may make control of their diabetes more difficult
- Asymptomatic elderly people – if there is only a short history of diabetes then long term complications may not be a concern within their lifetime
- People with mental health problems or other comorbidites that may mean they are unable to cope with insulin treatment
- People in whom the potential risks outweigh the potential benefits

## The simplest insulin regimen is the addition of an intermediate acting insulin to existing oral medication.

A recent review has shown no consensus in the choice of insulin regimen.[17] In general practice the simpler insulin regimens are easier to initiate and manage, however they will not suit everyone. Specialist advice may be required.

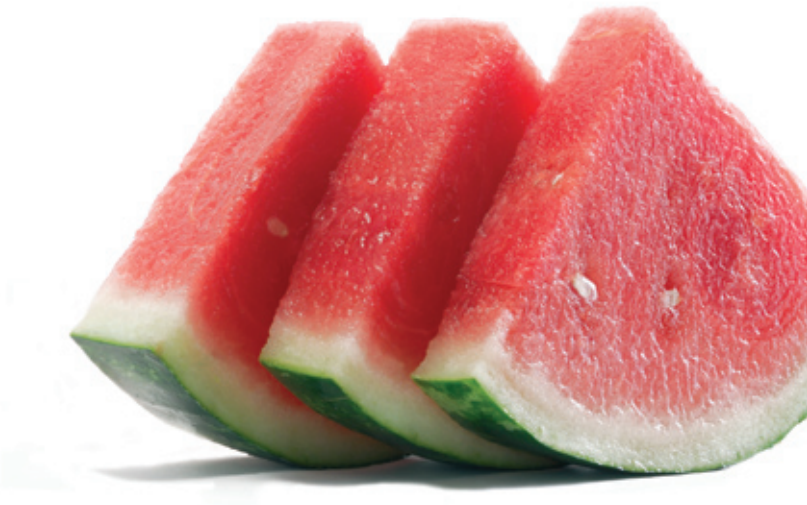
The simplest insulin regimen to initiate in general practice is the addition of an intermediate acting insulin to existing oral medication. Evidence supports the ongoing use of oral metformin,[17] however sulfonylureas should usually be stopped. The easiest approach is to stop the sulfonylurea when insulin is initiated, although some clinicians wean the dose over three months. Always reinforce the importance of continuing a good diet and maintaining exercise levels.

The advantages of combining oral therapy and insulin include:

- A simpler treatment regimen with minimum injections (at least initially)
- Less risk of hypoglycaemia because the starting dose can be lower and increases made gradually
- Better glycaemic control in the initial introduction and adjustment stage.
- Lower risk of weight gain

### Autoimmune diabetes in adults

In people with type 2 diabetes who have a BMI <25, a history of thyroid disease or who are younger it is worth checking GAD (glutamic acid decarboxylase) antibodies, as some will have an adult form of type 1 diabetes and may do better with early initiation of insulin alone.



## An example of a once daily insulin regimen

1. Start with 8–10 units of protophane or Humulin NPH usually before bed e.g. 9 to 11pm
2. Continue oral metformin at current dose e.g. 1 g twice daily
3. Minimum SMBG for this regimen is:
   - Pre-breakfast to titrate the dose and check for morning hypoglycaemia
   - Pre-evening meal to check for hypo or hyperglycaemia and give information for varying the regimen if control is not achieved
   - Two hours post-evening meal to check for surging glucose level as this may require a different insulin regimen

   Once stable, SMBG should be done as often as required to allow freedom from hypoglycaemia and to give information to keep $HbA_{1c}$ at the target level e.g. three to four times a day, two to three days per week.
4. Dose should be titrated aiming to achieve a pre-breakfast glucose of 6 mmol/L.

For the majority of patients, starting insulin as an evening dose is recommended. This is because high morning fasting glucose levels, due to excessive glucose production overnight, are characteristic of poorly controlled type 2 diabetes. Some elderly patients who have higher levels in the afternoon however may respond better to insulin given in the morning.

**Once initiated, adjust the insulin dose slowly**

Once initiated, slow increases in insulin dose are recommended.[16] This is likely to reduce the risk of hypoglycaemia and increase both patient and doctor confidence. Depending on fasting SMBG results, the dose of insulin should be increased every one to two weeks as necessary.

One suggested method of titration is to increase the insulin dose by: [16]

- 2 units if pre-breakfast glucose readings are consistently above 6 mmol/L
- 4 units if pre-breakfast glucose readings are consistently above 8 mmol/L

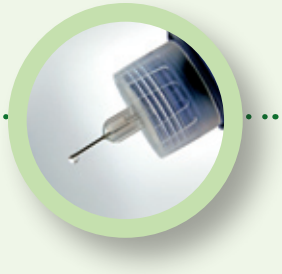
These gradual increases can continue for the first two to three months and then the $HbA_{1c}$ should be rechecked. Ideally there should be a reduction in $HbA_{1c}$ of about 1%. If this is not the case then check the patient is still using the insulin and also continuing to take their oral metformin.

Over the next six to twelve months, further gradual increases in insulin dose may be required depending on $HbA_{1c}$ levels. The majority of people with type 2 diabetes are insulin resistant so the insulin doses required may be higher than expected.[18] People who are obese and those who had high initial $HbA_{1c}$ levels are likely to need the highest doses.

If $HbA_{1c}$ remains above target level once fasting glucose levels are normalised, information from SMBG (pre-evening meal and two hours after meals) will help guide a change of insulin regimen. This may require a move to a twice daily premixed insulin regimen (e.g. Penmix 30:70 or Humalog Mix 25) or the addition of rapid acting insulin pre-meals. At this stage advice from a specialist diabetes team is often useful.

**Normalising blood sugar**

Slow is best. Sudden normalisation of long standing high blood glucose levels can in some cases cause temporary progression of complications e.g. diabetic retinopathy, insulin neuritis (acute symptomatic neuropathy) or pseudo hypos (hypo symptoms at normal glucose levels). These usually settle with time.



# Getting started with insulin

## A team approach is required

Successful initiation of insulin in a primary care setting requires education, resources and time and is likely to require input from GP, practice nurse, pharmacist and diabetic educators. Realistically in most general practices the education and support that the patient requires will be undertaken by the practice nurse.

There is a lot of information that needs to be given to the patient. Check that they fully understand what treatment with insulin involves. It may be useful to encourage them to talk to someone who is already doing well on insulin. If the patient is still uncertain or reluctant it may be helpful to suggest a three month trial.

Before starting insulin the patient needs to develop the technical skills to self monitor blood glucose (SMBG) and self inject. Generally once they have overcome the psychological barrier of the injections they will persist with treatment.

## What needs to happen once the decision to start insulin is made?

Initiating insulin is likely to require a longer consultation and multiple visits. How much and just what information is conveyed at each contact will depend on the individual patient and the complexity of the regimen to be started.[15]

The key information required should initially cover;

- SMBG techniques and frequency
- Injection technique including injection sites
- Reinforcement of the need for a good diet and maintaining exercise levels
- Hypoglycaemic awareness and treatment
- Storage of insulin, disposal of needles

## The choice of delivery device

For the simple regimen discussed on page 34 there is a choice of two insulin's (protophane or Humulin NPH) and therefore two pen devices available. Protophane is manufactured by Novo Nordisk and requires a NovoPen. Humulin NPH is manufactured by Eli Lilly and requires a Humapen. An insulin pen from one manufacturer will not fit insulin cartridges from another manufacturer.

Individual patient preference for a particular pen may determine the brand of insulin although in more complicated regimens the choice of a specific type of insulin will determine the type of pen (e.g. switching to Humalog Mix 25 requires a Humapen Luxura). Factors which may guide choice include the patient's manual dexterity, any visual impairment and the size of the dose likely to be required.

The reusable pen devices are usually preferred by patients as they are convenient and discrete and may improve compliance. Injections with pens are thought to be easier, faster and more accurate.

## How to help patients overcome their fear of injections

A good tool to help get over the fear of self injection is to give a "dummy injection". This can help with fears accompanying the thought of the actual injection – how easy is it, how do you do it, where does it go, does it hurt, what are the likely problems with injections. Once a patient has given a supervised injection they are often relieved how easy and relatively painless it is. A pen with placebo

may be given to the patient to practice at home prior to the next consultation. For patients who may have a needle phobia, the NovoPen 3 PenMate could be considered. It is an additional device that is used with a NovoPen 3 to conceal the needle.

## Check that the patient knows how to monitor their blood glucose

SMBG is not routinely recommended for patients with type 2 diabetes who are on diet or metformin alone, however once a patient is started on insulin it is necessary. It is important to check that patients have the equipment and skills to do this. How often they will need to perform SMBG will depend on their individual insulin regimen. For example with the simple insulin regimen discussed on page 34, this will initially be at least three times every day, until stable then perhaps three days per week. The key is that testing is done to guide dose changes and to look for trends in high and low glucose levels.

## Other practical issues at the time of initiation

1. When? The ideal time to schedule the first injection is earlier in the week so that the patient can be seen again if required. A low dose of intermediate acting insulin at night will seldom cause problems with hypoglycaemia in the day or overnight. Driving restrictions are not usually needed but patients should test before driving.
2. Where? Some patients prefer the surgery setting, for others home may be preferable.
3. Do they require a support person? Having a partner, friend, carer or family member present may help in recall of information, providing support and transport home.
4. Do they know who to contact in an emergency? Make sure they have appropriate contact numbers written down and consider a Medic Alert emblem.
5. Do they know how to store their insulin and what to do with sharps?
6. Do they know what to do if they are unwell, when they exercise, or if the weather is hot? (this may be learnt over time rather than at initiation)
7. Do they know that it is important to contact the practice regularly e.g. weekly to enable titration of doses?

## Regular follow up is required

Regular follow up will be required, usually weekly initially, with perhaps more frequent phone contact. This contact provides an ideal opportunity for dose titration, provision of more detailed dietary advice, reinforcement of good injection techniques and time for answering any questions that may have arisen. Written information to back up verbal instructions should be provided. Information pamphlets are widely available.

## LTSA requirements

People with type 2 diabetes who use insulin are generally considered fit to drive, however vocational drivers will need to see a diabetes specialist for individual assessment. If in doubt about any patient's driving risk, refer to a local diabetes team.

A person may be deemed unfit to drive if they have severe or recurrent hypoglycaemia or if they have hypoglycaemia unawareness i.e. they are unable to detect developing hypoglycaemia and to respond to it appropriately and in good time.

For further information see the LTSA website: **www.landtransport.govt.nz/licensing/medical-aspects/4.html**

## References:


1. Calvert MJ, McManus RJ, Freemantle N. Management of type 2 diabetes with multiple oral hypoglycaemic agents or insulin in primary care: retrospective cohort study. Br J Gen Pract. 2007;57:455-60.
2. Agarwal G, Nair K, Cosby J et al. GP's approach to insulin prescribing in older patients: a qualitative study. Br J Gen Pract. 2008;58:569-75.
3. van Adendonk MJP, Gorter KJ, van den Donk M, Rutten GEHM. Insulin therapy in type 2 diabetes is no longer a secondary care activity in the Netherlands. Prim Care Diab. 2008.
4. Riddle MC. The underuse of insulin therapy in North America. Diabetes Metab Res Rev. 2002;18:s42-s49.
5. Jones S, Benroubi M, Castell C et al. Characteristics of patients with type 2 diabetes mellitus initiating insulin therapy: baseline date from the INSTIGATE study. Curr Med Res Opin. 2009;25(3):691-700.
6. New Zealand Guideline Group. Management of Type 2 Diabetes. 2003. Available from www.nzgg.org.nz (Accessed February 2009).
7. Lehman R, Krumholz HM. Tight control of blood glucose in long standing type 2 diabetes. BMJ 2009;338:b800.
8. ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patient with type 2 diabetes. N Engl J Med. 2008;358:2560-72.
9. Duckworth W, Abraira C, Moritz T et al. Glucose control and vascular complications in veterans with type 2 diabetes. N Engl J Med. 2008;360:129-39.
10. Hayes RP, Fitzgerald JT, Jacober SJ. Primary care physician beliefs about insulin initiation in patients with type 2 diabetes. Int J Clin Pract. 2008;62(6):860-8.
11. Meneghini L. Demonstrating strategies for the initiation of insulin therapy: matching the right insulin to the right patient. Int J Clin Pract. 2008;62(8):1255-64.
12. Tibaldi J, Rakel RE. Why, When and how to initiate insulin therapy in patients with type 2 diabetes. Int J Clin Pract. 2007;61(4):633-44.
13. Hirsch IB, Bergenstal RM, Parkin CG et al. A real-world approach to insulin therapy in primary care practice. Clin Diab. 2005;23:78-86.
14. Aston-Mourney K, Proietto J, Morahan G, Andrikopoulos S. Too much of a good thing: why it is bad to stimulate the beta cell to secret insulin. Diabetologia. 2008;51:540-5.
15. Royal College of Nursing. Starting insulin treatment in adults with type 2 diabetes. 2004.
16. Wong J, Yue D. Starting insulin treatment in type 2 diabetes. Aust Prescr. 2004;27:93-6.
17. van Avendonk M, Rutten GEHM. Insulin therapy in type 2 diabetes: what is the evidence? Diab Obes Metab. 2009.
18. American Association of Clinical Endocrinologists Diabetes Mellitus Clinical Practice Guidelines Task Force. AACE Medical Guidelines for Clinical Practice for the Management of Diabetes Mellitus. Endocr Pract. 2007;13(Suppl 1).

www.bpac.org.nz keyword: bronchiolitis

# **Bronchiolitis** Update

Key reviewer: **Dr Philip Pattemore**, Associate Professor of Paediatrics, University of Otago, Christchurch

## Key Points:

- Bronchiolitis is the most common lower respiratory tract infection seen in infants less than 12 months of age
- Most cases are caused by Respiratory Syncytial Virus (RSV) but other viruses can be involved
- Bronchiolitis is a highly infectious viral illness and measures to prevent infection and recurrence of infection are important
- Māori and Pacific infants suffer proportionally more morbidity from bronchiolitis
- Risk factors for bronchiolitis (e.g. environmental factors, exposure to others with viral illness) should be managed if possible
- Management of bronchiolitis in general practice is supportive. There is no indication for bronchodilators, inhaled or systemic corticosteroids or antibiotics

In BPJ 5 (May, 2007) we discussed the assessment and management of bronchiolitis. With the bronchiolitis season on the horizon we provide an update with emphasis on differential diagnosis, treatment options, indications for referral and preventative strategies.

## Bronchiolitis is a seasonal viral disease commonly seen in infants

Bronchiolitis is the most common lower respiratory tract infection seen in infants less than 12 months of age, with a peak incidence at three to six months. Most cases are caused by Respiratory Syncytial Virus (RSV) but it can also be caused by rhinovirus and less commonly other viruses such as parainfluenza viruses, adenovirus and influenza A and B viruses. Certain adenoviruses can cause a severe bronchiolitic illness with pneumonia. This can damage small airways and lead to bronchiolitis obliterans and bronchiectasis.

The RSV season in New Zealand is from June to October with the peak for bronchiolitis admissions occurring in July and August.

## Symptoms of bronchiolitis

Bronchiolitis usually starts with a two to three day prodromal phase of coryzal symptoms. Other symptoms and signs include cough, rapid respiratory rate, hyperinflation and wheeze and crackles. Fever does not always occur but if present it is usually low grade (less than 39°C). Absence of fever should not preclude a diagnosis of bronchiolitis. In the first 72 hours of the illness infants may get worse before starting to improve.[2, 3]

Increased respiratory rate can be a marker of the severity of bronchiolitis, but apnoea may be a presenting feature, especially in very young or premature infants. Many infants will have poor feeding as result of dyspnoea and feeding problems are often a reason for hospital admission. Bronchiolitis can be assessed as mild, moderate or severe (Table 1).[2] Most infants with acute bronchiolitis will have mild disease and can be managed at home with

## Bronchiolitis in Māori infants

A five year bronchiolitis study at Lakes DHB from 2003-2007 found that 80% of children admitted were Māori and the majority (over 70%) were from the poorest housing deciles.[1] Bronchiolitis is easily spread in poorer, overcrowded households. Smoking is another significant factor.

Tu Kotahi Māori Asthma Trust provides a bronchiolitis service within the Hutt Valley where the majority of referrals received are young Māori whānau. The service offers home visits to assess the baby (oxygen level, chest, pulse and temperature). A key aspect of the service is the opportunity to reinforce understanding of the illness, its symptoms and the likely course it will take.

The main issues encountered by this service are a general lack of understanding of the disease and the reasons why medication is not prescribed. A clear explanation that bronchiolitis is a viral infection can help parents to understand and accept why medication is not required.

Situations frequently encountered by Tu Kotahi that increase the risk of bronchiolitis include:

- Damp housing
- Inadequate heating
- Overcrowding
- Whānau who are unable to provide adequate clothing for their children over the winter months
- Transport and access problems to health care resources

When whānau visit the GP, key questions about housing and the social environment should be asked. There are a number of options that can be investigated by community health workers regarding home insulation, possible subsidy of power bills and clothing banks.

**Table 1:** (adapted from New Zealand Guidelines).[2, 3]

| | Assessment of severity of bronchiolitis | | |
|---|---|---|---|
| | **Mild** | **Moderate** | **Severe** |
| **Respiratory rate** breaths/minute | < 2 months > 60/min<br>2–12 months >50/min | > 60/min | > 70/min |
| **Chest wall indrawing** | None/mild | Moderate | Severe |
| **Nasal flare and/or grunting** | Absent | Nasal flare possible, grunting absent | Present |
| **Feeding** | Normal | Less than usual<br>Frequently stops<br>Quantity > ½ normal | Not interested<br>Choking<br>Quantity < ½ normal |
| **History of behaviour** | Normal | Irritable | Lethargic |
| **Cyanosis** | Absent | Absent | Present |

support. However, it is important to provide caregivers with information on how to recognise deterioration in the infant's condition, and what to do if this occurs.

A recent consensus guideline from the UK defined bronchiolitis as a "seasonal viral illness characterised by fever (not always present), nasal discharge and dry wheezy cough. Cough is usually dry and wheezy and along with nasal symptoms is one of the earliest symptoms to occur in bronchiolitis.[3] On examination there are fine inspiratory crackles and /or high pitched expiratory wheeze.[4]

## Consider other causes of wheeze

Diagnosis is made clinically based on a typical history (e.g. wheeze with recent coryzal symptoms and/or cough) and findings on clinical examination. Wheeze is usually a prominent characteristic of bronchiolitis but can also occur in other conditions common in infants and young children, primarily, asthma, transient infant wheeze (see box) and rarely pneumonia.

The frequency of presentation of these wheezing phenotypes is influenced by age, with RSV bronchiolitis occurring almost exclusively in the first 12 months of life and peaking at six months.

Only a minority of infants who wheeze in the first year of life will have asthma. Some of these infants will have strong risk factors, such as parental asthma or eczema. A definite response to bronchodilators and asthma can be recognised from an early age. In others, the trend towards a recurrent wheezy illness responsive to bronchodilators, is only apparent after a period of months or years. Risk factors for asthma include eczema in the infant, wheeze without a cold (interval symptoms), more than two episodes of wheezing with a cold and family history of atopy.

Transient infant wheeze is thought to be due to smaller than normal airways and is associated with exposure to tobacco smoke and early viral infections. Acute attacks of wheezing tend to occur with viral upper respiratory tract infections.

Fine inspiratory crackles in all lung fields are a common finding in acute bronchiolitis but are not a characteristic of asthma. Infants with no crackles and only intermittent wheezing are unlikely to have true bronchiolitis but may have viral bronchitis with wheeze, or other acute or recurrent causes of wheeze.[3] Coarse crackles, which clear or change on coughing, indicate the presence of mucus in large airways which can occur in asthma.

The presence of wheeze, in addition to increased respiratory rate and indrawing, may indicate a diagnosis of bronchiolitis rather than pneumonia. However, it should be noted that wheeze may occasionally be seen in infants aged less than two months with pneumonia.[2]

### Inhaled corticosteroids

Although bronchodilators and corticosteroids appear to be frequently used in primary care to treat acute bronchiolitis there is no evidence to support this practice. Hospital based studies have shown no benefit from inhaled corticosteroids on respiratory symptoms or length of hospital stay, and a systematic review concluded that oral prednisolone did not prevent wheeze, when given for the first seven days of acute bronchiolitis.[3] Some trials have shown short term clinical benefits of inhaled beta-2 agonists, but their use does not appear to reduce hospital admission rates or the length of hospital stay. [3]

**Investigations are rarely necessary**

Investigations, with the exception of oximetry, are not routinely indicated in the diagnosis or in determining the severity of bronchiolitis. If there are concerns about hypoxia, or if oxygen saturation is less than 92%, the infant should be referred.

Routine blood and urine cultures are not recommended for infants presenting with uncomplicated bronchiolitis. FBC, ESR and CRP are not reliable predictors of disease severity and are not helpful for differentiating between bacterial and viral infection. Chest X-ray is not routinely indicated and is not useful for differentiating between viral and bacterial infection.

## Treatment is supportive

**Bronchodilators, inhaled or systemic corticosteroids or antibiotics are not recommended for the treatment of bronchiolitis in primary care.[2, 3]**

The management of bronchiolitis in primary care is focused on providing support and information. In the first 72 hours of the illness infants may get worse before starting to improve. An infant who is seen early in the course of the illness may need to be re-assessed to check for any deterioration.[2] Parents/caregivers of infants who have been assessed with mild or moderate illness, where symptoms have been present for more than 72 hours, need only reassurance.[2]

Caregivers should be given clear information about how to recognise any worsening of the infant's condition and asked to bring the infant back for reassessment if this occurs. It is also important to inform caregivers of the location of support services, such as after hours clinics or hospitals, in case the infant's condition deteriorates.

**When to refer**

Infants with severe symptoms or who deteriorate may require referral for consideration of oxygen, nasogastric feeding and intravenous fluids.

Refer all infants with:

- Respiratory rate > 70/min
- Nasal flare and grunting
- History of apnoea
- Poor feeding - lack of interest, choking, less than 50% of usual fluid intake in the preceding 24 hours
- Lethargy
- Severe chest wall recession
- Cyanosis

The threshold for referral to hospital should be lowered in infants less than two months of age, or those born at less than 32 weeks gestation, and infants with respiratory or cardiac comorbidity (e.g. chronic lung disease, congenital heart disease).[2]

Social factors such as the home environment, ability of caregivers to cope and distance to a hospital may also determine the need to refer.

A comprehensive fact sheet for caregivers is available from **www.kidshealth.org.nz** (keyword: bronchiolitis). A one page summary is shown on the opposite page. This can be also be downloaded from **www.bpac.org.nz** keyword: bronchiolitis.

### Re-infection is common

As re-infection is common, advice should be given on how to reduce the risk of infection, and how to prevent the spread of infection to other infants in the family/whānau.

- Take time to clearly explain bronchiolitis, what is meant by a viral infection and check the parents understanding. Provide simple written information if possible
- Ask about housing conditions and find out about services in your community that may be able to assist if needed
- Encourage parents to keep rooms, where the baby lives, at a constant comfortable temperature
- Encourage and support a smokefree environment
- Encourage parents to return or seek assistance if there are concerns about baby's breathing, ability to feed or general wellbeing
- Bronchiolitis is easily spread, so encourage good hygiene practices such as hand washing before and after handling the baby. People who have a cold or flu-like illness should try and avoid contact with infants.

## Post bronchiolitic wheeze

Acute bronchiolitis, especially when severe, is associated with a later risk of recurrent wheezing episodes.[3] It is not known if bronchiolitis is the cause, or whether there are prior genetic or environmental factors, that predispose to respiratory disease.

Approximately 10% of children will have wheezing episodes after age five.[2] But evidence shows that in the majority the increased risk of wheeze dissipates by the age of 13 years.[2] A recent Cochrane Review did not find any evidence that inhaled corticosteroids, given during acute bronchiolitis, are effective in the prevention of post-bronchiolitic wheezing.[5]

### References


1. Lakes DHB. Five year bronchiolitis study at Lakes District Health Board. Available from https://www.asthmanz.co.nz/files/PDF-files/CREW/REC2008/Presentations/Ngaroma_Grant.pdf (Accessed February 2009).
2. Paediatric Society of New Zealand. Wheeze and chest infection in infants under one year. Best practice evidence based guideline. Available from www.nzgg.org.nz (Accessed February 2009).
3. Scottish Intercollegiate Guidelines Network. Bronchiolitis in children. SIGN Guideline 91. November, 2006.
4. Lakhanpaul M, Armon K, Eccleston P et al. An evidence based guideline for the management of children presenting with acute breathing difficulty. Nottingham University, 2002.

   Available from; http://www.nottingham.ac.uk/paediatric-guideline/breathingguideline.pdf (Accessed, March 2009).
5. Blom D, Ermers M, Bont L, van Aalderen WM, van Woensel JB. Inhaled corticosteroids during acute bronchiolitis in the prevention of post-bronchiolitic wheezing. Cochrane Database Syst Rev. 2007 Jan 24;(1):CD004881.

# Caregiver advice for bronchiolitis

**Your child has bronchiolitis. This is very common in children under one-year-old and is caused by a virus. Bronchiolitis can usually be managed safely at home**

## 1. What to expect and how you can help your child

You can expect your child to get a lot better after the first three days, although their cough may linger for several weeks.

Medicines are not helpful for children with bronchiolitis but you can help keep your child comfortable by:

- Offering small feeds of breast milk or infant formula regularly
- Keeping your baby warm but not too hot
- Giving your baby as much rest as possible
- Don't smoke in the house or around your baby
- Keeping your baby's nose clear. If it is blocked or crusty you can use saline nose drops (from a pharmacy)
- Keeping your baby away from other children so as not to spread the disease

## 2. When should I seek help?

You can expect your child to improve so you should get urgent advice from a doctor or nurse if they get worse. Any one of the following may be a sign of the illness getting worse:

- Breathing fast, has noisy breathing and is having to use extra effort to breathe
- Looking unwell and/or very pale
- Taking less than half of their normal feeds
- Vomiting
- Has not wet a nappy for six hours

## 3. Danger signals

The following are danger signs. Dial 111 or contact a doctor immediately if your child has any of the following:

- Blue lips and tongue
- Severe difficulty breathing
- Is becoming less responsive
- Is pale
- Is floppy
- Periods of stopping breathing

**This note tells you:**

- What to expect and how you can help your child
- How to recognise when you should get urgent advice
- How to recognise danger signals

### Healthline is available for free, confidential health advice 24 hours a day

Healthline nurses do not diagnose over the phone but will assess the situation and provide advice as to the best course of action.

Call 0800 611 116 from either a landline or a mobile phone.

### Your child may need a further check up

Your Doctor or Nurse may want to check your child even if things appear to be going as expected. If you have been advised to have a check up, write the details here:

Check up time and date:

At the following location:

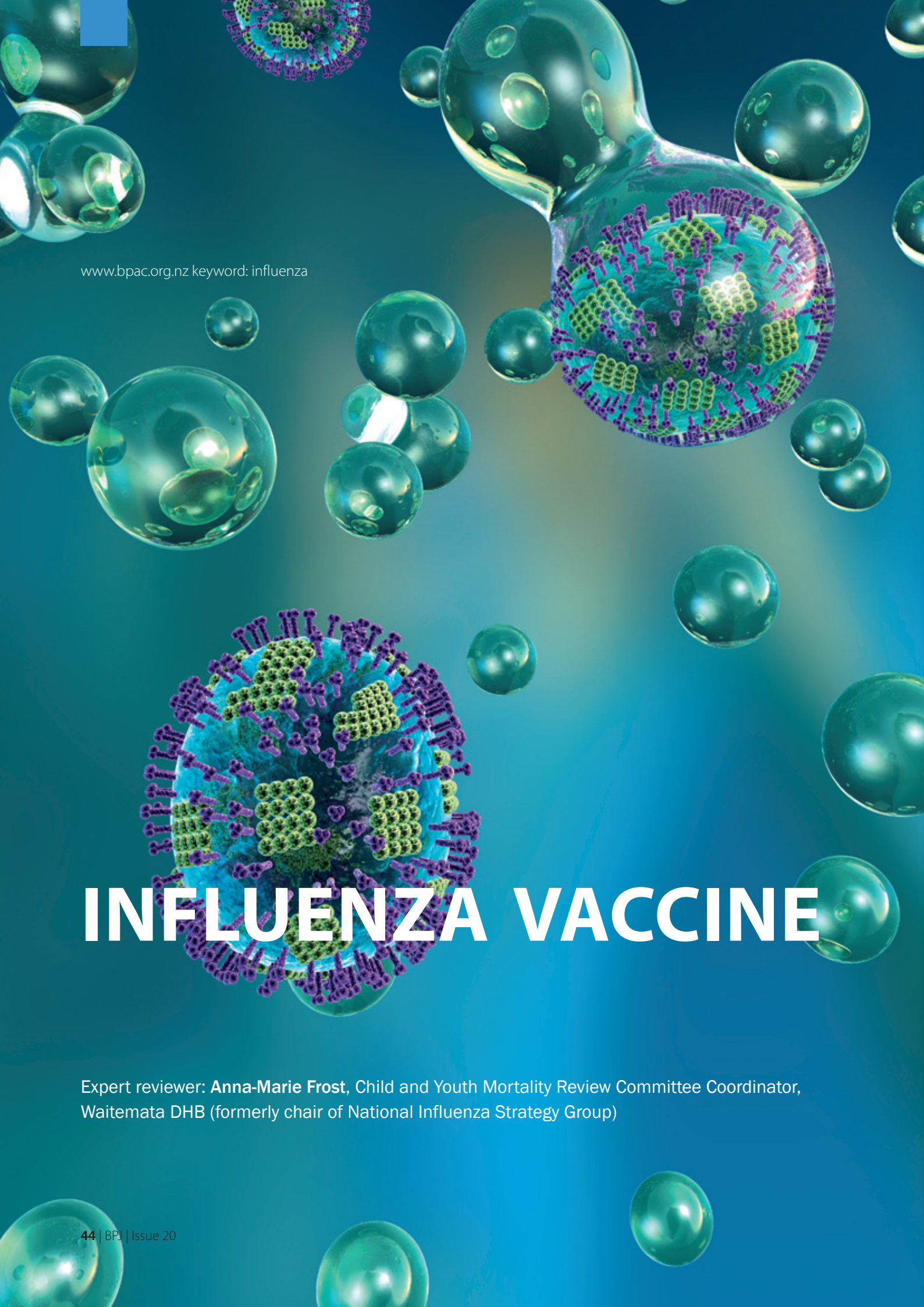
Name of person doing the check up:

Phone number:

For more information visit:

**www.kidshealth.org.nz**

www.bpac.org.nz keyword: influenza



# INFLUENZA VACCINE

Expert reviewer: **Anna-Marie Frost**, Child and Youth Mortality Review Committee Coordinator, Waitemata DHB (formerly chair of National Influenza Strategy Group)

# influenza

## Influenza is a highly infectious acute respiratory disease

Influenza is characterised by fever, headache, severe malaise, myalgia, cough, sore throat and runny nose. While cough and malaise can persist for weeks, acute illness usually only lasts for about three days.[1]

Seasonal rates of influenza vary from year to year. Mortality rates depend on spread and virility of the virus. Approximately one in five people will catch influenza each year and approximately 40 New Zealanders die from influenza annually.

## The influenza vaccine

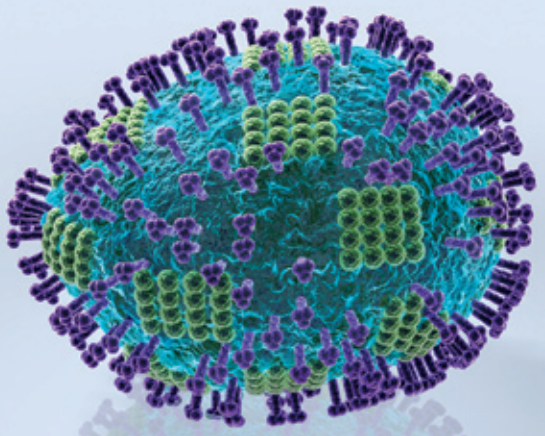
The influenza virus has a marked ability to mutate, therefore strains are surveyed each year and new vaccines against influenza are designed to match the circulating strains most likely to cause influenza activity over the winter months.[2]

Influenza vaccines for 2009, Fluvax and Vaxigrip, contain the following inactivated virus strains.[4]

- A/Brisbane/59/2007 (H1N1) – like virus
- A/Brisbane/10/2007 (H3N2) – like virus
- B/Florida/4/2006 – like virus

## Potentially deadly influenza strain for 2009

The "Brisbane strain", contained in this year's vaccine, killed six children in Australia last year and has medical authorities in Europe warning that it could be the most deadly influenza virus seen for 20 years. Oseltamivir-resistant strains have also been seen in the United States this season. These factors combined with low immunisation rates, seen in both the general public and in health professionals, could result in a potentially severe influenza season this year[3]



**Influenza immunisation is the most effective protection against influenza**

Influenza vaccination is approximately 70–90% effective at preventing infection in healthy adults, when the vaccine and circulating influenza strains are well matched.[4, 5] In elderly people, vaccination is less effective at preventing infection, however it reduces the risk of death from influenza by 48%, and reduces the risk of hospitalisation for pneumonia or influenza by 27%.[4]

**The vaccine is free for those at high risk of influenza and complications**

The incidence of influenza is usually higher in children, elderly people and those living in crowded conditions. Elderly people and people with chronic co-morbidity are most at risk of complications including pneumonia, bronchitis, exacerbations of chronic respiratory disease and death.[5]

Anyone can be immunised against influenza however the influenza vaccine is funded until June 30, 2009 for the following people:[4]

1. Anyone aged 65 years or over
2. Anyone over six months old with chronic medical conditions, such as:
   - Cardiovascular disease (ischemic heart disease, congestive heart failure, rheumatic heart disease, congenital heart disease, cerebrovascular disease)
   - Chronic respiratory disease (asthma if on preventive therapy; other chronic respiratory disease with impaired lung function)
   - Diabetes
   - Chronic renal disease
   - Cancer (patient currently has cancer), excluding basal and squamous skin cancers if not invasive
   - Other conditions (autoimmune disease, immune suppression, HIV, transplant recipients, neuromuscular and CNS diseases, haemoglobinopathies, children on long term aspirin*)

* aspirin therapy puts children at risk of Reye's syndrome if they develop a fever

People with the following conditions are **not** eligible for the funded vaccine:

- Asthma not requiring regular preventive therapy
- Hypertension and/or dyslipidaemia without evidence of end-organ disease
- Pregnancy in the absence of other risk factors that meet the eligibility criteria

### There are very few contraindications to the influenza vaccine

Influenza vaccine should not be given to people who have had an anaphylactic reaction to eggs, chicken proteins, neomycin, polymyxin B or any other vaccine components.[4] Vaccination should be delayed in people who have acute systemic illness or fever over 38°C.

### Pregnancy is not a contraindication to influenza immunisation

Maternal influenza immunisation has substantial benefits for both mothers and infants. One study showed that maternal immunisation against influenza reduced rates of respiratory illness with fever in both infants and mothers.[6]

Evidence shows there is no risk to the foetus from vaccinating pregnant women with inactivated viral vaccines. Influenza vaccination is safe for breastfeeding women.[3, 4]

In the UK, influenza vaccine is recommended for pregnant women who are in the high risk group, regardless of their stage of pregnancy. For other pregnant women, it is recommended that vaccination is delayed until after their first trimester.

In New Zealand, influenza vaccines are licensed for use after the first trimester (i.e. greater than 14 weeks gestation) and are recommended for women who are beyond their first trimester during the influenza season.[7, 8] Influenza vaccine is only funded for pregnant women with other risk factors that meet the eligibility criteria (see above).

### Children

Influenza immunisation of children with chronic co-morbidities is currently recommended and funded in New Zealand.

In the US, in addition to children with co-morbidities, it is recommended that all children aged less than five years are immunised, as well as caregivers of children aged under five years.[9]

Children have high rates of influenza and are often the major cause of influenza spread in the community. The benefit of influenza immunisation appears greater in children than adults. Immunising healthy children also results in less influenza in their families.[4]

Parents who wish to immunise their healthy children against influenza can purchase the vaccine.[4]

### Healthcare workers

Influenza immunisation is effective in healthy adults. Immunisation of healthcare workers has additional benefits because it protects patients who are at risk of serious complications of influenza.[2, 4]

However, there are low immunisation rates in New Zealand healthcare workers, with influenza vaccination uptake reported to be only approximately 20–40%.[10] One survey of Canterbury District Health Board employees, who were offered free influenza vaccine in 2004 and 2005, showed that uptake was greatest in laboratory workers and administration staff, followed by doctors and the lowest uptake was by nurses (estimated 16%).[11]

Consent is required prior to giving the injection. This can be written consent or documentation of verbal consent. It is good practice to record what was discussed and that consent was obtained.[8]

### Vaccine administration and dosage

Influenza vaccine can be given intramuscularly or subcutaneously.

It is usually given:[2]

- By intramuscular injection to the vastus lateralis muscle on the lateral thigh for infants under 15 months of age
- By intramuscular injection to either the vastus lateralis or deltoid muscle for young children over 15 months
- By intramuscular injection into the deltoid muscle for adults, adolescents and older children
- By deep subcutaneous injection for people with a bleeding disorder

Patients are required to stay for 20 minutes after receiving the influenza vaccine to allow monitoring for immediate allergic reaction.

See Table 1 for vaccine doses.

### Influenza vaccines are well tolerated

The most common adverse effect reported following vaccination, affecting 10–64% of individuals, is mild tenderness at the immunisation site. Rarely, systemic reactions such as fever, malaise, and myalgia occur and usually only last one to two days.[5] Immediate allergic reactions such as urticaria, bronchospasm and anaphylaxis are rare.[2]

### Influenza immunisation is required before the influenza season begins

In New Zealand, the influenza season usually occurs between May and September but may occur earlier or later.[4] In 2007, influenza activity peaked in July but was low overall compared to previous years.[12]

The effectiveness of the influenza vaccine does not rapidly diminish, however as there is significant change in influenza viruses circulating each year, annual immunisation is necessary. It takes up to two weeks for the vaccine to induce immunity therefore it is recommended that people are immunised against influenza as soon as the current year's vaccine is available and before the expected exposure to high influenza activity in May to September.

**Table 1:** Recommended vaccine doses in adults and children

| Age | Dose |
|---|---|
| Children aged 6 – 35 months | 0.25 mL; repeated 4 weeks later if receiving vaccine for the first time* |
| Children aged 3 – 8 years | 0.5 mL; repeated 4 weeks later if receiving vaccine for the first time* |
| Adults and children 9 years of age and over | A single injection of 0.5 mL |

*Two doses are required to produce a satisfactory immune response in children less than 9 years of age who have not previously received the influenza vaccine (i.e. in the first year they receive the vaccine).[8] Children under nine, who received only one dose in their first year of vaccination, should receive two doses the following year.

### Health professional endorsement of influenza vaccination increases uptake

Health professional endorsement of influenza vaccination is one of the most effective measures to increase vaccination uptake. An important message to give patients is that the influenza vaccine cannot cause influenza because it contains no live viruses.[4] Emphasise that the vaccine is made from inactivated virus which means it is incapable of producing infection within the body.

Influenza vaccinations can be carried out in dedicated "flu clinics", opportunistically when a patient presents for a consult, or in workplaces. When actively organising eligible patients to come in for influenza immunisation there is evidence that reminding patients by letters, postcards, telephone or face-to-face is effective in increasing vaccination rates. Reminding people by telephone and providing multiple reminders can be more effective but is also likely to cost more.[2, 13]

### www.influenza.org.nz

This website contains information and resources about influenza immunisation including:

- The "Influenza Kit" information booklet
- Posters and other materials for informing patients about influenza vaccination
- Example recall letters and PMS downloads for query builders



**References:**

1. Worrall G. Influenza. Can Fam Phys 2008; 54: 415-6.
2. Clinical Knowledge Summaries. Immunisations – Influenza. Available from http://cks.library.nhs.uk/immunizations_influenza (Accessed February 2009).
3. Frost AM. Giving flu jab your best shot. NZ Doctor 2009.
4. National Influenza Strategy Group. 2009 Influenza Kit. Available from: http://www.influenza.org.nz/ (Accessed February 2009).
5. Hall R. Influenza immunisation. Australian Prescriber 2002; 25(1): 5-7.
6. Zaman K, Roy E, Arifeen SE, et al. Effectiveness of maternal influenza immunisation in mothers and infants. N Engl J Med 2008; 359: 1555-64.
7. Sanofi Pasteur. Vaxigrip Datasheet. Available from: http://www.medsafe.govt.nz/profs/Datasheet/v/Vaxigripinj.htm (Accessed February 2009).
8. Ministry of Health. Immunisation Handbook 2006. Wellington: Ministry of Health. Available from: http://www.moh.govt.nz/moh.nsf/indexmh/immunisation-handbook-2006 (Accessed February 2009).
9. Committee on Infectious Disease. Prevention of Influenza: Recommendations for influenza immunization of children, 2007-2008. Pediatrics 2008; 121(4): e1016-e1031.
10. McLennan S, Celi LA, Roth P. The Health and Safety in Employment Act and the influenza vaccination of healthcare workers. N Z Med J 2007; 120(1250). Available from: http://www.nzma.org.nz/journal/120-1250/2442/ (Accessed February 2009).
11. Jennings L. Influenza vaccination among New Zealand healthcare workers: low rates are concerning. N Z Med J 2006; 119(1233). Available from: http://www.nzma.org.nz/journal/119-1233/1961/ (Accessed February 2009).
12. Influenza in New Zealand 2007. Available from: http://www.surv.esr.cri.nz/virology/influenza_annual_report.php (Accessed February 2009).
13. Jacobson Vann JC, Szilagyi P. Patient reminder and recall systems to improve immunization rates. Cochrane Database Syst Rev 2005; 3 (CD003941).

# THE SOCIAL RESPONSIBILITY OF SMOKERS

www.bpac.org.nz keyword: smoking

Key reviewer: **Dr Hayden McRobbie**, Senior Lecturer, Department of Community Health Development, School of Public Health and Psychosocial Studies, Auckland University of Technology

It is estimated there are approximately 600 000 smokers in New Zealand.[1] Each of these people will be at different stages of the quitting spectrum – from having absolutely no desire to quit through to a significant proportion having already made a quit attempt. But in the meantime, until the quit attempts are successful, those around them continue to be exposed to the risks associated with their smoking.

Many smokers are aware of the risk to others, and have already taken steps to minimise this. It is becoming more common for people to choose to make their homes and cars smokefree, and many people choose not to smoke around babies or young children.

Other smokers may not have considered that they are putting other people at risk. It is worthwhile ensuring all smokers are aware of the risks they pose to others. This risk is greater for babies and children where involuntary exposure is an issue.

Non-smokers can be exposed to smoke by two recognised ways:

- "Second hand smoke", which is exposure to cigarette smoke from someone smoking nearby, often described as "the exposure that occurs as an unavoidable consequence of breathing in a smoke-filled environment".[2]
- "Third hand smoke" – which is residual tobacco smoke and particles remaining after the cigarette is extinguished.

## Second hand smoke

Second hand smoke (also known as environmental tobacco smoke) is made up of approximately 85% "sidestream smoke" – smoke emitted from the burning end of the cigarette, and 15% "mainstream smoke" – smoke exhaled by smokers. Sidestream smoke poses the greatest risk because it has not been filtered.

### Second hand smoke – at home and work

Approximately 10% of New Zealanders are regularly exposed to second hand smoke in their homes, with Māori being more likely to be exposed.[3]

In a 2001 survey of Year 10 students, in which neither parent smoked, approximately 11% of children were exposed to second hand smoke in their homes, from either visitors or other household members.[4]

In the 1980s workplace exposure to second hand smoke was estimated at 34% for men and 23% for women.[5] There has however, been a marked drop in workplace exposure to second hand smoke, following the banning of smoking in most workplaces in the early 1990s.

### The effects of second hand smoke

There is no safe level of second hand smoke exposure. In New Zealand, second hand smoke is considered to contribute to over 350 deaths per year.[5] This represents an additional 8% over and above deaths due to first hand smoking. Numerous reviews have concluded that second

hand smoke is a significant contributor to disease. It is well recognised that people exposed to second hand smoke have an increased risk of lung cancer, coronary heart disease, stroke and sudden infant death syndrome. It has been estimated that in New Zealand, second hand smoke exposure in the home will contribute to approximately 15,000 episodes of childhood asthma annually, more than 27,000 medical consultations for child respiratory problems and 1500 operations to treat glue ear.[5]

Higher levels of exposure from second hand smoke are associated with higher risk.

However, second hand smoke poses risks even at lower levels. Brief exposure to second hand smoke, which is defined as 15–30 minutes exposure, has been demonstrated to produce measurable changes in coronary blood flow.[6]

People may be concerned by the potentially harmful effects of involuntary exposure to second hand smoke in outdoor settings, such as walking past someone smoking, or sitting next to a smoker. However, a recent study has demonstrated that in this situation the smoke is rapidly dispersed into the environment, and poses little risk.[7]

## Third hand smoke

"Third hand smoke" is a recently coined phrase that refers to the particles and gases that linger in a room after someone has smoked, or remain in the clothing, hair or possessions of people who have been exposed to smoke. Although "third hand" smoke is recognised as a risk to non-smokers, there is a lack of evidence to quantify the extent of this risk.

Some of the volatile components of cigarette smoke (e.g. nicotine, naphthalene) are absorbed into surfaces within minutes of emission, and can be re-emitted into the air over the following days and weeks. In cars, surfaces such as upholstery, carpets and roof liners act as reservoirs for residual tobacco smoke. There is also concern that residual tobacco smoke particles accumulating inside cars may be further potentiated by the effects of sunlight, extreme temperature and limited air exchange.

Children are generally considered more susceptible to the effects of third hand smoke because they may touch, mouth, play and crawl on contaminated surfaces.

## Keeping others safe

Most people (including smokers) accept that smoking is associated with adverse health outcomes. People continue to smoke for a number of reasons, and some will find it difficult to ever quit. But while they continue to smoke, it is important they think about the risks to those around them.

In 2004, the Smokefree Homes campaign was developed by the Health Sponsorship Council (HSC) and The Quit Group. The campaign aimed to increase protection for non-smokers by informing people about the dangers of second hand smoke, and to protect the health of non-smokers by encouraging smokers to smoke outside. The campaign emphasised the importance of smokers protecting their children from second-hand smoke, by using the message "taking the smoke outside".

In 2006, the Smoke Free Cars campaign was launched. This campaign encouraged smokers to protect their children from the harms of second hand smoke by not smoking in their car, even when they are alone. The key messages were that second hand smoke is dangerous to the health of children, and that winding down a window does not rid a car of the poisons contained in second hand smoke, as they linger long after the smoke has disappeared.

In addition to encouraging smokers to quit, health professional are well placed to educate patients to minimise the risk to others. There are a number of resources available to encourage people to make their cars and homes smoke free. These are available from:

**www.secondhandsmoke.co.nz**

**www.quit.org.nz**


www.quit.org.nz


www.secondhandsmoke.co.nz

Order this patient information from **www.bpac.org.nz**

keyword: resources

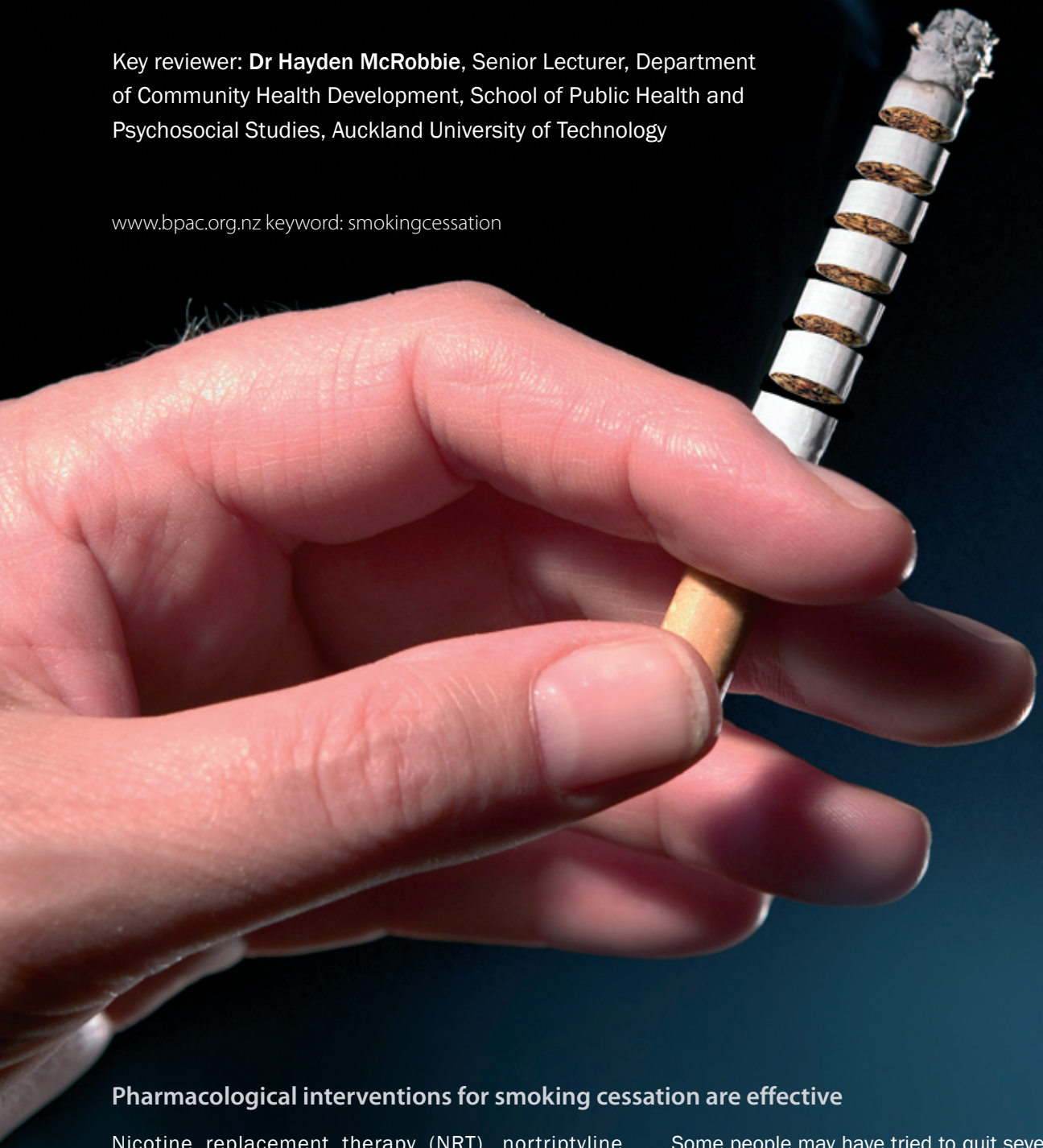

## References


1. Ponniah S, Bloomfield A. Sociodemographic characteristics of New Zealand adult smokers, ex-smokers, and non-smokers: results from the 2006 Census. N Z Med J 2008;121(1284):34-42.
2. Office of the Surgeon General. The health consequences of involuntary exposure to tobacco smoke.
3. Thomson G, Wilson N, Howden-Chapman. Smoky homes: a review of the exposure and effects of secondhand smoke in New Zealand homes. NZ Med J 2005;118:1213.
4. Scragg R, Laugesen M, Robinson E. Parental smoking and related behaviours influence adolescent tobacco smoking: results from the 2001 New Zealand national survey of 4th form students. N Z Med J. 2003;116(1187).
5. Woodward A, Laugesen M. Morbidity attributable to second hand cigarette smoke in New Zealand. Wellington: Ministry of Health; 2001. Available from http://www.moh.govt.nz/ (Accessed March 2009).
6. Otsuka R, Watanabe H, Hirata K, et al. Acute effects of passive smoking on the coronary circulation in healthy young adults. JAMA 2001;286(4):436-41.
7. Klepeis NE, Ott WR, Switzer P. Real-time measurement of outdoor tobacco smoke particles. J Air Waste Manag Assoc 2007 May;57(5):522-34.

# Smoking cessation – Pharmacological therapy

Key reviewer: **Dr Hayden McRobbie**, Senior Lecturer, Department of Community Health Development, School of Public Health and Psychosocial Studies, Auckland University of Technology

www.bpac.org.nz keyword: smokingcessation



## Pharmacological interventions for smoking cessation are effective

Nicotine replacement therapy (NRT), nortriptyline, bupropion and varenicline can be effective aids to smoking cessation. For people who have not tried any of the pharmacological therapies for smoking cessation, initial choice can be guided by preference.

Some people may have tried to quit several times before with medication. When choosing a pharmacological intervention for them it is advisable to select one that was previously effective in suppressing the urge to smoke.[1]

It is not advisable to use a medication that:[1]

- Previously caused significant adverse effects for the patient
- Was previously not very effective in suppressing the urge to smoke
- The patient does not believe works

It is useful to explain the risks and benefits of each treatment and allow the patient to help decide which is best for them.[1] NRT is often used initially because of long term experience with its use, its safety profile and cost-effectiveness.[2]

Approximately two to three percent of people who attempt to stop smoking, will quit with no pharmacological or behavioural intervention.[2]

### NRT is suitable for most people trying to stop smoking and is available subsidised via Quit Cards

NRT effectively aids smoking cessation, approximately doubling the chances of long term abstinence compared with no treatment.[2] Approximately one in 14 people who would have not otherwise stopped smoking, will do so for at least six months after completing a course of NRT, i.e., the number needed to treat (NNT) for NRT is 14 for abstinence at six months.[2]

NRT is available subsidised on Quit Cards which can now be distributed by general practitioners, nurse practitioners, midwives and dentists. Quit Cards can be ordered at: **http://www.quit.org.nz/page/providers/QuitCards.php**

This website also contains a useful flow chart for initiating people on NRT, including which type and strength NRT to choose, and recommendations for pregnant or breastfeeding women and people aged less than 18 years.

See article on page 58 for more information about NRT

### Nortriptyline almost doubles the chances of long-term abstinence from smoking

Nortriptyline is as effective as NRT or bupropion in aiding smoking cessation.[2] The NNT is 11 for abstinence at six months. The efficacy of nortriptyline appears to be independent of its antidepressant effects, and is not restricted to people with a history of depression or depressive symptoms, during smoking cessation.[3]

Common adverse effects associated with nortriptyline include drowsiness, dry mouth, constipation and nausea.[2] It can also be dangerous in overdose.[3]

**Dose**

Nortriptyline is started while the patient is still smoking and the quit date is set for ten to 28 days later. Initially 25 mg per day is taken and this may be increased up to 75 mg over ten days to five weeks as adverse effects allow. The maximum dose should be taken for eight to twelve weeks and tapered down at the end to avoid withdrawal symptoms.[1, 2]

### Bupropion approximately doubles the chances of long term abstinence from smoking

Bupropion therapy approximately doubles the likelihood of smoking cessation.[3] The NNT is 11 for abstinence at six months.[2] Adverse effects associated with bupropion include insomnia, dry mouth and nausea. It is also associated with an increased risk of seizures (estimated to be about one in 1000).[3] This risk is further increased for people with a pre-existing seizure disorder, anorexia nervosa or bulimia (or history), or those concomitantly using drugs that lower the seizure threshold.[4]

**Dose**

Bupropion is started while the person is still smoking. Initially 150 mg (one tablet) is taken daily for the first three days followed by 150 mg twice daily from day four. The evening dose can be taken early to avoid wakefulness however there should be at least eight hours between doses.[2]

**Table 1:** Comparison of drug treatments for smoking cessation [8]

| | NRT | Nortriptyline | Bupropion | Varenicline |
|---|---|---|---|---|
| **Effectiveness** | Approximately doubles the chances of long-term abstinence<br>NNT = 14 | Approximately doubles the chances of long-term abstinence<br>NNT = 11 | Approximately doubles the chances of long-term abstinence<br>NNT = 11 | Approximately doubles to triples the chances of long-term abstinence<br>NNT = 8 |
| **Clinically significant adverse effects** | – | Adverse effects on cardiovascular function (e.g. ECG changes, arrhythmias) | Increased risk of seizures (risk approximately 1 in 1000) | None noted but post-marketing cases of depression, suicidal ideation and myocardial infarction. Currently being monitored by IMMP |
| **Contraindications** | – | Acute recovery phase following an MI | History of seizures, eating disorders, bipolar disorder<br>Acute alcohol withdrawal<br>Breastfeeding | – |
| **Clinically significant drug interactions** | – | MAOI's – concomitant use is contraindicated | Any drug known to lower the seizure threshold (e.g. antipsychotics, antidepressants, quinolones, tramadol)<br>MAOI's | – |
| **Available as:** | Patch, gum, inhaler*, lozenge, sublingual tablet* | Tablet | Tablet* | Tablet* |
| **Efficacy affected by previous use** | No | Not known | Yes | Not known |
| **Use in pregnancy** | Yes – intermittent products such as gum or lozenges are preferred as total daily dose is lower than patches | Wide experience and considered safe however may be more appropriate to use NRT | Not recommended | Not recommended |
| **Use in people with CVD** | Yes | Best avoided | Yes | Yes |
| **Approximate cost to patient of one course of treatment** | $15 for 12-week course of patches, gum or lozenges ($5 per item) | $3 for a 12-week course | $400 for 8-week course | $700 for 12-week course |

* not currently subsidised

The quit date should be set for between days eight and 14 after starting bupropion. The person can continue to smoke normally up until that point, and should stop completely by day 14, aiming not to have a single puff after this time.[2]

The recommended duration of treatment with bupropion is seven to nine weeks, however longer treatment can be considered for those who need it.[4]

### Varenicline increases the chances of smoking cessation two to three fold

Varenicline approximately doubles to triples the chance of long-term smoking cessation compared with no pharmacological treatment.[5] The NNT is eight for abstinence at six months. Studies have shown varenicline to be more effective than bupropion.[5] One open-label trial showed it to be moderately more effective than NRT, at end of treatment, however this difference disappeared at one year follow up.[6] The efficacy of varenicline on abstinence rates beyond 12 months has not been clearly established.[5, 7]

Common adverse effects include nausea and abnormal dreams. Nausea is often mild to moderate, usually subsides over time and can be minimised by taking varenicline with food and water.[1] There have been reports of serious psychiatric adverse effects, including depression and suicidal thoughts and behaviours (see BPJ 13, May 2008 for further information). There have also been reports of serious cardiac adverse effects such as myocardial infarction. Varenicline is currently being monitored on the Intensive Medicines Monitoring Programme (IMMP), and all clinical events occurring in people taking this medication, should be reported.

#### Dose

The recommended dose of varenicline is:

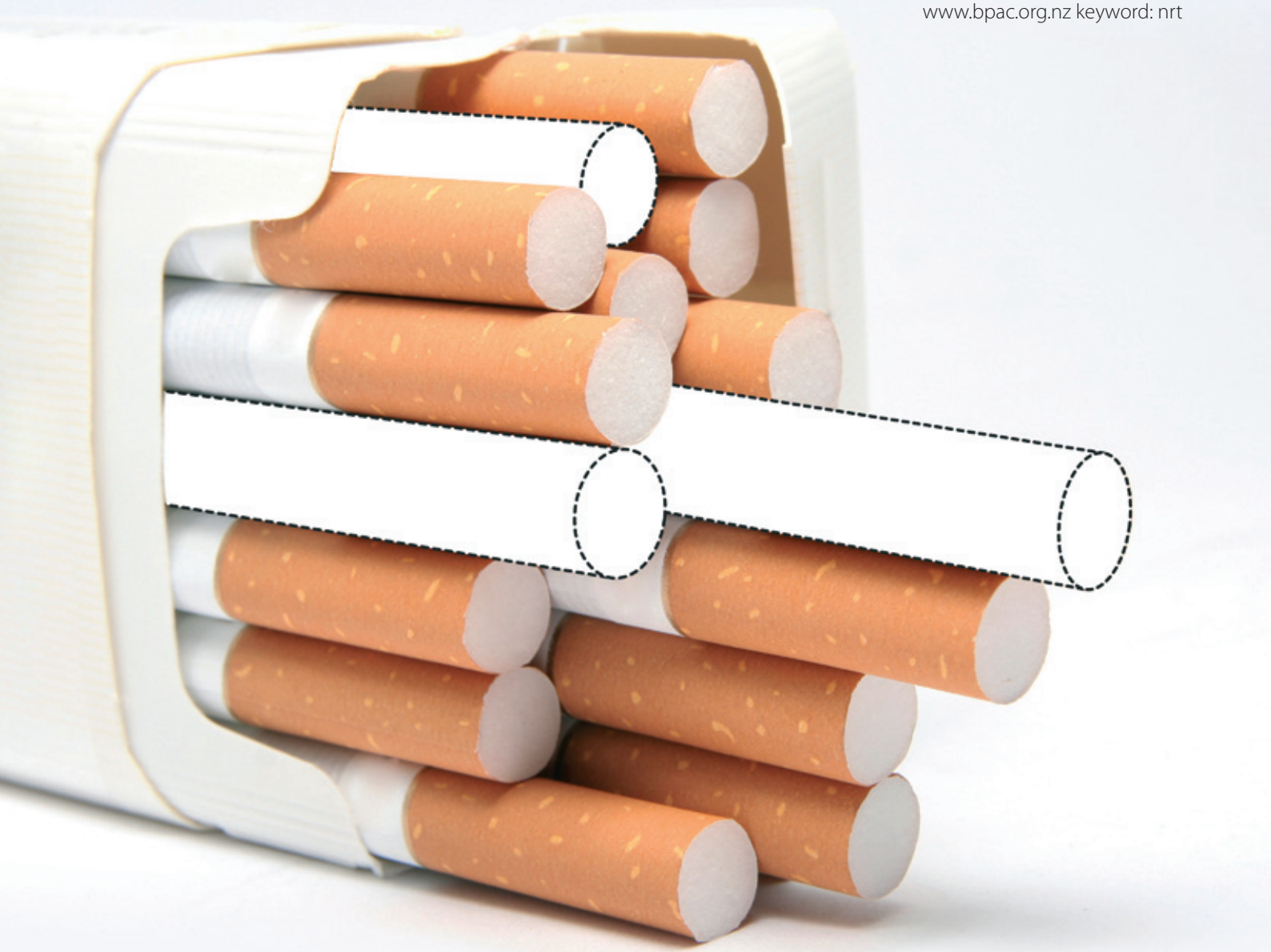
- 0.5mg daily for three days
- Followed by 0.5 mg twice daily for the next four days
- Continue with 1 mg twice daily starting at day eight and continuing through until the end of the 12 week course.

Varenicline is started while the patient is still smoking and they should stop smoking one to two weeks later. An initial course is 12 weeks long and patients who have successfully stopped smoking at 12 weeks, can continue on varenicline for an additional 12 weeks, to increase the chances of long term abstinence.[4]

See Table 1 for comparison of pharmacological treatments.

**References:**


1. Aveyard P, West R. Managing smoking cessation. BMJ 2007; 335: 36-41.
2. Ministry of Health. New Zealand Smoking Cessation Guidelines 2007. Wellington: Ministry of Health.
3. Hughes JR, Stead LF, Lancaster T. Antidepressants for smoking cessation. Cochrane Database of Systematic Reviews 2007; 1 (CD000031).
4. Rennard ST, Daughton DM. Management of smoking cessation. UpToDate 2008. Available from: www.uptodate.com (Accessed February 2009).
5. Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. Cochrane Database of Systematic Reviews 2008; 3 (CD006103).
6. Aubin HJ, Bobak A, Britton JR, et al. Varenicline versus transdermal nicotine patch for smoking cessation: results from a randomised open-label trial. Thorax 2008; 63(8): 717-724.
7. National Prescribing Service (NPS) RADAR. Varenicline (Champix) for smoking cessation. Available from: http://www.npsradar.org.au/ (Accessed February 2009).
8. Clinical Knowledge Summaries. Smoking cessation. Available from: http://cks.library.nhs.uk/smoking_cessation (Accessed February 2009).



# Getting the most out of **nicotine replacement therapy**

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It is known that the majority of people who smoke want to stop and nearly half will try each year.[1] However most will do it without any pharmacological or behavioural support – an approach that is associated with one of the lowest long-term quit rates (only 2–3% of people who quit in this way will succeed in stopping for at least a year). Quit rates can be increased by using a combination of pharmacotherapy and behavioural support.[2]

This article offers five key points that will help healthcare professionals and their patients get the best out of nicotine replacement therapy (NRT).

## 1. NRT is not a "magic cure" but it does help when used correctly

When recommending NRT, it is important to communicate positive and realistic expectations of what can be achieved. NRT roughly doubles the chances of quitting long-term, and this is independent of the degree of behavioural support utilised.[3] It works by reducing the severity of withdrawal symptoms associated with smoking cessation (urges to smoke, irritability, restlessness and poor concentration), and in doing so make quitting easier.[4] Despite strong evidence of effectiveness, NRT is not a "magic cure" and does not stop a person lighting up a cigarette. Some effort is still required.

NRT products are equally effective so the choice of product can be based upon individual preferences (Table 1) and to provide different types of relief. For example the patch may be best to relieve background craving while faster acting products such as nicotine gum or lozenges can relieve acute urges.

**NRT reduces the weight gain associated with stopping smoking**

For those people who are concerned about weight gain there is evidence to show that NRT can reduce weight gain. This effect appears to be dose dependent and continues for as long as the NRT is used.[5, 6]

**Correct use of oral products reduces adverse effects**

Oral NRT products have a hot or peppery taste, which some people may find unpleasant. This taste is due to the nicotine and although the manufacturers have attempted to disguise it with mint or fruit flavourings the gum and lozenges are still relatively unpleasant initially. People can be reassured that they will get used to the taste over a short period of time.

The nicotine from oral NRT products is absorbed through the buccal mucosa. The gum needs to be chewed for a few seconds, then parked against the side of the mouth for a few minutes, then the process repeated. Chewing NRT gum like confectionery chewing gum, or sucking the lozenge too vigorously results in more nicotine being swallowed. This is not harmful but results in less nicotine being absorbed and increases the likelihood of heartburn and hiccups.

## 2. Use enough NRT

People need a sufficient dose of nicotine to relieve withdrawal symptoms. NRT can be likened to analgesics – use enough to take the pain away. If people are struggling with stopping smoking, they may benefit from a higher dose of NRT, or use a combination of NRT products.

**Table 1:** NRT Products Available

| NRT Products Available on the Quit Card Scheme |
|---|
| Patches |
| Gum |
| Lozenges |

| Other NRT products available over the counter |
|---|
| Inhaler |
| Sublingual tablets (Microtabs) |

See the New Zealand Smoking Cessation Guidelines for more detail on product dosing:
**www.moh.govt.nz/moh.nsf/indexmh/nz-smoking-cessation-guidelines**

Combining NRT products (e.g. patch and gum) is safe and increases the odds of quitting smoking, compared with a single NRT product, by approximately 40%.[3]

**Prescribing NRT – dose and type**

The product labels often use cigarette consumption as a guide to NRT dose. For example the Nicotinell Patch data sheet recommends that people smoking 20 or more cigarettes per day should start on the full-strength (21 mg) patch, while those smoking less start on the medium strength (14 mg).[7] The problem with this approach is that consumption does not always correlate well with blood nicotine levels. Smokers can reduce their cigarette consumption but this may not change their blood nicotine levels due to compensatory smoking (smoking more from each cigarette).

In general most daily smokers can be started on a full strength (21 mg) patch and use an additional oral product for acute urges to smoke. If there is concern that this dose might be too high (e.g. in a long-term five-a-day smoker) then recommend the use of an oral product where the dose can be titrated more easily, i.e. people can use more or less gum or lozenges as required.

**High dependency smokers may require higher doses**

There is evidence that higher dose gum and lozenges are more effective in high dependency smokers (e.g. those who smoke their first cigarette of the day within 30 minutes of waking).[3] The evidence for using higher than standard dose patches e.g. 42 mg (two patches) versus 21 mg is less convincing.

However many of the smoking cessation specialists working within Aukati Kai Paipa (a national smoking cessation service for Māori) have been using a higher dose of patches on their clients with some success. Despite the limited evidence for increasing quit rates there are data to show that higher dose patch therapy is more effective in relieving withdrawal symptoms, in both smokers and smokeless tobacco users, when compared to standard doses.[8, 9]

## 3. Use it for long enough

It is generally recommended that NRT is used for eight to twelve weeks, however a good and simple message is to use it for as long as it takes until the patient feels 100% sure that they can give up smoking. NRT is subsidised

via Quit Cards for as long as it is required. People can be reassured that they are unlikely to become addicted to NRT, but some may need to use it for longer than others, especially those people who are more highly dependent.[10]

## 4. NRT is safe

Compared to smoking, NRT is a safe alternative. It is not associated with increased rates of cancer or heart disease and can be used in the vast majority of people who smoke. Compared to tobacco smoke, NRT supplies less nicotine less rapidly, and without harmful substances. Even in special groups of smokers, such as those who are pregnant and those with severe or acute cardiovascular disease, NRT use usually outweighs the risk of continued smoking.[11, 12]

## 5. Use NRT in a way that best suits the needs of your patient

The phrase "one size does not fit all" is often used in smoking cessation. People have different levels of nicotine dependence as well as different personal circumstances. Therefore different approaches are needed.

In New Zealand NRT is available to help smokers reduce the number of cigarettes smoked before quitting. This "cut down then stop" approach gives people who might be fearful of stopping straight away, a chance to make some positive changes with their smoking behaviour. It does not put people off from quitting altogether, but instead seems to increase the number of quit attempts, as smokers become more motivated and more self confident about quitting.[13]

### Helping people to stop smoking is not impossible

Stopping smoking can be a difficult task for some people but it is not impossible. The key to successfully helping people to quit, is to encourage them to keep trying and to use the available treatments, that will make their attempts more likely to succeed.

## References


1. Ministry of Health. New Zealand Tobacco Use Survey 2006. Wellington: Ministry of Health, 2007.
2. Ministry of Health. New Zealand Smoking Cessation Guidelines. Wellington: Ministry of Health, 2007.
3. Stead LF, Perera R, Bullen C, Mant D, Lancaster T. Nicotine replacement therapy for smoking cessation. Cochrane Database Syst Rev 2008(1):CD000146.
4. West R, Shiffman S. Effect of oral nicotine dosing forms on cigarette withdrawal symptoms and craving: a systematic review. Psychopharmacology (Berl) 2001;155(2):115-22.
5. Gross J, Johnson J, Sigler L, Stitzer ML. Dose effects of nicotine gum. Addict Behav 1995;20(3):371-81.
6. Dale LC, Schroeder DR, Wolter TD, Croghan IT, Hurt RD, Offord KP. Weight change after smoking cessation using variable doses of transdermal nicotine replacement. J Gen Intern Med 1998;13(1):9-15.
7. New Zealand Medicines and Medical Devices Safety Authority. Data sheet: Habitrol Patch. Available online http://www.medsafe.govt.nz/profs/Datasheet/h/HabitrolTTS.htm.
8. Shiffman S, Ferguson SG, Gwaltney CJ, Balabanis MH, Shadel WG. Reduction of abstinence-induced withdrawal and craving using high-dose nicotine replacement therapy. Psychopharmacology (Berl) 2006;184(3-4):637-44.
9. Ebbert JO, Dale LC, Patten CA, Croghan IT, Schroeder DR, Moyer TP, et al. Effect of high-dose nicotine patch therapy on tobacco withdrawal symptoms among smokeless tobacco users. Nicotine Tob Res 2007;9(1):43-52.
10. Hajek P, McRobbie H, Gillison F. Dependence potential of nicotine replacement treatments: effects of product type, patient characteristics, and cost to user. Prev Med 2007;44(3):230-4.
11. McRobbie HH, P. Nicotine replacement therapy in patients with cardiovascular disease: guidelines for health professionals. Addiction 2001;Nov;96((11)):1547-51.
12. Benowitz N, Dempsey D. Pharmacotherapy for smoking cessation during pregnancy. Nicotine Tob Res 2004;6 Suppl 2:S189-202.
13. McRobbie H, Whittaker R, Bullen C. Using Nicotine Replacement Therapy to Assist in Reducing Cigarette Consumption before Quitting Another Strategy for Smoking Cessation? Dis Manage Health Outcomes 2006;14(6):335-40.
14. Ministry of Health. Evaluation of culturally appropriate smoking cessation programme for Māori women and their whanau. Aukati Kai Paipa 2000. Wellington: Ministry of Health, 2003.


# Evidence That Counts

## Antibiotics to Prevent COPD Exacerbations?

*Journal Watch, Vol. 29, No.3, February 1, 2009*

Macrolide antibiotics have anti-inflammatory activity that appears to be distinct from their antibacterial activity. U.K. researchers — postulating that both properties of macrolides might be relevant in chronic obstructive pulmonary disease — conducted this single-centre, randomised trial of prophylactic therapy.

One hundred and nine patients with moderate-to-severe COPD, most of who already were using inhaled steroids and long-acting bronchodilators, received either erythromycin (250 mg twice daily) or placebo. At 12 months, the total number of moderate-to-severe COPD exacerbations was significantly lower in the erythromycin group than in the placebo group (81 vs. 125). Erythromycin recipients also experienced significantly fewer exacerbations per person (median, 1 vs. 2) and shorter duration of exacerbations (median, 9 vs. 13 days). The researchers found no differences between groups in serum and sputum inflammatory markers. Side effects were similar in the two groups, and routine sputum cultures did not reveal new bacterial resistance among erythromycin recipients.

**Comment:**

In this study, low doses of prophylactic erythromycin were associated with fewer and shorter COPD exacerbations. The study's duration and size were insufficient to rule out long-term bacterial resistance or drug toxicity, and the mechanism of benefit was unclear. Current recommendations against long term prophylactic antibiotics for COPD patients are based mainly on research from the 1960s. The current study alone is insufficient to change practice, but a larger NIH-funded multicentre trial (using azithromycin) is in progress.

— Allan S. Brett, MD

**References**

Seemungal TAR et al. Long-term erythromycin therapy is associated with decreased chronic obstructive pulmonary disease exacerbations. Am J Respir Crit Care Med 2008 Dec 1; 178:1139.

Kunisaki KM and Niewoehner DE. Antibiotic prophylaxis for chronic obstructive pulmonary disease: Resurrecting an old idea. Am J Respir Crit Care Med 2008 Dec 1; 178:1098.

Current recommendations for COPD can be found at http://www.goldcopd.com/ free of charge. Details about the larger trial that is in progress can be found at http://www.clinicaltrials.gov/ct2/show/NCT00325897 free of charge.

## Thickened Formula Reduces Reflux in Infants

*Journal Watch, Vol. 29, No.2, January 15, 2009*

Results of previous meta-analyses have suggested that thickening infant formula (e.g., with rice cereal or carob bean gum) does not reduce gastroesophageal reflux (GER), but findings of more-recent studies not included in those meta-analyses are more encouraging. To further evaluate the efficacy of thickened formula, investigators conducted a meta-analysis of data from 14 randomised, controlled trials that involved 877 infants (age, <24 months) with GER.

# Evidence That Counts

The findings were remarkably consistent. Compared with standard formula, thickened formula significantly reduced episodes of regurgitation and vomiting in infants as reported by parents and physicians. Use of thickened formula was associated with a significant increase in weight gain (about 4 g/day) but no significant difference in objective measures of GER by esophageal pH monitoring. Use of thickened formula was significantly associated with diarrhoea in two of the six studies that reported adverse effects.

**Comment:**

These findings confirm the observation of some clinicians that thickened formula reduces GER in infants. The negative results of pH monitoring suggest that signs and symptoms of infant GER cannot always be confirmed objectively. The authors of the meta-analysis were not able to determine whether one thickening agent was more effective than another. Given that thickened formula is inexpensive and generally safe, it is a reasonable intervention for infants with GER, if treatment is indicated.

— Howard Bauchner, MD

**Reference**

Horvath A et al. The effect of thickened-feed interventions on gastroesophageal reflux in infants: Systematic review and metaanalysis of randomised, controlled trials. Pediatrics 2008 Dec; 122:e1268.

Note: commercially thickened formulas are available in New Zealand

## Are UTIs Overdiagnosed in Older Patients?

*Journal Watch, Vol. 29, No.3, February 1, 2009*

Urinary tract infections (UTIs) often are diagnosed in older hospitalized patients. Sometimes, presumed UTI is the reason for admission; sometimes, it is a secondary or incidental diagnosis. Suspecting that clinically relevant UTIs are overdiagnosed in older patients, U.K. researchers performed a retrospective single-centre study of 265 hospitalized patients (age, ≥75) whose primary or secondary discharge diagnoses included UTIs.

Three presentations were considered to be consistent with UTI if a urine culture (collected before antibiotics were started) was positive: (1) acute urinary symptoms; (2) positive blood culture with known uropathogen; and (3) no reported urinary symptoms, but presence of a urinary catheter or a condition that might preclude accurate reporting of symptoms (e.g., dementia, delirium) plus evidence of a septic illness (e.g., fever, leukocytosis). Fully 115 of the 265 patients (44%) did not meet these criteria for UTI. In fact, 37 of these 115 patients had pre-antibiotic urine cultures that were negative — yet, their discharge diagnoses included UTIs.

**Comment:**

Although this study's retrospective design is an important limitation, the results ring true: Older patients commonly are treated with antibiotics for presumed UTIs even when little evidence supports the diagnosis. Reasons for overdiagnosis include the high prevalence of asymptomatic bacteriuria (which can be mistaken for pathogenic infection) in older patients, contamination of urine specimens by leukocytes and bacteria, and perhaps overemphasis on the idea that older patients with UTIs often do not present with specific symptoms.

— Allan S. Brett, MD

**Reference**

Woodford HJ and George J. Diagnosis and management of urinary tract infection in hospitalized older people. J Am Geriatr Soc 2009 Jan; 57:107.

## Imaging Does Not Alter Outcomes in Acute Low Back Pain

*Journal Watch, Vol. 29, No.6, March 15, 2009*

Many physicians continue to order lumbar imaging studies for patients with acute low back pain despite consistent guideline opposition to such imaging in the absence of "red flags" suggestive of serious disease (e.g., cancer, infection, cauda equina syndrome). Little evidence indicates that imaging helps with treatment decisions or improves outcomes, and imaging could result in unnecessary radiation and invasive procedures that are directed at anatomic lesions unrelated to back pain.

In a meta-analysis of six randomised trials, investigators compared clinical outcomes in 1804 patients with acute low back pain who were randomised to immediate lumbar imaging (plain radiography, computed tomography, or magnetic resonance imaging) or usual care without imaging. In all trials, patients with factors that suggested serious disease were excluded; pain and function were outcome measures in all trials. Follow-up ranged from 3 weeks to 2 years. Immediate imaging (plain or advanced) was not associated with any significant differences in short-term or long-term pain, function, quality of life, mental health, or general improvement.

**Comment:**

This meta-analysis strengthens the evidence supporting existing recommendations, but what will convince physicians to adhere to these guidelines? More than mere evidence might be required to overcome patient pressures, fears of litigation, and financial incentives that encourage unnecessary imaging.

— Bruce Soloway, MD

**References**

Chou R et al. Imaging strategies for low-back pain: Systematic review and meta-analysis. Lancet 2009 Feb 7; 373:463.

Kochen MM et al. Imaging for low-back pain. Lancet 2009 Feb 7; 373:436.

## Calcium Supplementation in Healthy Nonosteoporotic Men

*Journal Watch, Vol. 29, No.1, January 1, 2009*

One quarter of all hip fractures occur in men, and 30% of older men experience fragility fractures. However, data are lacking on calcium supplementation for prevention of osteoporosis in men. In a double-blind trial from New Zealand, 323 healthy men (mean age, 57) with normal bone density were randomised to placebo or to calcium supplementation (600 mg daily or 600 mg twice daily). Men with any major active disease or bone-mineral density (BMD) Z scores lower than –2 were excluded.

During 24 months, total body BMD remained stable in the placebo and low dose calcium groups but rose by 1.5% in the high-dose calcium group. Lumbar and mean total-hip BMD of high-dose patients rose relative to BMDs in placebo and low-dose patients. Additional biochemical testing, conducted in a randomly selected subgroup, showed a dosage-related decrease in parathyroid hormone and bone turnover. No significant differences were noted in rates of fractures or serious adverse events in all three groups.

**Comment:**

Many argue that sex bias — favouring men — permeates medical research and clinical medicine. Notably, this trial represents an attempt to redress the tendency to study osteoporosis exclusively in women. The results suggest that

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calcium supplementation is as important for men as it is for women. Additional studies will be required to determine precise dosing regimens (calcium 600 mg daily vs. 600 mg twice daily), the role of vitamin D supplementation in men, and supplementation's effect on fracture risk..

— Jamaluddin Moloo, MD, MPH

**Reference**

Reid IR et al. Randomised controlled trial of calcium supplementation in healthy, nonosteoporotic, older men. Arch Intern Med 2008 Nov 10; 168:2276.

## Are fish oil supplements recommended during pregnancy?

Dear bpac,
I have to say I do love your publication. The articles are well written and researched and of practical use in General Practice.

I have a question for Dr Lisa Houghton on nutrition and supplements during pregnancy.

Does she recommend fish oil during pregnancy? There seems to be a growing mass of evidence to suggest that it is useful to decrease allergies in the infant and helps with learning and mood etc.

**Susanna Kent**, GP, Wellington

*Fish oil supplements, which contain the omega-3 fatty acid docosahexaenoic acid (DHA), are increasingly being marketed to pregnant and lactating women to enhance cognitive development, visual acuity, nervous system maturity and immune function in the developing infant. At present, the potential benefits to the foetus of maternal DHA supplementation are suggested largely by randomised controlled studies in which supplements were given to the infants after birth.[1] Few clinical studies of DHA supplementation of pregnant women have been conducted. However the number of observational studies linking higher DHA status to favourable infant developmental outcomes has highlighted the need for more quality dose-response clinical trials.*

*Recent recommendations from the Perinatal Lipid Intake Working Group has suggested that pregnant and lactating women consume ≥200 mg/day of long chain polyunsaturated fatty acids, - DHA and EPA (eicosapentaenoic acid),[2] while the Canadian and American Dietetic Associations recommend an intake of 500 mg/day.[3] Both groups, however, emphasise consuming seafood. Evidence suggests that pregnant women consume low levels of DHA due to avoidance of specific sources of seafood because of their mercury content. Oily fish such as canned tuna, sardines, salmon, mackerel, eel, warehou and kahawai are an excellent source of DHA with little concern over the amounts eaten.*

**Dr Lisa Houghton**, Dietitian, University of Otago


1. Carlson SE. Docosahexaenoic acid supplementation in pregnancy and lactation. Am J Clin Nutr 2009;89(suppl):678S-84S.
2. Koletzko B, Cetin I, Brenna JT. Dietary intakes for pregnant women and lactating women BR J Nutr 2007;98:873-7.
3. Kris-Etherton PM, Innis S. Position of the American Dietetic Association and Dietitians of Canada: dietary fatty acids. J Am Diet Assoc 2007;107:1559-611.


## CVD and cholesterol

Dear bpac,
In BPJ 17 and 18 there was some good information on cardiovascular risk assessment and lifestyle interventions. I am finding that more and more of my patients, probably in light of some recent publications like the “Cholesterol Myth”, are becoming rather suspicious of the pharmaceutical industry and of medicine as a whole.

I have been having trouble tracking down the original studies, that showed that saturated fat causes increased heart disease, and that identified dyslipidaemia as a

cause of heart disease and therefore needing treating rather than just an indicator of risk. I understand that recent study has shown statins mechanism in reducing second heart attacks comes more from its influence on vascular smooth muscle rather than its cholesterol lowering ability.

I am currently feeling a little high and dry on evidence to support my recommendations to patients to lower their cholesterol and reduce the saturated fat in their diet. I would be grateful if you could provide some references to this effect and would be interested in your comment.

Mark Edmond, GP, Christchurch

*The so-called "Cholesterol Myth" is the real myth. It has been promulgated by journalists and other writers seeking controversy where there is none, in order to sell newspapers and books. The "false flames" of controversy have probably also been fanned by industries with vested interests in saturated fat production and these are powerful industries with huge propaganda resources. Unfortunately there is little money to be made from the truth, which is that almost everything new that has been learnt about saturated fat, blood cholesterol and congestive heart failure (CHD) in the last 30 years supports what we already knew back then, which is simply that "a diet high in saturated fat causes an increase in blood cholesterol which causes an increase in CHD".*

*With regards to local data, Jim Mann and colleagues undertook a great little trial randomising people to butter or margarine and showed clear evidence of worsening lipid profiles in those given butter which reversed when they were changed to margarine.[1] This evidence was unsurprisingly consistent with a huge body of international trial evidence from many decades of research demonstrating that saturated fat consumption increases blood cholesterol levels.*

*The New Zealand diet has changed significantly over the last 30 years and in particular there has been a significant reduction in saturated fat consumption. For example butter consumption – which alone accounts for one-fifth of our total saturated fat consumption – has fallen from a high of almost 20 kg/head in the late 1950s to about 10 kg/head this decade (www.fao.org). Also the increasing range of low fat milk and other dairy products has had an important impact on our saturated fat consumption. Most of these products were not available until the 1970s and 1980s.*

*This change in diet has been associated with a substantial reduction in blood cholesterol levels. Since the early 1980s a fall in blood cholesterol of about 0.5 mmol/L on average has been documented. During the same period CHD mortality has fallen by 2–3% per year in New Zealand – more than two-thirds reduction in CHD mortality in New Zealand since the late 1960s! It has been estimated that the decline in blood cholesterol levels between the early 1980s and early 2000s account for about one-third of this decline in CHD mortality.[2]*

*However the best evidence comes from systematic reviews of the literature that avoid the peculiarities and random error in single studies. An international meta-analysis of cohort studies published in the Lancet in 2007 described a ten year follow-up of almost one million people and demonstrated beyond doubt that blood lipids are strongly associated with CHD mortality.[3]*

*Almost every trial of statins, of which there are now many, support the cohort data described above. Moreover it exposes the other cholesterol myth that statins work primarily by their influence on smooth muscle rather than*

*their cholesterol-lowering ability. While statins may well work indirectly on smooth muscle, it is almost certainly secondary to their cholesterol-lowering ability because the different declines observed in CHD risk in the different statin trials, can be explained by their effect on lipid levels. This has been demonstrated in another international meta-analysis of almost 100,000 people in randomised trials of statins versus placebos, published in the Lancet in 2005.[4] The meta-analysis clearly shows a strong and consistent relationship between changes in blood lipids and changes in CHD risk.*

*The cholesterol myths are generated by people who cherry pick individual studies or parts of studies to support their need for controversy. The boring headline one never gets to read, based on a more systematic approach to the huge range of evidence, is that: "**We continue to confirm with almost every new study, that what we knew 30 years ago about saturated fat, cholesterol and CHD is still true – they are strongly related and the effects are reversible.**" The proof is also in the (low saturated fat) pudding. In New Zealand saturated fat consumption has been falling for over 30 years, blood cholesterol levels have been falling over the same period (it started before statins were invented), and so has CHD.*

**Professor Rod Jackson**, School of Population Health, Faculty of Medical and Health Sciences, Auckland University

**References:**

1. Chisholm A, Mann J, Sutherland W, et al. Effect on lipoprotein profile of replacing butter with margarine in a low fat diet: randomised crossover study with hypercholesterolaemic subjects. BMJ 1996;312:931-4.

2. Tobias M, Taylor R, Ken Huang L-C, et al. Did it fall or was it pushed? The contribution of trends in established risk factors to the decline in premature coronary heart disease mortality in New Zealand. Aust N Z J Public Health 2008;32:117-25.

3. Prospective Studies Collaboration. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55 000 vascular deaths. Lancet 2007; 370: 1829–39

4. Cholesterol Treatment Trialists' (CTT) Collaborators Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90 056 participants in 14 randomised trials of statins. Lancet. 2005; 366: 1267–78.

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