BEST PRACTICE

19

FEBRUARY 2009

SKIN

Impetigo

Scabies

Fungal Nail Infections

ANTIPLATELET DRUGS

bpac nz
better medicine

We would like to acknowledge the following people for their guidance and expertise in developing this edition:

Dr Michael Crooke, Wellington

Dr Rebecca Grainger, Wellington

Dr Hayden McRobbie, Auckland

Dr Amanda Oakley, Hamilton

Assoc. Prof. CK Wong, Dunedin

Dr Edward Wong, Auckland

Dr Neil Whittaker, GP Reviewer, Nelson

Best Practice Journal (BPJ)

ISSN 1177-5645

BPJ, Issue 19, February 2009

BPJ is published and owned by bpac^{nz}
Level 8, 10 George Street, Dunedin, New Zealand.

Bpac^{nz} is an independent organisation that promotes health care interventions which meet patients' needs and are evidence based, cost effective and suitable for the New Zealand context.

We develop and distribute evidence based resources which describe, facilitate and help overcome the barriers to best practice.

Bpac^{nz} is currently funded through contracts with PHARMAC and DHBNZ.

Bpac^{nz} has four shareholders: Procare Health, South Link Health, IPAC and the University of Otago.

Contact us:
Mail: P.O. Box 6032, Dunedin
Email: editor@bpac.org.nz
Free-fax: 0800 27 22 69

www.bpac.org.nz

This magazine is printed on an environmentally responsible paper managed under the environmental management system ISO 14001, produced using Certified ECF pulp sourced from Certified Sustainable & Legally Harvested Forests.

CONTENTS

CONTENTS

CONTENTS

Essentials

All web links in this journal can be accessed via the online version.

www.bpac.org.nz

New hope for genetic disorders

Pre-implantation genetic diagnosis

Pre-implantation genetic diagnosis (PGD) represents the latest technology in genetic testing. However it also opens up an ethical minefield between the balance of scientific advances and "playing God". The purpose of this article is to provide information about the issues, preparing GPs and primary care professionals for questions from patients.

> "It is vital that GPs and other health professionals know more about genetic testing and genetic services in New Zealand so they can better facilitate informed consent, know when to refer patients for testing and be able to offer some degree of genetic counselling if required." *Professor Mark Henaghan, Human Genome Research Project.*

What is pre-implantation genetic diagnosis?

Until recently the only testing option available for parents at risk of conceiving a child with a genetic disorder was prenatal diagnosis. This involves sampling foetal cells through the placenta (chorionic villus sampling) or the amniotic fluid (amniocentesis). Couples then decide whether to abort the foetus or continue with the pregnancy.

PGD is a procedure used in conjunction with in vitro fertilisation to test embryos for serious inherited genetic conditions and chromosomal abnormalities before they are transferred to the uterus. This enables parents to make a choice about the future of an affected embryo rather than an affected foetus.

Currently PGD can be used for three different abnormalities:

- Single gene defects e.g. cystic fibrosis, Huntington's disease, haemophilia
- Numerical chromosomal abnormalities (aneuploidy) e.g. Down syndrome, Turner syndrome
- Structural chromosomal abnormalities e.g. translocations

PGD can be used for couples who are carriers of a familial genetic disorder that would cause serious impairment for the child and for which there is a 25% or greater risk of an affected pregnancy.

It may also be used for couples who are having trouble conceiving due to advanced reproductive age or who have experienced recurrent implantation failure or miscarriage.

PGD involves:

1. Creation of an embryo via IVF
2. Removal of one or two cells from the embryo

3. Genetic testing of these cells for specific genetic conditions or chromosomal abnormalities
4. Transfer of unaffected embryos to the uterus

The Ministry of Health currently funds 40 cycles of IVF/PGD a year to detect serious inherited genetic diseases. There is limited availability of PGD in New Zealand (see page 7). PGD is most commonly used in New Zealand to test for Huntington's disease, cystic fibrosis and spinal muscular atrophy.

Patients considering PGD should be given relevant information, advice on alternatives and referral for genetic and psychosocial counselling from a trained genetic counsellor.

Gender selection

PGD can be used in New Zealand to select the gender of a child, if it prevents transmission of a sex-linked genetic condition such as haemophilia or Duchenne's muscular dystrophy, when a specific test is not available.

Gender selection for social reasons (e.g. family balancing) is not legal in New Zealand, although it is allowed in some other countries such as the United States. The use of PGD for any other social reasons e.g. beauty or intelligence, is not currently scientifically possible, nor would it be permitted.

Many people may perceive that gender selection for social reasons is an unimportant application for this technology. There is also concern that gender selection will result in unbalanced selection of male embryos. In the "Who gets born" report, the Bioethics Council of New Zealand found that there was insufficient cultural, ethical and spiritual reasons to prohibit the use of PGD for social reasons such as "family balancing". They have recommended that this use of PGD be re-examined in New Zealand.

> "I long for a daughter and sister for my four boys to 'balance' our family... I have thoroughly researched the new PGD technology available for sex selection, which is freely available in the US, and we are currently considering using this technology to weigh the chances of our next (and final) pregnancy being a girl. I believe I should have the right to decide whether or not to take advantage of such wonderful advancements in medical technology as PGD for sex selection. I don't believe it is up to the Government or policymakers to be able to make such personal choices on my behalf. We are a loving, hard-working family and have the resources to take care of another child; if there is a technology that allows us to increase our chances of it being a girl then we plan to take advantage of it." *Forum, Who Gets Born.*

Saviour siblings

Saviour siblings are children who are created in order to donate mast cells to an existing sick child in the family. PGD along with human leukocyte antigen (HLA) tissue typing can be used to select genetically matched sibling embryos. In New Zealand, saviour siblings are permitted for inherited disorders e.g. beta thalassemia, under the oversight of Ethics Committee on Assisted Reproductive Technology. Approval from the Minister of Health must be sought to use cord blood on a sibling. No saviour siblings have been born in New Zealand to date.

Saviour siblings may not be used in New Zealand for general illness e.g. leukaemia. Parents may store their child's umbilical cord blood, which can be used if the child becomes sick in the future. This is permitted for autologous use only (cannot be used by a sibling). Auckland CordBank, offers cord blood storage for an initial fee of $2500 plus $200 per year of storage.

The Human Genome Research Project group, sponsored by the New Zealand Law Foundation has recommended that the use of saviour siblings should be extended to include any serious or life threatening condition. They also recommend that the use of tissue, blood and bone marrow should be permitted. The donor child should have an appropriately qualified advocate and ethical

considerations include addressing potential feelings of the saviour sibling as a "spare parts factory".

> "The question over screening siblings' compatibility for medical procedures is the hardest one for me. Where does one child's right to life take precedence over another child's right to be left alone, when they can't make their own decisions legally?" *Forum, Who Gets Born.*

Considerations for PGD treatment

- Although PGD is diagnostically reliable, patients must still undergo prenatal diagnosis to ensure that PGD has been accurate and to screen for other abnormalities.
- The live birth rate for PGD is 20–30% per IVF cycle which is the same rate as for IVF in general.
- There is a lack of consistent evidence to show that PGD for aneuploidy screening (e.g. Down syndrome) improves the live birth rate of couples having fertility problems.
- Long term health risks of children born as a result of PGD are unknown. An advisory group has been established to examine long term health risks of assisted reproductive technology.
- PGD is expensive and may be inaccessible to many families. In New Zealand PGD costs around $11 000.
- There is a long waiting list for PGD with delays of a year or more.

Some suggest that PGD discriminates against people with disabilities and promotes the view that birth of children with disability should be prevented.

> "In applying and advancing scientific knowledge, medical practice and associated technologies, human vulnerability should be taken into account. Individuals and groups of special vulnerability should be protected and the personal integrity of such individuals respected." *Article 8 of the Universal Declaration on Bioethics and Human Rights 2005*

Who gets born?

The following discussion occurred during a public consultation forum for the Bioethics Council of New Zealand "Who Gets Born" report about pre-birth testing in New Zealand. This feedback provides insight into some of the ethical and social issues that PGD raises.

> "It comes down to your moral viewpoint on, where does life begin? Is it equally repugnant to you to destroy an eight-cell embryo as an eight week old foetus or as an eight month pregnancy? You probably draw the line somewhere along that spectrum. But where? And why?"

> "There is a shift in paradigm from pregnancy being a gift or fate, to the idea of a tentative pregnancy... where we have all the tests before deciding whether to continue with it."

> "As a carrier of cystic fibrosis and having witnessed what it can do to someone, I have no problem with testing for it. The guilt I would feel if I brought a child into this world with a death sentence attached is just not worth it (especially when I have the opportunity to avoid it)."

> "People need to know that it was shattering having this Down syndrome baby, but it passed; we love him and wouldn't be without him. He has every right to be here and while his life is more difficult in some ways, he's still having a great time. Every time we hear that a baby with Down syndrome has been terminated we feel sorry for the people (and the baby of course) because they don't know what they have missed out on."

> "Pre-birth testing raises many ethical challenges, and everyone has an opinion based on their own personal experience. Someone who was born with a genetic condition and raised in a loving family will argue vehemently against pre-birth testing. Someone who was born with the same level of disability but was not raised in a loving family – was

in fact mistreated and abused – will wish that pre-birth testing had been available before he/she was born."

"Imagine you are the parent of a child who has inherited a lethal genetic condition. Imagine the fear we feel going into a subsequent pregnancy, knowing that we have a 25%, or even 50% chance of conceiving a baby with the same genetic illness, and with the same outcome. Imagine living with that fear for 40 long, terrifying weeks if there is no diagnostic tool. Imagine trying to fight for your baby's life, knowing the second time that child will die. Now imagine there exists the medical technology to know for a fact whether or not that subsequent baby carries the genetic condition that will kill him or her. Imagine that you could spare a child that pain."

Fertility clinics offering PGD

In New Zealand PGD is currently offered by Fertility Associates based in Auckland, Hamilton and Wellington, Fertility Plus in Auckland and Repromed in Christchurch. Egg collection, IVF and embryo culture are performed in New Zealand then the embryos are biopsied and cells sent to Australia for most tests. Results are received within one to two days allowing embryos to be selected and transferred.

PGD for serious genetic conditions with a 25% chance of inheritance or greater may be publicly funded, with couples being offered up to two cycles of treatment. Women need to be aged 39 years or younger and meet some other criteria related to the chance of success with IVF for public funding.

Genetic counselling

Genetic services in New Zealand are limited and are based in Wellington and Auckland, with clinics held in some other centres. GPs may refer patients to these services.

Northern Regional Genetic Services
Private Bag 92024
Auckland Hospital Site
Grafton
Auckland
Ph (09) 307 4949 extn 5530
Toll free 0800 476 123
Fax (09) 307 4978
Email gensec@ashsl.co.nz

Central Regional Genetic Services
Wellington Hospital
Private Bag 7902
Wellington
Ph (04) 385 5310
Toll free 0508 364 436
Fax (04) 385 5822

Central Regional Genetic Services
Christchurch Hospital
Christchurch
Ph (03) 379 1898 or (03) 364 0640 extn 89777
Toll free 0508 364 436 (South Island callers)
Fax (03) 379 1343

Further reading

National Ethics Committee on Assisted Human Reproduction. Guidelines on preimplantation genetic diagnosis. March 2005.

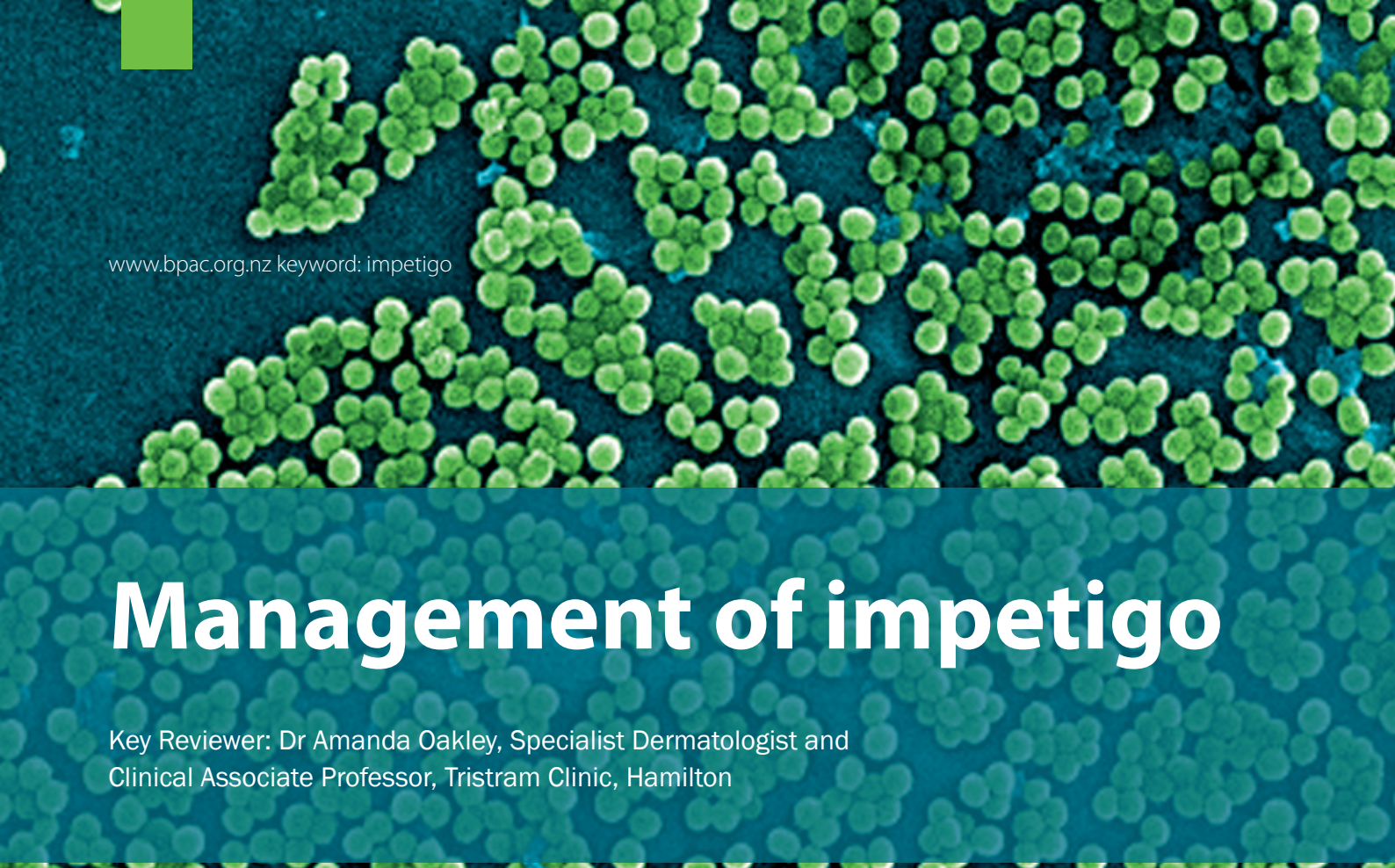
Available from: http://www.acart.health.govt.nz/moh.nsf/indexcm/acart-resources-guidelines-preimplantation

Bioethics Council. Who gets born? A report on the cultural, ethical and spiritual issues raised by pre-birth testing. June 2008.

Available from http://www.bioethics.org.nz/publications/who-gets-born-jun08/index.html

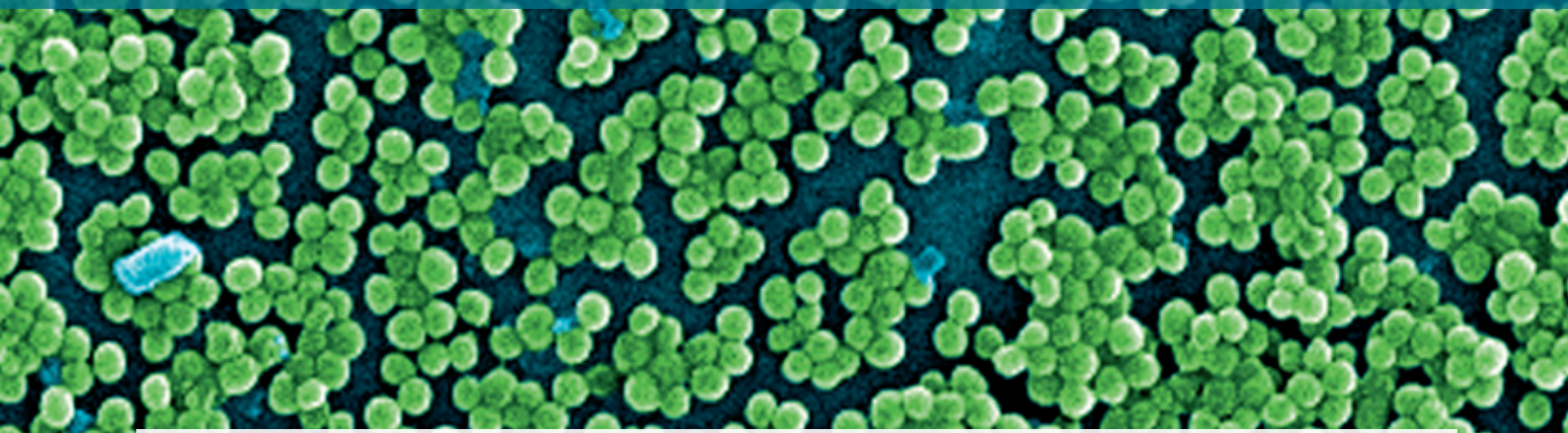
National Human Genome Research Institute. Frequently asked questions about genetic testing.

Available from: http://www.genome.gov/19516567



Management of impetigo

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



Key concepts

- Impetigo is a common, highly contagious bacterial infection of the skin
- Impetigo is usually diagnosed clinically. Swabs may be required for recurrent infections, treatment failure with oral antibiotics or where there is a community outbreak.
- Topical treatment is the initial therapy for small localised patches of impetigo
- Oral antibiotics should be used for extensive disease or systemic infection and when topical treatment fails

Impetigo is a common, highly contagious bacterial infection of the skin

Impetigo can affect any age group but most commonly occurs in young children (i.e. aged two to six years).[1, 2] *Staphylococcus aureus* and *Streptococcus pyogenes*, either alone or together, are the most common causes of impetigo. *S. aureus* is more common.[3] Impetigo can occur in previously healthy skin or can start from minor trauma that disrupts the skin barrier such as a graze, scratched scabies or eczema.[1, 4]

Impetigo is highly contagious and can be transmitted by direct contact, commonly spreading rapidly through families, day-care centres or schools.[2]

Impetigo is more common in;[1]

- Hot humid weather
- Conditions of poor hygiene or close physical contact (e.g. overcrowding, participation in contact sports)
- People who have skin conditions or experience trauma that impairs the normal skin barrier (e.g. eczema, scabies, fungal skin infections, insect bites)
- People with diabetes mellitus
- Intravenous drug users
- People who are immunocompromised (e.g. HIV, cancer, chemotherapy)

Two types of impetigo: bullous and non-bullous

Bullous and non-bullous are the two types of impetigo. Non-bullous (Figure 1) is much more common and can be caused by *S. aureus* or *S. pyogenes,* however *S. aureus* is the main cause. Lesions begin as a vesicle that ruptures and the contents dry to form a gold-coloured plaque. These lesions are often 2 cm in diameter and most frequently affect the face (especially around the mouth and nose) and limbs.[2, 3] Systemic signs are usually not present however with extensive impetigo, fever and regional lymphadenopathy may occur.[1]

Bullous impetigo (Figure 2) is only caused by *S. aureus*. It is characterised by larger fluid-filled blisters that rupture less easily. Systemic signs of infection such as fever and lymphadenopathy are more likely to occur and the torso is more likely to be affected.[1]

Impetigo is usually diagnosed clinically

Impetigo is usually diagnosed clinically and treatment decisions are rarely based on the results of skin swabs. Swabs may be required for recurrent infections, treatment failure with oral antibiotics or where there is a community outbreak and the cause needs to be identified. For recurrent impetigo nasal swabs can identify staphylococcal nasal carriage requiring specific management.[1]

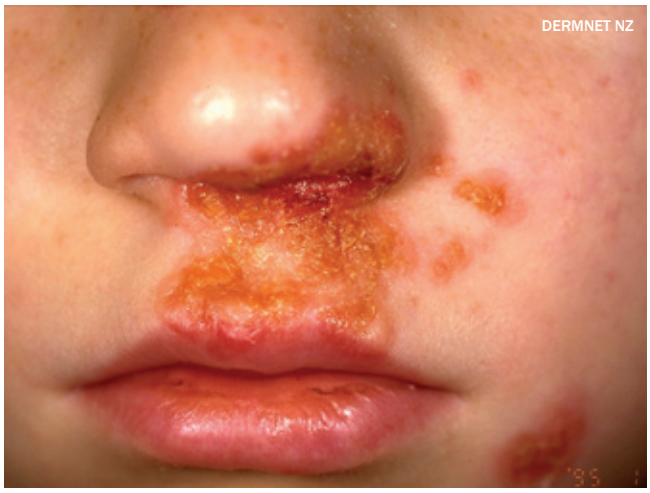


Figure 1: Nonbullous impetigo (*S. aureus*)

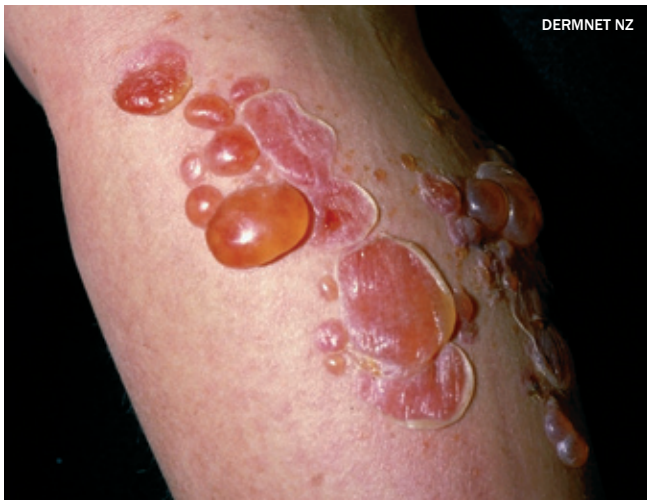


Figure 2: Bullous impetigo (*S. aureus*)

Treatment

The aim of treatment is to clear the eruption and prevent the spread of the infection to others.

Topical antibiotics are as effective as oral antibiotics for treating localised impetigo. The advantage of using topical antibiotics is that they are applied only where needed, avoiding systemic adverse effects such as gastrointestinal upset. Antiseptics such as hydrogen peroxide cream may also be effective.[5]

Impetigo caused by MRSA

The prevalence of impetigo caused by methicillin-resistant *S. aureus* (MRSA) is unknown, but is likely to be increasing.[6] Amongst *S. aureus* isolates in New Zealand 7% were resistant to oxacillin/methicillin in 2005.[10] Half of 664 MRSA laboratory isolates reported in New Zealand in August 2007 were from community patients.[11] However, MRSA is more likely to present with folliculitis or abscess. Some community strains of MRSA are also highly resistant to fusidic acid and mupirocin.[11] Trimethoprim/sulfamethoxazole, tetracyclines or clindamycin are usually effective against MRSA.[12]

Oral antibiotics are suitable for more extensive impetigo or when systemic symptoms are present because of the difficulty of applying topical antibiotics to large areas. Topical antibiotics are less suitable for recurrent infection, because the risk of inducing bacterial resistance is greater with topical antibiotics than with oral antibiotics.

Underlying conditions also need to be treated to reduce the risk of recurring impetigo.[6]

Topical treatment is the initial therapy for small localised patches of impetigo

Fusidic acid and mupirocin have been shown to be equally effective for small localised patches of impetigo. They are as effective as oral antibiotics.[6, 7]

Fusidic acid cream or ointment (Foban) is the first-line choice because mupirocin ointment (Bactroban) is effective against MRSA (see over page) and is best reserved for this reason.[8]

Seven days of topical antibiotic treatment appears to be effective.[9] It is not recommended to exceed ten days treatment as this may make contact sensitisation more likely and may encourage bacterial resistance.

Oral antibiotics should be used for extensive disease and for topical treatment failure

Flucloxacillin is the first-line choice as it is effective against *S. aureus* and Group A *streptococci*.[4, 13]

Erythromycin can be used for people who are allergic to penicillins, however gastrointestinal disturbances are more common and in some areas, resistance to erythromycin is increasing.[1, 14, 15]

Broad-spectrum antibiotics such as amoxicillin clavulanate are inappropriate because the organisms are known and are susceptible to narrow spectrum antibiotics.[1]

A seven day course of oral antibiotics is generally sufficient. If treatment fails after this time, compliance should be enquired about and swabs can be taken to check sensitivities.[16]

Children may find the taste of flucloxacillin syrup very unpleasant. Advise parents to offer a glass of fruit juice to their child directly after taking a dose.

Potential outcomes

The natural history of impetigo has not been extensively studied but it is believed that without treatment, minor cases would resolve spontaneously in two to three weeks. Scarring does not occur because the infection is limited to the epidermis.[6]

Recurrent infection

Recurrent infection may result from the nasal carriage of causative microorganisms or from fomite colonisation (colonistation of an inanimate object capable of carrying infectious organisms). If nasal carriage is suspected, a nasal swab is required to confirm this and a topical antibiotic applied inside each nostril, three times daily for seven days, is recommended. A household contact may be

an asymptomatic carrier of *S. aureus* and this person will require treatment too.[4]

Post-streptococcal glomerulonephritis is a rare complication of streptococcal impetigo

Post-streptococcal glomerulonephritis, which can lead to renal failure, is a rare (less than 1%) complication of streptococcal impetigo (see BPJ 7, August 2007). Treatment of impetigo may not prevent susceptible people developing this complication.[10]

Advice for patients with impetigo

To remove crusted areas:

If patients wish to remove crusted areas, soak a clean cloth in a mixture of half a cup of white vinegar in a litre of tepid water. Apply this compress to affected areas for about ten minutes several times a day and then gently wipe away crust.[4] Topical antibiotic can then be applied. Note: bullous impetigo should not be lanced.

To prevent the spread of infection:[1,4]

Children should stay away from day-care or school until the lesions have crusted over or they have received at least 24 hours of antibiotic treatment. This may be less important for older children (e.g. secondary school) because they may be less likely to spread the infection through touching each other.[6]

Cover the affected areas and wash hands after touching patches of impetigo or applying antibiotic cream or ointment.

Avoid close contact with other people.

Use separate towels, flannels, clothing and bathwater until the infection has cleared. Disinfect linen and clothing by hot wash, hot dry or ironing.

Use hand sanitisers and/or careful washing with household soap and water, several times daily.

Images contributed by NZ DermNet, the website of the New Zealand Dermatological Society.

References

1. Clinical Knowledge Summaries. Impetigo. Available from http://cks.library.nhs.uk/impetigo (Accessed January 2009).
2. Sladden MJ, Johnston GA. Common skin infections in children. BMJ 2004; 329: 95-9.
3. Cole C, Gazewood J. Diagnosis and treatment of impetigo. Am Fam Physician 2007; 75(6): 859-64.
4. Oakley, A. Impetigo. DermNet NZ 2007. Available from www.dermnet.org.nz (Accessed January 2009).
5. Christensen OB, Anehus S. Hydrogen peroxide cream: an alternative to topical antibiotics in the treatment of impetigo contagiosa. Acta Derm Venereol 1994;74(6):460-2.
6. Treating impetigo in primary care. Drug Ther Bull 2007; 45(1): 2-4.
7. Koning S, Verhagen AP, van Suijlekom-Smit LWA, et al. Interventions for impetigo. Cochrane Database Syst Rev 2003; 2: CD003261.
8. Health Protection Agency and Association of Medical Microbiologists. Management of infection guidance for primary care 2008. Available from www.hpa.org.uk (Accessed January 2009).
9. George A, Rubin G. A systematic review and meta-analysis of treatments for impetigo. Br J Gen Pract 2003; 53: 480-7.
10. Fadheel ZH, Perry HE, Henderson RA. Comparison of methicillin-resistant Staphylococcus aureus carriage rate in the general population with the health-worker population. NZ J Med Lab Sci, April, 2008.
11. Heffernan H. Annual Survey of all MRSA Public Health Surveillance ESR Ministry of Health. Available from http://www.surv.esr.cri.nz (Accessed January 2009).
12. Burdick EA, Camacho ID. Impetigo. Emedicine. Available from http://emedicine.medscape.com/article/1052709-overview (Accessed January 2009).
13. Australian Medicines Handbook 2006.
14. Lang S. Guide to pathogens and antibiotic treatment. Diagnostic Medlab 2004. Available from http://www.dml.co.nz/ (Accessed January 2009).
15. BNF 56. British National Formulary. 56th Ed. London: British Medical Association and the Royal Pharmaceutical Society of Great Britain; September 2008.
16. Brown J, Shriner DL, Schwartz RA, Janniger CK. Impetigo: an update. Int J Dermwatol 2003; 42: 251-5..

SCABIES

Diagnosis and management

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

Key concepts

- Scabies transmission occurs when there is transfer of a fertilised female mite by direct, (approximately five minutes) skin-to-skin contact with an infected person.
- Diagnosis is usually made clinically. Laboratory diagnosis is not usually necessary but may be useful for uncertain cases or cases in residential care.
- Malathion and permethrin are effective treatments for scabies.
- All recent contacts should be treated.
- The itch may persist for weeks even though the mite is gone. However itch beyond six weeks may indicate treatment failure.

Scabies is caused by the female scabies mite (*Sarcoptes scabiei*). The itchy skin rash is due to an allergic reaction that occurs to the mite's trail of debris, faeces and saliva. Scabies mites occur worldwide and are prevalent in New Zealand. Scabies infestation can affect all socioeconomic groups and is not a result of poor hygiene. It is however, more often associated with poverty and overcrowding.[1]

Transmission of scabies usually occurs by the transfer of fertilised female mites

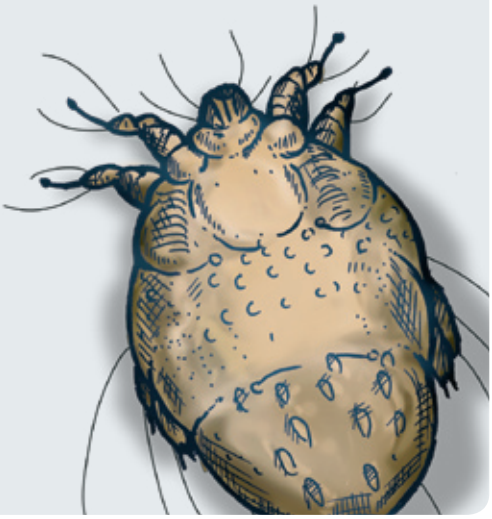
Scabies transmission occurs when there is transfer of a fertilised female mite by direct, prolonged (approximately five minutes) skin-to-skin contact with an infested person. Infection is easily spread to sexual partners and household members.

Transfer can also result from sharing clothing, towels and bedding as the mite can live for up to two to three days away from the human body.

In children, scabies transmission most commonly occurs at day-care centres, schools or sleepovers while in elderly people it most commonly occurs in residential care.

Life cycle of scabies mite

After mating the male mite dies. Newly mated female mites will lay two to three eggs per day (for her lifespan of one to two months) in burrows within the stratum corneum. After approximately two to four days, the eggs hatch and the larvae leave the burrow to stay on the surface of the skin, or in short burrows until they reach maturity in seven to nine days.



Diagnosis is usually made clinically

Scabies infestations can be difficult to diagnose. It should be considered whenever a patient complains of severe itch on the trunk and limbs, particularly when the visible signs are minor. Exposure to an infested person should promote a high index of suspicion.

There is usually a history of intense itch, worse at night and after a hot shower/bath.

The itch related to scabies can start at variable times after a person becomes infested, from hours (if the person has been infested before and therefore previously sensitised) to several weeks in an initial infestation.

A confident clinical diagnosis can be made if burrows are observed on the wrists, finger web spaces and/or on the sides and soles of the feet (Figure 1). Irregular clusters of inflammatory nodules in the axillae, genitalia or thighs are also highly suggestive of infestation.

Burrows are 5–10 mm long and they look like greyish pencil marks (Figure 2) on pale skin (in darker skin they may appear pale). Burrows can be difficult to identify when the skin has been scratched, is secondarily infected or in the presence of eczema.[2, 3] Burrows are best seen under magnification. Dermoscopy may reveal tiny grey triangular structures at the leading edge of the burrow (Figure 3).[4]

The rash is often widespread and polymorphic; there may be scratched papules and nodules, eczema, folliculitis and urticaria, usually sparing the head and neck. In infants, elderly and immunocompromised people, scabies

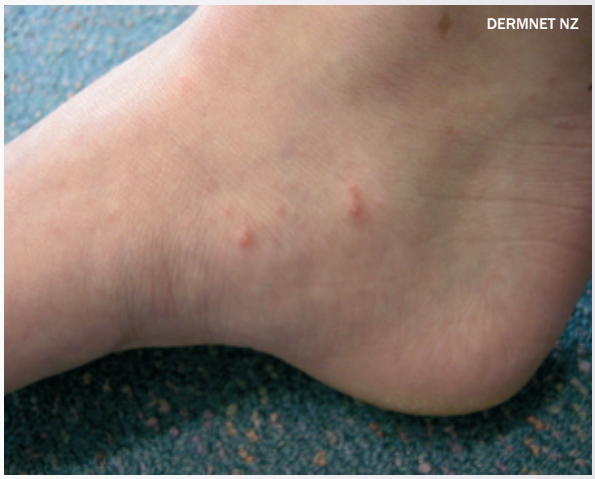


Fig 1: Burrows on foot of young adult patient

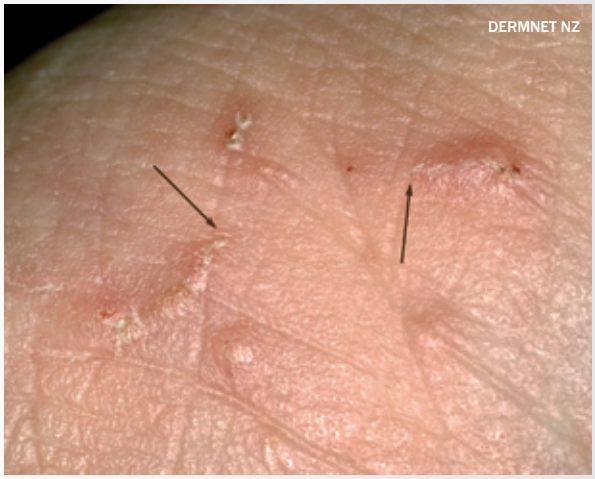


Fig 2: Scabies burrows with arrows to show where the mite can be seen on magnification

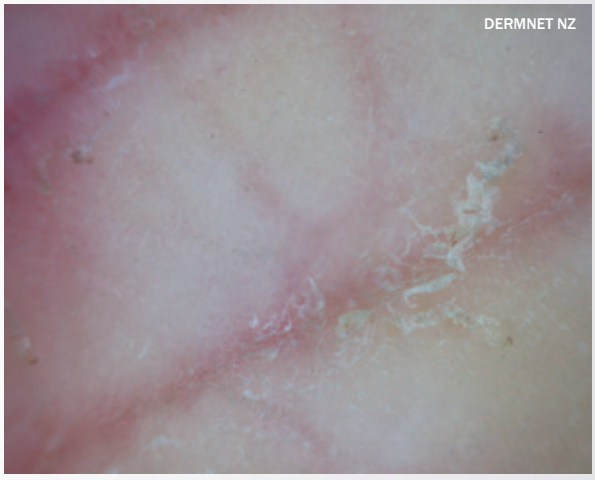


Fig 3: Dermoscopy reveals tiny grey triangles (the head of the female mite) at distal ends of burrows on fingers

may also affect the face and scalp.[2] Vesicles and pustules on the palms and soles are characteristic of scabies in infants, and may persist for several weeks after the mites have been successfully destroyed.[5]

Apply ink to burrows[2]

- Rub a non-toxic water-soluble felt pen over an area suspected of having burrows, wait a few moments and then wash off ink.
- In the presence of a burrow the ink will track down the burrow, forming a characteristic dark, zig-zag line.

Crusted scabies may occur in elderly, immuno-compromised or institutionalised people

Elderly, immunocompromised or institutionalised people may present with crusted or "Norwegian" scabies, a variant of scabies where extensive hyperkeratosis occurs (Figures 4 and 5). The diagnosis is often delayed because itch may be less severe and typical papules and nodules are frequently absent. The rash may resemble psoriasis. Thousands or even millions of mites are present in the crusts making this type of scabies easily transmissible. Crusted scabies is a common cause of institutional outbreaks (e.g. rest homes, prisons, or hospitals). Staff who are even minimally exposed to someone with crusted scabies (e.g. laundry workers, cleaning staff) are at risk of infestation.[6]

Laboratory diagnosis is not usually necessary

Microscopy of burrow contents, or scrapings from the hands of a patient with crusted scabies, may reveal mites, eggs or faeces. Laboratory diagnosis may be useful for scabies in residential care or in cases where the diagnosis is uncertain. However, even experienced dermatologists only recover a mite or egg in about 50% of scabies cases.[2, 4]

Treatment – malathion and permethrin are effective treatments for scabies

Permethrin and malathion are the most frequently used treatments for scabies. While both have been used extensively, the best evidence is for permethrin.[7] Researchers were unable to draw conclusions about malathion's effectiveness as there were no trials involving malathion.[7]

Gamma benzene hexachloride (Lindane) has been associated with aplastic anaemia and convulsions, possibly due to its application to broken skin. Lindane has been withdrawn in the UK and in Australia.[7]

Fully funded scabicides available in New Zealand are:

- 5% Permethrin cream – Left on for 8–14 hours before washing off. Reapplied after seven days.[8] Permethrin is a safer choice in pregnancy, lactating women and infants because of its low inherent toxicity and low percutaneous absorption.[9]
- 0.5% Malathion lotion – Left on for 24 hours before washing off. Reapplied after seven days.[8]
- 1% gamma benzene hexachloride cream (Lindane) – Left on for 8–12 hours. Not reapplied. Lindane should only be used if other treatments have failed, and should not be used in patients weighing less than 50 kg, those with a seizure disorder or pregnant and lactating women.

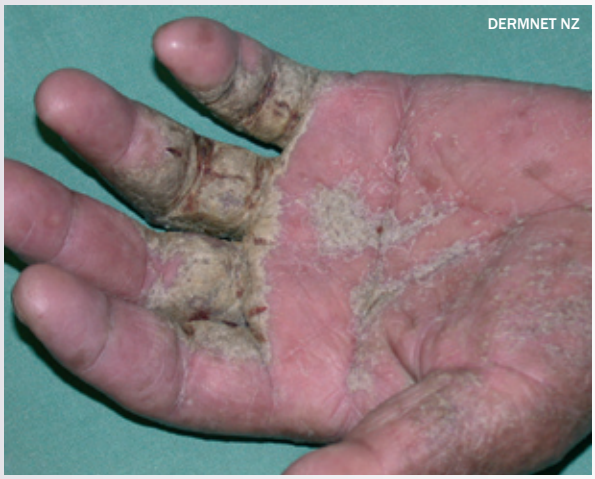


Fig 4: Typical crusted scabies in elderly hospitalised patient

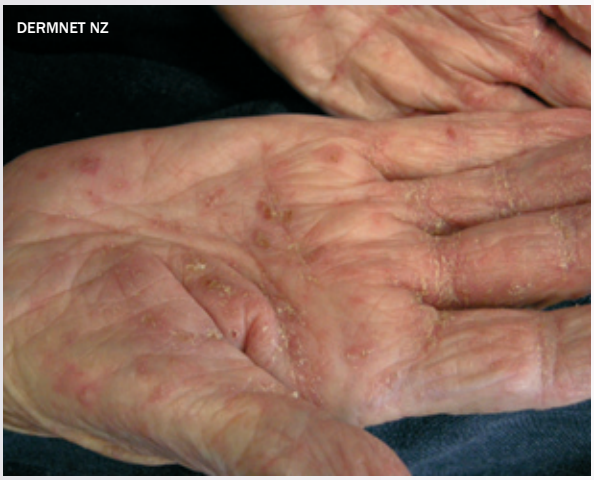


Fig 5: Crusted scabies in rest home resident: numerous burrows on palms

Scabicides should be applied to the entire body from the chin and ears downwards. The face and scalp should also be included for infants under two years, people who are immunocompromised and elderly people (but avoiding contact with eyes). Particular attention should be paid to the area between toes and fingers, genitals and under nails (a soft nail brush may be necessary).[8] This rarely causes stinging or irritation. Treatment needs to be reapplied to areas that are washed within the necessary application time (such as after hand washing). It can be helpful for a second person to assist with the application to areas that are not easily accessible.

Note: The BNF recommends application of scabicides to the entire body, including the head and neck for all people.[8]

Immunocompromised patients and those with crusted scabies may prove resistant to repeated topical therapy and require systemic insecticide therapy such as oral ivermectin (200 mcg/kg).[1, 9]

Retreatment may be necessary if symptoms and signs persist; or after oral antibiotics if there is crusting due to secondary impetigo.

Reducing transmission – treat all recent contacts

Household members and anyone with recent direct and prolonged body contact should be treated at the same time even if they are not itchy. This is because infestation may occur up to several weeks before symptoms and secondary rash appear.

Clothing, sheets, pillow cases, towels and facecloths that have been in contact with the patient within the previous few days should be machine washed in hot water and dried (hot cycle) or dry cleaned.

It is not generally necessary to wash blankets, duvets or quilts. They can be hung outside in the sun for a day. There is no need to treat furniture or carpets with an insecticide, except in the case of crusted scabies where numerous mites may be found on fomites.

The itch may persist for weeks even though the mite is gone

Do not assess treatment response until four weeks after treatment is finished. Overtreatment with scabicides can cause skin irritation and contact eczema.[6]

Itch or rash may persist for weeks after treatment due to the continuing allergic reaction to persisting antigens within the skin. Oral antihistamines, crotamiton (Eurax) cream, emollients and mild to moderate potency topical steroids can be useful.

Itch beyond six weeks after initial treatment may indicate treatment failure (particularly if itch persists at the same level or is increasing in intensity). This could be due to re-infestation, inadequate treatment of contacts, resistance to therapy, or an incorrect initial diagnosis. Consider an alternative diagnosis and re-examine the person. If the diagnosis of scabies is established, a different scabicide should be tried if all contacts were originally treated simultaneously, and the treatment was correctly applied.[2]

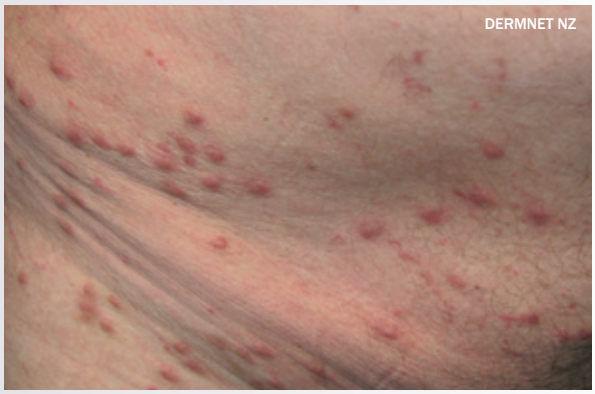


Fig 6: Nodular scabies

Even after successful treatment, pruritic nodules may persist in some people. Nodules are usually brownish red, can be up to 2 cm in diameter and are most often seen around the genitals and axillae (Figure 6). Treatment with topical corticosteroids may be useful.[9]

People with scabies can become secondarily infected with streptococci or staphylococci, which should be treated with oral antibiotics for seven days. Flucloxacillin is recommended as empirical treatment, erythromycin is an alternative for those with penicillin allergy.[2]

Images contributed by NZ DermNet, the website of the New Zealand Dermatological Society.

References

1. Heukelbach J, Feldmeier H. Scabies. Lancet 2006; 367: 1767-74.
2. Clinical Knowledge Summaries. Scabies. Available from http://cks.library.nhs.uk/scabies (Accessed January 2009).
3. Management of scabies in primary care. MeRec Bulletin 2008; 18(4): 8-10.
4. Scabies. DermNet NZ 2008. Available from www.dermnet.org.nz (Accessed January 2009).
5. Johnston G, Sladden M. Scabies: diagnosis and treatment. BMJ 2005; 331: 619-22.
6. Chosidow O. Scabies. N Engl J Med 2006; 354: 1718-27.
7. Strong M, Johnstone PW. Interventions for treating scabies. Cochrane Database Syst Rev 2007; 3: CD000320.
8. BNF 55. British National Formulary 55th Ed. London: British Medical Association and the Royal Pharmaceutical Society of Great Britain; March 2008.
9. Chouela E, Abeldano A, Pellerano G, Hernandez M. Diagnosis and treatment of scabies: a practical guide. Am J Clin Dermatolol. 2002; 3(1):9-18.

Management of **fungal nail infections**

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

Key concepts

- Laboratory diagnosis of onychomycosis is recommended before starting oral or topical treatment
- Onychomycosis is diagnosed with microscopy and culture of nail clippings
- Treatment may not be necessary for everybody and may be inappropriate for elderly people
- Oral terbinafine is first line treatment for dermatophyte infection of nails
- Itraconazole is the treatment of choice for onychomycosis due to candida infection
- Topical amorolfine or ciclopirox may be suitable for superficial or minor infection and for those unable to take oral antifungal therapy
- Treatment failure or relapse will require mycological confirmation and possibly alternative treatment

Fungal infection accounts for approximately half of all nail disease

Fungal infection of the nails or onychomycosis accounts for about 50% of all nail disease. It becomes more common with increasing age and mostly affects toenails (80% of cases). Other risk factors for onychomycosis include: nail trauma, frequent immersion in water, occlusive footwear, athletes foot, diabetes mellitus, immunosuppression and smoking.[1, 2, 3]

Dermatophytes are the most common cause of fungal nail infection

In 90% of cases onychomycosis is caused by a dermatophyte, mostly *Trichophyton rubrum*. Other causes of infection include yeasts; mainly *Candida* infection of the fingernails, which is often accompanied by paronchynia (inflammation of the proximal nail fold).[1] Non-dermatophyte moulds (*Fusarium, Scopulariopsis* and *Scytalidium*) account for about 2–3% of fungal nail infections.[2, 4]

Distal and lateral subungual onychomycosis is the most common morphology of fungal nail infection

Most cases of onychomycosis are characterised by thickening of the nail, discolouration (ranging from white to black) and onycholysis (separation of the nail from the nail bed).[1, 5]

There are different morphological types of onychomycosis, the most common being distal and lateral subungual onychomycosis (Figure 1), usually caused by dermatophyte infection.[1, 5] This begins in the distal or lateral part of the nail plate and spreads proximally under the nail.

Superficial white onychomycosis (Figure 2) is also mostly caused by dermatophyte infection (usually *Trichophyton interdigitale*) and accounts for about 10% of onychomycosis. It presents as small, white, powdery patches on the surface of the nail.[2, 6]

Proximal onychomycosis (Figure 3) is the least common type of onychomycosis and usually presents in patients who are immunosuppressed (e.g. HIV), have diabetes, or

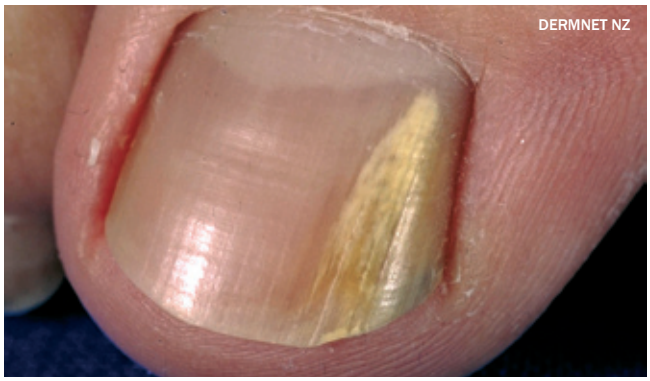


Figure 1: Typical lateral onychomycosis (*T. rubrum*)

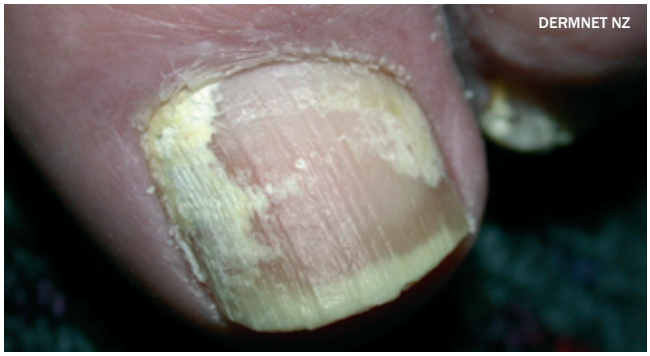


Figure 2: Extensive superficial white onychomycosis (*T. interdigitale*)

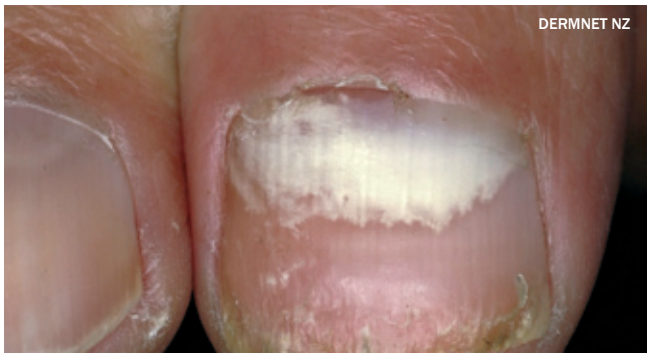


Figure 3: Proximal onychomycosis (*T. interdigitale*)

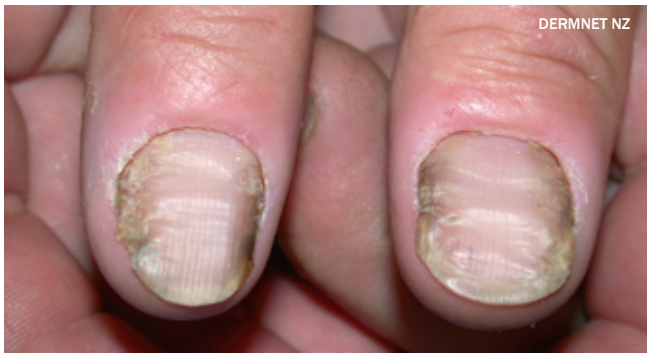


Figure 4: Typical onychomycosis and paronychia due to *C. albicans*

Differential diagnoses[1, 2]

Psoriasis affecting the nail – pitting, onycholysis, discolouration, thickening and irregular ridging. Look for psoriatic plaques on typical sites (scalp, ears, elbows, knees and flexures).

Onychogryphosis – thickening and distortion of the nails, most often the big toe. This is more common in elderly people.

Other differential diagnoses include – lichen planus, nail trauma, squamous cell carcinoma and malignant melanoma and nail dystrophy caused by systemic disease.

in those with peripheral vascular disease.[1, 2] This begins as discolouration of the proximal end of the nail.

Candidal onychomycosis (Figure 4) is often associated with paronchynia and most often occurs in the fingernails of people who frequently immerse their hands in water.[1, 2]

Laboratory diagnosis is recommended before any treatment is started

Laboratory diagnosis is recommended before starting treatment because other conditions (see differential diagnoses over page) can present similarly to onychomycosis, particularly psoriasis. Also, treatment of onychomycosis is lengthy, may have adverse effects and can be expensive.[1, 2, 3]

Diagnose onychomycosis with microscopy and culture of nail clippings[7]

Microscopy of a sample of affected nail plate can identify fungal elements and culture determines the causative organism.[8]

In most cases patients will be sent to the laboratory for collection of samples, however in some cases (e.g. rural practice) the doctor may collect the sample. Nail clippings (chiropody clippers may be the best tool to use) from the diseased part of the nail and curettings of subungual debris should be taken. If superficial white onychomycosis is suspected, a scalpel can be used to scrape the surface of the nail to obtain a sample.[1, 2]

It is best to provide the laboratory with a generous amount as there are usually few fungi in a typical specimen. If necessary, delay the investigation to allow the nail to grow longer.[2, 8]

Problems with laboratory tests – false negatives and delayed results

Accurate microscopy of specimens depends on the skill of the laboratory personnel. The false negative rate can be 30–40%.[5] Mycological culture increases the sensitivity but results may take several weeks because dermatophytes are slow growing. A culture plate is incubated for four weeks before it is declared negative.[9]

Treatment options

Treatment may not be necessary for everybody and may be inappropriate for elderly people

For patients who do not have troublesome symptoms, the decision to treat can be based on the patient's choice, after they have been informed of risks and benefits of treatment.

Patients should be informed about treatment including:[1]

- Nail may not look completely normal, even after treatment
- Treatment with oral antifungals is only successful in about 70-80% of cases (and clinical trials usually exclude people aged over 60 years) and can relapse.[8] Topical treatment is less effective.[10]
- Length of treatments: three months for oral medication and up to two years for topical medication

- Potential adverse effects and interactions with oral treatment

Treatment with oral antifungals may not be appropriate for elderly people, or people taking multiple medicines, as there is an increased risk of adverse effects and interactions.[2]

Treatment should be considered for those at risk of complications

People with diabetes, peripheral vascular disease or connective tissue disorders are at higher risk of complications such as secondary bacterial infections (e.g. cellulitis). In these people treatment should be considered. However, treatment is less likely to be successful in these patients, who also have higher rates of drug-induced complications.[1, 11]

Pharmacological treatments

Oral antifungals (terbinafine, itraconazole) and topical antifungals (ciclopirox, amorolfine) are available for the treatment of onychomycosis.

Oral treatment is more effective than topical therapy and is recommended for most people in whom treatment is appropriate

Oral antifungal treatment is more effective than topical treatment except for cases of superficial white onychomycosis or in a few cases of minor distal onychomycosis. Oral therapy is considered first line for most patients who opt for treatment.[8]

Terbinafine is first line for dermatophyte infection

Terbinafine and itraconazole are both effective for treating dermatophyte infection however terbinafine is more effective and is considered first line.[2, 8, 11]

In adults, 250 mg terbinafine is given once daily for an initial course of six weeks for typical fingernail infection, or 12 weeks for toenail infection.

Gastrointestinal effects such as dyspepsia, nausea and diarrhoea, skin reactions (morbilliform rash, urticaria) and taste disturbance are the most common adverse effects associated with terbinafine.[1, 2]

Rarely, serious skin reactions (e.g. Stevens-Johnson syndrome, toxic epidermal necrolysis, drug hypersensitivity syndrome and angioneurotic oedema) and haematological disorders have occurred with terbinafine therapy.[2] Psoriasis may be aggravated by terbinafine treatment.[2]

Oral terbinafine is not recommended for people with liver disease. Patients taking terbinafine should be advised to promptly report any symptoms that may suggest liver toxicity such as anorexia, nausea, vomiting or fatigue.[12] In elderly or unwell people, liver function and blood count should be monitored at baseline and then after four to six weeks of treatment.

Terbinafine interacts with a small number of drugs (Table 1).

Itraconazole is the treatment of choice for onychomycosis due to candida infection

Itraconazole is the most effective treatment for onychomycosis due to candida infection.[8, 11] Terbinafine can be used but is less effective.[1]

For the treatment of onychomycosis in adults, 200 mg itraconazole is taken twice daily for seven consecutive days of the month, for two months for fingernails and three months for toenails (although candidal onychomycosis is much less common in toenails).[8] Alternatively, 200 mg itraconazole can be taken once daily for three months. There is no evidence that continuous or intermittent regimens produce significantly different cure rates or adverse events.[13]

Adverse effects associated with itraconazole also include gastrointestinal effects and skin reactions as well as reversible increases in hepatic enzymes. Uncommon adverse effects include hepatotoxicity, severe skin conditions, nervous system disorders (peripheral neuropathy, headache, dizziness) and congestive heart failure.[2]

Table 1: Interactions with antifungals[2, 3, 14]

Drug or class	Terbinafine	Itraconazole
Benzodiazepines		Concurrent use of midazolam or triazolam is contraindicated, risk of excessive or prolonged sedation
Statins		Avoid concomitant use as rhabdomyolysis has been reported
Rifampicin	Decreased plasma levels of terbinafine possible	
Warfarin	Bleeding events reported rarely, however avoiding concurrent use is not necessary	Increased risk of bleeding, increased INR monitoring may be required
Calcium channel blockers		Increases the plasma level of felodipine which may increase its adverse effects, particularly ankle and leg oedema

N.B. This is not a comprehensive list of interactions

Itraconazole should not be used in patients with congestive heart failure or in those with liver disease or raised liver enzymes.

LFTs should be monitored at baseline and after four to six weeks of treatment for courses lasting more than one month.[1]

Itraconazole is an inhibitor of CYP3A4 and has a number of significant drug interactions (Table 1).

Topical treatment may be suitable for superficial infection and for those unable to take oral antifungal therapy

Topical therapies are less effective than oral therapies but may be useful for superficial white onychomycosis or in early distal and lateral subungual onychomycosis.[11, 15] Topical therapy can also be used where a patient is unable or unwilling to take oral antifungals.[11] Compliance with topical treatments can be an issue as they require application for extended periods, e.g. 6 to 12 months.

Amorolfine and ciclopirox nail lacquers are available topical antifungals

Amorolfine 5% (Loceryl) and ciclopirox 8% (Batrafen) are two topical antifungals available in New Zealand. While there is limited evidence that ciclopirox modestly improves symptoms of onychomycosis compared with placebo, there is a lack of evidence examining effectiveness of amorolfine.[16, 17]

Amorolfine is applied to the affected nail twice weekly until infection is resolved, usually six months for fingernails and 9 to 12 months or longer, for toenails. The nail needs to be filed, cleansed and de-greased before application.[1, 18] A transient burning sensation may occur after application of nail lacquer.[1]

Ciclopirox is applied to the affected nails every second day for the first month, then application is reduced to twice weekly for the following month, and then reduced to once weekly for up to six months or longer. The nail lacquer should be removed with nail vanish once weekly and the nail filed.[18] Irritation and pruritus may occur after application.

Both products are available over-the-counter as pharmacist-only-medicines or on prescription. There are part charges for both and these products may be too expensive for some patients.

Measure treatment response as nail grows

To determine if treatment is effective, photograph the nail, or make a groove with a nail file at the proximal end of the infected area. The infection should not progress proximal to this groove if treatment is effective. The groove may need to be redefined over time because it can take 12 months or longer for a big toenail to grow out.[2]

All people, whether they are being treated with medicines or not, should be provided with lifestyle advice

Foot care advice is integral to the treatment of onychomycosis and may lessen the discomfort of the infected nail(s).[2, 3, 15]

Advise patients to:[2, 3, 15]

- Keep feet cool and dry by wearing cotton socks and breathable footwear
- Trim nails and file down hypertrophic nails
- Avoid high heels and narrow toed shoes to prevent nail trauma
- Recognise and treat athletes foot if present
- Wear footwear in communal showers

Treatment failure or relapse

If initial treatment fails or infection recurs, the first step is to confirm mycology.[3] Earlier positive culture may have been secondary infection of nail dystrophy due to another cause. In addition, check adherence and if treatment is required, an alternative drug, a combination of oral and topical treatment or nail avulsion may be considered. However, there is little evidence that nail avulsion increases cure rates.[2, 11]

Images contributed by NZ DermNet, the website of the New Zealand Dermatological Society.

References

1. Clinical Knowledge Summaries. Fungal and candidal nail infections. Available from http://cks.library.nhs.uk/impetigo (Accessed January 2009).
2. How should fungal nail be treated? Drug Ther Bull 2008; 46(1): 3-8.
3. Rogers P, Bassler M. Treating onychomycosis. Am Fam Physician 2001; 63(4): 663-72.
4. Lang S. Guide to pathogens and antibiotic treatment. Diagnostic Medlab 2004. Available from http://www.dml.co.nz/ (Accessed January 2009).
5. olde Hartman TC, van Rijswijk E. Fungal nail infection. BMJ 2008; 337:295.
6. Fungal nail infections. DermNet NZ 2008. Available from www.dermnet.org.nz (Accessed January 2009).
7. The Royal College of Pathologists of Australasia Manual 2004. Available from http://www.rcpamanual.edu.au/ (Accessed January 2009).
8. Roberts DT, Taylor WD, Boyle J. Guidelines for treatment of onychomycosis. Br J Dermatol 2003; 148: 402-10.
9. Waikato Hospital. Available from http://www.waikatodhb.govt.nz/laboratory/tests/microbiology_tests/mycology_skin_scrapings.htm
10. Hainer BL. Dermatophyte Infections. Am Fam Physician 2003; 67(1):101-8.
11. National Prescribing Service. Onychomycosis (nail infections) – who needs treatment? NPS News 2008; 61.
12. Medsafe. Terbinafine: serious hepatic and haematological reactions. Prescriber Update 2006; 27(2):18-20.
13. Crawford F, Young P, Godfrey C, et al. Oral treatments for toenail onychomycosis. Arch Dermatol 2002; 138:811-6.
14. Baxter K (ed). Stockley's Drug Interactions. [online] London: Pharmaceutical Press. http://www.medicinescomplete.com (Accessed January 2009).
15. Finch JJ, Warshaw EM. Toenail onychomycosis: current and future treatment options. Dermatol Ther 2007; 20:31-46.
16. Hunt D. Fungal toenail infections. BMJ Clin Evid 2008; 12:1715.
17. Crawford F, Hollis S. Topical treatments for fungal infections of the skin and nails of the foot. Cochrane Database Syst Rev 2007; 3: CD001434.
18. MIMS New Ethicals Issue 10. Jan-Jun 2009. CMPMedica.

www.bpac.org.nz keyword: tia

Key Reviewer: Dr Edward Wong, Stroke Neurologist, Middlemore Hospital and Auckland City Hospital, Auckland

Transient Ischaemic Attack – a medical emergency

Key concepts[1]

- People with sudden onset of neurological symptoms should be screened for a diagnosis of stroke or TIA using a validated tool such as FAST
- If TIA is suspected:
  - Start aspirin immediately
  - Assess risk of stroke with the ABCD2 tool
  - If at high risk (ABCD2 ≥4) refer urgently for specialist assessment and investigation to occur within 24 hours of onset of symptoms
- As soon as a diagnosis of TIA is confirmed introduce secondary prevention

TIA is a warning

In one in four people a transient ischaemic attack (TIA) is a forerunner for a stroke,[2, 3] most of which occur in the first few days after a TIA.[4] Emergency referral for high-risk patients, urgent investigations and prompt treatment may prevent these strokes from occurring.

85% of strokes that follow a TIA will be fatal or disabling.[5] People with TIAs are also at high risk of non-stroke cardiovascular events e.g. myocardial infarction.

Benefit of early assessment and rapid intervention following TIA

There are several effective interventions for preventing stroke and other cardiovascular events following a TIA. Rapid diagnostic workup, appropriate early interventions such as carotid endarterectomy and commencement of secondary prevention have shown significant reduction in the 90 day risk of stroke following TIA (approximately 80% relative risk reduction).[6]

Guidelines for managing TIA and stroke may not be applicable to people with severe co-morbidities or a terminal illness but for most people the aim is to identify a TIA, start antiplatelet therapy and refer.

Recognising a TIA

A TIA may be thought of as a small stroke and shares similar signs and symptoms (Table 1):

- Rapid onset of symptoms – usually the patient or witness is certain when the event started
- Maximal neurological deficit at onset – progressive symptoms imply other diagnoses
- Focal symptoms typical of loss of blood supply to part of the brain
- Negative neurological symptoms (loss of function e.g. paralysis, weakness)

Most TIAs resolve within 60 minutes

Traditionally a TIA is defined as stroke signs and symptoms that resolve within 24 hours. However modern brain imaging now shows that most transient symptoms that last for more than one hour, are associated with detectable brain damage, and are in fact small strokes.

The clinical implications are that if symptoms are still present beyond one hour, then it can be assumed that this is likely to be a stroke.

Table 1: TIA symptoms (Adapted from NZ TIA Guideline 2008)[7]

Symptoms typical of TIA	Symptoms not typical of TIA*
Unilateral weakness: – face – arm – leg Unilateral altered sensation Dysphasia (speech deficit) Hemianopia Monocular Blindness	Generalised weakness or sensory symptoms Confusion (exclude dysphasia) Impaired consciousness or syncope Dizziness or light headedness Incontinence – bladder or bowel Amnesia Bilateral blurred vision or scintillating scotoma *If symptoms occur in isolation, without typical symptoms

Note – ataxia, vertigo, dysphagia, dysarthria and sensory symptoms to part of one limb or the face may be consistent with TIA if they occur in conjunction with other typical symptoms

Urgent assessment and intervention reduces the risk of stroke after TIA

Act FAST

The history of the event is crucial in making a diagnosis as often focal neurological signs have resolved by the time the patient presents. A witness's account can be invaluable.

A quick screening tool to aid the diagnosis of stroke or TIA is Face Arm Speech Test (FAST).[1] This may be performed on examination or retrospectively on history if the symptoms have resolved.

If time permits, further neurological examination to assess gaze and visual fields, limb ataxia and any sensory signs may be appropriate.

Likewise cardiovascular examination may be helpful to identify known risk factors:

- Neck bruit
- Atrial fibrillation
- Raised blood pressure
- Reduced or absent peripheral pulses
- Heart murmurs

Interventions

Step 1 – Medication

For those people with suspected TIA and no neurological deficit on examination, start aspirin (300 mg stat, and then 75–100 mg daily) if tolerated.[8]

If the patient is already on aspirin, special authority may be applied for to add dipyridamole.

Blood pressure reduction in the acute phase (prior to diagnosis being confirmed) is not recommended.

Step 2 – Speed of referral based on stroke risk

Urgency of referral depends on the stroke risk. This can be assessed with the ABCD2 tool.[9, 10]

High risk (≥4) – very rapid referral within 24 hours

ABCD2 scores of four and above are associated with higher likelihood of a true diagnosis of TIA and high risk of subsequent stroke (3.5% at two days and 5% at seven days.[11] Other high-risk patients include those with; symptoms at the time of assessment, more than one TIA in a week (crescendo TIAs), atrial fibrillation or those taking warfarin. High-risk patients require urgent assessment at a specialist centre, with access to brain and carotid imaging, within 24 hours of onset of symptoms.[12]

FAST

If possible check blood glucose. If <3.5 mmol/L treat and reassess once blood glucose is normal.

FACIAL WEAKNESS – Can the patient smile?

Ask patient to smile or show teeth.

- Look for new asymmetry – is there unequal smile or grimace, or obvious facial asymmetry?

ARM WEAKNESS – Can the person raise both arms?

Lift the patient's arms together at 90 degrees if sitting, or 45 degrees if supine, and ask them to hold in position for five seconds. Then let go.

- Does one arm drift down or fall down rapidly?

SPEECH PROBLEMS – Can the person speak clearly?

If the patient attempts conversation.

- Look for new disturbance of speech (check with witness)
- Look for slurred speech
- Look for word-finding difficulties. This can be confirmed by asking the patient to name commonplace objects that may be nearby, such as a cup, chair, table, keys, pen
- If there is a severe visual disturbance, place an object in the patient's hand and ask him/her to name it.

TIME TO REFER

If there is any neurological deficit, consistent with stroke or TIA, do not delay: Arrange to transfer the patient acutely to secondary care.

ABCD2 – prediction of stroke risk after TIA

	ABCD2 items (score: 0–7)	Points
A	Age: ≥ 60 years	1
B	Blood Pressure: ≥ 140/90mm Hg	1
C	Clinical features:	
	unilateral weakness or	2
	speech impairment without weakness	1
D	Duration of symptoms:	
	≥ 60 minutes or	2
	10–59 minutes	1
D	Diabetes: on medication/insulin	1

Low risk (≤3) – urgent referral within seven days

ABCD2 scores of three or less have a lower risk of stroke. These patients, plus those with higher scores but presenting more than one week following the TIA, may initially be managed in the community followed by specialist assessment and investigations within seven days of onset of symptoms. If the treating doctor is certain of the diagnosis, confident of initiating treatment and has ready access to brain and carotid imaging then specialist review may not be required.

Specialist review will confirm a diagnosis of TIA in approximately 50–80% of patients referred from the community.[13]

Initial investigations of TIA in primary or secondary care should include CBC, electrolytes, creatinine, fasting lipids, CRP, ESR (to rule out temporal arteritis) random glucose, INR (if on warfarin) and ECG.

Other possible investigations, usually performed in secondary care, are echocardiology, angiography, CXR, syphilis serology, vasculitis screen (ANA) and prothombotic screen (aPTT, PT).

Since TIA is a clinical diagnosis investigations include brain imaging to confirm cerebral ischaemia or haemorrhage and to exclude stroke mimics. Brain imaging is mandatory, to exclude intracranial haemorrhage as the cause of the current event, prior to commencing warfarin for atrial fibrillation.

Carotid imaging is appropriate in people, with carotid circulation symptoms (Table 2) who are fit for surgery. Urgent endarterectomy may be recommended for people with symptomatic severe stenosis of the internal carotid artery.

Step 3 – Begin early treatment as soon as TIA confirmed

As soon as a diagnosis of TIA is confirmed by a specialist, preventive measures to modify risk should be commenced. Antiplatelet and statin therapy should continue.

All patients should be offered information and personalised advice about how they can reduce their modifiable risks.[19] Any co-morbidities such as atrial fibrillation, diabetes, hypercholesterolaemia and hypertension should be intensively treated[20] (Table 3).

Secondary prevention to modify risk factors can reduce the risk of stroke by up to 80%.[21]

Table 2: Carotid and vertebrobasilar TIA symptoms

Carotid TIA	Vertebrobasilar TIA
▪ Monocular blindness ▪ Dysphasia ▪ Unilateral motor and/or sensory symptoms affecting face and limbs	▪ Cortical blindness ▪ Diplopia ▪ Isolated homonymous hemianopia or quadrantanopia ▪ Bilateral motor and/or sensory symptoms affecting face and/or limbs

Table 3: Modifiable risk factors for stroke following a TIA (excluding carotid endarterectomy). Adapted from LaRocque et al, 2008.[14]

	Risk	Recommendation
Lifestyle factors	Smoking	Smoking doubles stroke risk. All people who smoke should be strongly encouraged to stop immediately. (see BPJ 10 and smoking cessation guidelines)
	Alcohol	Avoid excessive alcohol: no more than two drinks/day for men and one drink/day for women.
	Body mass index	Encourage weight loss in those who are overweight. Aim for BMI of <25 kg/m^2 and waist circumference of <100 cm in men and <90 cm in women.
	Diet	Encourage a low fat, low sodium diet with 5+ portions a day of fruit and vegetables.
	Physical activity	Encourage an increase in physical activity to regular exercise 30–60 minutes most days of the week.
Medical therapies	Blood pressure lowering	Even small decrease in blood pressure reduces stroke risk by 20–25%. All people, whether normotensive or hypertensive should start antihypertensives within the first week, if tolerated. No specific blood pressure target can be recommended for all people.
		First-line ACE inhibitor +/– thiazide diuretic.
	Antiplatelet therapy,[8, 15] (see page 32)	Long term antiplatelet therapy should be prescribed to all people who are not on an anticoagulant.
		First-line aspirin plus modified release dipyridamole[16] (currently dipyridamole is only subsidised if a person continues to have TIAs while on aspirin, however this restriction is currently under review).
		Second-line aspirin or clopidogrel alone (not currently subsided for non-aspirin allergic patients).
	Anticoagulant therapy[17] (see page 38)	Should be used in all people who have atrial fibrillation, cardioembolic stroke from valvular heart disease or recent myocardial infarction once brain imaging has excluded intracranial haemorrhage.
	Cholesterol lowering	Statins should be prescribed for all people able to tolerate therapy. Aim for LDL <2.5 mmol/L.
	Diabetes management	Check for diabetes and manage in–line with national guidelines.[18]

Differential diagnoses

There is a wide differential diagnosis for a patient who presents with a history of transient neurological symptoms. Symptoms that make the diagnosis less likely are:

- Positive neurological symptoms – such as pins and needles, limb shaking or scintillating visual field abnormalities
- Global symptoms – such as confusion, faints, generalised numbness, bilateral blurred vision, isolated dizziness

Differential diagnoses of TIA:[7]

- Migraine aura, with or without headache
- Hypotension and/or syncope
- Transient episodes of non focal symptoms e.g. confusion
- Peripheral vestibular disorders – isolated vertigo that may have associated nausea and ataxia
- Partial (focal) epileptic seizures
- Anxiety and/or hyperventilation
- Transient global amnesia
- Drop attacks – sudden transient loss of postural tone causing falls
- Hypoglycaemia

Returning to driving after a TIA

In general driving is not safe in the early days and weeks after a TIA because of the significant risk of a stroke.

The Land Transport and Safety Agency recommend:

Single TIA

- Private licence: no driving for minimum of one month
- Commercial licence: no driving for minimum of six months and then specialist review.

More than one TIA

- Private licence: no driving for minimum of three months and return only if cause adequately investigated and treated.
- Commercial licence: no driving. Appeal possible with specialist support.

Resources

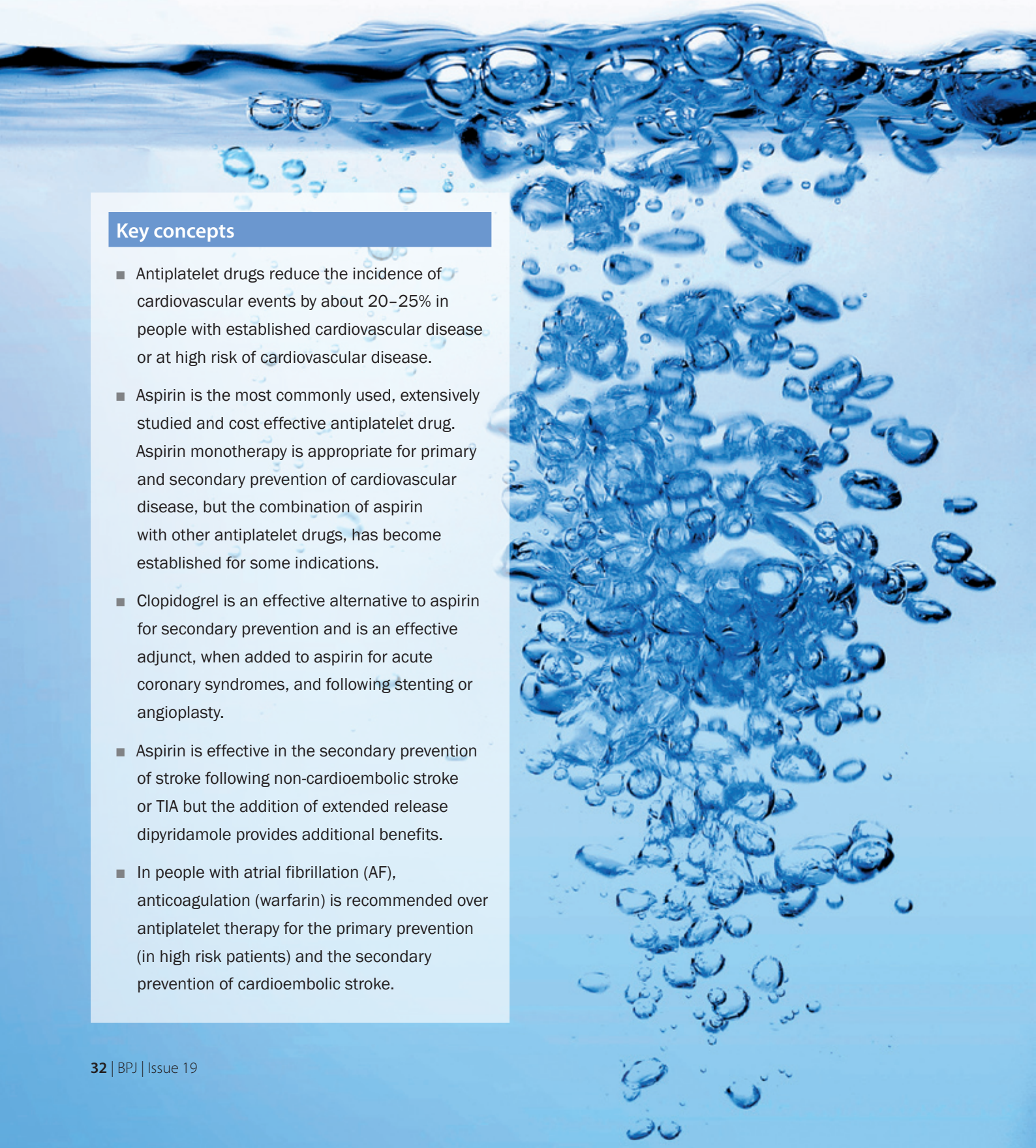
- Stroke Foundation of New Zealand TIA guideline 2008. www.stroke.org.nz
- New Zealand Guidelines Group. New Zealand smoking cessation guidelines, 2007. www.nzgg.org.nz
- New Zealand Guidelines Group. Assessment and management of cardiovascular risk, 2003. www.nzgg.org.nz
- New Zealand Guidelines Group. Management of type 2 diabetes, 2003. www.nzgg.org.nz
- Land Transport Safety Authority. New Zealand Medical fitness to drive, 2002. www.ltsa.govt.nznzlicensing/docs/ltsa-medical-aspects.pdf

References

1. National Collaborating Centre for Chronic Conditions. Stroke: National clinical guideline for diagnosis and initial management of acute stroke and transient ischaemic attack (TIA). London: Royal College of Physicians, 2008. Available from http://www.nice.org.uk/CG068 (accessed January, 2009).
2. Wu CM, McLaughlin K, Lorenzetti DL, et al. Early risk of stroke after transient ischemic attack: a systematic review and meta-analysis. Arch Intern Med 2007; 167(22):2417-22.
3. Giles MF, Rothwell PM. Prognosis and management in the first few days after a transient ischaemic attack or minor ischaemic stroke. Int J Stroke 2006;1:65-73.
4. Coull A, LovettJK, Rothwell PM et al. Early risk of stroke after a TIA or minor stroke in a population-based incidence study. BMJ 2004;328:326-8.
5. Johnston SC, Gress DR, Browner WS et al. Short-term prognosis after emergency department diagnosis of TIA. JAMA 2000;284:2901-6.
6. Rothwell PM, Giles MF, Chandratheva A et al. Effect of ugent treatment of transient ischaemic attack and minor stroke on early recurent stroke (EXPRESS study): a prospective population-based sequential comparison. Lancet 2007;370(9596):1432-43.
7. Stroke Foundation of New Zealand. NZ Guidelines for the Assessment and Management of Transient Ischaemic Attack (TIA). 2008. Available from www.stroke.org.nz (accessed January, 2009).
8. Sandercook PAG , Counsell C, Gubitz GJ, Tseng M-C. Antiplatelet therapy for acute ischaemic stroke. Cochrane Database Syst Rev 2008;4:CD000029.
9. Johston SC, Rothwell PM, Nguyen-Huynh MN, et al. Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack. Lancet 2007;369(9558):283-92.
10. Giles MF, Rothwell PM. Risk prediction after TIA: the ABCD system and other methods. Geriatrics 2008;63(10):10-16.
11. Josephson SA, Sidney S, Pham TN, et al. Higher ABCD2 score predicts patients most likely to have true transient ischaemic attack. Stroke 2008;49:3096-8.
12. Franklin M, McDiarmid T, Mackler L. Clinical Inquiries: Is an outpatient workup safe for patients with a transient ischaemic attack? J Fam Prac 2004;53(7):567- 9.
13. Lavallee PC, Mesequer E, Abboud H, et al. A transient ischaemic attack clinic with round the clock access (SOS-TIA): feasibility and effects. Lancet Neurol 2007;6(11):953-60.
14. LaRocque P, McBride P. Prevention of secondary stroke/transient ischaemic attack. CME Bulletin, American Academy of Family Physicians 2008;9(5):1-5.
15. Kirshner HS. Prevention of secondary stroke and transient ischaemic attack with antiplatelet therapy: the role of the primary care physician. Int J Clin Pract 2007;61(10):1739-48.
16. ESPRIT Study Group: Halkes PH et al. Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (ESPRIT): randomised controlled trial. Lancet 2006;367(9523):1665-73.
17. Sandercock PAG, Counsell C, Karmal AK. Anticoagulants for acute ischaemic stroke. Cochrane Database Syst Rev 2008;4:CD000024.
18. New Zealand Guidelines Group. Management of type 2 diabetes. 2003. Available from www.nzgg.org.nz (accessed January 2009).
19. Miller ET, Spilker J. Readiness to change and brief educational interventions: successful strategies to reduce stroke risk. J Neuro Nurs 2003;35(4):215-22.
20. Lip GYH, Kalra L. Stroke prevention. BMJ Clinical Evidence 2008;9:207.
21. Hackman DG, Spence JD. Combining multiple approaches for the secondary prevention of vascular events after stroke: a quantitative modeling study. Stroke 2007;38:1881-5.

The role of antiplatelet agents

Key Reviewer: Dr CK Wong, Associate Professor of Medicine and Cardiologist, Dunedin School of Medicine, University of Otago



Key concepts

- Antiplatelet drugs reduce the incidence of cardiovascular events by about 20–25% in people with established cardiovascular disease or at high risk of cardiovascular disease.
- Aspirin is the most commonly used, extensively studied and cost effective antiplatelet drug. Aspirin monotherapy is appropriate for primary and secondary prevention of cardiovascular disease, but the combination of aspirin with other antiplatelet drugs, has become established for some indications.
- Clopidogrel is an effective alternative to aspirin for secondary prevention and is an effective adjunct, when added to aspirin for acute coronary syndromes, and following stenting or angioplasty.
- Aspirin is effective in the secondary prevention of stroke following non-cardioembolic stroke or TIA but the addition of extended release dipyridamole provides additional benefits.
- In people with atrial fibrillation (AF), anticoagulation (warfarin) is recommended over antiplatelet therapy for the primary prevention (in high risk patients) and the secondary prevention of cardioembolic stroke.

The oral antiplatelet drugs include aspirin, clopidogrel and dipyridamole. This article provides an overview of their current place in therapy.

Antiplatelet drugs have a major role in the secondary prevention of thrombotic cardiovascular events. Aspirin is also widely used for primary prevention in those with high vascular risk. Clopidogrel is an alternative to aspirin in allergic or intolerant patients, and in combination with aspirin it is more effective than aspirin alone in secondary prevention, following acute coronary syndromes (ACS). The combination of dipyridamole and aspirin is more effective than aspirin alone for secondary prevention following stroke or TIA.

Evidence shows that antiplatelet drugs can reduce the incidence of cardiovascular events in people with established cardiovascular disease or in people at high risk of cardiovascular disease.[1,2] It is estimated that antiplatelet drugs reduce the risk of any serious vascular event by about 25% (this figure is calculated from a reduction in non-fatal MI of 34%, non-fatal stroke of 25%, and vascular death of 17%).[3] The benefits in these high risk groups outweigh the risk such as major bleeding.[4] The evidence for benefit of antiplatelet treatment (primarily aspirin) in people at low risk of cardiovascular disease (i.e. for primary prevention) is less clear.[4]

Aspirin

Mechanism of action

Aspirin works by irreversibly inhibiting the enzyme cyclo-oxygenase (COX-1) which is required to make the precursors of thromboxane within platelets. This reduces thromboxane synthesis. Thromboxane is required to facilitate platelet aggregation and to stimulate further platelet activation. Because platelets do not have a nucleus and therefore contain no DNA, no new cyclo-oxygenase can be produced, so the effect of aspirin on platelets persists until enough new platelets have been formed to replace affected ones. This takes approximately seven to ten days, i.e. the lifespan of a platelet. Therefore the risk of increased bleeding, caused by aspirin, persists for some days after aspirin treatment has been stopped.

Aspirin also alters the COX-2 form of cyclo-oxygenase which is required in the prostaglandin pathway. This is the mechanism for the anti-inflammatory effects of aspirin at higher doses.

Therapeutic uses

In the primary prevention of cardiovascular events in people at high risk (15–20% risk of an event over five years) aspirin is the antiplatelet drug of choice, however some controversy exists (see box below).

In the primary prevention of stroke in people with AF, warfarin may be preferable to aspirin after assessment of the risk of bleeding versus the risk of embolism (see page 38).

In patients who have had a non-cardioembolic TIA or stroke (including post TIA) the combination of aspirin plus dipyridamole is more effective than aspirin alone. In situations of concomitant AF and ischaemic stroke warfarin should be used instead.

Controversy surrounds the use of aspirin for primary prevention of cardiovascular disease

The use of aspirin for primary prevention is increasingly controversial and several well controlled trials have shown that aspirin has no benefit for primary prevention of cardiovascular events, even in people at higher risk.[5] The evidence base for aspirin in primary prevention mainly involved studies almost a decade ago when statins were much less commonly used. Statins now appear to have an emerging role in primary prevention in some groups.[6] The role of aspirin and statins for primary prevention will continue to be debated.

GI adverse effects and low dose aspirin

Risk factors associated with GI bleeding and NSAID use generally also apply to the use of aspirin. These include:

- A history of upper GI bleeding
- A history of peptic ulcer disease
- Concomitant use of drugs known to increase the risk of upper GI events

General measures to reduce the risk of GI bleeding may include:

- Ensuring that a low dose of aspirin (≤100 mg) is being taken
- Ensuring that there are no contraindications to the use of aspirin (e.g. active peptic ulceration)
- Reviewing medication – the risk of serious GI complications increases significantly in people who regularly take an antiplatelet drug and an NSAID (also consider OTC medication)

If dyspepsia develops in a person taking low dose aspirin or a person on aspirin is at increased risk of GI bleeding then:

- Consider if aspirin is necessary
- Consider the use of a PPI with ongoing low dose aspirin
- A check for *H. pylori* may be indicated
- Consider a switch to clopidogrel, although there is a lack of evidence that dyspeptic symptoms will resolve and clopidogrel is not subsidised for this indication. Taking aspirin with a PPI may be safer, and more effective at preventing recurrent ulcer bleeding in people with a previous aspirin induced bleeding ulceration, than switching to clopidogrel.[7]

For a number of indications including acute ST elevation myocardial infarction (STEMI), ACS, post intracoronary stenting and following coronary angioplasty the combination of aspirin with clopidogrel is more effective than aspirin alone and is currently subsidised for three to six months, depending on the indication. In the treatment of non-STEMI most benefit of clopidogrel occurs within the first three months. Once clopidogrel is stopped, aspirin alone should be continued.[8]

It is suggested that in ACS or in acute ischaemic stroke where an immediate anti-thrombotic effect is needed, a dose of 300 mg of aspirin should be given, to enable total inhibition of thromboxane dependent platelet aggregation.[1]

For emergency administration, patients should chew and suck uncoated aspirin tablet for quickest absorption. Peak plasma levels will be achieved after 30–40 minutes (it can take three to four hours to reach peak plasma levels when using enteric coated aspirin unless the tablets are chewed).[1]

Risks and benefits

Ten to twenty fatal and non-fatal vascular events can be prevented for every 1000 people, at high risk of vascular disease, treated for one year with low dose aspirin.[9] There is an approximately two-fold increase in the risk of major bleeding (predominately upper GI) with long term treatment with low dose aspirin. For the majority of high risk people the benefit of avoiding a serious vascular event is greater than the increased risk of bleeding.

The presence of uncontrolled hypertension in a person taking low dose aspirin may increase the risk of a haemorrhagic stroke or major GI bleeding.

Gastrointestinal effects

Aspirin use has long been associated with an increased risk of GI bleeding.[10] The risk of GI bleeding with aspirin use increases as the dose increases. A meta-analysis of

31 randomised controlled trials showed people taking aspirin at a dose of more than 100 mg daily, had a rate of bleeding complications that was approximately three times higher, than for people taking aspirin doses of less than 100 mg.[11]

The risk of GI bleeding in people taking low dose aspirin is lower than the risk for people taking standard doses of NSAIDs (a two-fold increase in risk compared to a five fold increase in bleeding in people taking NSAID for musculoskeletal pain).[12]

There is no convincing evidence that enteric coated aspirin reduces the risk of GI bleeding when low doses (75–100 mg) are used and some evidence that the enteric coating significantly reduces the bioavailability of aspirin particularly for people with a higher BMI.[13]

If dyspepsia becomes a concern in a person taking low dose aspirin it is recommended that general measures are taken to reduce risk (see box). Other medication that can cause dyspepsia should be reviewed e.g. NSAIDs, corticosteroids.

Clopidogrel

Mechanism of action

Clopidogrel is a thienopyridine that reduces platelet activation and aggregation by inhibiting the binding of ADP to its platelet receptor. Clopidogrel appears to have a similar permanent effect on platelet function to aspirin. After the drug is stopped, normal platelet function is only restored as new platelets are produced.[3]

Therapeutic uses

In the secondary prevention of atherothrombotic disease, the CAPRIE study[14] demonstrated that clopidogrel is at least as effective as aspirin but its higher cost has prevented it from superseding aspirin for this indication. In practice, monotherapy with clopidogrel is mainly used for secondary prevention as an alternative in people who are allergic to or intolerant of aspirin. There is little evidence to support the use of clopidogrel for primary prevention.

Combination therapy with clopidogrel and aspirin is now established in acute STEMI, ACS, post intracoronary stenting and following coronary angioplasty. For these indications, several major trials (CURE, CLARITY, COMMIT)[15–17] have shown reduced secondary events and decreased mortality with the addition of clopidogrel to aspirin compared with aspirin monotherapy.[5] Taking both clopidogrel and aspirin is not routinely recommended for people who have had a TIA or ischaemic stroke because of an increased risk of haemorrhage.[14]

The recent ProFESS trial,[18] on over 20,000 patients within 120 days of a non-cardioembolic ischaemic stroke, has provided good quality evidence that clopidogrel alone (75 mg daily) is as effective as aspirin (25 mg) plus dipyridamole (slow release 200 mg twice per day) in the secondary prevention of ischaemic stroke, but clopidogrel is not currently subsidised for this indication.

Clopidogrel is available on special authority as an additional antiplatelet agent for patients who have had one of the following:[19]

- An acute MI
- Chest pain at rest for more than 20 minutes duration, requiring hospital admission for more than 24 hours
- A troponin T or troponin I test result above the upper limit of the reference range
- A revascularisation procedure
- Patients awaiting revascularisation, post stenting and documented stent thrombosis
- Aspirin allergy (defined as a history of anaphylaxis, urticaria or asthma within four hours of ingestion), and any of the indications listed above and also for TIA or stroke, or severe symptomatic peripheral vascular disease.[19]

Dipyridamole

Mechanism of action

Dipyridamole has both antiplatelet and vasodilating properties. It is thought to act primarily to reduce platelet aggregation but it also has other inhibitory effects on various enzymes that are required for normal platelet function.

Therapeutic uses

For the secondary prevention of stroke following non-cardioembolic TIA or stroke, combination treatment with dipyridamole (as the extended release formulation) and low dose aspirin has been shown to produce more benefit than aspirin alone.

Most of the evidence comes from two trials; ESPS-2 and ESPRIT.

In ESPS-2, the stroke rate at 24 months follow up was significantly reduced in the aspirin plus dipyridamole group compared with aspirin alone (absolute risk reduction 3%).

In the ESPRIT trial, death from all vascular causes, non-fatal stroke, non-fatal MI, or major bleeding complication after a mean follow-up of 3.5 years, was significantly lower in the combination group compared with aspirin alone (absolute risk reduction 1% per year).

Therefore there is considerable debate about the cost effectiveness of adding dipyridamole to aspirin for these indications and some experts still consider that aspirin alone should remain the first line treatment. However most current international guidelines recommend aspirin plus dipyridamole (or clopidogrel monotherapy in aspirin allergic patients) as the preferred treatment.[20]

Aspirin plus dipyridamole is recommended for up to two years after the most recent ischaemic event. After this time aspirin alone can be used (unless there are ongoing ischaemic events).[21]

Currently dipyridamole is only subsidised if a person continues to have TIAs whilst taking aspirin or is aspirin intolerant (aspirin induced asthma, urticaria, anaphylaxis, or significant aspirin induced bleeding excluding bruising). This restriction is currently under review.

Dipyridamole is also available on special authority for use in patients who have prosthetic heart valves and after CABG surgery.[19]

Adverse effects

Dipyridamole can cause a range of unpleasant adverse effects. Effects such headache, dizziness, nausea and diarrhoea may occur but are usually short lived and most patients can persevere with treatment. Rarely symptoms of ischaemic heart disease, particularly angina, can become worse with dipyridamole use. Dipyridamole should therefore be used cautiously in people with severe coronary artery disease including unstable angina, recent MI and heart failure. It may also exacerbate migraine, postural hypotension and myasthenia gravis.

References:

1. Patrono C, Garcia Rodriguez LA, Landolfi R, Baigent C. Low-dose aspirin for the prevention of atherothrombosis. N Engl J Med 2005;353:2373-83.
2. Patrono C, Bachmann F, Bode C et al. European Society of Cardiology expert consensus document on the use of antiplatelet agents. The Task Force on the Use of Antiplatelet Agents in Patients with Atherosclerotic Cardiovascular Disease of the European Society of Cardiology. Eur Heart J 2004;25:166-81.
3. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction and stroke in high-risk patients. BMJ 2002;324:71-86.
4. Krötz F, Sohn H-Y, Klauss V. Antiplatelet drugs in cardiological practice: Established strategies and new developments. Vasc Health Risk Manag 2008;4(3):637-45.
5. Hiatt WR. Aspirin for prevention of cardiovascular events. BMJ 2008;337:a1806.
6. Mills EJ, Rachlis B, Wu P et al. Primary prevention of cardiovascular mortality and events with statins. A network meta-analysis involving more than 65000 patients. J Am Coll Cardiol 2008;52(22):1769-81.
7. Chan FKL, Ching JYL, Hung LCT et al. Clopidogrel versus aspirin and esomeprazole to prevent recurrent ulcer bleeding. N Engl J Med 2005;352:238-44.
8. National Institute for Health and Clinical Excellence (NICE). Clopidogrel in the treatment of non-ST-segment-elecation acute coronary syndrome. Technology appraisal 80. 2004. Available from www.nice.org.uk. (Accessed December 2008).
9. Patrono C, Baigent C, Hirsh J, Roth G. Antiplatelet Drugs. American College of Chest Physicians Evidence-based Clinical Practice Guidelines (8th Edition). Chest 2008;133:199S-233.
10. Derry S, Loke YK. Risk of gastrointestinal haemorrhage with long term use of aspirin:meta-analysis. BMJ 2000;321:1183-7.
11. Serebruany VL, Steinhubl SR, Berger PB et al. Analysis of risk of bleeding complications after different doses of aspirin in 192036 patients enrolled in 31 randomised controlled trails. Am J Card 2005;95(10):1218-22.
12. National Institute for Health and Clinical Excellence (NICE). Dyspepsia: management of dyspepsia in adults in primary care. Clinical guideline 17. 2004. Available from www.nice.org.uk. (accessed December 2008).
13. Cox D, Maree AO, Dooley M et al. Effect of enteric coating on antiplatelet activity of low-dose aspirin in healthy volunteers. Stroke 2006;37:2153-8.
14. CAPRIE Steering Committee. A randomised, blinded trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). Lancet 1996;348:1329-39.
15. Yusuf S, Zhao F, Mehta SR, et al. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med. 2001 16;345(7):494-502.
16. Sabatine MS, Cannon CP, Gibson CM et al. Effect of clopidogrel pretreatment before percutaneous coronary intervention in patients with ST-elevation myocardial infarction treated with fibrinolytics. The PCI-CLARITY study. JAMA. 2005;294:1224-32.
17 COMMIT collaborative group. Addition of clopidogrel to aspirin in 45 852 patients with acute myocardial infarction: Randomised placebo-controlled trial. Lancet 2005; 366:1607-21.
18. Sacco RL, Diener HC, Yusuf S et al. PRoFESS Study Group. Aspirin and extended-release dipyridamole versus clopidogrel for recurrent stroke. N Engl J Med. 2008 Sep 18;359(12):1238-51.
19. Parmaceutical Management Agency. New Zealand Pharmaceutical Schedule, December 2008.
20. UpToDate Version 16.3, www.uptodate.com.
21. Simmons BB, Salzman BE. Aspirin + clopidogrel therapy: How does your care compare to the evidence? J Fam Pract 2008;57(1):26-32.

www.bpac.org.nz keyword: warfarinaspirin

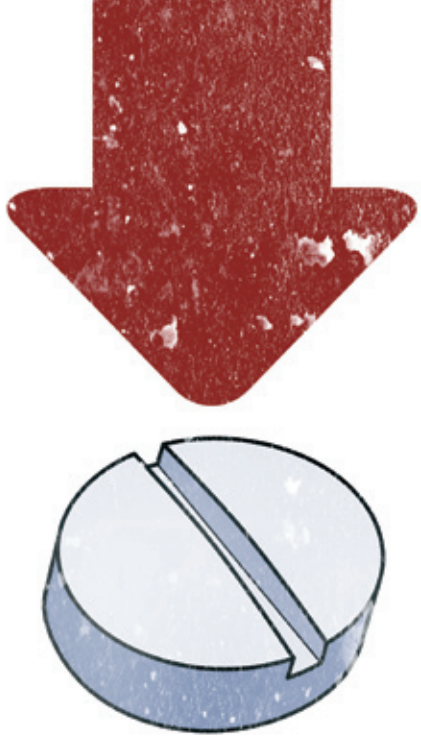
WARFARIN vs. ASPIRIN

FOR THE PREVENTION OF ATRIAL FIBRILLATION RELATED STROKE

Key Concepts

- In atrial fibrillation (AF) warfarin is more effective than aspirin for stroke prevention.
- Warfarin is preferred in people at high risk of stroke and aspirin for those at low risk. In people at intermediate risk the choice of treatment is determined by assessment of the benefits versus risks on an individual basis.
- The risk of bleeding with warfarin is increased in elderly people however with correct monitoring it appears to be as safe as aspirin.
- Clear communication and monitoring is required for the safe and effective use of warfarin in all people, particularly the elderly.

Key Reviewer:
Dr CK Wong, Associate Professor of Medicine and Cardiologist, Dunedin School of Medicine, University of Otago



Both warfarin and aspirin are indicated for the prevention of stroke in people with AF. Over 50% of strokes occur in people over the age of 75 years.[1] Stroke risk doubles approximately every ten years after age 55. The prevalence of AF increases at a similar rate with age. Elderly people therefore are at increased risk of AF and stroke and are likely to benefit from anticoagulation.

The decision whether to choose aspirin or warfarin for stroke prevention is often not clear cut. Although most people can take warfarin safely, it is under utilised in both primary care and hospital practice, particularly in elderly people.[2, 3]

Warfarin is more effective for prevention of stroke than aspirin

There is evidence to show that treatment with warfarin can reduce stroke risk more effectively than aspirin in patients with AF. A recent meta-analysis showed that warfarin reduced AF related stroke by 64% compared to 22% for aspirin therapy.[4] If warfarin is contraindicated (see box over page), not indicated or is declined by the patient, aspirin should be prescribed, as it reduces the risk of stroke compared to placebo.

Which therapy to choose depends on the risk of stroke

Current guidelines recommend the use of warfarin for those at high risk of stroke and aspirin for those at low risk (Table 1).[2, 5] For those at intermediate risk of stroke the benefits of warfarin may not always outweigh the risks. Individual patient preference and the availability of effective monitoring may be the most important deciding factors.[6]

Table 1: Choice of therapy guided by thromboembolic risk. Adapted from New Zealand guidelines for management of atrial fibrillation and flutter, 2005.[2]

Thromboembolic risk – 5 years	Therapy
High risk of stroke ≥15%	Warfarin usually advantageous
Intermediate risk of stroke 10–14%	Warfarin may be advantageous but patient preference may influence decision
Low risk of stroke <10%	Aspirin usually preferred

Contraindications to warfarin use include:

- Haemorrhagic tendencies and blood dyscrasias
- Past history of intracranial haemorrhage
- Recent history of GI or GU bleeding (previous six months)
- Uncontrolled hypertension
- Severe liver disease
- Alcoholism
- Recurrent unexplained syncope
- Planned surgery
- Pregnancy

Other aspects to consider when prescribing warfarin include:

- Comorbidities
- Concomitant use of medications
- Poor compliance with medication and monitoring (e.g. cognitive impairment, confusion, mental illness, inability to access services)
- Activities that increase the risk of trauma
- Increased risk of bleeding in elderly people
- Potential for falls
- Changes in diet, supplement use and general wellbeing (e.g. new illness)

$CHADS_2$: alternative method of stroke risk assessment

Another method to assess stroke risk that is widely used in research, but which may be applicable to daily clinical practice, is the $CHADS_2$ risk stratification scheme.[7]

$CHADS_2$ assigns a score to independent risk factors for stroke and guides drug selection. (Figure 1).[1] Scores are calculated as follows:

CHF	(1 point)
Hypertension	(1 point)
Age 75 years or older	(1 point)
Diabetes mellitus	(1 point)
previous **S**troke or TIA	(2 points)

Coronary heart disease and female gender which are weaker risk factors for stroke are not included.

A calculated $CHADS_2$ score for example, in an 80 year old (+1) patient, with hypertension (+1), and a history of a previous stroke (+2) would be 4.

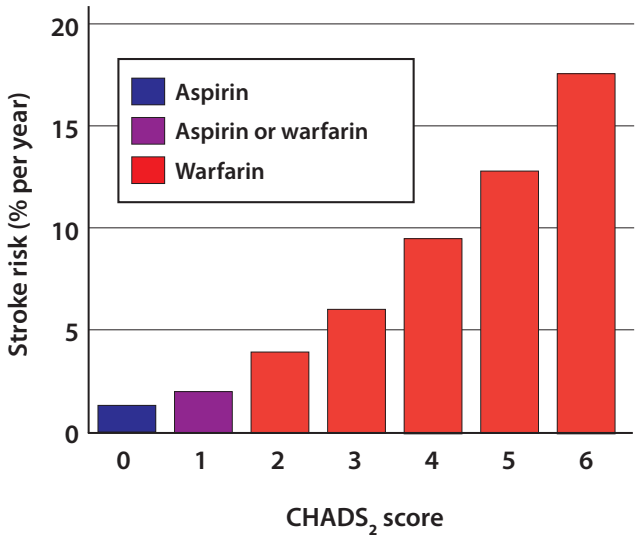


Figure 1: Stroke risk in patients with AF according to the $CHADS_2$ risk index. The colour coded bar graphs indicate the appropriate antithrombotic treatment strategy.[1]

Bleeding risk of aspirin and warfarin

Aspirin

The risk of major bleeding with aspirin therapy varies according to the dose taken. The rate of major bleeding with low dose aspirin is reported as approximately 1–2% per year.[3, 8] Mortality data is similar to that for warfarin. Other dose dependent adverse effects of aspirin use can include gastrointestinal irritation and bleeding and tinnitus.

Warfarin

The risk of major bleeding with warfarin varies from 1% to 7.2% per year in clinical trial data. Of those that have a major haemorrhage on warfarin, up to 1% will die. Intracranial bleeding is associated with the highest risk to the patient, with up to 60% of major intracranial haemorrhages resulting in death.[9] The incidence of more minor bleeding is difficult to quantify.

Risk of bleeding with warfarin is higher in elderly people

There is an increased risk of bleeding with warfarin use in elderly people. This is thought to be due to several factors. Elderly people are more likely to have co-morbid conditions and to be on multiple medications with increased interaction potential, therefore increasing the risk of bleeding. Age related changes in the pharmacodynamics and pharmacokinetics of warfarin may also contribute to the increased bleeding risk.

A recent study in patients over the age of 65 years found that those at the greatest risk of stroke were also the patients who experienced more problems with bleeding while on warfarin.[10] The risk of bleeding while taking warfarin was greatest in those aged 80 years or over (13.1 %) and the risk was higher in the first three months of treatment.[10]

Warfarin can be used safely in elderly people with atrial fibrillation

The BAFTA study was a randomised controlled trial that looked at the use of warfarin versus aspirin for stroke prevention in primary care and was the first to include only people aged 75 years or older. The conclusions of the study were that:[3]

- Advanced age alone is not a contraindication to warfarin use
- Warfarin, in elderly patients with AF, is more effective for stroke prevention than aspirin
- Warfarin is as safe as aspirin (when monitored correctly)
- Warfarin use should be considered in all people with AF aged 75 years or older, unless there are contraindications to its use or the patient declines treatment
- Target INR should be 2–3

Limitations of the study arise from possible selection bias as patients were excluded if there were clear clinical indications to use, or not to use, warfarin. Those who were included therefore were patients in whom there was clinical uncertainty. Although these are the very patients that we need guidance for, those in the study group were also shown to have a lower level of stroke risk than participants in other studies.[11] Critics suggest that this may give a false sense of safety with warfarin use.[12] The authors response to this, however is that they are likely then to have "underestimated the benefits of warfarin treatment over aspirin".[13]

Effective communication and monitoring is required for safe use of warfarin in all people, particularly elderly people

Safe use of warfarin depends on many factors but effective communication and monitoring are essential.

Useful strategies for safe warfarin use may include:

- Give clear verbal and written information.
- Ensure patients know which symptoms may signal abnormal bleeding
- Educate patients about the effects of diet, alcohol, acute illness and other medications (including herbal medicines and supplements) on INR control
- Encourage effective sharing of information between patient, whanau, carers, clinicians and pharmacists
- Use one brand only
- Use one tablet strength only during initiation (remind yourself what colour each strength of tablet is)
- Set up an alert on your practice software for patients on warfarin
- Consider ways to minimise the inconvenience of regular INR monitoring (e.g. most convenient place to have blood drawn, best way to convey results)

The results of the recent ACTIVE-W[15] trial (warfarin vs aspirin and clopidogrel) indicate that the benefits of warfarin also depend on individual factors and how well treatment is managed or monitored. Implications from the results of this trial include:

- Some patients may have an unstable INR which is difficult to manage
- Compliance or monitoring problems may compromise the benefits of warfarin
- The benefits of warfarin are mainly seen in patients who maintain a therapeutic INR most of the time

Aspirin with warfarin in people with atrial fibrillation and vascular disease

Recent guidance has re-emphasised that for patients with AF and associated stable vascular disease, the risks from combined treatment with both warfarin and aspirin are greater than the benefits. Adding aspirin to warfarin increases the risk of bleeding and does not provide additional prevention from stroke.[6, 14]

However, this issue remains controversial amongst cardiologists, mainly because of the well proven benefit of antiplatelet agents in vascular disease versus more doubtful benefit of warfarin in this situation. So if a patient with severe vascular disease had AF as well, many cardiologists may still give combination therapy.

References:

1. Blaauw Y, Crijns H. Treatment of atrial fibrillation. Heart 2008;94:1342-9.
2. New Zealand Guidelines Group (NZGG). Management of people with atrial fibrillation and flutter. May 2005. Available from www.nzgg.org.nz (Accessed January 2009).
3. Mant J, Jobbs R, Fletcher K et al. Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation treatment of the Aged Study, BAFTA): a randomised controlled trial. Lancet 2007;370:493-503.
4. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: Antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med 2007;146:857-67.
5. National Institute for Clinical Excellence (NICE). The management of atrial fibrillation. Clinical guideline 2006. Available from www.nice.org.uk. (accessed December 2008).
6. Aguilar MI, Hart RG, Pearce LA. Oral anticoagulants versus antiplatelet therapy for preventing stroke in patients with non–valvular atrial fibrillation and no history of stroke or transient ischaemic attacks (Review). The Cochrane Collaboration 2008. Available from www.thecochranelibrary.com (accessed December 2008).
7. Gage BF, Waterman AD, Shannon W et al. Validation of clinical classification schemes for predicting stroke. JAMA 2001;285(22):2864-70.
8. Wiedermann CJ, Stockner I. Warfarin-induced bleeding complications – clinical presentation and therapeutic options. Thromb Res 2008;122(suppl 2):S13-S18.
9. Hylek EM, Evans-Molina C, Shea C et al. Major Hemorrhage and tolerability of warfarin in the first year of therapy among elderly patients with atrial fibrillation. Circulation 2007;115:2689-96.
10. Borosak M, Choo S, Street A. Warfarin: balancing the benefits and harms. Aust Prescr 2004;27:88-92.
11. Garcia D, Hylek EM. Stroke prevention in elderly patients with atrial fibrillation. Lancet 2007;370:460-1.
12. Diug J, Lowthian J, Evans S. Warfarin versus aspirin for stroke prevention (BAFTA). Lancet 2007;370:1606.
13. Mant J, Hobbs R, Fletcher K et al. Warfarin versus aspirin for stroke prevention (BAFTA) – Authors' reply. Lancet 2007;370:1606-7.
14. Lip GYH. Don't add aspirin for associated stable vascular disease in a patient with atrial fibrillation receiving anticoagulation. BMJ 2008;336:614-5.
15. The ACTIVE Writing Group on behalf of the ACTIVE Investigators. Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial. Lancet. 2006;367(9526):1903-12.

Sexually transmitted infections in New Zealand

Key findings from the 2007 New Zealand Annual STI Surveillance Report:

- *Chlamydia trachomatis* was the most commonly diagnosed STI
- Between 2003 and 2007, diagnoses of chlamydia increased by 19% and gonorrhoea by 56%
- Genital warts were the most common viral infection
- There were 71 cases of infectious syphilis in 2007, up 4% from 2006
- People aged less than 25 years accounted for 72% of cases of chlamydia, 62% of gonorrhoea, 43% of genital herpes and 62% of genital warts

This article on the prevalence of sexually transmitted infections (STIs) in New Zealand begins our series on sexual health. Upcoming articles in future editions of Best Practice Journal and Best Tests will include:

- **Overview of common STI pathogens – how to recognise**
- **Testing for STIs – how to select the best test and obtain the best sample**
- **Treating STIs – latest evidence**
- **Safer sex – talking to patients about safer sex**

Every year the STI Surveillance Team at the Institute of Environmental Science and Research (ESR) collects data on STIs in New Zealand. This data is submitted voluntarily from sexual health clinics, family planning clinics, student health clinics and laboratories. Data collection does not cover all areas in New Zealand but this is the most complete source of information on STIs currently available.

Chlamydia is the most common STI in New Zealand

Chlamydia trachomatis is the most common STI in New Zealand and rates are increasing. Chlamydia is asymptomatic in approximately 70%–90% of females and up to 73% of males (Ministry of Health. Draft Chlamydia Management Guidelines, 2008). If left untreated, chlamydia infection can lead to pelvic inflammatory disease and ectopic pregnancy in females, urethritis, epididymo-orchitis and reactive arthritis in males, as well as infertility in both males and females. Infection can also be passed on to infants born vaginally, which may result in neonatal conjunctivitis or pneumonia.

In 2007, 5% of people who attended a sexual health clinic were diagnosed with chlamydia (4501 cases, Table 1). The rate of chlamydia detected in Māori and Pacific peoples was double that of Europeans. Māori and Pacific peoples were also more likely to present with complications of chlamydia.

Chlamydia screening guidelines

In 2008 the Sexual Health Advisory Group, established by the Ministry of Health, published the Chlamydia Management Guidelines with the purpose of increasing opportunistic testing for chlamydia in New Zealand. The implementation of these guidelines is currently being piloted, with national distribution anticipated for early 2009.

A copy of the current guideline is available at: **www.moh.govt.nz/moh.nsf/pagesmh/8210**

Table 1: STIs in sexual health clinics in New Zealand in 2007

	Chlamydia	Gonorrhoea	Genital herpes	Genital warts	Syphilis	HIV (AEG data)
No. cases	4501	925	746	3797	71	195
European	53%	38%	74%	71%	52%	43%
Māori	34%	44%	dns	dns	6%	11%
Pacific	7%	11%	dns	dns	10%	4%
Other	5%	6%	dns	dns	30%	36%
Mean age	23	25	29	25	37	39

dns = data not supplied

Total sexual health clinic visits for 2007 = 89208

AEG = AIDS Epidemiology Group

Laboratory surveillance data from Auckland, Waikato and Bay of Plenty regions shows that the rate of chlamydia has risen by 20.6% between 2003 and 2006. More sensitive diagnostic techniques have been introduced over this time period but this would only partly explain the increase.

Rates of gonorrhoea are increasing

Although not as prevalent as chlamydia, the diagnosis of *Neisseria gonorrhoeae* is increasing at a greater rate. Māori accounted for more cases of gonorrhoea diagnosed in sexual health clinics than any other ethnic group (Table 1). Approximately 95% of males with gonorrhoea will be symptomatic (compared to 50% of females) therefore males are more likely to seek treatment. Untreated gonorrhoea infection can lead to pelvic inflammatory disease in females, epididymo-orchitis in males and severe conjunctivitis in infants born to infected mothers.

First presentations of genital herpes

The actual burden of disease caused by genital herpes is much greater than the rates of initial infection as reported in STI clinics (Table 1). Genital herpes can be difficult to diagnose clinically as around 60% of cases present with atypical symptoms and 20% are asymptomatic. Typical painful lesions are only seen in 20% of cases. Recurrent infection of genital herpes is common and prevalence in the population increases with age. Mothers with active infection pose a high risk to their infant when giving birth. Genital herpes can cause severe systemic disease in neonates and those who are immune suppressed. Ulcerative lesions can also facilitate the transmission of HIV infection.

Genital warts is the most common viral STI

Genital warts are caused by human papillomavirus (HPV) infection. In 2007, genital warts were the most frequently reported viral STI, with the number of cases increasing by 19% from the previous year in sexual health clinics (Table 1).

Some types of HPV infection (mainly types 16 and 18) are associated with cervical, penile and anal cancers. However approximately 90% of genital warts are caused by HPV types 6 or 11, which are not associated with cervical cancer.

Syphilis cases increasing

Infectious syphilis is caused by *Treponema pallidum*. In recent years this disease has resurfaced. Although a relatively uncommon STI, the number of cases in 2007 (71 cases, Table 1) has more than doubled since 2003 (30 cases). The majority of syphilis cases in 2007 were in males (92%) and occurred in the Auckland region (69%).

The first stage of infectious syphilis presents as a painless, solitary ulcer that heals spontaneously. If left untreated, secondary syphilis develops in two to eight weeks. In approximately one-third of cases, tertiary syphilis develops several years later. Untreated syphilis during pregnancy can be transferred directly to the foetus via the placenta, or through contact with lesions during vaginal delivery, resulting in congenital infections and complications or foetal death.

HIV in New Zealand

The AIDS Epidemiology Group, based at the University of Otago is responsible for HIV and AIDS surveillance in New Zealand.

In 2007, 195 people were newly identified with HIV (Table 1). Rates of HIV have decreased in New Zealand since a peak of 218 new cases in 2005. Of the new cases of HIV in 2007, almost half were males who contracted the virus through sex with other males. Cases of heterosexual transmission predominantly occurred in people, who were either infected overseas, or infected by a partner who contracted the virus overseas. Only one person was infected through intravenous drug use. Eight children, five of whom were born overseas, were infected with HIV in 2007 through mother to child transmission. The remaining

three children were born in New Zealand to mothers who were unaware of their HIV positive status.

Improvements in the effectiveness of HIV treatment has resulted in a decrease in the number of people being diagnosed and dying from AIDS. In 1995 64 people were diagnosed with AIDS in New Zealand and 62% died within the following two years. In 2005 only 23% of the 35 people diagnosed with AIDS had died by 2007. Progression from HIV to AIDS is dependent on many factors and may occur within one year of initial infection to up to 15 years later.

Further reading

STI Surveillance Team. Sexually transmitted infections in New Zealand. Annual Surveillance Report 2007. Population and Environmental Health Group. Institute of Environmental Science and Research. Wellington, 2008. Available from **www.surv.esr.cri.nz**

AIDS Epidemiology Group (AEG). AIDS – New Zealand 2008;61. Available from **www.moh.govt.nz/moh.nsf/indexmh/aids-nz-issue61**

How does New Zealand compare to the rest of the world?

There is no universal method for collecting STI surveillance data and numbers are also influenced by individual country's testing practices. Therefore it is unknown how the rate of STIs in New Zealand compares to the rest of the world. In addition, there is no national data for New Zealand.

In general it is known that:

- Regional chlamydia rates in New Zealand are two to three times higher than national chlamydia rates in Australia, the UK and the US.
- Regional gonorrhoea rates in New Zealand are three to four times higher than national gonorrhoea rates in Australia and the UK, but considerably less than in the US.

Key Reviewer: Dr Hayden McRobbie, Consultant, Inspiring Ltd, Auckland

WHY PEOPLE SMOKE

Clinicians who want to encourage people to quit smoking are likely to be more successful if they have some understanding and empathy for why people start smoking and continue to smoke. This understanding and empathy is unlikely to come from experience as statistics show only 3.4% of New Zealand medical practitioners are regular smokers and 81.4 % have never smoked.[1]

In this article we look at what are commonly perceived by smokers as the "benefits" of smoking, along with some of the more significant barriers to quitting.

Why do people start smoking?

It has been estimated that 80% of adult smokers begin smoking as children, and about 30% of children have tried smoking by the age of 11.[2]

There is no single reason why young people begin to smoke.

Predisposing factors such low socioeconomic status, adverse childhood experiences and mental illness are generally not easily changed. Knowing about these factors is useful because they can help identify which young people might be at greatest risk for smoking and in greatest need of support to resist smoking.

Influencing factors provide the opportunity for young people to experiment with smoking. Friends and the presence of people around them who smoke are major influencing factors. Understanding these influencing factors is useful as many of them are able to be changed.[3]

It is important to ensure young people avoid starting to smoke in the first place as nicotine addiction can occur rapidly. In one study, 10% of children who became regular smokers showed signs of nicotine dependence within two days of first inhaling from a cigarette, and 25% within a month.[4] Within a year of starting to smoke, it has been reported that children will be inhaling the same amount of nicotine as adults, will experience cravings when they do not smoke, will make quit attempts and will suffer withdrawal symptoms.[5]

Why do people continue to smoke?

Because of the effects of nicotine

The primary reason why people smoke is that they are nicotine dependent.

When inhaled, nicotine reaches the brain in 10 to 16 seconds (faster than if it was delivered intravenously), and has a terminal half life of about two hours. Given this short half life, regular cigarettes are required to maintain nicotine levels and avoid symptoms of withdrawal.

Nicotine activates nicotinic acetylcholine receptors in the midbrain, inducing the release of dopamine and

Table 1: Symptoms of nicotine withdrawal[5]

Symptom	Duration	Incidence (%)
Lightheadedness	<48 hours	10
Sleep disturbance	<1 week	25
Poor concentration	<2 weeks	60
Craving for nicotine	<2 weeks	70
Irritability or aggression	<4 weeks	50
Depression	<4 weeks	60
Restlessness	< 4 weeks	60
Increased appetite	< 10 weeks	70

exerting dependence producing effects, in a similar way to amphetamines and cocaine. Nicotine demonstrates a biphasic effect, meaning it can both invigorate and relax a smoker, depending on how often they smoke. In new users, nicotine improves reaction time and sustained performance, but tolerance soon develops and these effects are not seen in chronic users.

Nicotine withdrawal has significant physical and psychological effects starting within hours of the last cigarette and peaking within the first week.

Because of the behavioural rewards

Continued smoking is also influenced by non-nicotine effects, including the sensory-motor effects of smoking as well as smoking-associated behaviours that become reinforced.

A person smoking a pack of cigarettes a day can accrue over 70 000 deliveries of nicotine per year. The sight, smell and sensations of smoking have a behavioural conditioning effect on the brain. While nicotine replacement therapy can be very successful in achieving smoking cessation, it does not address the non-nicotine effects of smoking.

Smoking has been shown to elicit a strong Pavlovian response for many people. For example, having a cup of coffee, concluding a meal, seeing another person smoke or smelling smoke may trigger the psychological desire to smoke. The Pavlovian response is considered a reason a number of light smokers, with low nicotine dependence, continue to smoke.[6]

Social norms play a role in continued smoking. In some cases this will discourage smoking, e.g. the increasing number of smoke free public areas and work places and the increasing number of smoke free messages. On the other hand, in groups where the smoking prevalence is high, this may constitute the social norm; therefore there may be less of an expectation to quit.

Because cigarettes help people deal with stress

Many people think they need cigarettes to help them relax and cope with stressful situations. Many smokers report they feel calmer and have improved concentration after a cigarette. However, it is more likely that declining nicotine levels begin to cause symptoms of withdrawal including agitation, and smoking another cigarette simply restores nicotine levels alleviating these effects.

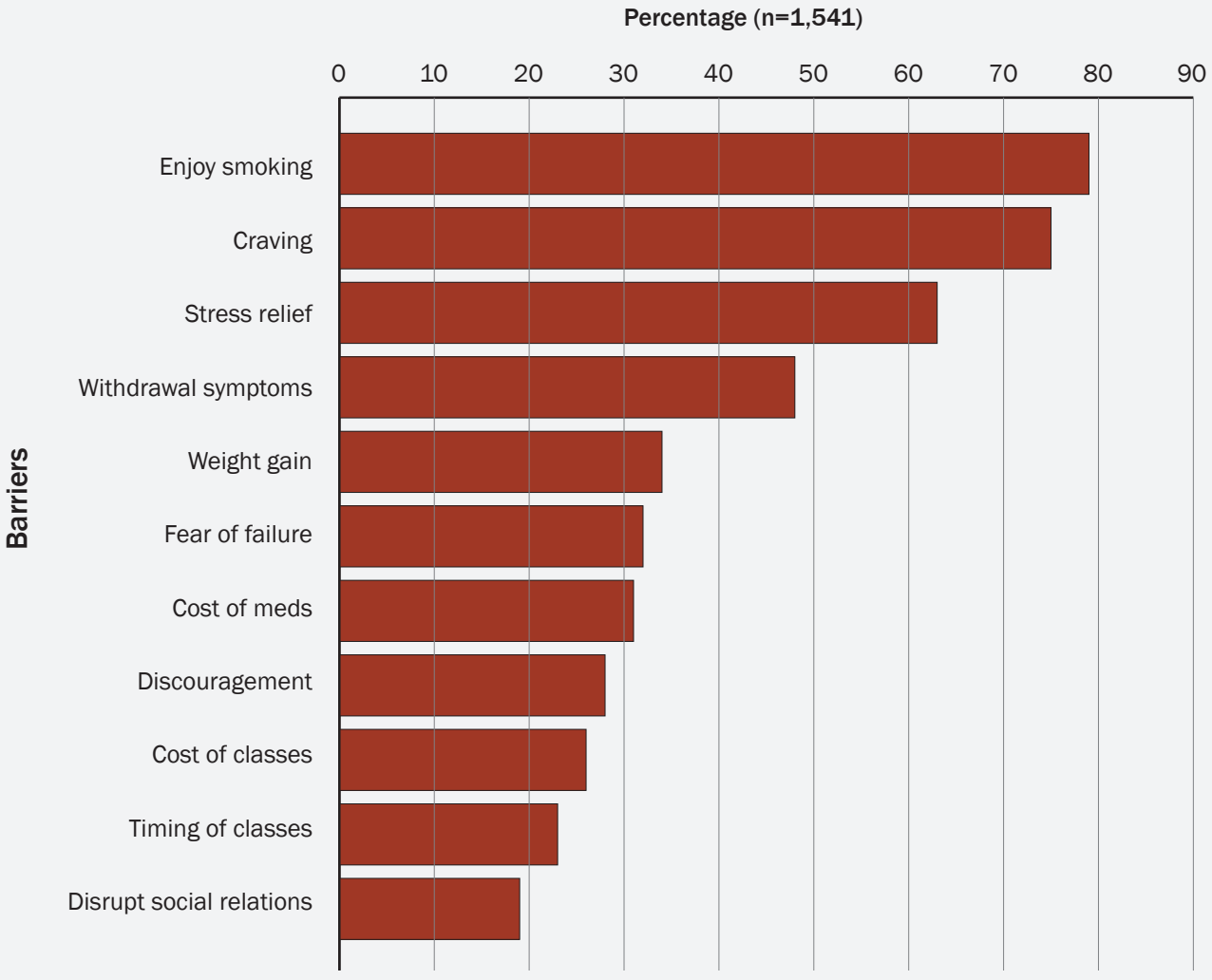
It is also worth considering the actions associated with smoking. For example people may go outside to smoke, removing themselves from the stressful environment and creating an opportunity to "clear their head". Furthermore, the smoke is often inhaled and exhaled in a slow and often deliberate manner – similar to relaxation breathing techniques. Each of these are useful methods in their own right for dealing with stress, so it may be useful to remind people they already have the skills to manage stress, even if they don't realise it.

Because of concern of weight gain on stopping

Many people, especially young women, believe that smoking helps them to maintain a lower body weight. Following smoking cessation, weight gain occurs in approximately 75% of people,[7] with an average gain of around 7 kg.[8]

It is thought some of this weight gained is caused by a decrease in metabolic rate following smoking cessation. In some people the metabolic rate may slow down even further and return to normal over a period of weeks or months.

Figure 1: Barriers to quitting smoking (adapted from UW Center for Tobacco Research and Intervention, 2005)[7]



The lifetime benefits of quitting

Many of the major risks associated with smoking decrease within two to five years of quitting smoking. For some conditions a residual risk remains and never returns to the level of a non-smoker. This is summarised in Table 2.

Table 2: Modification of risk upon quitting smoking (adapted from Dresler et al 2006)[9]

Disease	Risk lower in former smokers than continuing smokers	Time for risk reduction	Returning to level of non-smoker
Lung cancer	✓	5–9 years	Never
Laryngeal cancer	✓	60% after 10–15 years after cessation	Not for at least 20 years
Oral and pharyngeal cancer	✓	Inadequate data	20 years
Stomach cancer	✓	Decreases with continued abstinence, lower risk associated with younger age at cessation	Inadequate data
Pancreatic, renal cell, and bladder cancer	✓	Decreases with continued abstinence	Pancreatic – 15 years Renal cell – 20 years Bladder cancer – 25 years
Coronary heart disease	✓	35% in 2–4 years	Variable: 10–15 years, others small risk after 10–20 years
Cerebrovascular diseases	✓	Marked reduction in 2–5 years	Variable: some say 5–10 years, other say residual risk after 15 years
Abdominal aortic aneurysm	✓	Inadequate data	Residual risk may always remain higher
Peripheral arterial disease	✓	Inadequate data	Residual risk may always remain higher
COPD	✓	Improvement in FEV_1 during first year	After 5 years the age related decline of ex-smokers reverts to that of non-smokers
Chronic bronchitis	✓	Inadequate data	Symptoms are same as non-smokers within 5 years

Following smoking cessation, many people have an increased appetite, which may last for two to three months.

There are also several behavioural aspects that may influence weight gain. Ex-smokers may miss the familiar mouth and hand actions of smoking and replace this with snacking. People that smoke to deal with stress, boredom or loneliness may replace their smoking rituals with increased food intake.

While smokers should be aware they may gain weight when they stop smoking, it is not inevitable. It is important to incorporate advice on a healthy diet and exercise into a quit-plan. However a recent Cochrane Review concluded that advice alone on healthy lifestyles is not effective and may reduce abstinence. More focused intervention is required.[8]

Barriers to quitting

There are a number of barriers that make it difficult for people to stop smoking. These barriers vary depending on age, gender and number of cigarettes consumed.

In a survey of 1500 smokers, over 80% wanted to quit, but factors such as enjoyment, craving and stress relief reduced their desire to attempt quitting (Figure 1).[7]

People who live with others smokers find it more difficult to quit and this is associated with a higher incidence of relapse.

Conclusion

Understanding why an individual smokes and what their barriers are to quitting will assist in counselling them to stop smoking and stay stopped.

People smoke because;

- They are addicted to nicotine
- Withdrawal from nicotine causes unpleasant symptoms
- Smoking is associated with strong behavioural rewards
- Smoking is perceived to help deal with stress
- Concern about weight gain upon stopping

The Prevalence of Smoking in New Zealand

Contributed by Sharon Ponniah

Smoking is the single largest preventable cause of death and disease and is a major contributor to health inequalities. The burden of smoking on the public health system is substantial and approximately 5000 deaths are attributable to smoking in New Zealand every year. While a comprehensive approach to tobacco control including preventive health, education strategies and cessation interventions has been employed to reduce prevalence rates, wide social and ethnic inequalities in New Zealand continue.

Trends in smoking

Large decreases in the prevalence of smoking were observed between 1976 and 1990. These decreases have slowed and between 1996 and 2006, the prevalence of daily smoking in New Zealand decreased by 3% (from 23.7% to 20.7%), which represents around 100,000 less smokers.

The smoking population

A current snapshot of smoking in New Zealand indicates smokers to more likely be aged 20–49 years, identify with Māori and Pacific ethnic groups, have lower personal incomes and be unemployed. Smoking prevalence increases with level of socio-economic deprivation, a trend that is particularly marked among Māori.

Table 1: Prevalence of daily cigarette smoking, 15+ years (%) by ethnic group and socioeconomic deprivation (NZDep06)

Deprivation decile	European	Māori	Pacific Peoples	Asian	Other Ethnicity	Total
Decile 1	10.8%	21.9%	19.9%	7.5%	9.7%	10.7%
Decile 2	13.7%	28.2%	24.2%	8.9%	12.1%	13.6%
Decile 3	15.4%	30.3%	25.8%	9.7%	13.3%	15.3%
Decile 4	17.1%	33.4%	25.9%	9.7%	15.1%	17.0%
Decile 5	18.8%	35.9%	26.9%	10.6%	16.3%	18.8%
Decile 6	20.8%	38.8%	28.8%	11.4%	18.3%	21.0%
Decile 7	22.8%	41.0%	28.9%	11.9%	19.7%	23.1%
Decile 8	25.5%	43.7%	30.6%	12.5%	21.9%	26.1%
Decile 9	28.1%	46.8%	31.2%	12.9%	23.9%	29.5%
Decile 10	33.9%	52.9%	32.8%	15.1%	27.6%	36.5%
Total	19.4%	42.2%	30.3%	11.1%	16.5%	20.7%

Source: 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.

References

1. Ponniah S, Bloomfield A. An update on tobacco smoking among New Zealand health care workers, the current picture, 2006. N Z Med J 2008;121:1272.

2. Conrad, Km, Flay BR, Hill D. Why children start smoking cigaretteS: predictors of onset. Br J Addict 1992;87:1711-24.

3 Health Canada. Youth and Tobacco Report. 1999. Available from www.hc-sc.gc.ca/hl-vs/pubs/tobac-tabac/youth-jeunes/index-eng.php (Accessed February 2009).

4. DiFranza JR, Savageau JA, Fletcher K, et al. Symptoms of Tobacco Dependence After Brief Intermittent Use. Arch Pediatr Adolesc Med 2007;161:704-10.

5. Jarvis MJ. ABC of smoking cessation. Why people smoke. BMJ 2004;328:277-9.).

6. Thewissen R, Havermans RC, Geschwind N, et al. Pavlovian conditioning of an approach bias in low-dependent smokers. Psychopharmacology 2007;194:33-9.

7. UW Center for Tobacco Research and Intervention. Barriers to Quitting Smoking. February 2005. Series 2, Paper Number 2. Available from: http://www.ctri.wisc.edu/Publications/publications/BarrierstoQuitting.2.28.pdf (Accessed December 2008).

8. Parsons A, Shraim C, Inglis J, et al. Interventions for preventing weight gain after smoking cessation. Cochrane Database Syst Rev 2009;CD006219.

9. Dresler CM, Leon ME, Straif K, et al. Reversal of risk upon quitting smoking. Lancet 2006;368:348-9.

Quiz feedback:

Bones & Joints/CVD risk assessment

In BPJ 17 (October 2008) we covered several issues in relation to "bones and joints" including prevention of osteoporosis, symptomatic management of osteoarthritis and monitoring of disease modifying anti-rheumatic drugs (DMARDs) in rheumatoid arthritis.

We also covered the PHO performance indicator of "cardiovascular risk assessment".

GPs were invited to complete a quiz about the articles in the journal. Dr Rebecca Grainger and Dr Michael Crooke provide expert commentary on several key issues that were highlighted.

A full version of the quiz feedback can be found online at **www.bpac.org.nz** (search by Publication/CME Quiz feedbacks).

Bones and Joints

Osteoporosis

Who should receive calcium supplementation and what interactions are important (i.e. what drug/food combinations should be avoided)?

Total calcium intake of 1 g per day should be recommended for all patients taking bisphosphonates for osteoporosis or Paget's disease, due to the theoretical risk of mild hypocalcaemia. For most patients this is in the form of calcium supplements. However, recent data from the Auckland Calcium Study showed calcium supplementation was associated with an increased rate of myocardial infarction in elderly women, and other recent studies have also observed this trend. Therefore daily 1 g calcium supplements should be avoided in people over the age of 70 years and those with known coronary heart disease. An alternative in the over 70 age group is a 500 mg calcium supplement and increased dietary calcium to ensure total calcium intake of 1 g daily. Calcium supplements can continue to be used in younger women without coronary heart disease who wish to optimise bone health with supplemental calcium.

Calcium supplements can decrease the absorption of fluroquinone and tetracycline antibiotics, thyroxine and phenytoin. These agents should be taken one to two hours before or four hours after calcium supplements. Calcium supplements can potentially decrease levels of digoxin or increase risk of digoxin toxicity via hypercalcaemia. Thiazide diuretics can increase the risk of hypercalcaemia and hypercalciuria. Monitoring of electrolytes in patients

The questions and answers to the bones, joints foods and CVD risk assessment quiz are shown in the following table. The right hand column shows the percentage of GPs that selected each answer.

1.	Assessment of bone mineral density by DEXA scan is:	
	☐ The gold standard for diagnosing osteoporosis	96%
	☐ Indicated for all postmenopausal women	4%
	☐ Required for all people who have had an osteoporotic fracture	13%
	☐ Reported as a T score when compared to the young adult mean	85%
	☐ Required before treatment with a bisphosphonate can commence	9%
2.	Risk factors for generalised osteoporosis include:	
	☐ Crohn's disease	85%
	☐ Thyrotoxicosis	94%
	☐ Use of regular inhaled corticosteroids	24%
	☐ Diabetes	67%
	☐ Māori ethnicity	5%
3.	Core therapies for osteoarthritis include:	
	☐ Rest for reducing pain induced movement	7%
	☐ Weight reduction (if overweight)	98%
	☐ Using shock absorbing shoes	69%
	☐ Learning psychological strategies for coping	67%
	☐ Acupuncture	4%
4.	Recommended pharmacological treatments for osteoarthritis include:	
	☐ Topical NSAIDs	89%
	☐ Capsaicin cream	92%
	☐ Heat rub e.g. Deep Heat	23%
	☐ Oral NSAIDs	93%
	☐ Codeine	79%
5.	Disease modifying anti-rheumatic drugs (DMARDs):	
	☐ Should be initiated as soon as possible after diagnosis of rheumatoid arthritis	95%
	☐ Should not be tried unless all other pharmacological treatment has failed	2%
	☐ Should never be used in combination with each other	3%
	☐ Have an onset of action between two to six months	84%
	☐ Can be associated with blood dyscrasias	92%

6.	By what age should cardiovascular risk assessment begin for a European woman with no risk factors?	
	☐ 35 years	<1%
	☐ 45 years	6%
	☐ 55 years	93%
7.	For the woman above, what risk factors would indicate performing cardiovascular risk assessment earlier?	
	☐ Sedentary lifestyle	25%
	☐ Drinking >14 units alcohol per week	31%
	☐ Smoking	98%
	☐ Truncal obesity	91%
8.	What is the best approach for undertaking cardiovascular risk assessments?	
	☐ Scheduling a formal cardiovascular risk assessment with high risk patients	86%
	☐ Opportunistic risk assessment with eligible patients	83%
	☐ Building a picture over time by collecting details of risk factors over several consultations	39%
	☐ Only undertaking cardiovascular risk assessments when requested by patients	0%
9.	Which of the following statements about communicating cardiovascular risk are true?	
	☐ Understanding risk can be confusing for many people	91%
	☐ Crowd diagrams are the most powerful tool for communicating risk	15%
	☐ Analogies should be tailored to situations familiar to the patient	94%
	☐ At the first consultation it is best to outline all the changes a patient should make	7%
10.	Which of the following statements are true?	
	☐ Māori and Pacific men aged over 35 are at increased risk of CVD	97%
	☐ Māori and Pacific rates of assessment for CVD are low compared with European New Zealanders	62%
	☐ Māori and Pacific people are less motivated to make lifestyle changes	22%
	☐ Whānau can play an important role in healthcare decisions	97%

taking digoxin and thiazide diuretics should include serum calcium. Calcium reduces absorbance of bisphosphonates so these agents should never be taken at the same time.

There are some theoretical food interactions affecting dietary calcium absorption but these are unlikely to be of practical concern. Caffeine has a small effect on calcium absorption and can temporarily increase calcium excretion. The calcium deficit generated by one cup of brewed coffee is estimated to be 2–3 mg, which is easily offset by other sources of dietary calcium. Alcohol can potentially inhibit calcium absorption directly and indirectly by decreasing liver conversion of vitamin D to its active form. The amount of alcohol that has a measurable impact on calcium balance is unknown. It seems that minimising intake of caffeine containing beverages and alcohol may be prudent advice for people interested in optimising calcium intake.

Should all people at risk of deficiency be given regular vitamin D supplementation?

Vitamin D supplementation can be given to all individuals at risk of deficiency, without need for vitamin D testing. The vitamin D recommendation remains cholecalciferol (Cal-d-Forte) once daily for 10 days and then one monthly thereafter. This subject has been discussed in detail at; **www.bpac.org.nz keyword: vitamind**

The most common osteoporotic fracture sites are the spine, hip and wrist. However can fractures at other sites be classified as fragility fractures?

A fragility fracture is one that occurs with mechanical forces that would not ordinarily cause a fracture in a healthy young adult. Since osteoporosis is a systemic disease, fractures at other sites could be considered fragility fractures by this definition. Other sites might include humerus, ankle, pelvis and tibia. Any previous fragility fracture increases risk of subsequent fracture.

Is there any evidence of benefit for the use of hip protectors?

Hip protectors are undergarments with padding over the trochanters which disperse the impact of a fall. A recent Cochrane review of hip protectors, found a marginally statistically significant reduction in hip fracture incidence with hip protector use in individuals in residential care, but no decrease in community dwelling populations. Although safe and non-invasive, non-compliance over the long term limits the practical use of hip protectors.

Is the use of inhaled corticosteroids a risk factor for osteoporosis?

There is data that higher cumulative doses of inhaled corticosteroids are associated with loss in bone mineral density. Bone mineral density and osteoporosis prevention should be considered for patients who have reached a cumulative inhaled steroid dose of 5000 mg e.g. dose > 1 mg/day (beclomethasone 250 mcg four puffs per day) for greater than 14 years or cumulative equivalent.

Why is diabetes a risk factor for osteoporosis? Is this both type 1 and type 2 diabetes?

There is increased risk of osteoporotic fracture for women with both type 1 and type 2 diabetes. Women with type 1 diabetes are at risk of low bone mineral density, which is often worse because of the longer duration of diabetes. Type 2 diabetes is often associated with higher body mass, usually protective against loss of BMD, however microvascular disease affecting bone quality may contribute to the observed higher fracture rate in type 2 diabetes. People with diabetes are also at increased risk of falls due to peripheral and autonomic neuropathy, visual impairment from retinopathy or cataracts and hypoglycaemia.

Osteoarthritis

Although self management strategies for coping are very important, in practice this is an area that is often neglected in a consultation, due to lack of time and resources.

Although doctors may not have the time or training to assist their patients in self management strategies, there are community based organisations that can provide this support. Arthritis New Zealand has excellent information and resources for patients, provides support through arthritis educators and runs self-management courses in the community. More information can be found at: www.arthritis.org.nz

The vast majority of people with osteoarthritis are using supplements or alternative remedies.

When patients ask about complementary products, it could be suggested that they use a weekly symptom diary to assess efficacy. It is recommended they keep the diary for one month before and three months after starting an agent, perhaps rating on one to ten their symptoms and making a few notes about how they feel. Then after the three month trial, review the diary, take account of the cost of the agent and decide if the benefits justify continuing use.

Many patients with osteoarthritis avoid eating particular foods such as acidy tomatoes. Is there any basis to the claim that these foods exacerbate symptoms?

There is no good data to support the claim that certain foods exacerbate symptoms of osteoarthritis. The most important interaction between diet and osteoarthritis is that increased weight is a risk factor for onset and more rapid progression of osteoarthritis. Patients should follow standard nutritional guidelines to maintain a healthy body weight and if certain foods exacerbate their symptoms, avoid them.

Rheumatoid arthritis and DMARDs

What are the monitoring tests 6-TGN and 6-MMP useful for?

Measurement of 6-TGN and 6-MMP may assist dosing adjustment in patients, who have had a good therapeutic response to azathioprine, but develop haematological toxicity. These tests should be ordered after discussion with the treating specialist rheumatologist.

6-TGN (6-thioguanine nucleotides) and 6-MMP (6-methylmercaptopurine) are metabolites of azathioprine required for clinical effects (efficacy and toxicity). The metabolism of azathioprine is complex and patients have highly variable 6-TGN and 6-MMP concentrations for a given dose of azathioprine. Algorithms for optimisation of azathioprine dosing in inflammatory bowel disease using 6-TGN and 6-MMP levels have been developed but these are not yet available for rheumatic diseases.

Cardiovascular risk assessment

Can alcohol itself cause ischaemic heart disease or is the effect in combination with other risk factors?

Alcohol is not a risk factor for ischaemic heart disease. There is a dose related association with hypertension. Some studies indicate that moderate alcohol consumption decreases both risk of CVD events and overall cardiovascular mortality but much of the data is confounded. Heavier drinking, in excess of 14–18 drinks per week in women, is associated with increased mortality from other causes and there are similar data for men who take more than three to four drinks daily. The balance of risks and benefits of even light to moderate alcohol consumption are difficult to assess, as there is no long term trial data, and observational data has serious limitations.

Waist circumference seems to have a stronger correlation with cardiovascular risk than BMI. What waist measurement in males and females indicates risk?

Some studies have confirmed that both waist circumference and BMI are indicators of CVD risk but that when adjusted for BMI, waist circumference is a stronger predictor than BMI alone. In other studies the extra strength of waist circumference has been in predicting diabetes with no benefit over BMI in predicting CVD. Waist to hip ratio may be a more powerful indicator of obesity associated CVD risk than any other single measure of obesity. It is true that BMI may be confounded in some individuals but there are considerable practical difficulties in accurately measuring waist circumference in a standardised manner in routine practice. The New Zealand guidelines continue to indicate that BMI ≥ 30 or waist circumference ≥100 cm (men) or ≥90cm (women) should be considered as risk factors. These figures apply mainly to those of European descent.

Is there any evidence to support increased benefit in terms of CVD outcome, with formal organised clinics devoted to screening?

Most guidelines recommend opportunistic screening at a certain age as the minimum requirements but scheduling formal assessments with high risk patients should be a high yield activity. Building a picture over time may be very valuable, especially in younger patients who may have obvious risk factors, but who will not have very high current absolute risk. Using the concept of risk trajectory may be very useful in such individuals, as outlined in the second edition of the New Zealand Cardiovascular Guidelines Handbook (2009), now available online at **www.nzgg.org.nz**

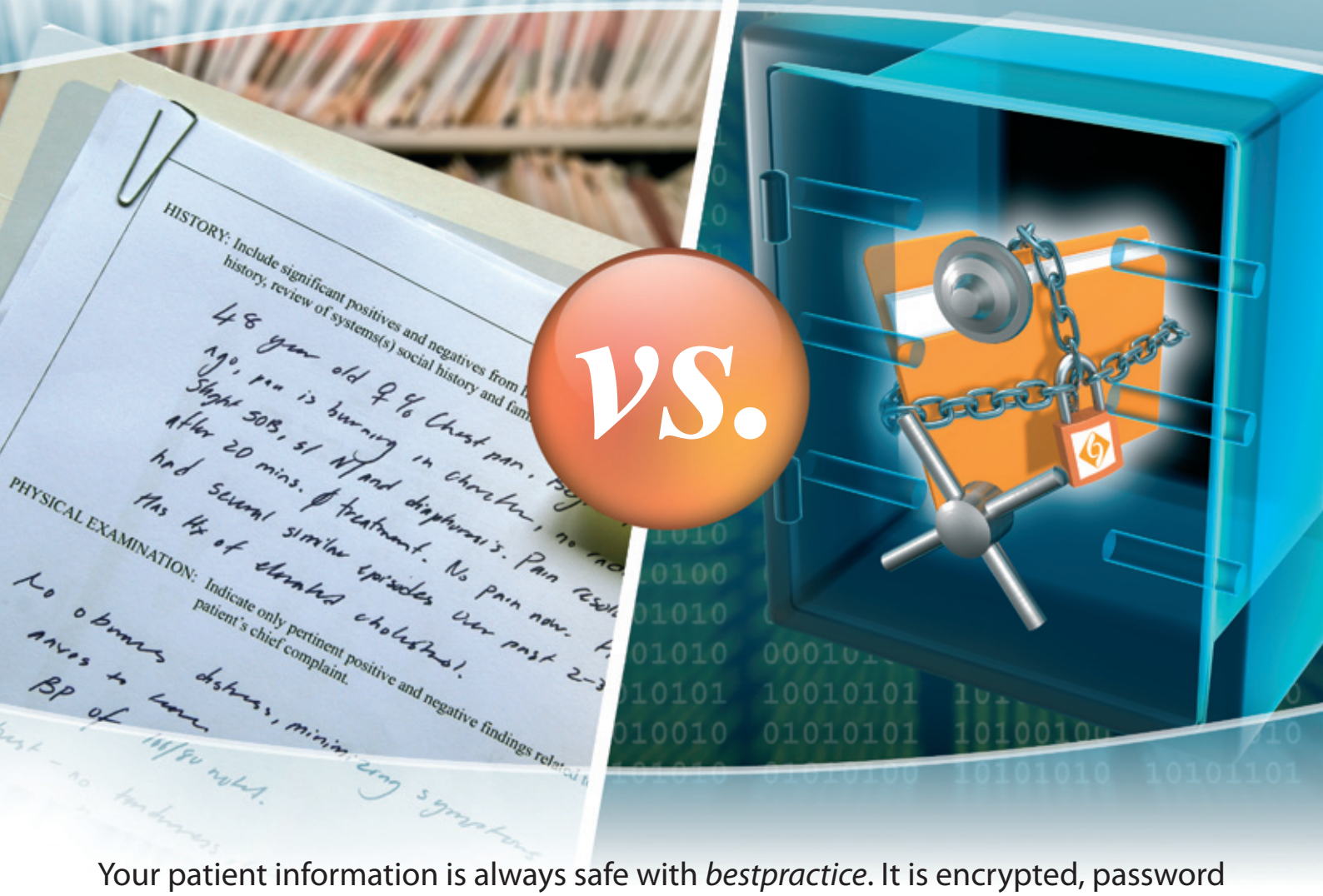
There does not appear to be any data that proves the value of formal clinics devoted to screening, and such a study would be very difficult to complete.

Are rates of CVD assessment for Māori and Pacific peoples lower compared to other New Zealanders?

There is a wealth of data showing ethnic and socioeconomic disparities in the prevalence of cardiovascular disease in New Zealand, and recognised in the recommendation to begin screening ten years earlier in Māori and Pacific peoples. There seems to be no hard data on rates of assessment for risk in different ethnic groups but there is evidence that this earlier time of assessment is not being fully achieved.

bestpractice
DECISION SUPPORT FOR HEALTH PROFESSIONALS

Feel **safe** and **assured**.



Your patient information is always safe with *bestpractice*. It is encrypted, password protected and can't be used for any other purpose, without your permission.

Enquire now to access the latest innovation to improve patient management

Contacts:
Murray Tilyard or **Kaye Baldwin**
Level 8, 10 George Street, PO Box 6032, Dunedin
phone: **03 479 2816**
email: **murray@bpac.org.nz** or **kaye@bpac.org.nz**

Evidence That Counts

More Data on Statins in Primary Prevention — The JUPITER Study

Journal Watch, Vol. 28, No.24, December 15, 2008

The role of statin therapy in primary prevention is uncertain for patients whose cholesterol levels are not markedly elevated. Among such patients, elevated levels of high-sensitivity C-reactive protein (hsCRP) are associated with excess cardiovascular risk. In this international industry-sponsored study, 17,802 people (men's age ≥50; women's age ≥60) without known cardiovascular disease and with LDL cholesterol levels <130 mg/dL (<3.36 mmol/L) and hsCRP levels 2 mg/L were randomised to receive daily rosuvastatin (Crestor; 20 mg) or placebo. Exclusion criteria were numerous and included diabetes, uncontrolled hypertension and various other chronic diseases.

The trial was stopped early, after a median follow-up of 1.9 years. Rosuvastatin lowered mean LDL cholesterol level by 50% and hsCRP level by 37%. The incidence of the primary endpoint (first major adverse cardiovascular event, including unstable angina, myocardial infarction, stroke, arterial revascularisation, or death from cardiovascular causes) was significantly lower in the rosuvastatin group than in the placebo group (0.77 vs. 1.36 per 100 person-years; hazard ratio, 0.56); occurrence of all components of the composite endpoint was lower in the rosuvastatin group, as was the overall mortality rate (HR, 0.8). Physician-reported new-onset diabetes was significantly more common in the rosuvastatin group; median glycosylated haemoglobin (HbA_{1c}) level at 24 months also was higher with rosuvastatin.

Comment:

In this study of apparently healthy subjects with elevated hsCRP levels, statins lowered the incidence of adverse cardiovascular events; this result supports expanded use of statins in primary prevention. An editorialist sounds several cautionary notes, however, mentioning the high proportion of patients who were excluded from enrolment, the relatively modest absolute effect size (about 100 people need to be treated for almost two years to prevent one event) the higher incidence of diabetes, and the lack of long-term data on hazards of statin therapy. He also reminds us that this is a randomised trial of statin therapy, not of hsCRP testing, and he advocates selective, rather than routine, use of hsCRP testing.

— Kirsten E. Fleischmann, MD, MPH

Ridker PM et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med 2008; 359:2195.

Hlatky MA. Expanding the orbit of primary prevention — Moving beyond JUPITER. N Engl J Med 2008; 359:2280.

C-Reactive Protein and Atherosclerosis: No Case for Causality

Journal Watch, Vol. 28, No.24, December 15, 2008

Elevated plasma C-reactive protein (CRP) levels are associated with increased risk for cardiovascular events. However, scientists debate whether elevated CRP levels are a causative factor in, or just a marker of, ischaemic vascular disease.

To assess the effects of genetically determined lifelong elevated CRP levels, investigators studied more than 50,000 Danish individuals from the general population of Copenhagen, including one large prospective cohort, one large cross-sectional cohort and two small case-control groups. The researchers measured high-sensitivity plasma CRP levels and genotyped individuals for four single nucleotide polymorphisms (SNPs) in the CRP gene and for two SNPs in the apolipoprotein E gene (positive

controls). All of the genetic variants are known to affect plasma levels of their respective gene products.

The investigators found an association of ischaemic heart or cerebrovascular disease, with elevated CRP levels, as expected. They also confirmed that the four CRP polymorphisms were associated with increases in CRP levels by up to 64%, which would amount to an increase in predicted risk for ischemic vascular disease of up to 32% for heart disease and up to 25% for cerebrovascular disease, independent of other risk factors. However, none of the CRP genotypes was associated with an increase in risk for either heart or cerebrovascular disease. By contrast, the apolipoprotein E genotypes were associated with both elevated cholesterol levels and increased risk for ischemic heart disease.

Comment:
These findings strongly suggest that genetic variants associated with lifelong elevations of CRP levels are not associated with an increase in cardiovascular risk. Thus, increased CRP levels appear to be simply a marker for atherosclerosis or cardiovascular events, and future drugs targeting CRP are unlikely to provide any preventive benefit.

— Beat J. Meyer, MD

Zacho J et al. Genetically elevated C-reactive protein and ischemic vascular disease. N Engl J Med 2008; 359:1897.

Aspirin Does Not Affect Cognitive Function in People at Moderate CV Risk

Journal Watch, Vol. 28, No.19, October 1, 2008

Cardiovascular disease (including cerebrovascular disease) is associated with declining cognitive function in old age (JW Aug 1 1995 and BMJ 1994; 308:1604). Regular aspirin use lowers risk for adverse cardiovascular events in patients with peripheral vascular disease (JW Mar 15 2002 and BMJ 2002; 324:71). Aspirin might similarly prevent atheroma- or thrombosis-related strokes and, thereby, preserve cognitive function. However, aspirin might also promote cognitive decline if it raises risk for brain haemorrhage. Previous observational data suggest either no association between regular aspirin use and cognitive decline or, at best, a modest protective benefit. To investigate this association, investigators randomised 3350 men and women (age range, 50–75) in Scotland to daily low dose aspirin (100mg) or placebo. Participants were at moderately high cardiovascular risk (ankle brachial index, ≤0.95 in both legs) but without prior myocardial infarctions or strokes.

Participants underwent cognitive testing at baseline and after a median of five years of treatment. An intent-to-treat analysis revealed no significant differences in summary cognitive scores (reflecting general cognitive ability) or in individual measures of memory, executive functioning, nonverbal reasoning, mental flexibility and information processing between the aspirin and placebo groups after five years.

Comment:
Daily low-dose aspirin does not appear to affect cognitive function in middle- aged and older patients at elevated cardiovascular risk. Whether aspirin use at higher doses or for longer durations has salutary or deleterious effects on cognitive function remains unclear.

— Paul S. Mueller, MD, MPH, FACP

Price JF et al. Low dose aspirin and cognitive function in middle aged to elderly adults: Randomised controlled trial. BMJ 2008; 337:a1198.

Evidence That Counts

Let Them Eat Nuts (and Popcorn)! Neither Causes Diverticular Complications

Journal Watch, Vol. 28, No.18, September 15, 2008

Patients with diverticulosis often are instructed to reduce their intake of popcorn, nuts and corn to prevent diverticular complications. This advice is based on a rather intuitive notion that colonic luminal trauma from these foods might initiate inflammation or bleeding within diverticula. In a prospective cohort study of 47,228 male health professionals without prior diagnoses of diverticular disease, inflammatory bowel disease or non–skin cancer, investigators explored this issue. At regular intervals, from 1986 through 2004 participants provided health-related information and completed food-frequency questionnaires.

During 18 years of follow-up 801 incident cases of diverticulitis and 383 incident cases of diverticular bleeding occurred. Analyses that were adjusted for potential risk factors yielded a hazard ratio (HR) of 0.80 for diverticulitis in participants who ate nuts at least twice weekly, compared with those who consumed nuts no more than once monthly. In a similar analysis of popcorn consumption, the HR was 0.72. Corn consumption was unrelated to risk for diverticulitis and none of the three foods were associated with diverticular bleeding.

Comment:
Another bit of "common medical wisdom" has been disproved. If anything, these data suggest that eating popcorn and nuts is somewhat protective against diverticulitis.

— Thomas L. Schwenk, MD

Strate LL et al. Nut, corn, and popcorn consumption and the incidence of diverticular disease. JAMA 2008; 300:907.

Are PPIs Culprits in the C. difficile Epidemic?

Journal Watch, Vol. 28, No.21, November 1, 2008

Use of proton-pump inhibitors (PPIs) has been implicated as a factor in the recent epidemic of Clostridium difficile –associated diarrhoea (CDAD), although, in many studies, the evidence has been indirect at best (JW Feb 1 2006, JAMA 2005; 294:2989, JW Nov 15 2006 and CMAJ 2006; 175:745). In the present study, researchers compared 94 adults who acquired CDAD as inpatients at a single hospital in Saudi Arabia with 94 controls who were matched for duration and nature of antibiotic treatment, hospital ward, room type and other factors.

In univariate and multivariate analyses, PPI use correlated significantly with risk for CDAD, as did renal failure (developing either before or after admission). Histamine-2 (H2)-blocker use did not contribute significantly to risk, nor did gastrointestinal disease, diabetes, immunosuppression, or presence of a malignancy.

Comment:
This capably conducted study adds to the literature that implicates PPI use in CDAD. An editorialist points out, however, that some of the usual criteria for assigning causality have yet to be met, including any evidence of a dose-response pattern. He endorses the authors' goal of eliminating unnecessary PPI use from hospital wards, but notes that the drugs are too valuable to abolish completely, and that far better evidence supports standard infection-control measures to contain CDAD.

— Abigail Zuger, MD

Aseeri M et al. Gastric acid suppression by proton pump inhibitors as a risk factor for Clostridium difficile-associated diarrhoea in hospitalised patients. Am J Gastroenterol 2008 Sep; 103:2308.

Metz DC. Clostridium difficile colitis: Wash your hands before stopping the proton pump inhibitor. Am J Gastroenterol 2008 Sep; 103:2314.

Choose to chew: nicotine gum and pregnancy

Journal Watch, Vol. 28, No.24, December 15, 2008

At least 10% of women smoke during pregnancy, raising their risk for delivering low birth weight or premature babies. Is nicotine-replacement therapy effective in this setting?

In a randomised trial, researchers assessed use of a 1 mg nicotine gum versus placebo gum in 194 pregnant women, many of whom were socioeconomically disadvantaged. Mean gestation at entry was 17 weeks, and mean number of cigarettes smoked daily before pregnancy was 18. Both groups received extensive tobacco counselling; participants were instructed to chew one piece of gum each time they otherwise would have smoked (not exceeding 20 pieces daily; treatment duration, six weeks).

Women in the nicotine group had significantly greater reductions in mean number of cigarettes smoked daily, than did those in the placebo group (-5.7 vs. -3.5) and delivered babies with significantly higher birth weights (mean 3287 g vs. 2950 g) and at later gestational ages (mean 38.9 weeks vs. 38.0 weeks). The most common side effects were headache, dizziness, fatigue, heartburn, nausea and vomiting.

Comment:

Nicotine gum might be a useful and safe adjunct to smoking-cessation counselling in pregnant women. Enrolment was curtailed early because the effect size was not as large as anticipated, and thus, the originally designed study was under-powered. Nevertheless, the results suggest improvement in some neonatal outcomes and little risk associated with nicotine gum for pregnant women who are trying to cut back on smoking.

— Sandra Ann Carson, MD

Oncken C et al. Nicotine gum for pregnant smokers: A randomised controlled trial. Obstet Gynecol 2008;112:859.

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

for **BEST PRACTICE** online

visit us at **www.bpac.org.nz**

Call us on **03 477 5418**

Email us at **editor@bpac.org.nz**

Freefax us on **0800 27 22 69**

www.bpac.org.nz

bpac nz
better medicine