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A how to guide for a sexual health checkup

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better medicine

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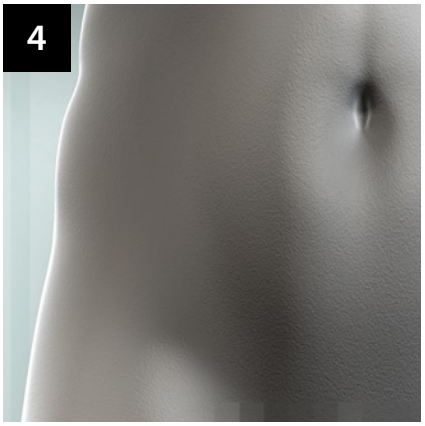
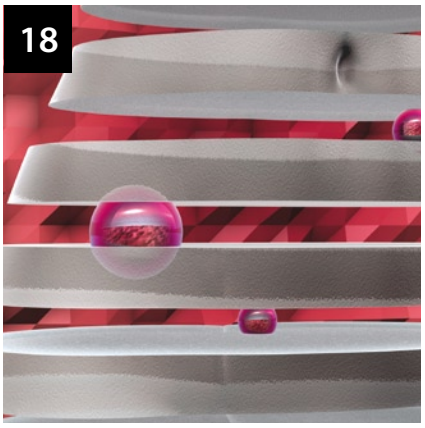
CONTENTS

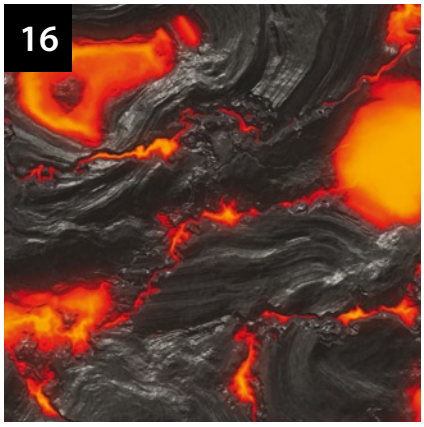
Issue 52 April 2013





CONTENTS

Issue 52 April 2013



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Print is still very important to us, and we will continue to produce printed copies of our publications, however, we realise the importance of the online world as a means to distribute information "24/7". Consequently, over the past few months we have been working hard on redeveloping and rebuilding our website.

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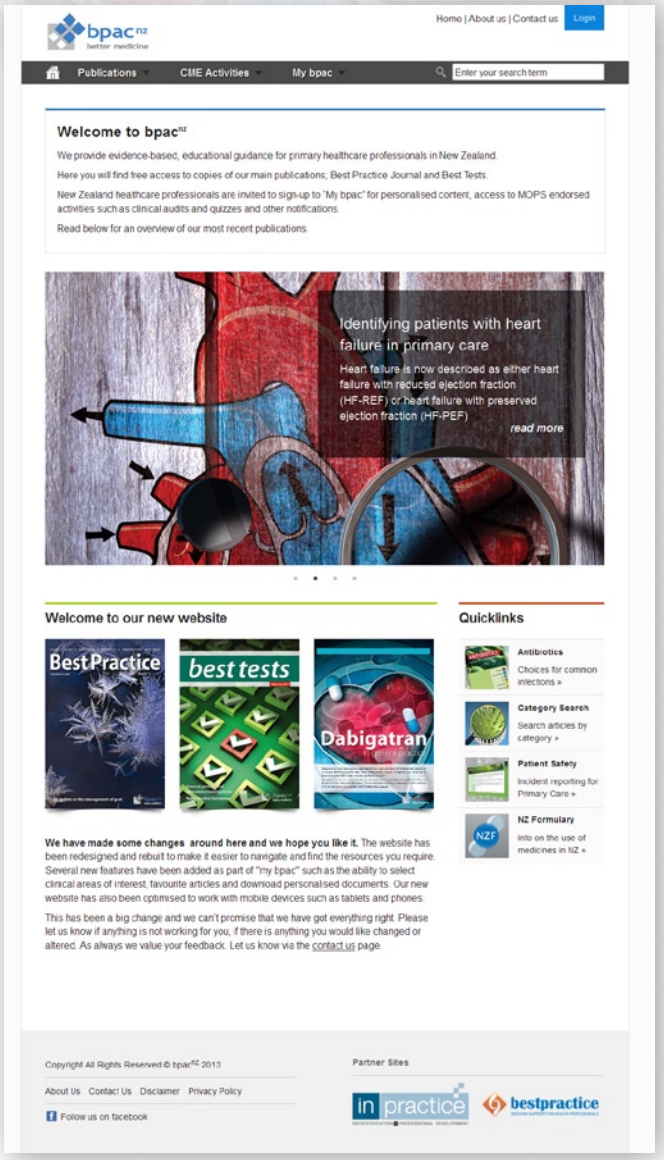

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A "how-to guide" for a sexual health check-up

Good sexual health is about achieving both physical and psychological wellbeing, free from disease, coercion or abuse. Reaching and maintaining good sexual health requires a positive and respectful approach to sex and sexual relationships, as well as the ability to have pleasurable and safe sexual experiences. Primary care plays an important role in the provision of all aspects of sexual health care, including educating about sexually transmitted infections (STIs) and safer sex and providing testing and treatment for STIs.

New Zealand has a high rate of sexually transmitted infections

In New Zealand, the prevalence of bacterial sexually transmitted infections (STIs), e.g. chlamydia and gonorrhoea, is high compared to other developed nations, such as Australia and the United Kingdom. Chlamydia is the most commonly reported STI in New Zealand, with a reported incidence in 2011 of 786 new cases per 100 000 people.[1] More than 70% of reported chlamydia infections occurred in people aged 15 – 24 years,[1] and the number of diagnoses in community laboratories in females was 2.8 times higher than in males (indicating significantly greater uptake of STI testing in females).[1] Gonorrhoea is the second most commonly reported STI, with an incidence of 67 cases per 100 000 people, followed by genital warts, genital herpes, non-specific urethritis and syphilis.[1] The prevalence of chlamydia and gonorrhoea is higher in Māori and Pacific Peoples and in people aged under 25 years.[1] Syphilis is much more commonly diagnosed in men who have sex with men (MSM), accounting for 83% of cases diagnosed in sexual health clinics in 2011.[2] The prevalence of viral STIs such as human papillomavirus (HPV) and herpes simplex virus is less well known, as most infections are asymptomatic.

There are multiple cultural, behavioural and economic factors contributing to current disparities in sexual health indices in different population groups in New Zealand. Primary care is ideally situated to address these issues by improving the sexual health knowledge of patients and facilitating the diagnosis and treatment of STIs.

When should you take a sexual health history?

Questions about sexual health should be routinely included as part of a general history for all patients seen in primary care. The purpose of taking a sexual health history is to assess risk of STIs, identify problems with sexual function, identify issues of past sexual abuse or risk of future abuse, and to assess overall sexual wellbeing and knowledge.[3]

In general, a sexual health check should be undertaken:

- As part of a routine preventative healthcare check-up in all sexually active people (particularly those aged under 25 years)[4]
- For sexual contacts of someone with a bacterial STI, pelvic inflammatory disease or epididymo-orchitis
- For people who have had a recent partner change or multiple partners
- For females attending for routine contraceptive or cervical screening visits
- Prior to intrauterine device (IUD) insertion
- During routine antenatal testing
- Before termination of a pregnancy
- For people presenting with specific anogenital symptoms
- For people who have been sexually assaulted
- For people who request a sexual health check

How to open a dialogue about sexual history

Ensure that the patient feels comfortable and able to speak openly. It is important that practitioners are also comfortable with asking questions about sexual health in order to help put patients at ease. It should be clear from the outset that the consultation is confidential, and the tone of the conversation should aim to normalise the clinical encounter, e.g. "*We routinely discuss sexual health with all our patients, is it ok if I ask you some questions?*" or: "*Chlamydia is very common in sexually active young people, so can I ask you some questions to see if you need a check-up?*"

General points for taking a sexual history

All questions in the sexual history should be gender neutral until the gender of sexual contacts is known. Avoid using the term "partner" (or husband/wife) unless the person has stated they are in a relationship.

It is important to discuss confidentiality, and its limitations, in case any significant safety issues are identified.

It may be helpful to briefly explain why each question is being asked and that the questions are routine, e.g. "*We ask everyone the same questions, they may seem intrusive but I'm just trying to find out risks and what tests you may need.*"

It may not be possible to take a full sexual history at the initial presentation, especially if this was not the primary reason for the visit. The most relevant information is whether the patient is currently symptomatic, whether any test is indicated at that visit, whether they are at risk of unwanted pregnancy and whether they have risk factors for HIV, syphilis, hepatitis or other infections. Asymptomatic, young people can be referred to the Practice Nurse for a more in-depth sexual health history and testing if there is insufficient time during the consultation, or be encouraged to return for an additional consultation. New Zealand research shows that nurse-led education and self-collection of samples is an effective strategy for increasing uptake of opportunistic chlamydia testing in people aged 16 – 24 years.[5]

The range of questions that may be included as part of a complete sexual history are:[3]

- Do you have any specific problems or symptoms? Mention specific symptoms such as, for females: unusual vaginal discharge, lower abdominal pain, abnormal bleeding, urinary symptoms and dyspareunia; for males: dysuria, penile discharge; and for both sexes: genital itch, rashes, sores or blisters, anorectal symptoms.
- Are you sexually active at present? Are you in a relationship?
- When was the last time you had sex? (important to establish whether it is an appropriate time to test)
- Was this with a regular or casual sexual contact/partner?
- Was this sexual contact/partner male or female?
- Do sexual encounters usually include vaginal, oral or anal sex?
- How many sexual contacts/partners have you had in the previous two months? (important for partner notification purposes)
- Do you use condoms – always, sometimes or never?*
- For females – when was your last period? Do you use hormonal contraception? When was your last cervical smear?**
- Have you ever had any STIs before?
- Have you had all your routine recommended vaccinations? e.g. Hepatitis B, HPV?**
- Do you ever have sex while under the influence of alcohol or other drugs? Have you ever injected drugs?
- Have you ever traded sex for money or drugs?
- Have you ever had any unwanted sexual contact?
- Have you ever been afraid in a relationship, or been hurt by a partner?
- Have you ever had a non-professional tattoo, genital piercing, or received medical or dental treatment overseas in a developing nation? (important to assess risk of blood-borne viruses)

Once relevant information has been gathered, ask again if the patient has any questions or if they want to add anything before assessing their risk of infection.

* Modify to "protection" for women who exclusively have sex with women

** If thorough patient notes are available, hormonal contraception use, cervical smear information and vaccination questions may be skipped

Assess the patient's risk profile for STIs

The key behaviours that increase risk of any STIs are:[6]

- Misuse of alcohol or other recreational drugs
- Early onset of sexual activity
- Inconsistent condom use
- Multiple or frequent change of sexual contacts (more than ten in the previous six months)
- A history of sexual assault or intimate partner abuse

- Commercial sex work (if not using condoms consistently), or having unprotected sex with a commercial sex worker

The key groups at risk of HIV are:[6]

- Men who have sex with men (MSM)
- People from a country where there is a high HIV prevalence, e.g. Sub-Saharan Africa, South-East Asia, India, Eastern Europe, South America
- Injecting drug users
- Sexual partners of people in the above categories

People at increased risk of blood-borne infections, e.g. hepatitis C, include:[3]

- Injecting drug users – past or present
- HIV positive MSM
- People who have received medical or dental treatment in a developing nation
- People who have had non-professional tattooing or piercing

Physical examination and appropriate testing

The information gained from the sexual history will guide the extent of physical examination and laboratory testing required.

Generally, routine STI testing should occur annually where appropriate, but this depends on risk factors. Testing should be repeated more frequently (i.e. three to six monthly) if the patient's history suggests higher risk sexual behaviours.

If there is a specific sexual event that the patient is concerned about and they are currently asymptomatic then it is recommended that testing be deferred until two weeks after the event. If they are unlikely to come back for testing or if they have current anogenital symptoms then testing should be done at the time of presentation.

Any patient with atypical anogenital ulceration should be referred to or discussed with a sexual health physician (for further information see New Zealand Sexual Health Society genital ulcer disease summary: www.nzshs.org).

STI test availability varies throughout New Zealand, and testing should always be guided by local laboratory recommendations. Most laboratories now offer combined nucleic acid amplification tests (NAAT) for chlamydia and gonorrhoea on a single PCR swab or urine specimen (talk to your laboratory about the preferred specimen collection swab/receptacle).

Give advice about safer, healthier sex

Individualised advice should be given about practising safer and healthier sex, based on information gained from the patient's sexual history.

Consistently and correctly using condoms is the most important advice for reducing the risk of pregnancy and STIs. It is recommended that a water-based lubricant is used with condoms to reduce risk of breakage during vaginal or anal sex. Thicker condoms do not offer any additional protection against STIs and HIV.[7] Discuss the use of the emergency contraceptive pill with women who are not using other forms of contraception. This can be prescribed by a clinician or purchased from an accredited pharmacist in a community pharmacy.

Advice on condom use can be excluded in women who have sex exclusively with women, although other methods of STI protection and not sharing sex toys, should be suggested.[7]

Talking about alcohol and drug use is recommended, particularly in younger people, as this may predispose them to higher-risk sexual behaviours such as unprotected sex.[7] Offer information on local drug and alcohol counselling services if appropriate.

Traditionally, advice on safer sex included abstinence. There is now a large body of evidence showing that the promotion of abstinence has no benefit in preventing unintended pregnancy and STIs.[7] Therefore, abstinence should only be discussed as one of a range of strategies to reduce risk.[7]

Ideally, an examination should be performed as part of a sexual health check-up, and samples for testing taken during the examination. However, self-testing is a safe and effective method for opportunistic testing in asymptomatic patients or those who decline examination.[8, 9]

It is important to tell patients how and when they will be notified of test results. For low-risk patients it is usually appropriate to tell them that they will only be contacted if there are any abnormal results. For higher risk patients, e.g. MSM having unprotected anal sex, it is recommended that they are asked to re-attend to discuss their results in person.

Females

Routine examination and testing for females should include:[3]

- Physical examination of the vulval and perianal skin, inguinal nodes, vestibule, introitus, cervix and vagina, looking for skin lesions, rashes, ulceration and abnormal vaginal discharge
- If requiring speculum examination, i.e. symptomatic or a contact of a person with gonorrhoea:
  - Endocervical swab(s) for chlamydia and gonorrhoea testing (one swab if the laboratory offers combined NAAT testing)
  - If a sexual contact of someone with gonorrhoea an additional endocervical swab for culture and antibiotic susceptibility testing should be taken*
  - High vaginal swab for bacterial vaginosis, candida, and trichomoniasis
- Serology for hepatitis B (if not immunised), syphilis and HIV
- Hepatitis C serology if the patient has risk factors
- Viral swab for herpes simplex virus if ulcers are present

A self-collected vaginal swab is appropriate for opportunistic testing for chlamydia in an asymptomatic female, or if a genital examination is declined. Instruct the patient to remove the swab from its container, insert it approximately 4 cm into the vagina, rotate and then replace in the swab container.

A first void urine (first 30 mL of the stream) is not the first-line recommendation for chlamydia testing in women as it has lower sensitivity than a vaginal swab, but is useful if the patient declines examination and does not want to self-collect a swab.

Males

Routine examination and testing in males should include:[3]

- Physical examination of the genital and perianal skin, inguinal lymph nodes, penis, scrotum, and testes looking for skin lesions, urethral discharge, rashes and genital ulceration
- First void urine for chlamydia testing (and gonorrhoea if the laboratory offers combined NAAT testing)
- If symptomatic with dysuria, urethral itch or discharge, or urethral discharge is noted on examination or a contact of a person with gonorrhoea:
  - Take a urethral swab for gonorrhoea culture,* using the smallest available bacterial culture swab (e.g. thin, blue per-nasal swab inserted approximately 1 cm into the urethral canal)
- Serology for hepatitis B (if not immunised), syphilis, and HIV
- Hepatitis C serology if the patient has risk factors
- Viral swab for herpes simplex virus if ulcers are present

N.B. Urine samples do not have to be early morning urine. Ideally the patient should not have passed urine in the previous two hours, however, if the patient is unlikely to return for testing, a specimen should still be collected and tested. A study has shown that the voiding interval does not significantly alter results of the Cobas PCR assay when testing for chlamydia in males.[10]

Men who have sex with men (MSM)

Testing as recommended for all males should be offered at least annually, depending on sexual history. Additional tests, regardless of stated sexual practices, should also be included for MSM.

N.B. MSM with anorectal symptoms should be referred to, or discussed with, a sexual health physician.

Additional tests (i.e. also follow recommendations for all males) for MSM include:[3]

- A pharyngeal NAAT test for gonorrhoea
- An anorectal NAAT test for chlamydia and gonorrhoea. Anorectal swabs should be collected by inserting the

* Discuss with laboratory as swabs for gonorrhoea culture are not always processed (or are subject to specific criteria)

swab 4 cm into the anal canal, rotating and replacing in the swab container. If the patient is a sexual contact of a person with gonorrhoea, an additional anorectal swab for gonorrhoea culture* and antibiotic susceptibility testing should be taken.

- Hepatitis A serology (if not immunised) – offer vaccination if susceptible (not funded; once a patient is recorded as having been vaccinated, annual testing is no longer required)

N.B. NAAT tests are now recommended for testing rectal and pharyngeal infection in MSM. A positive NAAT test from an extra-genital site needs to be confirmed by supplementary testing, which is done automatically by the laboratory.[11]

Best Practice Tip: Test kits can be bundled up and tied with a band in groups for a "male check-up", "female check-up" and "MSM check-up" to help speed up the testing process and ensure that all the necessary tests are done.

Treatment of common STIs

Treatment should be initiated if testing reveals a positive result for an STI, or if there is a high index of suspicion, e.g. signs and symptoms or contact with a person with a confirmed STI.

Patients should be advised to avoid unprotected sexual intercourse until seven days after treatment has been initiated for any STI, and at least seven days after sexual contacts have been treated, to reduce risk of re-infection. Partner notification should be discussed at the time of treatment (see "Partner notification").

All patients should be routinely followed up one week after treatment to check adherence, symptom resolution and whether partner notification has occurred. This role is often undertaken by the Practice Nurse. Re-treatment is necessary if there has been unprotected sex with untreated sexual contacts during the week after treatment initiation. Patients should be advised to have a repeat sexual health check in three months, as reinfection is common. Entering a recall in the practice management system can be helpful.

Referral may be necessary

Referral to, or discussion with, a sexual health physician is recommended for patients with:[12]

- Recurrent urethritis
- Genital warts (difficult or resistant cases)

Partner notification

Partner notification, or contact tracing, is the process of identifying sexual contacts of a person with a STI and ensuring that they are aware of their possible exposure. This helps to prevent reinfection in the index case, and allows identification of undiagnosed STIs and prevention of possible complications in their contacts. Partner notification should be discussed at the time of treatment for a STI and is recommended when the following conditions are identified: chlamydia, gonorrhoea, trichomoniasis, non-gonococcal urethritis, pelvic inflammatory disease and epididymo-orchitis. Partner notification is not necessary for people diagnosed with genital warts or genital herpes although regular sexual partners may benefit from an assessment and a routine sexual health check. Management of partner notification for syphilis or HIV is more complex and referral to, or discussion with, a sexual health physician is recommended.

The most common method of partner notification is for the index case to notify their sexual contacts themselves.[13] All sexual contacts in the previous two months should be notified.[13, 14] Discuss with the patient how they will notify their contacts, e.g. in person or over the phone, email or text, and provide them with the information that they will need, such as fact sheets and suitable websites on the condition and advice on returning for testing.[13]

If the patient does not wish to notify their contacts due to concerns about confidentiality or safety, e.g. there are issues of partner violence, notification can be done by clinical staff, with every effort to maintain confidentiality of the index case. If a patient attends as a contact of someone who has been infected, the index case must not be identified to the contact. Referral to appropriate agencies should be facilitated if there is ongoing risk of violence from a current relationship.

The General Practitioner, or usually the Practice Nurse, should follow up with the patient after one week to confirm that relevant sexual contacts have been notified, as well as to check symptom resolution, adherence to medication and whether there has been any unprotected sex.[13]

Sexual health clinics can assist with partner notification if required.

- Suspected or confirmed syphilis
- Suspected or confirmed HIV
- Any STI during pregnancy
- Problematic, recurrent or chronic vaginal discharge
- Chronic genital pain or sexual dysfunction

Referral is also needed for patients who require specific sexual health counselling, or for follow-up of patients or contacts who fail to attend for treatment.

In New Zealand some conditions must be reported to the Medical Officer of Health, including acute hepatitis A, B and C and AIDS (but not HIV).

For more detailed information on the treatment of STIs, refer to the New Zealand Sexual Health Society Best Practice Guidelines, available from: **www.nzshs.org**

Chlamydia

The first-line recommended treatment for people with chlamydia (and males with non-gonococcal urethritis), and their sexual partners is azithromycin 1 g, stat, or alternatively (if not pregnant), doxycycline 100 mg, twice daily, for seven days.

Azithromycin is safe for use in women who are pregnant (category B1*),[15] and has better efficacy than alternatives.

* Therapeutic Goods Administration Australia pregnancy category

Patients with a symptomatic rectal chlamydia infection, should be referred to, or discussed with, a sexual health physician.[16]

All patients treated for chlamydia and gonorrhoea should be advised to have a repeat sexual health check in three months, as re-infection is common. A test of cure is unnecessary, except in women treated during pregnancy or if a non-standard treatment has been used. This should be carried out five weeks after treatment was initiated.[16]

Gonorrhoea

The first-line recommended treatment for people with gonorrhoea, and their sexual partners is ceftriaxone 500 mg, IM, stat (make up with 2 mL lignocaine 1%, also see "Updated guidance on using ceftriaxone"), **plus** azithromycin 1 g, stat. Co-infection with chlamydia is very common, and azithromycin should always be co-administered, even if the chlamydia test is negative as the medicines act synergistically and reduce the risk of development of resistance.[17]

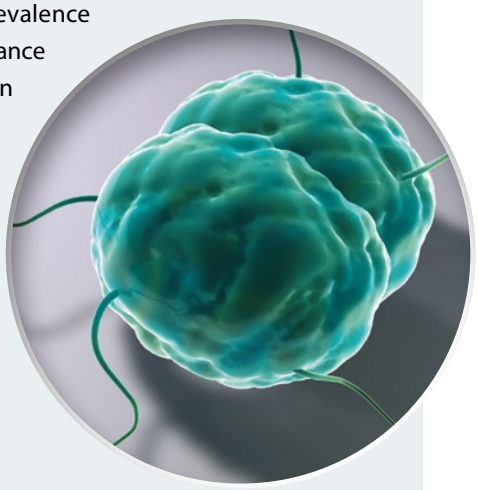
If the isolate is known to be ciprofloxacin sensitive, a 500 mg stat dose of ciprofloxacin can be used instead of ceftriaxone (but not in women who are pregnant).

A test of cure for gonorrhoea is not usually required unless there is a risk of re-exposure, symptoms do not resolve or a non-standard first-line medicine has been used (test in five weeks). Patients should be encouraged to return in three months for a sexual health check.[17]

Updated guidance on using ceftriaxone to treat gonorrhoea

Ceftriaxone injection is used for treating gonorrhoea if the antibiotic susceptibility is unknown, if the isolate is ciprofloxacin resistant, and for females who are pregnant or breast feeding (ciprofloxacin is contraindicated in pregnancy). The recommended dose of ceftriaxone for the treatment of gonorrhoea has increased from 250 mg ceftriaxone IM, to 500 mg IM stat.[17]

This increase in the dose for ceftriaxone has been recommended to overcome emerging cephalosporin resistance in *Neisseria gonorrhoeae*. Although the relevant subsidy requirement for ceftriaxone is "treatment of confirmed ciprofloxacin-resistant gonorrhoea", the prevalence of ciprofloxacin resistance is as high as 54% in some areas in New Zealand, and treatment where susceptibility is not known should be with ceftriaxone.[17]



Trichomoniasis

The first-line recommended treatment for people with trichomoniasis, and their sexual partners is metronidazole 2 g, stat, or alternatively if not tolerated, metronidazole 400 mg, twice daily, for seven days. Metronidazole may be given to women who are pregnant (category B2) or breast feeding, but they should be advised to avoid breast feeding for 12 – 24 hours after the dose.[18] Ornidazole 1.5 g, stat may be used instead of metronidazole, but is not recommended in women who are pregnant as no study data is available.

A test of cure for trichomoniasis is not usually required unless there is a risk of re-exposure. Culture of urethral swabs is rarely positive in males, due to low sensitivity, therefore empirical treatment of male partners is recommended without testing for trichomoniasis. Male contacts should, however, have a routine sexual health check for other STIs.[18]

Bacterial vaginosis

Women with bacterial vaginosis are often asymptomatic. It is not usually necessary to treat bacterial vaginosis unless symptoms are present or an invasive procedure is planned, e.g. insertion of an IUD or termination of pregnancy.

If treatment is required, first-line is metronidazole 400 mg, twice daily, for seven days.[19] Metronidazole 2 g stat, may be given if adherence is an issue, however, the stat dose is thought to be associated with a higher rate of relapse in women with bacterial vaginosis. Ornidazole 500 mg, twice daily, for five days, or 1.5 g, stat, is an alternative if metronidazole cannot be tolerated.

Treatment of male sexual partners of women with bacterial vaginosis is not usually necessary.

Pelvic inflammatory disease

Pelvic inflammatory disease (PID) is usually caused by a STI, particularly in women aged under 25 years, women who have had recent change of sexual partner or women with a previous history of gonorrhoea or chlamydia. Diagnosis of PID is clinical, taking into account the history, clinical findings and results of tests. However, STI tests will often be negative and a low threshold for treatment is appropriate, given the potential long-term consequences of infection and diagnostic uncertainty. Treatment should cover infection with gonorrhoea, chlamydia and anaerobes.

First-line treatment is ceftriaxone 500 mg, IM, stat **plus** doxycycline 100 mg, twice daily, for 14 days **plus** metronidazole 400 mg, twice daily, for 14 days. Metronidazole can be discontinued in women with mild PID symptoms, if it is not tolerated.[20]

Note: If adherence is in doubt, azithromycin 1 g stat, with a repeat dose in seven days, may be used instead of doxycycline.[20] Ornidazole may also be considered as an alternative to metronidazole, if it is not tolerated.

Epididymo-orchitis

Epididymo-orchitis may occur due to a variety of pathogens. STI pathogens are more likely in younger males (< 35 years) with a history of more than one sexual partner in the past 12 months and urethral discharge.[21] It is important to test for STIs prior to initiating antimicrobial treatment.

If STI pathogens are suspected as the cause, first-line treatment is ceftriaxone 500 mg IM, stat, followed by doxycycline 100 mg, twice daily, for 14 days. If symptoms are severe, refer immediately to hospital.[21]

If UTI pathogens are suspected as the cause, first-line treatment is ciprofloxacin 500 mg, twice daily, for 10 days or (if contraindications to quinolones) amoxicillin clavulanate 500/125 mg, three times daily, for 10 days.

Patients should be reviewed within 24 – 48 hours to assess response to treatment, and should be referred to hospital (urology) if signs and symptoms are worsening or do not improve.[21]

Genital herpes

Lesions (genital ulcers, sores or fissures) may be detected during the physical examination. If there is uncertainty, refer to, or discuss with, a sexual health physician. Referral is recommended for women who have their first clinical episode during pregnancy as serology may be required. A viral swab of lesions for herpes simplex should be taken, but a negative result does not exclude infection.[22]

The recommended first-line treatment is aciclovir 200 mg, five times daily, or 400 mg, three times daily, for five days (safe to use during pregnancy).[15] Lignocaine gel 2% may be given for topical analgesia (not subsidised), but oral analgesia may be required, particularly if symptoms are severe.[22]

For further resources on managing herpes, including in women who are pregnant, see: **www.herpes.org.nz**

Genital warts

Lesions can be identified on clinical examination. If warts are extensive, atypical, intravaginal/cervical or if there is uncertainty about the diagnosis, refer to, or discuss with, a sexual health physician.[23]

Treatment is mainly for cosmetic purposes, and may not be desired in all cases, e.g. if the warts are not visible externally and not extensive.

Podophyllotoxin solution 0.5%, twice daily, for three consecutive days per week, for five weeks, is appropriate for lesions which can be easily seen, e.g. pubic or penile shaft warts. It is not recommended to use podophyllotoxin for females with vulval warts or for people with perianal warts, as misapplication will cause significant irritation.

Imiquimod cream 5%, once daily, three times per week, for up to 16 weeks, is fully subsidised with Special Authority, for patients with warts not responsive to podophyllotoxin or for use in more sensitive areas, e.g. vulval or perianal warts or warts under the foreskin.[23]

Cryotherapy, laser, diathermy or surgical excision may be options if other treatments are not effective.[23]

N.B. The HPV vaccine prevents infection with HPV types 6 and 11 which cause 90% of anogenital warts.[23]

For further resources on managing HPV, including in women who are pregnant, see: **www.hpv.org.nz**

Syphilis

It is recommended that all patients with suspected syphilis be referred to, or discussed with, a specialist sexual health service if the practitioner does not have experience in managing syphilis.

For further information see: "Syphilis: testing for the great imitator", Best Tests (Jun, 2012).

What to do if other sexual health issues are raised

Occasionally in the course of a sexual health consultation a patient may state or indicate that they have sexual health issues beyond disease or infection.

Sexual dysfunction such as erectile dysfunction or loss of libido, are likely to be the most common non-STI issues encountered in primary care. A key requirement for the evaluation of sexual dysfunction is to determine whether the issue is associated with stress or anxiety. The presence of any serious medical condition is likely to impair sexual function not only because of the condition itself, but also due to the associated impact on psychological wellbeing.

For further information on sexual dysfunction in women, see "Selected topics in women's health", Best Tests (Sept, 2010).

For further information on sexual dysfunction in men, see "Selected topics in men's health", Best Tests (Sept, 2010).

Sexual violence is common in New Zealand. Most offenders are known to the victim and there is a high rate of intimate partner violence in New Zealand. Identifying people who are currently experiencing abuse or have been recently abused is likely to be difficult and will rely on interpreting the person's responses to sexual history questions and explicitly asking about abuse. These people will usually require referral to the appropriate services and if there are children in the household who are witnessing violence then referral to Child Youth and Family Services (CYFS) is required.

It is important to be aware of what counselling support services are available locally. Counselling may be funded by ACC. People who disclose a recent sexual assault may wish to report it to the police and a forensic examination may be required. Doctors for Sexual Abuse Care (DSAC) is an organisation that provides advice and support on the management of sexual abuse to New Zealand doctors. DSAC provides guidelines and an educational service, as well as patient information.

For further information, see: **www.dsac.org.nz**

Selected topics in sexual health

Special consideration for people who are lesbian, gay, bisexual and transgender

Lesbian, gay, bisexual and transgender (LGBT) people have different risks from those seen in the majority of patients. There is a large body of evidence that LGBT people are likely to report greater perceived barriers to quality healthcare as a direct result of their sexual or gender identity.[24] Asking about sexual preference during a sexual health consultation provides an ideal way in which to broach the subject in order to offer better care.

The uptake and frequency of cervical cancer screening is significantly lower in females who identify as lesbian or bisexual (ten times less likely to have had a test in the previous three years) than in heterosexual females.[24] Cervical cancer is caused by sexually transmitted high-risk HPV types, and there may be a false perception among both patients and healthcare providers, that women who do not have penetrative sex with males are not at risk from cervical cancer. However, there is significant clinical evidence that HPV is easily transmitted by oral sex and digital penetration. Health care providers should encourage cervical screening in all females aged 20 years and over, regardless of sexual preference or identity, and routine STI testing should be offered to all sexually active women regardless of sexual preferences.

Men who have sex with men have different sexual health risk factors than exclusively heterosexual men. HIV and syphilis are more common in MSM, and STIs such as gonorrhoea and syphilis can easily be transmitted by oral sex. Encouraging the use of condoms, and assessing recreational drug and alcohol use in this group is particularly important. Regular testing for STIs is recommended at least annually, with more regular testing depending on sexual history, rate of partner change and consistency of condom use.[25] Frequent testing (three to six monthly) is recommended for men reporting regular, unprotected anal sex, more than ten sexual partners in six months, engagement in group sex or use of recreational drugs during sex.[25, 26] Testing for syphilis at least annually is recommended in HIV-positive MSM.[25]

Some patients may express concern over certain problems believed to be related to anal sex, such as piles and anal fissures; however, these issues are no more common in MSM than in heterosexual people.[27] These problems are usually related to straining at stool or constipation, and should be managed within this context (see "Anal Fissures", Page 16). Faecal-oral spread of illnesses such as giardiasis and hepatitis A can occur via oral-anal sexual contact. Episodes of diarrhoea may be due to faecal exposure via oral-anal contact with another person, but are usually self-limiting. If diarrhoea persists, stool culture should be requested to identify any potential bacterial cause.[27] STIs such as chlamydia, gonorrhoea, herpes and syphilis may cause symptoms of proctitis (anal bleeding, discharge and tenesmus) even if there is no history of receptive anal intercourse. Therefore it is recommended that all MSM with anorectal symptoms be referred to or discussed with a sexual health physician.

Homosexuality and bisexuality, of both men and women, has been associated with higher rates of psychological and behavioural disorders, including depression, anxiety, mood disorders, suicidal ideation and planning, eating disorders, alcohol and substance abuse, and tobacco use.[28] While these issues are not exclusively related to sexual health, identifying a same-sex or bisexual sexual identity in a sexual health consultation presents an opportunity for the practitioner to discuss these other significant issues.

Ensuring the safety and health of sex workers

Sex workers, both male and female, have high-risk lifestyles and, as a group, are often marginalised by society. In general, sex workers exhibit higher than average knowledge about STI and HIV transmission.[29] Sex workers self-report an overall high adherence rate to condom-use, safe sex practices and health-seeking behaviours.[29] However, sex workers often have poor control over work-place safety and may not have complete

control over safe-sex practices; condom use may be poor in certain circumstances, particularly where there is concurrent drug or alcohol use.[29] In addition, rates of abuse, sexual assault and psychological issues are higher among sex workers than in the general population.[29]

When assessing the health of sex workers, include questions about intravenous drug use and exposure to abuse.

Six-monthly screening for STIs and HIV is sufficient for sex workers; more regular testing does not increase STI prevention if condoms are used consistently.[30]

Assessing the mental health of sex workers is important, both directly and indirectly as a method of preventing further sexual health issues. Sex workers who are psychologically distressed or have identified mental health issues report less consistent condom use, riskier behaviour and fewer sexual health checks-ups.[29]

For further information and a resource to which sex workers can be directed, see: **www.scarletalliance.org.au** and **www.nzpc.org.nz**

For further information on what to do in the case of sexual abuse or exploitation, see: **www.dsac.org.nz**

Genital piercing and STIs

Performing a sexual health check-up in a person with a genital piercing may be difficult: physically, it may be complicated to obtain urethral swabs, and certain piercing locations may increase the risk of blood borne infection.

Male genital piercing, most commonly through the glans penis and external urethra, known as a "Prince Albert", can cause scarring and urinary problems. As urethral swabs in males are inserted one centimetre into the urethra, some piercings may affect testing. First void urine is unlikely to be affected. Female genital piercing is usually through the clitoris, clitoral hood or labia, and it is therefore unlikely to impact on examination or swab collection.

Genital piercing, like any procedure that penetrates the skin, can lead to a viral or bacterial infection. Post-procedural infection with bacteria, such as *Staphylococcus aureus*, pseudomonas and group A streptococcus, is common.[31] There is limited evidence as to whether the prevalence of STIs is increased in people with genital piercings. In general, genital piercing in females, unless at a non-typical site, is unlikely to directly affect STI prevalence or exposure. However, there is case study evidence that the prevalence of genital warts is higher in males with genital piercings.[31] This may be causative, as the trauma and epithelial damage from piercing may increase the ease of transmission of high-risk HPV strains, or correlative, in that males with genital piercing may be prone to higher-risk behaviours.[31]

Important information may be revealed by enquiring about the reason for getting a piercing. Genital piercing in females has been linked with an increased incidence of past physical, emotional and sexual abuse (this link has not been studied in males).[32] In many of these females, genital piercing was viewed as a way to reclaim their bodies or their sexuality.[32] While the absolute number of females with genital piercing who have been exposed to abuse is likely to be low, the relative number appears to be high compared to the overall population.

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A quick guide to **managing anal fissures**

Anal fissures: tear-inducing tears

Anal fissures are small tears in the epithelium of the anus that can be intensely painful.

Most anal fissures are caused due to straining during bowel movements, constipation or repeated diarrhoea. They are equally common in both sexes, and most frequently affect people aged 15 – 40 years.[1] Women giving birth are at increased risk of developing anal fissures due to pressure on the perineum. Spasm of the anal sphincter or local ischaemia can predispose people to, or worsen, anal fissures.

Atypical anal fissures may develop in people with Crohn's disease, sexually transmitted diseases (particularly HIV, syphilis and herpes simplex), anal cancer, local trauma (anal intercourse), tuberculosis or receiving chemotherapy.[2, 3]

Spontaneous resolution occurs in one-third of people, usually within six weeks. Anal fissures that persist longer than this are considered chronic and should be managed more intensively. Topical glyceryl trinitrate is now available, fully subsidised, with Special Authority, as a treatment option for people who have had an anal fissure for at least three weeks. Where medical management fails to resolve symptoms and help heal the fissure, referral to secondary care for surgery or botulinum toxin treatment is usually required.

Symptoms and history usually indicate anal fissures

Anal fissures can usually be diagnosed based on the patient's description of their condition and a brief history, although an examination is also required.

Intense pain during defecation that often persists for one to two hours afterwards is the primary symptom of an anal fissure.[1] Patients will usually also have noticed the presence of blood on the toilet paper, and may report a tearing sensation during bowel movements.

Complications may occur in some people, including: failure to heal/chronic fissure, an anorectal fistula, infection and/or abscesses may develop or faecal impaction can occur due to intense and intolerable pain during defecation.

Perform an examination to help confirm a diagnosis

Anal fissures are not always visible on examination; however, examination is useful for ruling out other causes of pain and bleeding such as haemorrhoids, abscesses and viral ulcers. In 90% of cases, anal fissures form on the posterior midline of the anus. Typical features of a chronic anal fissure include an ulcerated lesion, a sentinel pile at the base of the fissure (resulting in a permanent skin tag) and enlargement of the anal papillae.

The management of anal fissures

Initial management involves lifestyle changes and symptomatic relief

Advise the patient to increase dietary fibre and fluid intake to keep bowel motions soft. The importance of correct anal hygiene and the need to keep the anal area dry should be emphasised. Regular sitz baths (sitting in warm water up to the hips) can help to relax the sphincter.[1] The patient should also be advised to avoid undue straining during bowel movements.

If lifestyle and dietary interventions are insufficient, or if the fissure is severe, a stool softener, e.g. oral docusate sodium, and mild local analgesia, e.g. lidocaine (not subsidised), may be prescribed.[1]

More intensive treatment may be required in some patients

If the fissure fails to heal within three to six weeks, topical nitrates or topical calcium channel blockers should be used. All topical treatments for anal fissures should be applied for at least six weeks to allow re-epithelialisation of the fissure.[1]

A topical nitrate, e.g. glyceryl trinitrate 0.2% ointment (see opposite), should be considered if the fissure has been present for at least three weeks. The patient should insert 1 – 1.5 cm of ointment into the anal canal, three times daily.[1] Nitrate ointment increases blood flow to the anus and reduces pain on defecation.[1] Dose escalation is not recommended as it does not increase the healing rate and may lead to more adverse effects.[4] Headache is the most common adverse effect,[5] and advising the patient to stop the medicine for a day or two if headaches become intolerable is recommended.[5]

Topical calcium channel blockers are also commonly used to manage anal fissures, although this is an unapproved use.[1] If the use of topical nitrates has not improved symptoms or where the adverse effects of nitrates are intolerable, topical diltiazem 2% (requires pharmacy preparation), two to three times daily, may be used.[1] The most common adverse effect is headache, although this has a lower incidence than with topical nitrates.[3, 4]

What to do if medical management fails to resolve symptoms

If the fissure has not healed after six to eight weeks of topical treatment and dietary changes, the patient should be referred to secondary care to assess the appropriateness of other treatments, usually botulinum toxin or surgery.

Subsidy changes to glyceryl trinitrate

Topical glyceryl trinitrate ointment is now available, fully subsidised, as of 1 April, 2013, for use in adults with anal fissures. The medicine can be prescribed by any General Practitioner, under Special Authority. The Special Authority criteria limit the use of the medicine to adults who have an anal fissure that has persisted for longer than three weeks.[6]

Topical glyceryl trinitrate is available as a 0.2% ointment, in 30 g packs. This medicine was previously available, but was not subsidised for anal fissures.

Botulinum toxin injected into the internal anal sphincter is used to paralyse the sphincter for several months. This treatment is most useful for females where the anal sphincter has been damaged following childbirth.[1]

Surgical techniques commonly used for anal fissures which aim to relax the internal sphincter include; open lateral sphincterotomy, closed lateral sphincterotomy and posterior midline sphincterotomy.[3] Surgery is consistently superior to medical management options, although it should only be considered in people with chronic, non-healing anal fissures where medical treatments have failed.[3] There is a slight risk of flatus and faecal incontinence following surgery.[4]

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The pharmacological management of ENDOMETRIOSIS

Endometriosis is a gynaecological condition in which endometrial tissue is present outside the uterine cavity, causing cyclic symptoms and, often, reduced fertility. A "working diagnosis" can be made based on the patient's symptoms and evaluation of risk-factors, although laparoscopy is required for a definitive diagnosis. Medical management involves the hormonal suppression of endometriotic lesions and, where possible, the surgical ablation and excision of ectopic endometrial tissue.

Endometriosis: a challenging diagnosis

Endometriosis is defined as the presence of endometrial tissue, glands and stroma outside the uterine cavity. The condition generally has three distinct manifestations: endometrial implantation on the peritoneum causing lesions and endometriomas (generally within the pelvic region, e.g. on the bladder, in the Pouch of Douglas), ovarian cysts (chocolate cysts) and endometriotic nodules in the tissue between the rectum and vagina (see opposite for definitions).[1]

The clinical presentation of women with endometriosis varies widely. Some women may be completely asymptomatic (and therefore not aware of the condition) while some women will have chronic pelvic pain, dysmenorrhoea, dyspareunia (pain during sexual intercourse) and painful defecation.[2] As endometriotic lesions are hormonally-responsive, symptoms will usually be worse at the time of menstruation. During periods of anovulation, such as pregnancy, lactation, menopause and hormone-induced amenorrhoea, symptoms are reduced or eliminated.[3] Endometriosis can have a significant effect on female fertility, and many women with undiagnosed endometriosis may first present with difficulty conceiving (See "Endometriosis and fertility", Page 24).

The exact prevalence of endometriosis is unknown, but it is estimated to affect 5 – 10% of women of reproductive-age, as many as half of all women with reduced fertility,[1, 2] and 70 – 90% of women with chronic pelvic pain.[1] The peak incidence is in women aged between 25 – 30 years.[4] Endometriosis rarely occurs in younger females and in post-menopausal women.[3] Endometriosis is also possible in males taking high-dose oestrogen, although this is extremely rare.[4]

The terminology of endometriosis

Endometriotic lesion – Lesions that occur when endometrial tissue seeds outside the uterus. Bleeding may occur from these lesions at the time of menstruation.

Endometrioma – An oestrogen-dependant lesion that is usually enlarged and filled with old blood. When they occur on the ovaries they are often referred to as chocolate cysts.

Endometriotic adhesion – Internal scar tissue that can bind organs together, causing organ dislocation and pain. The fallopian tubes, uterus, ovaries, bowel and bladder are the most commonly affected organs.

Endometrial stromal nodule – An uncommon, non-infiltrative, confined growth of endometrial stromal cells, which can develop into a rare type of cancer; an endometrial stromal sarcoma, which frequently metastasises.

The cause of endometriosis is unknown

The pathology of endometriosis is not well understood. Retrograde menstruation, where menstrual fluid flows back up the fallopian tubes and into the peritoneum, is believed to be central to the development of endometriosis.[2, 3] Endometrial cells are thought to move back up the fallopian tubes with the menstrual fluid, and possibly through the lymphatic and vascular network. The cells deposit in various tissues, seeding and developing into endometriotic lesions and endometriomas. When this occurs, internal bleeding and inflammation can lead to fibrosis and adhesion development, which in turn contributes to the symptoms and the physical distortion of pelvic anatomy that is seen in women with more severe endometriosis.

Although retrograde menstruation is estimated to occur in 90% of women, only a portion of these women will go on to develop endometriosis.[5] Current research is focused on investigating the genetic components of endometriosis.[6] Hormonal, immunological and environmental components are also implicated in the initial development of the condition.

Risk-factors for endometriosis

Risk factors for endometriosis include:[1, 4]

- A first-degree female relative (mother or sister) with endometriosis
- Shorter-than-normal menstrual cycle (< 27 days)
- Longer-than-normal menstruation (> five days)
- Low body-mass index
- Early menarche
- Nulliparity
- Müllerian anomalies – anomalies that arise during the formation of parts of the female reproductive organs
- Outflow obstructions, e.g. cervical stenosis, a transverse vaginal septum or an imperforate hymen

The distribution of ectopic endometrial tissue is influenced by age. Pelvic endometriomas typically occur in women aged 25 – 30 years.[4] Ectopic endometrial tissue outside the pelvic area typically occurs in older women, most commonly in those aged 35 – 40 years.[4]

Making a 'diagnosis' of endometriosis

Making a clinical diagnosis of endometriosis can be difficult as symptoms are often non-specific, there are limited clinical signs on examination, laboratory testing is not helpful and imaging is of only limited benefit.[7, 8] Laparoscopy is therefore required to make a definitive diagnosis.[7] On average, there is a delay of seven to twelve years between the development of symptoms and diagnosis of endometriosis, which impacts significantly on the patient's quality-of-life.[7] The presumptive diagnosis and medical management of endometriosis in primary care is, therefore, important in reducing avoidable pain and discomfort and managing fertility.

Symptoms are non-specific and common

Approximately one-third of women with endometriosis will be asymptomatic. Most women with symptomatic endometriosis will have cyclical symptoms, such as pelvic pain which is the most frequently occurring symptom. Pain generally begins several days prior to menstruation and ceases within one to two days of menstruation.[4] Deep pain may also be present during or after sexual intercourse. If endometriotic lesions are present in the bladder or rectum, pain may be present during urination or defecation.[3] In severe cases, pain may become constant as the condition worsens and deep endometriotic lesions and adhesions develop.[5]

Rarely, endometriotic lesions can occur outside of the abdominal cavity, such as in the lungs, and can cause pain and other symptoms, such as haemoptysis, coinciding with the menstrual cycle.[5]

Common symptoms of endometriosis include:[4, 9]

- Severe dysmenorrhoea
- Bloating
- Lethargy
- Pelvic pain
- Constipation
- Lower abdominal or back pain
- Dyspareunia
- Painful defecation
- Infertility
- Heavy menstruation or pre-menstrual spotting (may also indicate co-existing adenomyosis, see opposite)
- Cyclic pain upon urination or urinary frequency
- Pain during exercise

Acute exacerbations of pain, swelling or fever may occur due to chemical peritonitis if leakage of blood from an endometriotic lesion or cyst occurs.[4]

Clinical examination may be helpful to rule out other conditions

Most women with endometriosis will have normal examination findings; however, diffuse pelvic or posterior fornix tenderness or palpable pelvic masses are sometimes present. In some women, uterosacral ligament nodules may be palpable on a bimanual vaginal examination.

Examination is therefore primarily for the purposes of differential diagnosis, and should include assessment for sexually transmitted infections (STIs), cervicitis, abnormal vaginal discharge and any other gynaecological abnormalities, such as cervical excitation and adnexal masses.

Imaging and laboratory tests are of limited benefit

Imaging is not usually helpful. If available, transvaginal ultrasound imaging can be considered; however, if cysts and nodules are small or not situated on the ovaries or near the uterus the imaging will not be of any use.[10]

There is no laboratory test that can reliably identify endometriosis.[11] Investigation of full blood count, ferritin and TSH may be useful in the differential diagnosis.

Other diagnoses are always a possibility

Women with endometriosis often present with diverse, non-specific symptoms, and other possible diagnoses should always be considered.

Acute symptoms caused by STIs, urinary tract infections (UTIs) and pelvic inflammatory disease often mimic endometriosis, however, given the chronic nature of endometriosis, it is likely that these conditions can be ruled out early.

Some long-term conditions have symptoms that overlap with endometriosis and it may be difficult to rule these out. Differential diagnoses that should be considered in women with pelvic pain include adenomyosis, diverticulitis, irritable bowel syndrome, uterine fibroids and interstitial cystitis.

Adenomyosis occurs when endometrial tissue, is present within the muscles of the uterus (as opposed to endometriosis which occurs outside the uterine cavity). It is usually found in women in an older age group than endometriosis (age 35 – 50 years), and often after childbirth. It is almost symptomatically identical to endometriosis and can usually only be distinguished after laparoscopy. Adenomyosis also commonly co-exists with endometriosis.

Generally, presentation and patient history will shift the balance of probabilities for a diagnosis, e.g. uterine fibroids are more common in an older age-group and a patient with irritable bowel syndrome is less likely to present with painful defecation.[10] However, some conditions will be nearly impossible to rule out until laparoscopy is performed or a therapeutic trial of treatment is undertaken.

Always consider the possibility of colon and ovarian cancer which may present concurrently, even in women with laparoscopically diagnosed endometriosis. In addition, in a small number of women, uterine and müllerian abnormalities, both of which are risk-factors for endometriosis, may be present and complicate diagnosis and treatment.

When should a patient be referred for further assessment?

The management of suspected endometriosis depends on the patient's age, desire for conception, the degree of pain, the impact on their capacity to work and their overall quality of life.[8] Generally, a three-month therapeutic trial with hormonal treatment can be used to help strengthen a working diagnosis. However, this is not appropriate in certain instances.

Referral to secondary care for further assessment should be undertaken if:[10]

- Endometriosis is strongly suspected and immediate fertility is desired
- A trial treatment with analgesia and a hormonal medicine is unsuccessful
- The patient has persistent, constant pelvic pain, or significant bowel or bladder pain
- A pelvic mass, especially if tender, is found on examination
- The patient has pain or other symptoms that require a significant amount of time off work or school

Medical management of endometriosis

The aim of medical management is to control symptoms, either prior to, alongside or instead of more curative surgical interventions. Medical management is based on hormonal suppression of endometriotic lesions and is particularly effective when amenorrhoea occurs via down-regulation of the hypothalamic-pituitary-ovarian axis.[12]

Endometriosis is a chronic and often recurrent condition and long-term treatment is usually required. Approximately 50% of women will have a recurrence of symptoms within five years if medical management is stopped. Menopause usually leads to a complete cessation of symptoms, even if hormone replacement treatment is used.[6]

A step-wise treatment strategy

The first-line treatment for females with endometriosis who do not wish to conceive in the near future is a hormonal medicine, and analgesics if required.[9] Combined oral contraceptives are the most widely used hormonal treatment, followed by progestin hormone treatment.[8] Other hormonal treatment options include androgenic medicines and gonadotropin-releasing hormone analogues: both of which have comparable efficacy.[4, 5, 12] However, adverse effects limit gonadotropin-releasing hormones to a second-line choice and androgenic medicines are now rarely used due to their adverse effects.

Pain relief

Non-steroidal anti-inflammatory analgesics (NSAIDs), such as ibuprofen, naproxen or mefenamic acid are recommended for acute pain relief as an adjunct to all medical management options and prior to surgery in women who wish to conceive.[10,13] All NSAIDs have similar efficacy in the management of endometriosis.[13] Opioids should generally be avoided due to issues with long-term use.[12]

Combined oral contraceptives

Combined oral contraceptives are widely used as the first-line pharmacological treatment for women with suspected endometriosis, as these medicines are generally well tolerated with less adverse and metabolic effects than other options.[8]

The choice of combined oral contraceptive should be based on any previous use by the patient. If no combined oral hormonal contraceptives have been previously used, a trial of a levonorgestrel + ethinyloestradiol contraceptive, e.g. Ava, is recommended.

Combined oral contraception should be used continuously or semi-continuously, e.g. three or six-month cycles, as monthly uterine bleeds are likely to be painful, although less so than normal menstruation.[8, 10] Patients should be advised that this may result in irregular spotting and occasional breakthrough bleeding.

Adverse effects of combined oral contraceptives are generally mild.[10] They include gastrointestinal disturbance, headache, migraine, metabolic and weight changes, irritability, changes to libido, cramping and spotting in early cycles. Venous thromboembolism is also possible, although rare, in women taking combined oral contraception. Combined oral contraceptives will need to be discontinued if migraines occur.

Progestins and anti-progestins

High-dose progestins (medroxyprogesterone acetate 10 – 100 mg daily or norethisterone 10 – 45 mg daily) are commonly used to treat endometriosis, and are an alternative to combined oral contraceptives.[10] At these doses, progesterone suppresses the hypothalamic-pituitary axis to inhibit ovulation and reduce circulating oestrogen levels.[3] Progestins also have an additional, direct effect on the endometrium, causing atrophy to both normal endometrium and endometriotic lesions.[3] They are relatively well tolerated and have a more limited metabolic impact than androgenic analogues and gonadotropin-releasing hormones, and are less expensive than these options.

Progestin-only contraceptives are available in a variety of formulations, including oral medicine, implants and depot injections. Adverse effects of progestins include bone mineral density loss, weight-change, acne, oedema, mood changes, depression and headaches.[14] There is little difference in efficacy effect between formulations, however, patients administered depot progestin may experience more adverse effects.[14]

Oral medroxyprogesterone acetate (Provera) 10 mg, three times daily, for ninety days is approved for use in endometriosis. Oral medroxyprogesterone acetate should be started on day one of the menstrual cycle.

Depot medroxyprogesterone acetate (Depo-Provera) 50 mg weekly or 100 mg every two weeks, for at least six months is also approved for use in women with endometriosis.[15] N.B. vials come in 150 mg/mL.

Norethisterone (Primolut) 5 mg, twice daily, for six months is approved for use in women with endometriosis. Norethisterone

should be initiated between days one and five of the menstrual cycle.

The levonorgestrel intra-uterine device (Mirena) has been shown to be effective in managing the symptoms of endometriosis. However, this is an unapproved indication. The device is placed into the uterine cavity, usually at the onset of menstruation and may prevent endometriosis symptoms in some women, for up to five years.[8, 15]

Gonadotropin-releasing hormones

Gonadotropin-releasing hormone (GnRH) analogues are used in women with endometriosis to induce hypo-oestrogenic, medical menopause.[3] They modify the release of pituitary gonadotropins through interaction with the GnRH receptor, resulting in decreased production of FSH and LH. They are typically considered if oral contraceptives or progestins are ineffective or cannot be tolerated.[10] GnRH analogues are usually only prescribed in consultation with a gynaecologist.

Two GnRH analogues are available, fully subsidised, in New Zealand; goserelin acetate (implant) and leuproreolin (injection). Dosing regimens are dependent on the size of the dose, generally every 28 days or every three or six months. They are usually only used for a maximum of twelve months.

GnRH analogues are associated with several short-term adverse effects, mainly hypo-oestrogenic symptoms, including menopausal symptoms, loss of libido and emotional lability. Several long-term adverse effects may also be seen, most notably bone-mineral density loss.

Because of these adverse effects, "add-back" therapy is recommended if a GnRH analogue is continued for more than six months. Add-back therapy involves concurrently prescribing a synthetic progestin, e.g. norethisterone, plus either a bisphosphonate or oestrogen with GnRH in order to reduce the adverse effects of GnRH treatment. GnRH plus add-back treatment becomes considerably more expensive than other endometriosis treatment options.

Androgenic medicines

Androgenic medicines, e.g. danazol, were, in the past, often used to manage endometriosis due to their ability to induce a hypo-oestrogenic state.

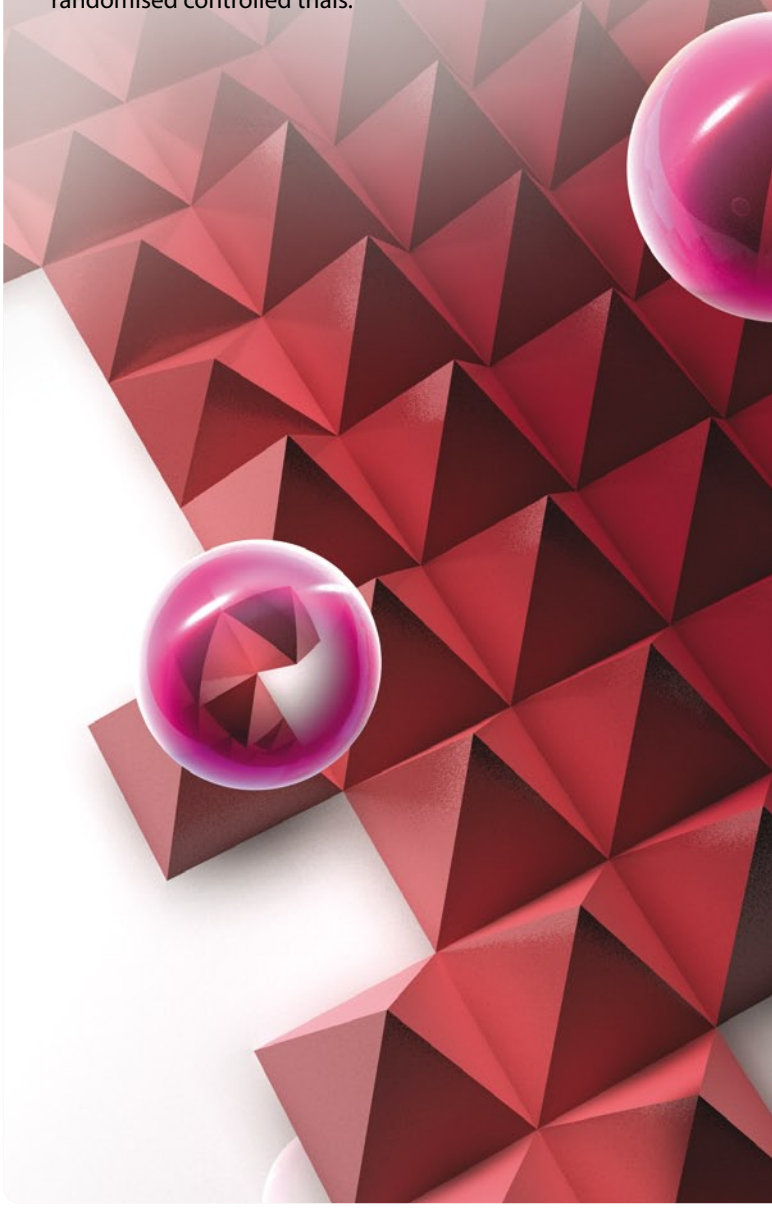
However, the adverse effects associated with androgenic medicines are significant and generally mean that androgenic medicines are no longer prescribed other than in females for

Emerging medical treatments

Several other, new treatment options for women with endometriosis are currently being investigated. One of the primary focuses of new research is finding an effective medical treatment that does not prevent or preclude pregnancy. Medicines currently being investigated include:[10, 12]

- Metformin
- Aromatase inhibitors
- Selective progesterone receptor antagonists
- Orally-active GnRH antagonists
- Selective oestrogen receptor-beta agonists

Several other medicines, such as immunomodulators and anti-TNF-alpha agents, have been trialled but either failed to show benefit or were proven to have no benefit in randomised controlled trials.



Endometriosis and fertility

The pathophysiology of infertility in women with endometriosis is not well understood. Inflammation of the pelvic cavity, structural abnormalities, the presence of endometriomas of the ovaries, alterations of sperm-oocyte interaction and reduced endometrial receptivity are all thought to be involved.[8]

It is not possible to differentiate between those women with endometriosis who will experience reduced fertility and those who will retain normal levels of fertility, even if a laparoscopy is performed.

Surgery to ablate and excise endometriomas, adhesions and scar tissue is the most common treatment for women with endometriosis who wish to conceive, but cannot.[2, 17] Recent evidence into endometriosis treatments indicates that lipiodol (oil soluble contrast medium) flushing of the uterus, fallopian tubes and ovaries in women with endometriosis increases the rate of pregnancy, and may be considered in the setting of a specialist fertility clinic.[19]

Assisted fertility treatments are likely to be beneficial for most women with endometriosis who have reduced fertility.[9]

Traditionally, hormonal treatment was used in women with reduced fertility for a short period, e.g. six months, and then stopped, as it was thought that this created "rebound" fertility. However, a Cochrane review found that there is no increase in fertility after treatment with hormonal medicines for women with endometriosis.[20] In addition, some medicines, particularly medroxyprogesterone acetate and some androgenic agents may have lasting effects of ovulation suppression beyond the duration of treatment, although typically not more than a few months.

whom no other treatment is effective or appropriate. Adverse effects include venous thromboebolism, weight gain, voice changes, skin reactions, mood and libido changes, oedema, myalgia, acne, oily skin and hirsutism or male pattern baldness, which may be permanent.[16] There is also limited evidence that androgenic medicines increase the risk of ovarian cancer.[10] They should not be prescribed to women with liver disease or hyperlipidaemia. They are contraindicated in women who are pregnant as they can virilise the foetus and cause other androgenic effects.

Danazol is titrated to achieve amenorrhoea, at a dose of 200 – 800 mg, in two to four divided doses, daily (capsules are 100 mg or 200 mg). It is generally used for a maximum of six months due to adverse effects.[3] Symptomatic improvement has been shown to remain up to six months after treatment is stopped.[16] Patients will need to be advised to use a non-hormonal form of contraception, usually condoms, throughout treatment, and pregnancy should be excluded prior to initiating.

Surgical treatment

Surgical treatment is highly effective for symptom and pain reduction and can increase fertility in sub-fertile women.[17, 18] However, access to surgery is limited, and even when performed, recurrence rates are high: approximately 50% of women will re-develop symptoms within five years of surgery.[3]

The success rate of surgical treatment of endometriosis depends on the severity of the condition, its location, and the extent of the symptoms as well as the age of the patient (effectiveness is reduced in younger women). Surgery for endometriosis is divided into two strategies: surgery with preservation of fertility and surgery if fertility is not desired.

Surgery with preservation of fertility involves laparoscopy to excise or ablate all visible lesions and restore pelvic anatomy. It is the more common surgical option, which significantly reduces pain in the majority of patients and has the ability to retain, and in some cases increase, fertility in women.[10] The rate of symptom recurrence is higher than with more aggressive, non-preservative techniques, however, the ability to maintain fertility outweighs this for many women.[10] A prophylactic appendectomy is sometimes performed during surgery, especially if the patient presents with right-sided pain, as abnormal appendix pathology has a high prevalence in women with endometriosis.[10]

Radical surgery is limited to women with endometriosis who do not wish to conceive, and after all medical treatments have been unsuccessfully trialled.[9] More aggressive surgical

options that do not preserve fertility involve hysterectomy, adnexectomy (removal of the fallopian tubes), oophorectomy (removal of the ovaries). The excision of all visible peritoneal lesions is standard alongside all aggressive treatments. Patients undergoing radical surgery should be counselled about the possibility of symptoms persisting even after complete bilateral oophorectomy and hysterectomy, and the adverse effects associated with early, medically-induced menopause. Oestrogen-replacement treatment may be required and should be discussed with the consulting surgeon.[10]

Complications

Long-term complications are common in women with endometriosis. Common complications are adhesion formation and ovarian failure post-surgery.

Adhesions are thought to result from the inflammation of peritoneal surfaces. The risk of this occurrence is not well known, and may be increased by surgical intervention. Sequelae may include pain, structural changes to the pelvic and reproductive organs and bowel obstruction.

Ovarian failure occurs in 2.4% of women after ablation of ovarian endometriomas, even with the less aggressive surgical interventions.[10]

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Cold season in primary care:

Advice is the best medicine

Every year New Zealanders spend significant amounts of money on supplements, over-the-counter, complementary and alternative medicines for the common cold. For most people, symptoms of the common cold are mild and self-limiting, and the products used to treat it are often expensive, lacking evidence of effectiveness and in some cases, have potentially serious adverse effects. Patients should be given advice on prevention and management and where possible, given unbiased, evidence-based information on the benefits and adverse effects of over-the-counter and alternative products.

There is no cure for the common cold

The common cold is a benign, self-limiting upper respiratory tract infection (URTI), with a multitude of symptoms caused by over 200 different respiratory viruses.[1] There is no "cure" for a cold, and few effective symptomatic treatments. Colds are a significant cause of lost work or school-days and account for a large number of presentations at general practice clinics in the winter season.

URTIs are the most common illnesses in humans, with adults experiencing on average two to five acute URTIs per year and children experiencing seven to ten per year.[1, 2] A mild winter cold is so common that self-diagnosis and self-treatment are normal. This has created a multi-billion dollar industry to supply the demand for over-the-counter and complementary and alternative medicines (CAMs). Most colds have a similar natural history, with symptoms increasing in severity over several days, followed by a gradual decline over one to two weeks.[1] The risk of complications is generally only increased in immunocompromised people, or very young or very elderly people. Because of this short, predictable natural history it often appears that CAMs, supplements and over-the-counter medicines have a curative effect, when in fact an improvement in symptoms reflects the usual course of the illness.

What is recommended for the management of the common cold?

Patients should be reassured that colds generally do not result in serious health problems, such as pneumonia, bacterial infections or hospitalisations, and that they are not the same illnesses as influenza and pandemic infections, e.g. coronavirus.

Preventative measures

The most effective management strategy for the common cold is to avoid contracting it. Practitioners should give patients, particularly families with young children, advice on preventing and reducing the spread of illness during the winter season.

Regular hand washing, for 20 seconds with warm water and soap followed by 20 seconds of drying, is likely to be the most significant protective action for common viral illnesses. Hands should also be washed after any contact with a person with a cold. When coughing or sneezing, cover the nose and mouth with a tissue, or use the inside of the elbow, rather than the hand. Avoid touching the eyes, nose and mouth when unwell, or when others in the house are unwell.[3]

Having a "healthy home" is also important, particularly for children. A smoke-free home with adequate heating and insulation, warm clothing and good nutrition should always be encouraged.

Analgesia

Paracetamol can be used for general "aches and pains" and to reduce fever in children and adults. However, mild fevers (< 38°C) do not need to be treated, as fever is a beneficial immune response that reduces the duration of most infections.[4, 5]

NSAIDs, such as ibuprofen, may be used as an alternative to paracetamol, or used concurrently. A Cochrane systematic review found that NSAIDs are effective for relieving pain and myalgic symptoms in people with URTIs, but that they had no effect on relieving respiratory symptoms.[6] Advise patients to remain well hydrated if taking NSAIDs, as renal complications are possible, particularly in children who become dehydrated.

Antibiotics should be avoided

Antibiotics are not necessary for most acute URTIs as they are caused by viruses. For the majority of people with a respiratory illness antibiotics will cause more adverse effects than benefit and will contribute to the continuing development of antibiotic resistance.[7]

However, there are some clinical instances when antibiotics are appropriate; such as when a secondary bacterial infection develops, or the initial diagnosis was incorrect. For example, there is currently a pertussis epidemic in New Zealand. The initial stage of pertussis (the catarrhal stage) is symptomatically similar to a mild cold. Antibiotics are necessary for the treatment and prophylaxis of suspected cases of pertussis. Another example where use of antibiotics may be appropriate is in the management of suspected Group A streptococcal (GAS) pharyngitis, due to the risk of rheumatic fever. In some cases, empiric treatment with antibiotics is appropriate, depending on the presence of risk factors.

 See Heart Foundation algorithm 4 for sore throat management: **www.heartfoundation.org.nz**

It is important to note that secondary bacterial infection is rare in people with the common cold, and usually will only occur with more serious URTIs or in people with pre-existing co-morbidities. Even when a bacterial aetiology is suspected, antibiotics are not always appropriate. In general, for illnesses that may require antibiotics, they should only be prescribed if:

- Symptoms are significant or severe
- There is a high risk of complications
- The infection is not resolving on its own

 For further information on the use of antibiotics, see: "Antibiotic treatment for common infections", bpac^{nz} . Available from: **www.bpac.org.nz**

Medicated cough and cold preparations

Cough and cold preparations are designed to provide symptomatic relief from viral respiratory infections.

Preparations commonly contain:

- Mucolytics/expectorants – loosen phlegm from the respiratory tract, making it easier to expel, e.g. bromhexine, guaifenisin
- Antitussives – reduces the urge to cough, e.g. pholcodine, dextromethorphan
- Nasal decongestants or sprays – reduces nasal symptoms through vasoconstriction and reduced nasal inflammation, e.g. phenylephrine, pseudoephedrine, xylometazoline, oxymetazoline
- Antihistamines – used based on the premise that they reduce similar symptoms in allergies (rhinitis, sneezing), e.g. promethazine, diphenhydramine

Although widely used, most cough and cold preparations containing these medicines, or combinations, are not particularly effective at reducing symptoms.[8] Antitussives, antihistamines, antihistamine/decongestant combinations and antitussive/bronchodilator combinations are no more effective than placebo in alleviating symptoms of the cold in either children or adults.[8, 9, 10, 11] There is insufficient evidence to evaluate expectorants or mucolytics, although they appear to have some limited benefit.[8, 12]

The common cold affects children and adults differently, and products which may be effective for adults may not work or be appropriate for children.

It is recommended that the use of CNS-acting medicines in children is avoided. Most cough and cold preparations contain either a central nervous system (CNS) depressant, e.g. chlorpheniramine, leading to possible sedation, psychomotor impairment, dizziness and hallucinations or a CNS stimulant, e.g. phenylephrine leading to possible insomnia, tremor, hallucinations and palpitations.[8]

Medicated nasal sprays containing ipratropium, such as Otrivin Plus, are effective in reducing rhinorrhoea but not nasal congestion.[13] They are associated with some adverse effects such as blood-tinged mucous and mucous membrane dryness. Patients are also likely to experience rebound effects after stopping the medicine, if the medicine is used for more than five days consecutively, therefore products should not be used for more than three to five days.

The placebo effect can play a significant role in the perceived effectiveness of cough and cold preparations.

Aromatic inhalants

Aromatic decongestant treatments, containing menthol and other "natural" products, are a popular over-the-counter product for colds. Preparations generally involve adding a compound to hot water and inhaling the vapour or applying a decongestant compound as a rub to the chest or neck. There is insufficient evidence to recommend the use of any such preparation.

A systematic review of steam inhalation concluded that there was insufficient evidence to determine whether there was any beneficial clinical effect when used for the common cold in adults.[14] Steam inhalation may worsen symptoms of congestion for some people. In addition, accidental ingestion of aromatic oils, even in small amounts, is associated with a significant risk of CNS depression (due to toxicity) and aspiration (due to volatility).

Nasal irrigation

Nasal saline irrigation is another common treatment for congestion in people with colds. It is one of the few treatments that can be safely used in infants. A Cochrane systematic review stated that "nasal irrigation with saline is a safe treatment that may be mildly beneficial to some patients".[15] There was limited evidence of benefit found in children and adults using nasal irrigation to manage URTI symptoms.[15] Symptoms and illness duration were statistically similar to control groups. The study did find that there was a reduction in days off work or school among people that used nasal saline irrigation. Adverse effects of nasal irrigation include minor nosebleeds in some children and mild discomfort.

What about complementary and alternative medicines?

Complementary and alternative remedies are frequently used for the purpose of managing or preventing the symptoms of the common cold. Some may have a small effect on reducing symptoms, however, in most cases there is limited evidence to support their use or evidence has shown that they are ineffective.

The recommended approach for advising patients about the use of CAMs

If a patient asks for advice about using CAMs, it may be helpful to consider the following points:

- Does it have any positive effect?

Some medicines should not be used in children

Preparations containing the following medicines should not be used in children aged less than six years:

- Antihistamines – brompheniramine, chlorpheniramine, diphenhydramine, doxylamine, promethazine or triprolidine
- Antitussives – dextromethorphan or pholcodine
- Expectorants – guaifenesin or ipecacuanha
- Decongestants – phenylephrine or pseudoephedrine

Preparations containing the following should not be used in children aged less than two years:

- Mucolytics – bromhexine
- Decongestants – xylometazoline or oxymetazoline

Cough and cold preparations are required to be labelled as such, and must include details containing active ingredients on the packaging.

A list of cough and cold preparations available in New Zealand that are affected by these restrictions is available from: **www.medsafe.govt.nz/hot/alerts/coughandcold/affectedmedicinesoct2009.asp**

What does the law say about doctors and alternative medicine?

The Medical Council of New Zealand states that practitioners providing information on CAMs have to inform patients "*of the nature of the alternative treatment offered and the extent to which it is consistent with conventional theories of medicine and has, or does not have, the support of the majority of practitioners*".[16] For those practitioners who do prescribe or recommend CAMs, the Medical Council of New Zealand and the Health Practitioners Competence Assurance Act 2003 state that: "*No person may be found guilty of a disciplinary offence merely because that person has adopted and practised any theory of medicine or healing if, in doing so, the person has acted honestly and in good faith*".[17] Careful attention to the process of informed consent is important whenever a patient wishes to use a potentially unproven, harmful or expensive alternative treatment.

Potential changes to the laws governing claims made by natural products

The "Natural Health and Supplementary Products" Bill is currently going through the New Zealand House of Parliament. The Bill will put in place stricter controls for the claims of benefit made by the manufacturers or importers of natural health and supplementary products. The Bill does not cover foods or prescription medicines covered under the Medicines Act 1981. It will require any claims of health benefit to be supported by either scientific research or by traditional practice evidence. Traditional use is defined as the "use of a substance based on knowledge, beliefs or practices passed down from generation to generation". The Director-General of Health determines what claims of health benefits are "allowable", on the basis of the evidence presented and the risks associated with allowing these claims. The Bill prohibits claims of health benefits on product labels or advertisements that are not allowable claims. The Bill also regulates the ingredients of natural health and supplementary products, and the manufacturing facilities of these products.

The Bill is currently awaiting its third reading, and may change the way products are advertised, and potentially how they are used. No date has been set for the third reading as yet.

To read the full Bill, see **www.legislation.govt.nz/bill/government/2011/0324/latest/DLM3984610.html**

- Will it cause harm?
- Will it interact with a current conventional medicine?
- Is it likely to replace a conventional medicine?
- Could it be a financial burden?

Practitioners should always attempt to give unbiased, evidence-based advice to patients about the treatments that they are using or wish to trial. Discuss the benefits, or lack of benefits, and the potential harms. Remind the patient that most winter illnesses are brief and will resolve without treatment.

What evidence is there for the use of complimentary medicines and alternative remedies?

There is a large range of commercial products that claim to have beneficial effects on the course of winter ills. Few treatments have a strong evidence base, and often when evidence is available a strong industry bias or significant design flaws are present.

Table 1 (over page) covers a small selection of the more commonly available CAMs. Wherever possible, the results of high-level randomised controlled trials (RCT) or meta-analysis of RCTs, generally from the Cochrane Database of Systematic Reviews, were used. Of the remedies and medicines reviewed, few had a strong, positive evidence base illustrating their effectiveness. Zinc, probiotics and vitamin C were the only medicines reviewed that had a symptomatic benefit illustrated by a reasonable evidence base. Many, such as garlic and ivy leaf have evidence of small symptomatic benefits, however, in almost all instances this was tempered by the authors indicating that the reviewed studies were poor, biased or flawed. Other commonly used remedies, such as Buccaline and olive leaf extract, lack meta-analysis or RCTs of sufficient size or quality to safely recommend for or against their use. In almost all cases, a large amount of primary research is available on CAM remedies. These individual studies are generally more positive, however, the risk of bias is higher and the quality of the studies varies. In addition, primary research-level studies often use individual brands, rather than generics or classes of medicine, and are funded directly by the manufacturer further limiting what can be said about the product based on the findings of a given study.

Some 'classes' of CAM, such as traditional Chinese medicines, are difficult to investigate due to the large variety of products available. There is also significant variation in the level and type of active ingredients in most CAMs, and significant variation in the additional substances included. As such, even high-level

meta-analyses are unable to identify sufficient quantities of evidence to make broad statements. For example, a Cochrane systematic review of 430 studies on Chinese traditional medicine, of which 17 studies met the inclusion criteria (patient sample size = 3212), found that there was insufficient available evidence to recommend the use of any Chinese herbal medicine for the common cold.[18] A review of 13 RCTs (sample size = 640) found no evidence to support the use of Chinese medicine in the treatment of severe acute respiratory syndrome.[19]

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Table 1: Supplements, herbal remedies and products for preventing or treating the common cold

Product	What is it used for?	Evidence of clinical benefit	Direct adverse effects*	What is the evidence?
Buccaline tablets**	Prophylaxis of bacterial infection secondary to URTIs	Inconclusive	Inconclusive	No RCTs were identified and primary research has significant bias and/or flaws
Echinacea	Preventing and managing acute URTIs	No	None	A Cochrane systematic review of 16 included studies out of 58 (sample size = 2601), testing a range of preparations, from different parts of the three main species of Echinacea found highly inconsistent evidence indicating no preventative benefit for the common cold, although there may be some symptomatic benefit if the aerial section (leaves, stems, etc) of the plant is used early in the illness.[20] Multiple preparations are available, and there may be difference in effect with different brands.
Garlic	Preventing and reducing the duration of the common cold	Possible, but inconclusive	Some participants reported malodour	A Cochrane systematic review of one included study out of six trials, which randomised participants to garlic capsules or placebo, found that garlic may slightly reduce the incidence of common cold.[21] However, the sample size was too small to gain strong statistical significance.
Homeopathy (a system of alternative medicine)	Multiple suggested uses	No	None	Meta-analysis and aggregations of meta-analyses have concluded that there is no evidence that homeopathy is more efficacious than placebo for any clinical condition.[22–24]
Honey	Symptomatic treatment of the common cold	Inconclusive	None N.B. Honey should not be used in children aged < 1 year due to a rare association with infant botulism[25]	A Cochrane systematic review of two included trials out of 79 (sample size = 268), stated that honey may be better than "no treatment" for acute cough in children, but that there was insufficient evidence to strongly suggest for or against honey.[26]
Ivy leaf extract	Relief of respiratory symptoms	Possible effect on respiratory symptoms	Inconclusive	A literature review of RCTs concluded that ivy leaf preparations have some effect on improving respiratory function, but there is insufficient evidence to make any recommendations for their use. A strong industry bias was present.[27]

Olive leaf extract	Prevention of the common cold	Inconclusive	Inconclusive	A review of the available literature was unable to identify any sound, unbiased evidence.
Probiotics (e.g. BLIS)	Prevention of the common cold and sore throat	Reasonable benefit for preventing respiratory infections	Adverse effects are minor: nausea, rarely vomiting	A Cochrane systematic review of 14 included studies out of 27 (sample size = 3451), found there may be some reduction in the incidence in URTI.[28] No RCT studies on the use of probiotics for sore throat were identified. There is a strong industry bias in the available evidence.
Vitamin C	Prevention of the common cold and duration reduction	Small preventative benefit against URTI; no symptomatic effect, no reduction in URTI duration	None	A Cochrane systematic review of 55 included studies out of 173 (sample size prophylaxis = 23587; sample size therapeutic action = 5957), found limited evidence for prophylaxis and for therapeutic treatment of the common cold with vitamin C; a prophylactic benefit was observed, but no benefit in duration or symptom reduction was found. The effect was slightly greater in children.[29]
Zinc	Prevention of the common cold	Reasonable evidence for positive effect in URTI	Toxic in high doses (> 40 mg/day in adults). Mild adverse effects are common (nausea, constipation, diarrhoea, abdominal pain, irritation)	A Cochrane systematic review of 15 included studies out of 57 (sample size = 1394), found a significant reduction in duration, severity and incidence of common cold in patients using zinc supplementation.[2] An independent meta-analysis of 683 studies yielding 17 trials (sample size = 2121) found similar results; that zinc reduces the incidence, severity and duration of the common cold, but has adverse effects.[30]

* Only direct adverse effects, from the substance, have been included

** An oral antibacterial product that contains inactivated bacteria. The product claims to increase immune response to the included bacteria, thereby creating a protective immunity

Hazards to Health:
e-notification to your Medical Officer of Health

Hazardous substances disease and injury notifications

A new electronic notification system has been designed for general practices to report incidents related to exposures to hazardous substances. The system has been developed by *bestpractice* Decision Support (BPAC Inc) and the Centre for Public Health Research, and is funded by the Ministry of Health.

General Practitioners in the Capital and Coast, Hutt Valley and Wairarapa regions are the first in New Zealand to use the system to electronically notify cases of hazardous substance disease and injury, and lead poisoning, seen in primary care. The notification system will be introduced throughout New Zealand in 2013; practices will be notified by their local Medical Officer of Health when the module is available in their area.

What is defined as a hazardous substance injury or disease?

A hazardous substance is anything that can explode, catch fire, oxidise, corrode or be toxic to humans, as defined in the Hazardous Substances and New Organisms Act 1996. The Act requires medical practitioners to notify cases of injury or disease caused by exposure to a hazardous substance to the Medical Officer of Health.

There are a multitude of possibilities of exposure to hazardous substances, such as: ingestion of cleaning products or cosmetics by children, overdose with agrichemicals, carbon monoxide poisoning, illness caused by exposure to solvents or chlorine, contact dermatitis due to chemicals, a fireworks burn or eye injury and "huffing" (inhaling) of butane.

How should a case be notified?

If you are in the Wellington, Hutt Valley or Wairarapa regions look for the "Hazardous Substances and Lead notifications" module on the *bestpractice* Decision Support dashboard (see Figure 1 for an example). Submitting the form will send it to your local Medical Officer of Health via a secure system.

If your practice does not currently have access to this electronic form, contact your local Public Health Unit to notify them of a case.

Lead notifications

Cases of non-occupational lead exposure, in which a patient has a blood lead level ≥0.48 µmol/L, are required to be notified under the Health Act 1956. The electronic form can be used for these notifications.

Chemical contamination of the environment

Cases of poisoning arising from chemical contamination of the environment (including from agrichemical spray drift) are also required to be notified under the Health Act 1956, and this can be done via the electronic form.

Why notify?

The Medical Officer of Health and Public Health Unit staff will assess the information about the exposure and determine if further follow-up with the patient is required.

Primary care notifications allow identification of substances which are causing harm, and can lead to controls being put in place to prevent disease or injury. For example, exposure to lead from deteriorating lead-based paint can be reduced through a range of remedial actions. In another example, regulatory changes have been made to the pH of dishwasher powder following reports of injuries to children (see over page).

For further information about reporting exposures to hazardous substances, contact your local Public Health Unit, or for more information about the new e-notification tool, contact:

Dr Saira Dayal
s.dayal@massey.ac.nz
04 801 5799 extn 63104

Helene Marsters
t.h.marsters@massey.ac.nz
0800 588 265

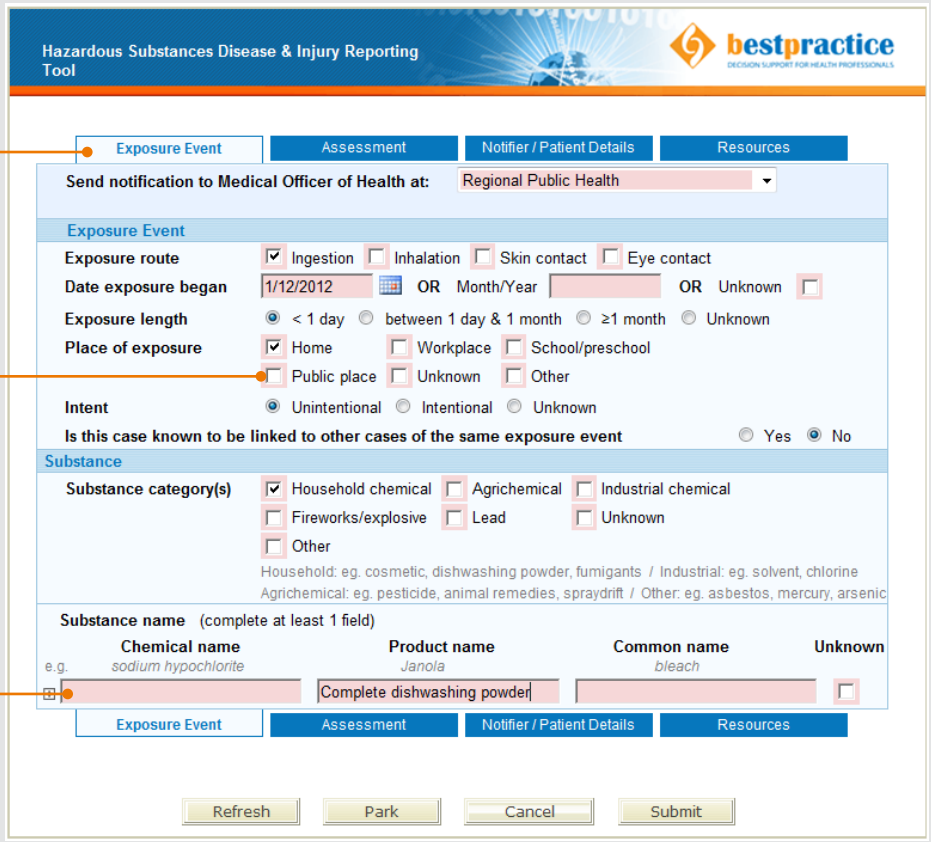
cphr | hsss Hazardous Substances Surveillance System

Figure 1: Example of the Exposure Event tab of the notification form – ingestion of dishwashing powder

1 **The notification form has four tabs:** Enter details into Exposure event and Assessment, Notifier/Patient details is pre-populated from the PMS and useful Resources

2 Tick boxes summarising the patient history

3 Enter the name of the substance (at least one field is required)



Reporting of poisonings in children ingesting dishwasher powders resulted in changes to legislation

In 2005 caustic dishwasher powders were recognised as an area of public health concern due to considerable numbers of reports of children ingesting them and requiring medical attention. Between January, 2003 and January, 2005 there were 610 calls to the National Poisons Centre and 11 admissions to Starship Hospital. Five children required intensive care, including intubation and multiple procedures for upper airway and oesophageal injuries.[1]

The reports from the National Poisons Centre and Starship Hospital were used to inform public health action (at the time, data on dishwasher powder ingestions managed in primary care were not available). A Safekids awareness campaign was initiated, and in 2007 the Environmental Risk Management Authority (ERMA) made changes to the group standard prohibiting the sale in New Zealand of dishwasher powders with a pH of greater than 12.5.[2] As a result of these actions the number of children referred for medical attention following a call to the National Poisons Centre for dishwasher powder ingestion has decreased considerably.[3]

The notification of hazardous substances injuries and diseases seen in primary care as part of the overall Hazardous Substances Surveillance System, aims to identify strategies that will reduce future morbidity and mortality resulting from exposure to hazardous substances.

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1. Bertinelli A, Hamill J, Mahadevan M, Miles F. Serious injuries from dishwasher powder ingestions in small children. J Paed Child Health 2006;42(3):129-33.
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Assessors required to undertake Regular Practice Review visits

Inpractice is the recertification programme for doctors registered in a general scope of practice, and is administered by bpac[nz]

Regular Practice Review is a formative process based on a supportive and collegial review of the doctor's practice by a peer, in the doctor's usual practice setting. This component of Inpractice is currently under development and is due for implementation in July 2013.

Inpractice is seeking expressions of interest from suitably qualified General Practitioners to act as assessors, who will undertake Regular Practice Review visits for doctors participating in the Inpractice Recertification Programme. Assessors will need to be able to undertake up to 10 reviews per year including out of town travel. Travel expenses, accommodation, and professional fees will be paid by bpac[nz].

For these positions we are seeking doctors with:

- Vocational registration with the Medical Council of New Zealand as a medical practitioner
- Relevant experience and knowledge that will assist with the assessment of doctors
- The ability to communicate confidently and effectively with doctors and other health professionals

To register your interest, or for more information please contact Tony Fraser, Inpractice Manager

Email: tony@bpac.org.nz or

Phone (03) 477 5418

www.inpractice.org.nz

in practice

RECERTIFICATION + PROFESSIONAL DEVELOPMENT

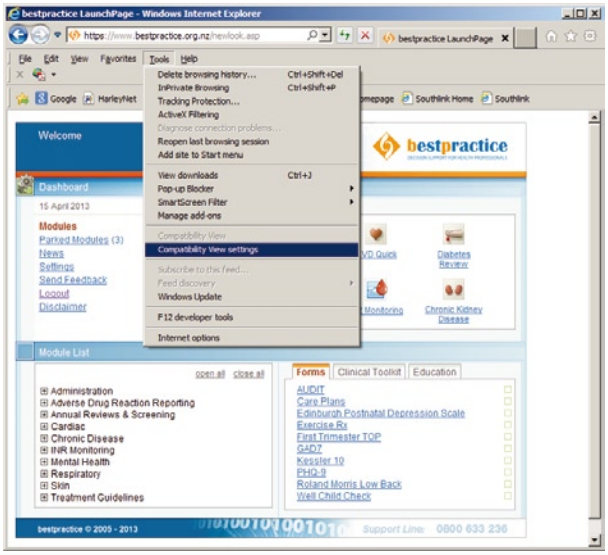
bestpractice TIPS & TRICKS

Setting up Internet Explorer Version 10

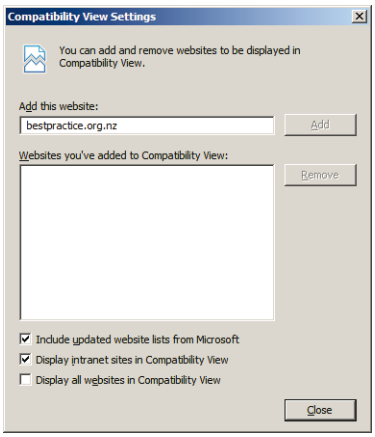
If you plan to use the new release of Internet Explorer - version 10 - with *bestpractice*, you will need to make a minor change to your computer settings to ensure that the *bestpractice* software continues to function correctly.

To make the change, proceed as follows:

- Using Internet Explorer 10, go to the *bestpractice* website (https://www.bestpractice.org.nz)
- Click on the **Tools** menu in Internet Explorer
- Select the **Compatibility View settings** menu option (see screenshot below)



- The Compatibility View settings dialog box is displayed (see screenshot below)



- If not already there, enter "bestpractice.org.nz" into the **Add this website** box as shown above
- Click the **Add** button
- Click Close. Internet Explorer 10 is now configured to run *bestpractice* correctly.

bestpractice

DECISION SUPPORT FOR HEALTH PROFESSIONALS

Statins and the risk of acute kidney injury: **keep calm – carry on**

THERE HAVE BEEN RECENT REPORTS in the literature associating the use of statins with acute kidney injury (AKI). A study by Hippisley-Cox and Coupland of over 225 000 patients starting statin treatment for the first time in England and Wales found a dose-response association between statin treatment and acute kidney injury (AKI).[1] Over 70% of these patients were taking simvastatin.[1] The increased risk of AKI was observed within one year of initiation and remained for the first five years of treatment, returning to normal within one to three years of treatment ceasing.[1]

In their analysis, Hippisley-Cox and Coupland calculated numbers needed to harm (NNH) and numbers needed to treat (NNT) for statin treatment in patients without cardiovascular disease, with a cardiovascular risk ≥ 15%. The NNT with any statin to prevent one case of cardiovascular disease over five years was 44 for females and 38 for males.[1] For females the NNH for an additional case of AKI over five years was 593, and for males the NNH was 447.[1] Potential harms and benefits both increased in patients with cardiovascular risks ≥ 20%.[1] For patients with elevated cardiovascular risk, the benefits of statin initiation therefore clearly outweigh any increased risk of AKI.

A larger, and more recent study by Dormuth *et al* investigated the use of high and low-dose statins in more than two million people in Canada, Great Britain and the United States. High-dose statin use was defined as ≥ 40 mg simvastatin, ≥ 20 mg atorvastatin or ≥ 10 mg rosuvastatin daily.[2] A 34% increase in the relative risk of hospitalisation for AKI within 120 days of initiation of high-dose statins, compared to low-dose statins, was reported in people without chronic kidney disease (CKD).[2] This risk remained elevated for at least two years of treatment, which was the maximum follow-up period for each patient.[2] Interestingly, the rate of hospitalisation for AKI did not increase significantly in patients with existing CKD.[2]

Dormuth *et al* also calculated a NNH for high-dose statin use. They estimated that 1700 patients without CKD need to receive high-dose statin treatment for 120 days (rather than low-dose statins), for one additional hospital admission due to AKI to occur.[2]

Rhabdomyolysis is proposed as a mechanism linking statin treatment to AKI, although there was no evidence of this among patients who had experienced an episode of AKI following statin treatment in the Dormuth study.[2] Another possible explanation is statin blockage of co-enzyme Q10, a fat soluble enzyme with antioxidant properties.[2] Human and animal studies have reported co-enzyme Q10 to be linked to improved kidney function in subjects with kidney disease.[2]

What do these studies mean for primary care?

The benefits of statins in reducing cardiovascular risk are well known. Given that the increased risk of AKI in patients taking statins is modest and the mechanism for this association is unknown, there is currently insufficient evidence to alter the prescribing of statins in primary care. However, in older patients with reduced kidney function there may be a need for increased vigilance when initiating high-dose statin treatment.

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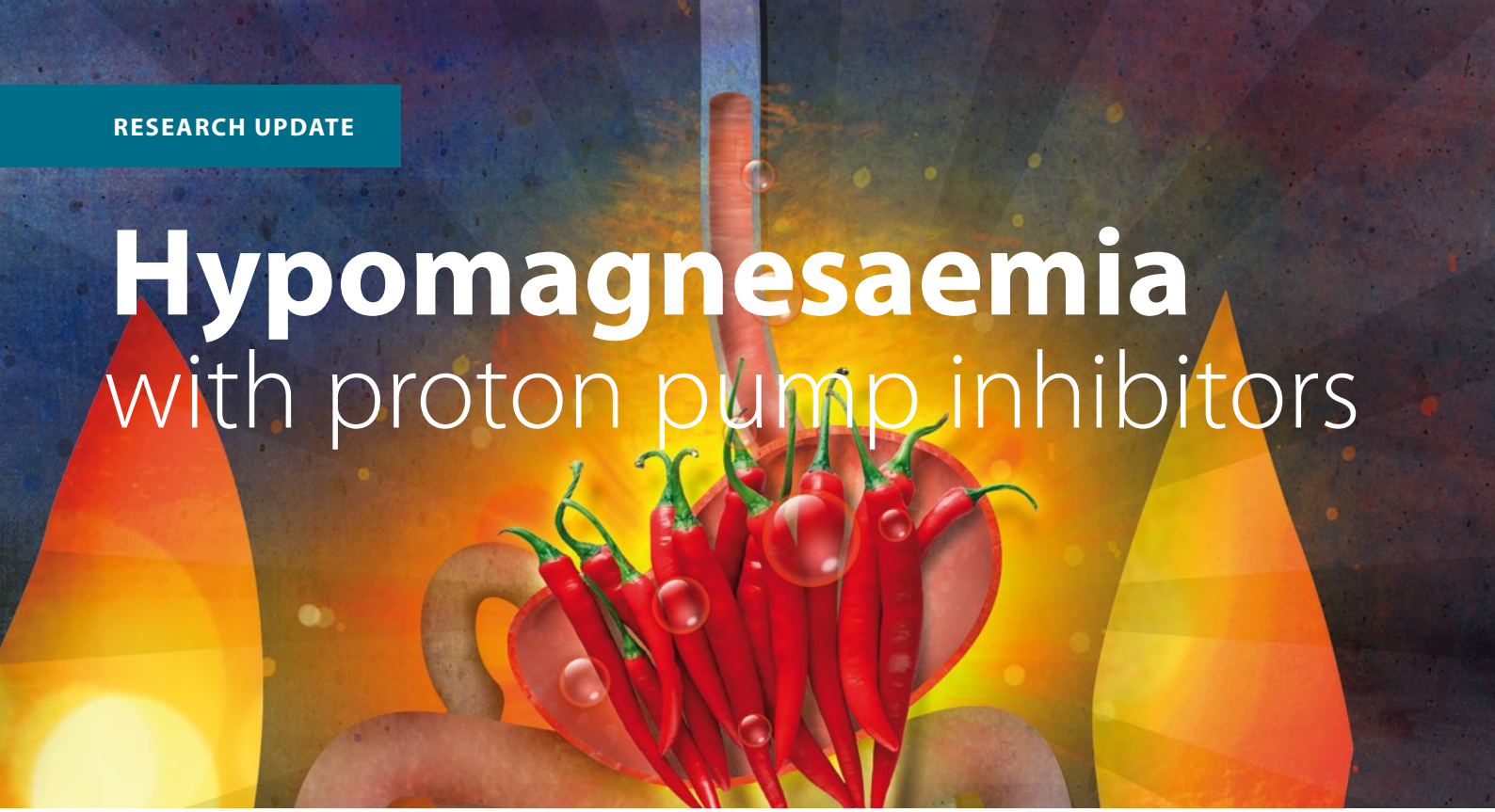
An alternative explanation for the association between statins and acute kidney injury

The finding by Dormuth *et al* that patients with existing CKD who were on high-dose statin treatment were not at significantly increased risk of AKI is unexpected. This may signal the need for caution when interpreting the results of this study.

Patients are prescribed statins because they have elevated vascular risk factors. These patients may therefore also be at increased risk of renal atherosclerosis. Statin treatment could therefore be a confounding factor in both studies that study design and analysis strategies may be unable to completely compensate for. High-dose statins are likely to be prescribed for patients with higher vascular risk, and this could account for the increased rate of AKI associated with high-dose statin use as reported by Dormuth *et al*. Furthermore, atherosclerosis is an ongoing process which may explain why Hippisley-Cox and Coupland observed an increased risk of AKI for patients who used statins six months after the medicine was stopped. The relative incidence rate ratio of AKI during use of simvastatin for males and females combined was 1.57, compared to 2.21 during the six-month washout period.[1]

RESEARCH UPDATE

Hypomagnesaemia with proton pump inhibitors



IN DECEMBER, 2012 MEDSAFE published a warning on the risk of hypomagnesaemia for people taking any proton pump inhibitor (PPI).[1] This follows a previous Medsafe warning in 2010 about hypomagnesaemia associated with omeprazole,[2] the most commonly prescribed PPI in New Zealand.

Despite two decades of clinical use of omeprazole without concern about electrolyte changes, a "safety signal" was detected in 2008 after spontaneous reports to the Centre for Adverse Reactions Monitoring (CARM) of hypomagnesaemia in association with omeprazole. At this time, there was not enough evidence locally, or internationally, to confirm an adverse medicine reaction. More intensive monitoring of PPIs was encouraged in New Zealand by listing them on the Medsafe monitoring scheme: "M²" (see below). Further reports to CARM of hypomagnesaemia with a PPI, and similar international evidence,[3] has confirmed an association between PPIs (omeprazole, pantoprazole, lansoprazole) and hypomagnesaemia. In 2012 Medsafe recommended that hypomagnesaemia (and the possibility of hypocalcaemia) be added to New Zealand datasheets as a possible adverse effect of PPIs.[2] A suggested mechanism for the effect is interference with magnesium absorption by the PPI, however, this has not been determined by research.

What is a "Safety Signal"?

A safety signal can be described as information that arises from one or more sources (including observations, research and spontaneous reporting by health care providers, health authorities and lawyers) that suggests a potentially causal association between an intervention, e.g. a prescribed medicine, and an adverse event. A safety signal may be a new association, or a new aspect of a known association that helps define subgroups of patients who are at increased risk.

In New Zealand, CARM is responsible for assessing safety reports and determining the likelihood of an association. CARM may recommend that a safety warning be issued by Medsafe about a specific medicine, or class of medicines, with recommendations about a change in prescribing or monitoring practice. Alternatively a medicine maybe listed on Medsafe's Medicines Monitoring scheme "M²", to gather more information about the safety signal.

The purpose of M² is to highlight potential safety issues from reports of suspected adverse medicine reactions, and to stimulate further case reports from practitioners. Placing a medicine on M² does not mean that a change in prescribing practice is recommended at that time.

For further information see "M² Medicines Monitoring", available from: **www.medsafe.govt.nz/profs/M2MedicinesMonitoring.asp**

Who is at risk? What should I do?

All general practices will have a significant number of patients who are being treated with a PPI. Although hypomagnesaemia is classed as a rare adverse effect of PPIs, given their frequency of use, practitioners will need to be alert to the possibility of hypomagnesaemia occurring, and minimise the risk for certain patients.

Most reports of hypomagnesaemia with PPIs have occurred at doses of omeprazole 20 – 40 mg daily, and after 12 months or more of use; however, some cases of hypomagnesaemia were detected after three months of PPI treatment.[1, 2]

Symptoms of hypomagnesaemia are non-specific and include muscle cramps, weakness, fatigue, irritability and confusion. More serious symptoms include delirium, convulsions, tetany and arrhythmias. Some symptoms may occur gradually and therefore be easily overlooked.

People taking PPIs who are most at risk of hypomagnesaemia are:

- Those taking other medicines associated with hypomagnesaemia, e.g. diuretics, ciclosporin, aminoglycosides
- Those whose condition puts them at risk of deterioration should hypomagnesaemia occur, e.g. taking digoxin, with cardiac conduction concerns

Patients should be informed of the possibility of hypomagnesaemia when prescribed a PPI, particularly if treatment is anticipated to be long-term. Patients who are concerned can be advised to increase dietary magnesium intake with milk, wholegrain cereals, wholemeal bread, green leafy vegetables (spinach, parsley, cabbage), lean meat, nuts, seeds, bananas and peas.

If a patient who has been taking a PPI long-term, especially those at increased risk, presents with unexplained symptoms that may be suggestive of hypomagnesaemia, consider requesting a magnesium level.

If hypomagnesaemia is present, increased dietary intake of magnesium rich foods or magnesium supplementation may be sufficient to improve serum magnesium levels while continuing the PPI. For some patients the PPI will need to be stopped; if the indication for using the PPI is strong, a re-challenge while monitoring magnesium can be undertaken. It is reported that hypomagnesaemia can occur more rapidly in a person who has already experienced hypomagnesaemia while taking a PPI.[1]

Omeprazole is a "Pharmacy only" medicine

Be aware that your patients could be taking a PPI without a prescription. Omeprazole 10 mg and 20 mg tablets can be purchased in pharmacies for the short-term relief of reflux-like symptoms in people aged 18 years or older. If there is no improvement in symptoms after two weeks of treatment, patients are advised to consult a doctor (or pharmacist

There are no magnesium-only supplements subsidised on prescription; these can be purchased over-the-counter. N.B magnesium supplements can cause diarrhoea. The only product that could be prescribed for magnesium supplementation that has a prescription subsidy (partial only) is Mylanta P liquid, although it is approved for use in indigestion, heartburn, upset stomach and as an anti-flatulent. Mylanta P contains approximately 340 mg of Mg^{2+} per 20 mL dose, which is approximately the recommended daily magnesium intake for an adult; the dose for indigestion and as an anti-flatulant is 10 – 20 mL up to four times daily. Mylanta P also contains aluminium and simethicone, and can interfere with the absorption of other medicines, and therefore should not be taken within two hours of other medicines.

What about calcium?

Low magnesium is often associated with low calcium levels, which causes similar symptoms to hypomagnesaemia. If measuring magnesium levels in a symptomatic patient taking a PPI, consider measuring calcium also.

References

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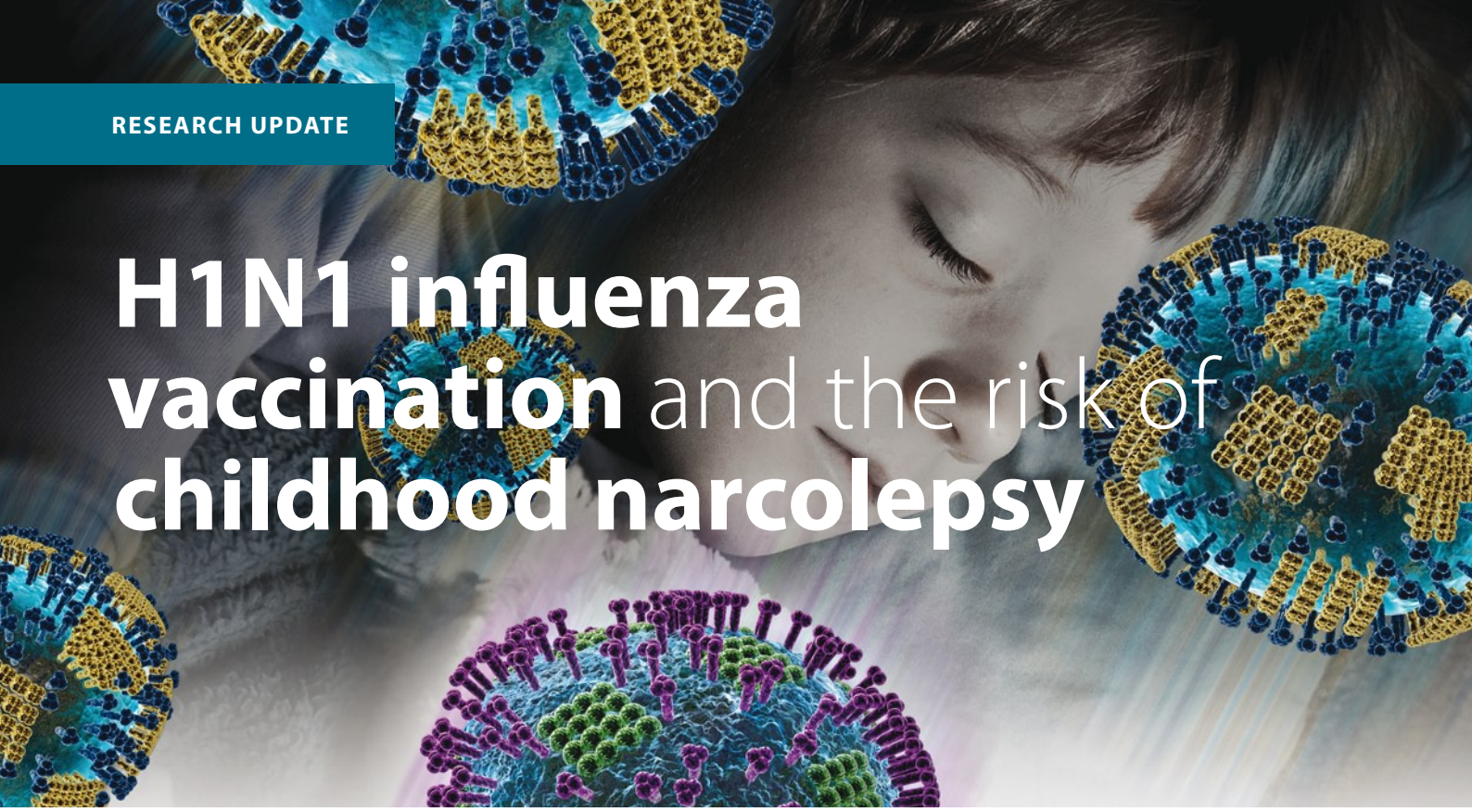

H1N1 influenza vaccination and the risk of childhood narcolepsy

IN MARCH, 2012 A SIGNIFICANT INCREASE in the rate of childhood narcolepsy associated with the influenza vaccine Pandemrix (GlaxoSmithKline) was reported in Finland.[1] This vaccine was administered to over 30 million people in Europe to provide protection during the 2009 H1N1 pandemic. Following the observation in Finland, the European Centre for Disease Prevention and Control commissioned two reports to investigate the rates of narcolepsy in Sweden, Finland, Denmark, Italy, France, the Netherlands, Norway and the United Kingdom. The report concluded that:[2]

1. There was no increase in the rates of narcolepsy due to the 2009 pandemic itself
2. An increase in the rate of childhood narcolepsy in Finland and Sweden had occurred with Pandemrix vaccination
3. There was no detectable association between influenza vaccination and childhood or adult narcolepsy in the Netherlands, Italy, the United Kingdom, Norway* and Denmark**
4. A significantly increased risk of narcolepsy in adults, associated with Pandemrix vaccination did occur in France, although the risk of selection bias could not be excluded. This result should be interpreted with caution and is being investigated further.

* The data from Norway is problematic as individuals presenting with narcolepsy prior to 2008 could not be clearly identified

** An increase in the rates of narcolepsy was detected in Denmark, however, this trend started before the introduction of the vaccination campaign.

In February, 2013, a study from the United Kingdom also reported an increase in childhood narcolepsy associated with Pandemrix vaccination. This study retrospectively reviewed the medical records of 245 young people aged four – 18 years, who had been identified by an expert panel as being likely to have narcolepsy.[3] In April, 2013, a Swedish study of 37 children with narcolepsy, found that nine of the children had onset of narcolepsy symptoms before vaccination with Pandemrix, and 28 had onset post-vaccination.[4] The authors calculated the incidence of narcolepsy to be 25 times higher after vaccination compared with the period before vaccination.[4]

Within the literature, estimates of the number of children who need to be vaccinated with Pandemrix for one instance of childhood narcolepsy to develop ranges from 13 000 to 57 500 children.[1, 3]

Influenza vaccination guidelines remain unchanged in New Zealand

Any association between influenza vaccination and narcolepsy does not appear to be a worldwide phenomenon.[5] There have been no reports linking influenza vaccination to narcolepsy in New Zealand. In Canada, a vaccine similar to Pandemrix was used and no increases in narcolepsy have been reported.[5] The United States Centres for Disease Control and Prevention continues to recommend influenza vaccination to protect individuals from influenza and its complications, and there have been no reports of narcolepsy associated with vaccination.[6]

The following points should also be considered when placing the results of European studies on narcolepsy risk and influenza vaccination into a New Zealand context:

- Pandemrix is the only vaccine, for any disease, that has ever been associated with an increased risk of narcolepsy
- Pandemrix has never been used in New Zealand
- The use of Pandemrix is now restricted in people aged under 20 years[5]
- The strain of inactivated virus contained in the 2013 New Zealand influenza vaccines Fluarix (GlaxoSmithKline) and Fluvax (CSL) is different to Pandemrix (Table 1)
- Pandemrix uses an oil-in-water adjuvant to boost the individual's immune response. Fluarix and Fluvax both use a phosphate-buffered saline adjuvant
- Pandemrix was specifically created for the 2009 H1N1 influenza pandemic whereas Fluarix and Fluvax also provide protection against three seasonal influenza strains: A/California (N1N1pdm09), A/Victoria (H3N2) and B/Winsconsin
- The influenza vaccines used in New Zealand in 2009 were also different to Pandemrix and provided protection against seasonal A(H1N1), A(H3N2) and B/Florida strains of influenza

Table 1: H1N1 vaccines and the strains of virus used to generate the 2009 Pandemrix and 2013 Fluarix and Fluvax vaccines[2, 7, 8]

Vaccine	H1N1 strain used in vaccine production
Pandemrix	X-179A
Fluarix	NIB-74xp
Fluvax	NYMC X-181

How could Pandemrix cause an increase in childhood narcolepsy?

Narcolepsy is a rare condition caused by the selective loss of cells in the hypothalamus that regulate arousal. An autoimmune mechanism for narcolepsy has been proposed that includes both genetic and environmental factors.[4] Most children with narcolepsy share the same leukocyte antigen and in the Swedish study it was reported that all the children who developed narcolepsy following vaccination with Pandemrix had this antigen. Therefore it is possible that rather than increasing the prevalence of narcolepsy, Pandemrix may have caused earlier onset of narcolepsy in young people who may have been predisposed to develop the condition later in life.

Reports of an increased risk of narcolepsy may also have heightened awareness of narcolepsy causing an increase in the number of people presenting with the condition. Long-term follow-up and a subsequent decrease in the rates of narcolepsy diagnosis would be needed to confirm if either of these possibilities had occurred.

ACKNOWLEDGMENT: Thank you to **Associate Professor Lance Jennings**, Virologist, University of Otago, Christchurch and Canterbury Health Laboratories, Canterbury DHB for expert guidance in developing this article.

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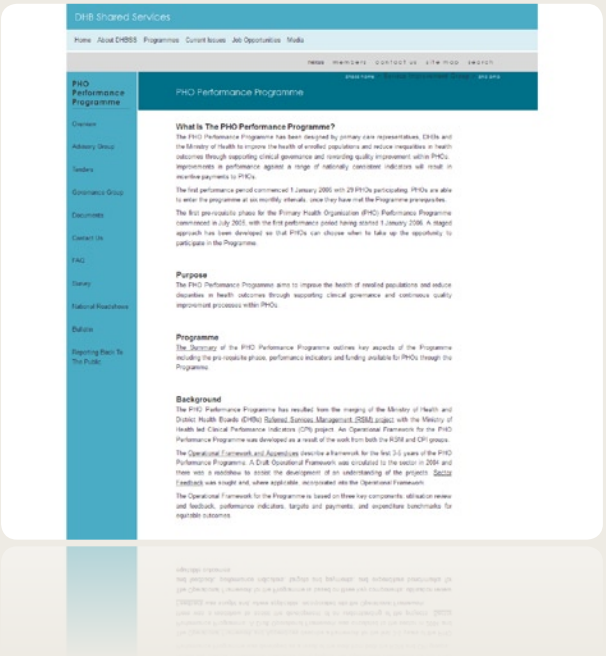
Influenza vaccination is a PHO Performance Programme indicator

Influenza vaccination in people aged 65 years and over accounts for 9% of the PHO Performance Programme funding; 3% for the total population and 6% for the high need population. High need populations include Māori and Pacific Peoples and people living in Quintile 5 (most deprived) socioeconomic areas. The target is assessed by counting the enrolled patients aged 65 years and over who have received an influenza vaccination during the most recent campaign (the numerator). This number is then divided by the number of enrolled patients aged 65 years and over at the beginning of the most recent campaign period (the denominator).

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

Further information about the PHO Performance Programme, including a summary of all performance indicators is available from: **www.dhbsharedservices.health.nz/Site/SIG/pho/Default.aspx**



Funding for influenza vaccination now extended

PHARMAC have announced that from 1 April, 2013 children aged from six months to four years (i.e. until their fifth birthday) with a significant respiratory illness are now eligible for fully subsidised influenza vaccination. In Canterbury DHB all children aged under 18 years are also eligible for free influenza vaccination.

This is in addition to pregnant women, people aged over 65 years and people with specific long-term health conditions, for whom influenza vaccination is already subsidised.

People eligible for subsidised vaccination must receive their influenza vaccination before 31 July, 2013.

For further information on influenza subsidy, see: **www.pharmac.health.nz**

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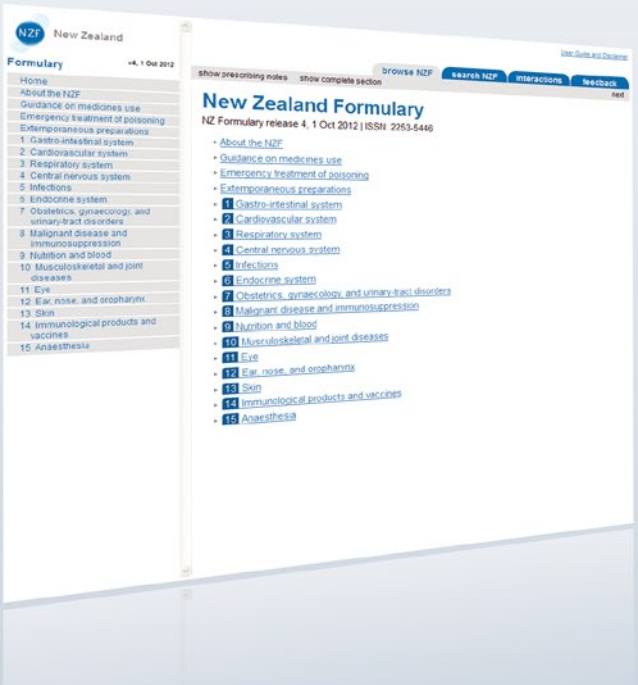

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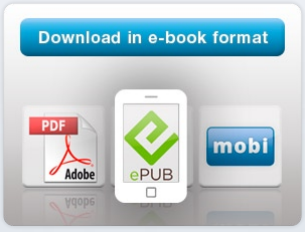

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An international perspective on the use of dabigatran

Dear Editor,

One of the promoted advantages of dabigatran over warfarin, on the basis of the RE-LY trial, was the unexpectedly high intracranial haemorrhage rate in the control (warfarin) arm of the trial. However, a Canadian study involving "real world" data from 125 195 patients in Ontario, the intracranial haemorrhage rate over a mean period of five years, was calculated at 0.2% per person year.[1] This compares to dabigatran 150 mg bid at 0.3% per person year in RE-LY.

The INR percentage time in therapeutic range (TTR) is unknown in this study, but presumably was in the mid fifties. What would these results look like in an environment where TTRs are in the range of 75% or greater, such as was achieved in the University of Auckland's Community Pharmacist-led Anticoagulation Management Service study? Also, there is latitude to improve warfarin management through the use of computer decision support software and INR point of care testing. With dabigatran, there is no such potential.

Finally, as the time within therapeutic range affects the hemorrhagic stroke rate, the stroke and systemic embolism rate, the total bleeding rate and the mortality rate, perhaps the RE-LY data should be adjusted to properly place it in context with the real world in Canada, as the valid transferability of the RE-LY (Rocket-AF and Aristotle) findings to Canada (and perhaps New Zealand) is highly in question in our minds.

***Dr Murray Trusler**, MD, MBA, FCFP*
BC, Canada

1. Gomes T, Mamdani M, Holbrook A, et al. Rates of hemorrhage during warfarin therapy for atrial fibrillation. CMAJ 2013;185(2)E121-7.

Thank you for your comments regarding recent BPJ articles on the role of dabigatran in the reduction of thromboembolism in patients with atrial fibrillation (BPJ 50, Feb 2013 and BPJ 38, Sept 2011). We believe the RE-LY multi-centre study provides valuable information for improving patient focused decision making for therapeutic options for patient with atrial fibrillation in New Zealand.

Your comments raise a number of questions:

Are the rates of intracranial haemorrhage over-represented in the New Oral Anti-Coagulant Trials (RE-LY, Rocket-AF and Aristotle)?

The intracranial haemorrhage rate is influenced by the characteristics of the group studied. Cohorts with a higher prevalence of hypertension, previous TIA/stroke and those with higher average $CHADS_2$ scores will be at increased risk of intracranial haemorrhage.[1] The concurrent use of aspirin was the most important modifiable independent risk factor for intracranial haemorrhage in RE-LY.[2]

The Canadian review looked at a real-world population initiated on warfarin for atrial fibrillation, and followed up for five years. The intracranial haemorrhage rate in this study was 0.4% per person year in the first 30 days and 0.2% over the subsequent five years.[3] The two year RE-LY study had an intracranial haemorrhage rate of 0.23% for dabigatran 110 mg, twice daily, 0.32% for 150 mg, twice daily and 0.76% for the matched warfarin arm.[4] Individuals enrolled in the RE-LY and Canadian studies had similar risk factors for intracranial haemorrhage (mean $CHADS_2$ scores of approximately 2 and similar rates of previous stroke and hypertension). However, participants in the RE-LY study had nearly twice the rate of aspirin use which may account in part for the higher intracranial haemorrhage rate.

The Rocket- AF trial had a cohort that were much more "at risk" for intracranial haemorrhage. Past history of TIA and stroke was 52% compared to 21.3% in the Canadian study, mean $CHADS_2$ score was 3.48 as opposed to just over 2 and an aspirin use was 29% as opposed to 20% in the Canadian study. The intracranial haemorrhage rate for the warfarin arm in Rocket was 0.7%. The higher rate of intracranial haemorrhage can be, in part, explained by the different cohort characteristics.[5]

What are the benefits of dabigatran over well-managed warfarin, as represented by time in therapeutic range (TTR)?

For patients taking warfarin, the TTR also has an effect on intracranial haemorrhage rates.[3] In RE-LY the INR control was relatively poor (TTR – 64%).[6] TTR was not evaluated in the Canadian AF warfarin study.

To analyse the effect of warfarin control on the end points of the study, RE-LY looked at two measures: the individual time in therapeutic range (iTTR) and the mean time in therapeutic range for each study centre (cTTR).[6]

The table below illustrates the reduction in end point events with improving TTR for individual patients taking warfarin in RE-LY. The greater the time in the therapeutic range, the better the outcomes.

	AF Warfarin patients – Percentage Time in Therapeutic Range (iTTR) Divided up in quartiles i.e. 25% of patients fell into following groups[6]			
Events:	**< 53.6 %**	**53.6 – 67.2 %**	**67.2 – 78.4 %**	**> 78.4 %**
Stroke and systemic embolic episodes	2.34%	1.72%	1.42%	1.25%
Major bleeding	4.95%	3.71%	2.98%	2.65%
Total mortality	7.48%	3.30%,	2.27%	2.65%
Composite	12.32%	7.35%	5.55%	5.4%

Irrespective of the centres quality of warfarin management (cTTR) the rate of intracranial bleeds was lower for both doses of dabigatran than with warfarin, and this did not change even for centres that had a cTTR of > 72.6%. However, dabigatran 150 mg was not superior to warfarin in reducing the risk of non-haemorrhagic stroke when the cTTR was > 72.6%. Also, there were no advantages for dabigatran over warfarin for outcomes such as non-haemorrhagic events and mortality, when cTTR for warfarin was >72.6%.[6]

These results show the importance of clinicians understanding the mean cTTR for all patients in their practice taking warfarin, and calculating individual iTTRs when considering changing patients from warfarin to dabigatran.

What are the implications for clinicians making decisions on treatment options for individual patients?

From "The use of dabigatran in general practice", BPJ 38 (Sep, 2011):

Patients with non-valvular atrial fibrillation **who may benefit** from dabigatran include those who:

- Require anticoagulation but are currently on no treatment, e.g. patients who have declined treatment with warfarin or aspirin or those taking medicines that are contraindicated with warfarin
- Are already on warfarin but where there are difficulties with monitoring, e.g. difficult venous access, problems with accessing lab facilities due to mobility issues, cost or lack of time, those who are non-compliant with monitoring
- Are already on warfarin but have INR values that are often sub-therapeutic or difficult to control
- Wish to change for convenience

Patients who **may not benefit** from dabigatran include those who:

- Are on warfarin with a stable (or easy to control) INR and who are comfortable with the need for INR monitoring.
- Patients on warfarin who have INR values that are consistently within the therapeutic range are less likely to benefit from a switch to dabigatran.
- Are unlikely to be compliant with the twice daily dosing required for dabigatran
- Prefer to continue with warfarin (some patients may like the reassurance of periodic monitoring)
- Require blister packed medicines

Decision support tools for warfarin management

We agree with the correspondent that every effort should be made to improve TTR when warfarin is the preferred therapeutic option for preventing thromboembolism in atrial fibrillation. Decision support has an important role in:

1. Deciding to initiate oral anticoagulants over aspirin/ clopidogrel in atrial fibrillation.
2. Deciding when TTR for warfarin is insufficient to be comparable to dabigatran.
3. Advising on warfarin dose and review periods to maintain cTTR above 72.6% at practices.

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1. Lip G, Andreotti F, Fauchier L, et al. Bleeding risk assessment and management in atrial fibrillation patients: a position document from the European Heart Rhythm Association. Europace 2011;13(5):723-46.
2. Hart R, Diener H, Yang S, et al. Intracranial hemorrhage in atrial fibrillation patients during anticoagulation with warfarin or dabigatran: the RE-LY trial. Stroke 2012;43(6):1511-7.
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4. Connolly S, Ezekowitz M, Yusef S, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009;361(12):1139-51.
5. Singer D, Hellkamp A, Piccini J, et al. Impact of global geographic region on time in therapeutic range on warfarin anticoagulant therapy: Data from the ROCKET AF clinical trial. J Am Heart Assoc 2013;2(1):e000067.
6. Wallentin L, Yusef S, Ezekowitz M, et al. Efficacy and safety of dabigatran compared with warfarin at different levels of international normalised ratio control for stroke prevention in atrial fibrillation: an analysis of the RE-LY trial. Lancet 2010;376(9745):975–83.

Escitalopram also associated with QT interval prolongation

Dear Editor,

The risk of QT interval prolongation with citalopram has been well described in your article "Prescribing citalopram safely: an update", BPJ 42 (Feb, 2012). However, your suggestion to switch to "a lower risk SSRI such as escitalopram might be more appropriate" may not be true. Escitalopram overdose leading to prolongation of the QTc interval has been previously described in the literature. The recommendation suggested in this update may be misleading to the prescribers.

Dr Prasad Nishtala, *Clinical Pharmacist*
Dunedin

When safety warnings first emerged in regards to the risk of QT prolongation with high-dose citalopram, it was advised that the recommended maximum daily dose be lowered to 40 mg. As escitalopram already had a recommended maximum daily dose of 10 – 20 mg, which is equivalent to the lowered maximum dose of citalopram, the same warnings were not issued for escitalopram.[1]

Prescribers were advised to review patients taking high doses of citalopram, and reduce their daily dose to ≤ 40 mg. A suggested alternative was to switch to a standard dose of escitalopram, which is considered safer in terms of cardiac toxicity, than a high dose of citalopram. However, the correspondent is correct in that escitalopram is not "a lower risk SSRI".

After evaluating case and trial data, the United States Food and Drug Administration (FDA) found that QT interval prolongation increased, with increasing doses of citalopram; there was a mean prolongation of 8.5 ms with 20 mg/day, 12.6 ms with 40 mg/day and 18.5 ms with 60 mg/day. The QT interval was also prolonged with increasing doses of escitalopram, but to a lesser extent; there was a mean prolongation of 4.5 ms with 10 mg/day, 6.6 ms with 20 mg/day and 10.7 ms with 30 mg/day.[2] Therefore the recommended daily dose of escitalopram (10 – 20 mg) is associated with a lower clinical risk of cardiac adverse effects than an equivalent dose of citalopram (40 mg), but still has a higher risk than some other antidepressant medicines.

Fluoxetine, paroxetine and sertraline are considered unlikely to cause prolonged QT interval when used at recommended doses in people without risk factors. Prospective studies have not found any evidence of QT prolongation with these medicines, however, case reports (some of limited validity) exist linking all SSRIs, except paroxetine, to QT interval prolongation and/or Torsades De Pointes.[3] All tricyclic antidepressants can cause QT interval prolongation.[3]

In summary, patients with risk factors for QT prolongation, taking other medicines that can cause QT prolongation or with severely reduced renal function, may be cautiously prescribed citalopram or escitalopram, provided that QT interval is monitored at baseline and intermittently throughout treatment, and that doses do not exceed maximum daily recommendations (≤ 40 mg for citalopram and ≤ 20 mg for escitalopram). Sertraline may be a more appropriate antidepressant for people at increased cardiac risk, as it has few medicine interactions, has not been consistently linked to QT prolongation, and is the most studied antidepressant medicine in patients with cardiac abnormalities.[3]

To switch to sertraline, the patient can stop citalopram or escitalopram, then start sertraline the next day. Sertraline is started at 50 mg daily, tapered upward, in steps of 50 mg at intervals of at least one week to a maximum of 200 mg daily, until a positive clinical benefit is observed. The usual maintenance dose for most people is 50 mg daily.[4]

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