Sleep disturbances: managing parasomnias
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Obstructive sleep apnoea in adults
Obstructive sleep apnoea affects many adults in New Zealand, and is especially common among Māori and Pacific peoples. Moderate to severe obstructive sleep apnoea is associated with a significant risk of cardiovascular morbidity and mortality, along with an increased risk of motor vehicle accidents, due to daytime sleepiness and fatigue. In most cases, an overnight sleep study is required to confirm the diagnosis. Continuous positive airway pressure (CPAP) devices are the mainstay of treatment.

Sleep disturbances: managing parasomnias in general practice
The term “parasomnia” describes a group of sleep disorders associated with unnatural movements, behaviours, emotions, perceptions and dreams that occur while falling asleep, during sleep, between sleep stages or upon waking. Most people experience a parasomnia during their lifetime. In the majority of cases, parasomnias are benign and, although frightening, no cause for concern. Reassurance, advice on methods to maximise sleep (sleep hygiene) and making the sleep environment safe are the key factors in managing people with parasomnias.

When and how to use a syringe driver in palliative care
Syringe drivers are often required to provide medicines for symptom management in patients who are terminally ill. They provide continuous subcutaneous administration of medicines to enable effective symptom control when medicines given by other routes are inappropriate or no longer effective. With guidance and support from the local hospice or district nursing services, General Practitioners can arrange a syringe driver infusion for a patient in their home or in a residential care facility, prescribe and monitor the appropriate mix of medicines and manage breakthrough symptoms.
Initiating interventions in people with intermediate hyperglycaemia (“pre-diabetes”)

Intermediate hyperglycaemia is a biochemical state in which a person has glucose levels above the normal range, but does not yet meet the criteria for a diagnosis of diabetes. The primary aim of management of intermediate hyperglycaemia is to prevent progression to diabetes. Intervention involves structured lifestyle changes, and for people with a high risk of progression to diabetes who do not achieve normoglycaemia, treatment with metformin.
Lung cancer is the leading cause of cancer death in New Zealand. In 2004, Dr Wendy Stevens, from the University of Auckland, conducted an audit of lung cancer care, from presentation in secondary care to treatment. At this time, five year survival from lung cancer was 10.2% in New Zealand, compared to 13% in Australia and 15% in the United States.

The audit revealed a number of disturbing findings:

- More patients presented to secondary care via an acute admission (36%) rather than as an outpatient referral to respiratory medicine via their General Practitioner (29%)
- Patients presenting via the emergency department more often had advanced, incurable disease
- Diagnosis and treatment was often subject to lengthy delays, particularly noticeable in outpatients (often with potentially curable disease)
- Only 28% of patients were presented at a thoracic multidisciplinary meeting (considered to be the gold standard approach to management)
- Rates of delivery of anti-cancer treatments (surgery, radiotherapy, chemotherapy) were low, and below those in comparable countries
- Māori were 2.5 times more likely to have locally advanced disease, and four times less likely to receive curative treatment than Europeans (multi-variate analysis)

When the four Cancer Networks were formed in New Zealand, these sobering findings helped to ensure that lung cancer was chosen as the first tumour with a dedicated “project stream”. This brought together relevant clinicians to try to improve the lung cancer pathway for people in New Zealand.

In 2007, a multidisciplinary study, funded by the Health Research Council, was set up and lead again by Dr Wendy Stevens. The study, entitled “Barriers to the timely diagnosis and management of lung cancer and description of best practice solutions”, involved a number of healthcare providers, including Auckland, Counties Manukau and Lakes DHBs; Procare and Tamaki PHOs; and the University of Auckland. The research included an audit of patients diagnosed with lung cancer in 2008, from initial presentation to treatment, patient interviews, General Practitioner focus groups and primary and secondary care provider surveys. The 2008 audit findings were very similar to 2004 – patients were more commonly presenting acutely to secondary care (rather than via a primary care referral) and presenting with advanced disease. Slower work-up times were encountered for outpatients/early stage patients.

As a result of these findings, it was recommended that systems be developed to expedite the diagnosis of patients with early stage disease, such as day-stay or “rapid access” clinics. Of the patients who presented directly to secondary care, 60% had seen their General Practitioner within the preceding six months, which suggests there may be an opportunity for earlier diagnosis. Patients interviewed or in focus groups (who had presented to hospital with advanced disease) tended to feel that most of the delays in the lung cancer pathway occurred in primary care, although in fact the median time from presentation to referral for the whole study population was quite short overall.

The 2008 audit found that the percentage of patients that were presented at a thoracic multidisciplinary meeting had improved to 56%. It has subsequently been recommended that all cases of lung cancer should be discussed at a multidisciplinary meeting.

Other key findings from the 2008 study are given in Table 1 (over page), along with solutions and recommendations.

One of the key issues highlighted from the 2008 study is use of radiology services in primary care. It was found that, on presentation to secondary care, only 64% of patients had undergone chest x-ray examination. Chest x-ray was, however, often a strong pointer either to a diagnosis of lung cancer or to a referral to secondary care, where lung cancer was
subsequently diagnosed. The New Zealand Guidelines Group guidelines for cancer diagnosis outline referral criteria for lung cancer. However, in the surveys and focus groups, General Practitioners felt that these referral criteria were not helpful.

**So where to from here?**

Implementation of the recommendations from this study is likely to make some difference in lung cancer survival rates, but not a large difference. This is due to the intrinsic nature of lung cancer (often asymptomatic until a late stage) and the poor responses to treatments such as conventional chemotherapy. Such changes would help to streamline the patient journey, and improve patient and family/whānau satisfaction with care received along that journey. However, it is important to also actually measure patient and family/whānau satisfaction directly, as a “one size fits all” approach may not be appropriate in all settings or cultures.

There are also other developments and strategies which may reduce deaths from lung cancer in the future.

<table>
<thead>
<tr>
<th>Finding</th>
<th>Solution and/or recommendation</th>
</tr>
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<tbody>
<tr>
<td>Pacific peoples more commonly presented with metastatic disease and were more commonly referred for acute admission.</td>
<td>Social marketing campaigns – ongoing rather than one off, national, targeted to and developed in conjunction with Māori and Pacific peoples.</td>
</tr>
<tr>
<td>Māori and Pacific peoples were more likely than Europeans to not attend appointments or initially decline investigation or referral.</td>
<td>Development of information resources – particularly targeted to Māori and Pacific peoples.</td>
</tr>
<tr>
<td>Delays documented in the clinical records occurred due to system factors (10%) such as lost referrals or lack of follow up of abnormal results, or to patient factors (10%) such as not attending appointments or declining investigation/referrals. Patients felt that the worst part of the pathway was waiting for investigations and appointments, coupled with lack of information, particularly leading up to diagnosis.</td>
<td>“Aunties” (primary care coordinators). Secondary care coordinators/lung cancer nurses. Systems/safety nets to follow-up incidental findings and abnormal results. Obtain formal feedback from patients and their whānau/family.</td>
</tr>
<tr>
<td>The most common presenting symptom of lung cancer was cough (49%); only 15% had haemoptysis. At initial presentation, General Practitioners took specific action, e.g. chest x-ray or referral, for 50% of patients with lung cancer. For the other 50%, the General Practitioner’s index of suspicion was not raised, usually because of co-morbidities.</td>
<td>Upskilling of General Practitioners and primary care workers, by respiratory team. Improve utilisation of chest x-rays (lower threshold for ordering); have defined guidelines in a user-friendly format.</td>
</tr>
<tr>
<td>Spirometry was rarely recorded in primary care notes. Smoking status was not well recorded, particularly for ex-smokers.</td>
<td>Risk assessment – recording smoking status accurately (including dose in pack-years). Better access to spirometry for General Practitioners.</td>
</tr>
<tr>
<td>General Practitioners referred patients to secondary care by a wide variety of ways (mainly paper-based such as fax) and were not informed of their patient’s progress along the pathway. Referrals sometimes got lost leading to delays as well as frustration. Although General Practitioners complained about the difficulty obtaining a timely specialist appointment, the median time from referral to first specialist appointment was 11 days, suggesting that information about secondary care services was lacking.</td>
<td>E-referral systems (rather than fax) with regionally consistent investigation and referral pathways. Expedite investigations and specialist assessment; systematic approach to action referrals to secondary care in a timely and appropriate manner. Improve communication between primary and secondary care, and with the patient/family/whānau.</td>
</tr>
</tbody>
</table>
Targeted chemotherapy

The molecular nature of lung cancer is being explored, and oral treatments have been developed to target any specific mutations present. In New Zealand, the tyrosine kinase inhibitors gefitinib and erlotinib, which target epidermal growth factor receptor, have been made available for suitable patients. As yet, only a minority of patients have been identified with such mutations and therefore have a good response to these medicines. These patients do better with the targeted medicines than with conventional chemotherapy, and usually have fewer adverse effects. However, these medicines are also expensive, and resistance develops, eventually leading to disease relapse or progression.

Minimally invasive surgery

Lobectomy may now be performed thoracoscopically, which has a longer procedure time but is associated with reduced post-operative pain, shorter hospital stay and faster recovery. This may enable older patients or patients previously considered “marginal” to undergo resection. The shorter recovery times may also enable adjuvant chemotherapy to be more consistently delivered to those who may benefit (large Stage 1B, and Stage 2 and 3A tumours).

Screening

The fundamental problem with screening for lung cancer is the very high false positive rate – small nodules are very commonly found on chest CT scans, and most turn out to be benign. A 2010 meta-analysis suggested that if 1000 asymptomatic smokers were screened with CT, nine curable Stage 1 lung cancers would be found but also 235 “false positive” nodules would be found, many of which would require follow up to ensure they were benign; four thoracotomies would also be performed for what turned out to be a benign process.1

The United States NLST trial found that CT screening at zero, one and two years led to a relative reduction in death from lung cancer of 20% compared to chest x-ray screening.2 Although there was no control group with “no screening” in this study, these findings suggest that chest x-ray screening of asymptomatic smokers in primary care is not useful.

Questions remain about the cost effectiveness of lung cancer screening, especially compared to smoking cessation strategies. The NLST targeted current or ex-smokers with >15 pack-years; however, recent evidence suggests a common genetic susceptibility shared between COPD/emphysema and lung cancer. Future research needs to find a better definition of the highest risk group of smokers, with algorithms which may include spirometry, presence of emphysema on CT, family history and possibly evaluation of genetic susceptibility. Many screening studies have also failed to evaluate whether smokers would be willing to participate in screening outside of the context of research trials – unlike successful “whole population” screening programmes such as cervical smears, smokers are a subgroup who are already engaging in risky behaviour.

Tobacco control

Ultimately, prevention of lung cancer would be the best strategy. Effective treatments for smoking cessation in primary care include brief advice or more intensive counselling, nicotine replacement therapy (NRT), bupropion and varenicline. The Aspire 2025 project aims to support the government objective of making New Zealand tobacco free by 2025, via research into a number of potential smoking cessation and tobacco control strategies.

Further information about Aspire 2025 is available from: www.aspire2025.org.nz

Overall, this is a rapidly evolving time in lung cancer care. Dr Stevens’ studies have helped to enable significant progress to be made in offering quality lung cancer services, earlier and more rapid diagnosis and staging, and more effective and less toxic treatment. It is to be hoped that such advances in local care and international practice will translate into reduced morbidity and mortality from lung cancer in New Zealand in the coming years.

Detailed reports on “Barriers to the timely diagnosis and management of lung cancer and description of best practice solutions” are available from: www.northerncancernetwork.org.nz

“Recommendations to expedite the diagnosis of lung cancer”, the final report of the HRC_DHBNZ funded project was released in July, 2012 and is also available at the above web address. It contains a number of recommendations that are specific to primary care. An article on these recommendations will appear in a future edition of Best Practice Journal.

ACKNOWLEDGEMENT: Thank you to Dr Chris Lewis, Respiratory Physician, Auckland District Health Board, Chair, Lung Tumour Stream, Northern Cancer Network for contributing this article.


Obstructive sleep apnoea in adults
Obstructive sleep apnoea is common in adults

Obstructive sleep apnoea is a sleep-related breathing disorder resulting in recurrent, partial (hypopnoea) or complete (apnoea) obstruction of the upper airways. It is caused by relaxation of airway muscles during sleep which allows soft tissue in the pharynx to collapse and block the upper airway. As a result of not breathing, oxygen saturation levels in the blood rapidly fall, and carbon dioxide increases, and eventually the brain triggers a brief arousal to resume breathing. Pauses in breathing usually last between ten and 30 seconds, but may persist for one minute or more. This cycle of events can occur hundreds of times a night and leads to broken, poor quality sleep. This night time “marathon” causes daytime sleepiness, which is the characteristic feature of obstructive sleep apnoea syndrome (OSAS). Recurrent hypoxaemia also results in negative health consequences such as cardiovascular morbidity and mortality.

Upper airway resistance syndrome and central sleep apnoea are less common than obstructive sleep apnoea, but may be associated with similar symptoms. People with upper airway resistance syndrome do not experience airway blockage, however, they are frequently aroused from sleep due to the increased work required to breathe. Central sleep apnoea is caused by instability or imbalance in the control mechanisms that drive respiration. This causes respiration to cycle between apnoea and hyperpnoea (deep breaths). Referral to a sleep physician is generally required to differentiate upper airway resistance syndrome and central sleep apnoea from OSAS.

Apnoea-hypopnoea index

The severity of obstructive sleep apnoea is quantified by recording the number of pauses in breathing each hour that last longer than ten seconds. This is referred to as the apnoea-hypopnoea index (AHI).

<table>
<thead>
<tr>
<th>Obstructive sleep apnoea severity</th>
<th>Apnoea-hypopnoea index (AHI)</th>
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</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Less than 5</td>
</tr>
<tr>
<td>Mild</td>
<td>5 – 15</td>
</tr>
<tr>
<td>Moderate</td>
<td>16 – 30</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt; 30</td>
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</table>

Traditionally, the AHI is determined following a full sleep study carried out in an attended sleep laboratory (polysomnography). However, partial studies conducted by appropriately trained sleep technicians in the patient’s home can accurately diagnose obstructive sleep apnoea in the majority of patients.

Obstructive sleep apnoea is reported to affect 4% of adult males and 2% of adult females. In New Zealand, it is twice as common in Māori adults males compared to non-Māori. Moderate to severe obstructive sleep apnoea is associated with a significantly increased risk of cardiovascular morbidity and mortality. People with mild symptoms and an absence of risk factors can often be managed with lifestyle interventions. However, people with more significant symptoms, such as excessive daytime sleepiness, will usually require treatment with a continuous positive airway pressure (CPAP) device.
How common is obstructive sleep apnoea in New Zealand?

The prevalence of OSAS in New Zealand is reported to be 4% in adult males and 2% in adult females. However, rates are elevated among Māori and Pacific peoples. Obstructive sleep apnoea is twice as common in Māori males compared to non-Māori males. Māori and Pacific peoples also tend to present with more severe forms of OSAS and increased co-morbidities. Higher rates of obesity among Māori and Pacific peoples is thought to be the principle reason for the increased prevalence of OSAS in these ethnic groups.

Obesity is a major risk factor for obstructive sleep apnoea

Between 40 – 90% of people with OSAS are obese. Obesity increases the risk of OSAS because excess fat tissue around the neck exerts pressure on the upper airways, increasing the likelihood of upper airway collapse occurring during sleep. Abdominal obesity has also been shown to reduce lung volumes, which can further increase the risk of upper airway collapse. It has been estimated that a 1 kg/m² increase in BMI in a person who is obese, results in a 30% increase in the relative risk of clinically significant sleep apnoea occurring in the next four years. Sleep loss caused by OSAS is also likely to further contribute to obesity.

Smoking is also associated with an increased prevalence of OSAS, and alcohol use can increase sleep apnoea duration, possibly by reducing muscle tone.

The incidence of OSAS is increased in people with hypothyroidism and females with polycystic ovary syndrome. The severity of untreated sleep apnoea may be worsened in males using testosterone supplementation.

Severe obstructive sleep apnoea increases mortality risk

Moderate to severe obstructive sleep apnoea is independently associated with an increased risk of all-cause mortality. A study of more than 77 000 patients found that increasing OSAS severity was associated with increasing all-cause mortality in patients aged younger than 50 years, after adjustments were made for BMI and age. This elevated risk has been estimated to be equivalent to an increase in age of 17.5 years or a 29 mmHg increase in mean arterial blood pressure.

Obstructive sleep apnoea is associated with increased cardiovascular risk. A predominant feature of OSAS is chronic, intermittent hypoxia, which is associated with the development of hypertension and hypertensive cardiomyopathy. Co-existing coronary artery disease, diabetes and obesity add to this risk. A large study found that, following adjustment for known risk factors, e.g. BMI, people with mild and moderate obstructive sleep apnoea had an approximately two and three-fold respectively, increased risk of hypertension compared to people without sleep apnoea. Treatment of OSAS in people with severe disease has been reported to result in a reduction in arterial blood pressure of approximately 4 mmHg, and may improve some cardiac dysfunction, although further trials are needed. Insulin resistance and abnormal lipid metabolism have also been independently associated with obstructive sleep apnoea. Both of these factors are likely to further increase the cardiovascular risk of people with OSAS.

Motor vehicle and occupational accidents are increased in people with OSAS due to impaired cognitive function caused by disrupted sleep. A study of over 900 adults undergoing sleep assessment in the United States found that males with mild sleep apnoea had a four-fold increased risk of having a motor vehicle accident compared to people without a sleep-breathing disorder. A small study of 40 injured drivers admitted to the Wellington Hospital Emergency Department (mean age 44 years) found that over one-third had obstructive sleep apnoea. The rate of traffic accidents involving people with OSAS has been reported to be significantly reduced after treatment for OSAS.

Clinical features of obstructive sleep apnoea

The clinical features of OSAS can be divided into symptoms that occur when the patient is either awake or asleep (Table 2).
Generally all people with obstructive sleep apnoea snore. But not all people who snore have sleep apnoea (see “Snoring alone is not a good predictor”).

Excessive daytime sleepiness and witnessed apnoeas are the symptoms most suggestive of obstructive sleep apnoea. Partners who have witnessed apnoeas report a sudden halt to snoring followed by a loud snort and resumption of snoring. Sleep apnoeas are more commonly reported by the partners of males. Females with obstructive sleep apnoea often report constant fatigue and lack of energy.

Assessment tools for suspected obstructive sleep apnoea

The Epworth Sleepiness Score (ESS) is a subjective assessment of daytime sleepiness. It is recommended that this score is calculated prior to referral for sleep testing. Patients are asked to assign a numerical value to each of the following situations to indicate the likelihood that they might fall asleep:

1. Sitting and reading
2. Watching television
3. Sitting in a public place, e.g. a theatre or meeting
4. As a passenger in a car for an hour
5. Lying down to rest in the afternoon
6. Sitting while conversing
7. Sitting after lunch (without alcohol)
8. As a passenger in a car stopped in traffic for a few minutes

Score: 0 = would never sleep, 1 = a slight chance of sleeping, 2 = a moderate chance of sleeping, 3 = a high chance of sleeping. A total score greater than ten is considered abnormal and a score greater than 16 indicates pathological daytime sleepiness.

The British Lung Foundation has an online version of the Epworth Sleepiness Score available at: www.blf.org.uk/Page/Obstructive-Sleep-Apnoea

The Mallampati score can be used to assess the degree of airway obstruction. Decreased upper airway size is associated with increased sleep apnoea prevalence and is more likely in people who are obese or who have anatomical abnormalities such as a large tongue, or enlarged tonsils, airway walls or soft tissue. To determine the Mallampati score, ask the patient to protrude their tongue, assess the visibility of the tonsils, uvula and soft palate and classify according to the degree of obstruction (Figure 1). A Mallampati score of class III or IV is useful for predicting obstructive sleep apnoea severity due to soft palate and tongue abnormalities.

Snoring alone is not a good predictor of obstructive sleep apnoea

Snoring is caused by the vibration of the soft palate and throat during inspiration. It affects between 20 – 60% of the adult population, and is a frequent cause of relationship strain. However, because snoring is so common among otherwise healthy people, it is not a good predictor of OSAS. Snoring may also be associated with obesity, nasal congestion, craniofacial abnormalities, hypothyroidism, acromegaly and soft tissue hypertrophy within the palate. Severe snoring has been linked to hypertension, cardiovascular disease and cerebrovascular disease. However, it is not known if snoring itself is an independent risk factor for cardiovascular disease.

Snoring can often be reduced with lifestyle interventions, such as weight reduction (if overweight), avoiding alcohol, smoking and avoiding sleeping on the back. If lifestyle measures such as these do not result in reduced snoring, oral appliances such as a mandibular splint or assessment for surgical tightening of the soft palate may be considered.
**Excessive daytime sleepiness can be a symptom of other disorders**

Simple causes should be considered first when encountering a patient with excessive daytime sleepiness. Lifestyle factors in the patient’s history should be explored to uncover insufficient sleep, primary insomnia and secondary causes of insomnia, such as depression or anxiety. Circadian rhythm disorders, e.g. jet lag, shift work or delayed sleep phase syndrome, and sedating medicines should also be excluded.

Chronic conditions such as cardiac, respiratory or neuromuscular diseases can cause fatigue, hypoventilation and daytime sleepiness. Carbon dioxide retention due to hypoventilation associated with severe obesity, central hypoventilation syndrome, or chronic obstructive pulmonary disease can result in increased daytime sleepiness, which may or may not be accompanied by breathlessness.

Unusual causes of excessive daytime sleepiness are considered last and are usually suggested by specific clinical features. Endocrine disorders, e.g. hypothyroidism, adrenal insufficiency or diabetic ketoacidosis, and neurological causes of drowsiness, e.g. subdural haematoma, encephalitis or intracranial neoplasm, may be a consideration, especially when the presentation does not fit well with OSAS.

OSAS frequently occurs in conjunction with other sleep disorders such as periodic limb movement of sleep (including restless leg syndrome), primary insomnia and narcolepsy.

For further information see: “Sleep disturbances: managing parasomnias in general practice” Page 16.

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**Sleep apnoea prediction tools**

There are several tools available to stratify the likelihood of a patient having severe obstructive sleep apnoea. However, these should be used as a guide only, as they do not provide sufficient information to make definitive decisions about referral or treatment urgency for individual patients.

The adjusted neck circumference calculation (Table 3) can be used to assess the probability of a patient having obstructive sleep apnoea, but it does not categorise potential severity.

The OSA50 screening questionnaire combined with overnight pulse oximetry can be used in patients in a primary care setting to rule out moderate to severe obstructive sleep apnoea. This tool relies on access to an electronic pulse oximeter with data recording functionality (or referral to a private sleep clinic). The process involves asking the patient specific questions (Table 4), and for patients who score five or more, arranging overnight pulse oximetry (equivalent to a level IV sleep study – see “Sleep studies”). Patients who experience 16 or more occurrences per hour of a 3% drop in oxygen saturation, are suspected to have moderate to severe sleep apnoea. The positive predictive value for the OSA50 tool (questionnaire and oximetry) is 55 – 65%, i.e. the patient has moderate to severe sleep apnoea, and the negative predictive value is 97 – 99%, i.e. they have mild sleep apnoea or no sleep apnoea. The greatest value of this approach is therefore in ruling out moderate to severe obstructive sleep apnoea.

Refer patients with suspected obstructive sleep apnoea for a sleep study

For most patients, an overnight sleep study (see “Sleep studies”) is required to confirm a diagnosis of obstructive sleep apnoea. In New Zealand, there is an absence of nationally agreed referral criteria for this service and availability is the limiting factor in determining when a patient receives a publicly funded sleep assessment.

For information about availability of sleep clinic services, contact your local DHB.

Patients at high-risk should be promptly referred for testing, e.g. sleepy drivers with a history of a sleep-related accident or near-miss, occupational drivers or machine operators. Sleepiness should be assessed using the Epworth Sleepiness Score (Page 9). Co-morbidities such as hypertension, cardiovascular disease and diabetes should also influence the urgency of referral.

Patients who do not report daytime sleepiness may not benefit from referral as treatment is aimed primarily at
Table 3: Adjusted neck circumference calculation to assess probability of sleep apnoea, adapted from Skjodt, 2008\textsuperscript{18}

<table>
<thead>
<tr>
<th>Measure</th>
<th>+</th>
<th>Add</th>
<th>Adjusted neck circumference*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck circumference in cm</td>
<td></td>
<td>3 cm for snoring history</td>
<td>&lt; 43 cm is low risk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 cm for history of witnessed apnoeas</td>
<td>43 – 47.9 cm is intermediate risk</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 cm for history of hypertension</td>
<td>≥ 48 cm is high risk</td>
</tr>
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* Low risk equals a 17% probability of sleep apnoea. High risk equals 81% probability of sleep apnoea.

Table 4: OSA50 screening questionnaire for moderate to severe obstructive sleep apnoea\textsuperscript{19}

<table>
<thead>
<tr>
<th>Criteria</th>
<th>If yes, SCORE</th>
</tr>
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<tbody>
<tr>
<td>Obesity: Waist circumference\textsuperscript{*} – Males &gt;102cm or Females &gt;88cm</td>
<td>3</td>
</tr>
<tr>
<td>Snoring: Has your snoring ever bothered other people?</td>
<td>3</td>
</tr>
<tr>
<td>Apnoeas: Has anyone noticed that you stop breathing during your sleep?</td>
<td>2</td>
</tr>
<tr>
<td>50: Are you aged 50 years or over?</td>
<td>2</td>
</tr>
</tbody>
</table>

TOTAL SCORE /10 points

If score ≥ 5, proceed to overnight pulse oximetry

* Waist circumference to be measured at the level of the umbilicus.
improving daytime symptoms. Treatment of OSAS is usually with continuous positive airway pressure (CPAP), which is often poorly tolerated by people without significant daytime sleepiness.12 Daytime sleepiness due to insufficient sleep should be excluded prior to referral (see: “Consider the presence of other sleep disorders”, Page 10).

Additional referral information that is likely to be required to receive a publicly funded sleep assessment includes:

- Patient history, e.g. snoring, witnessed apnoeas
- Details of any previous otolaryngological assessments or procedures
- Co-morbidities, including cardiovascular, metabolic and psychiatric
- Social circumstances, including any current psychosocial stressors
- Occupational risk, especially if sleepiness is threatening the patient’s employment
- Current medicines
- BMI and history of any recent weight change

Private sleep clinics and/or home-based partial sleep studies are an alternative to referral to specialist sleep laboratories where there are significant service delays. In New Zealand some private clinics are resourced by respiratory physicians. However, considerable debate exists about the validity of portable testing for the diagnosis of OSAS, compared with testing in dedicated sleep clinics. The diagnostic value of private studies is dependent on the variables that are measured. The 2007 American Academy of Sleep Medicine guidelines recommend level III sleep studies (see “Sleep studies”) as a diagnostic minimum.20 It is important for clinicians referring to private services to be aware of the level of sleep study used. Interpretation of the results from home-based partial sleep studies should be undertaken with the full clinical context of the individual patient.

Suggested contraindications to unattended home diagnostic sleep studies include:18

- Congestive heart failure
- Stroke
- Cor pulmonale
- Chronic obstructive pulmonary disease
- Hypoventilation
- Other serious medical disorders, e.g. seizures, psychosis, valvular heart disease, asthma, kidney or liver failure

Sleep studies

Level I studies, referred to as polysomanography, are performed in a sleep laboratory with a technician present and are the diagnostic gold standard. These studies include monitoring and recording of EEG (electroencephalography), EOG (electro-oculography), EMG (electromyography), heart rate, blood oxygenation, nasal flow, thoracic and abdominal movement, limb movements and body position.

Level II studies are unattended sleep studies recording the same parameters as Level I studies.

Level III studies record airflow, respiratory effort, blood oxygenation and heart rate. This level should be regarded as the minimum standard when diagnosing patients with obstructive sleep apnoea.

Level IV studies record two parameters, typically blood oxygenation and heart rate. Some level IV studies also record nasal flow. This level of sleep study should be used with caution as oximetry only detects apnoea-hypopnoea episodes leading to oxygen desaturation and are not sensitive enough to detect some instances of obstructive sleep apnoea, e.g. mild sleep apnoea. For this reason a negative result will usually require a higher level study if obstructed sleep apnoea continues to be suspected.
Treatment for obstructive sleep apnoea

Lifestyle interventions are the simplest approach to reducing OSAS severity and improving other health parameters. Studies have shown that weight loss in patients with mild, moderate and severe OSAS results in improvements in OSAS symptoms. A weight loss programme and a healthy lifestyle alone may provide clinical benefit for patients with mild OSAS. In patients with more severe OSAS, lifestyle interventions should be used in conjunction with CPAP or other interventions.

All patients with OSAS who smoke should be offered smoking cessation advice in the ABC format (Ask, Brief advice, Cessation support).

Avoidance of medicines or drugs that may contribute to OSAS. There is no conclusive evidence that alcohol, benzodiazepines or opioids exacerbate OSAS. However, in theory, these substances could relax upper airway dilatory muscles, reduce ventilator drive or diminish the likelihood of arousing from an apnoea. If required, opioids and benzodiazepines should be prescribed at the lowest effective dose. Alcohol should be avoided, especially in the few hours prior to bedtime.

Continuous positive airway pressure (CPAP)

CPAP treatment is reported to be 100% effective at eliminating obstructive sleep apnoea, if tolerated. It is recommended as first-line treatment for people with moderate or severe OSAS. A meta-analysis of 23 randomised controlled trials found that CPAP significantly reduced daytime sleepiness in patients with moderate or severe OSAS. CPAP treatment in people with OSAS has also been found to improve cognitive function, reduce arterial blood pressure and reduce the rate of motor vehicle accidents by up to 83%. Some studies have demonstrated improved glycaemic control in patients following CPAP initiation. However, CPAP treatment is not associated with weight loss.

Generally, CPAP treatment is not considered to be appropriate for people with milder OSAS without significant symptoms, as the inconvenience of the device is thought to outweigh the benefits, resulting in poor adherence to treatment.

CPAP prevents upper airway collapse by delivering positive air pressure through a mask which is worn during sleep. There are two forms of CPAP; fixed CPAP delivers constant pressure throughout the night, and auto-titrating CPAP devices adjust the pressure delivery as the patient breathes. Auto-titrating devices can be used to monitor treatment effectiveness and titrate CPAP pressure in patients commencing treatment. Both forms of CPAP have been shown to effectively control OSAS. Patient preference and economic considerations often determine which form of CPAP is provided.

Correct mask selection and treatment adherence are essential. Many patients find masks uncomfortable and may experience a sensation of claustrophobia. CPAP mask leakage can result in treatment failure. Patients should be encouraged to persevere with treatment for at least four weeks, as treatment acceptance often improves over time. Patients should also be encouraged to use the device throughout their sleep as increased treatment time is associated with increased benefit. Patients may report difficulties with adherence due to nasal dryness or bleeding, throat irritation, skin irritation, local sweating, pressure intolerance or a poor mask fit. It is essential that the operation of the device is understood, and any issues that may affect adherence are addressed. CPAP machines with built-in humidifiers and the use of silicon gels or plasters and facial shaving may alleviate some of these adverse effects. It has been reported that adherence to CPAP treatment among Māori with OSAS may be less than adherence among New Zealand Europeans.

Mandibular advancement devices

Mandibular advancement devices can prevent sleep apnoeas by widening the upper airway and pushing the pharyngeal fat pads laterally and moving the tongue base muscles anteriorly. These may be a suitable treatment for patients with mild to moderate disease, or as a second-line treatment for patients who cannot tolerate CPAP. There are many types of mandibular device available. Adverse effects, including teeth and jaw pain, are likely to influence treatment adherence. A New Zealand study assessing the use of a mandibular advancement splint in 18 males and one female, with varying severities of obstructive sleep apnoea, found that treatment resulted in significant improvements in the apnoea-hypopnoea index and other indices associated with OSAS, including snoring volume. However, the device was poorly tolerated with approximately one-quarter of participants reporting that adverse effects prevented regular use of the device. In general, mandibular splints can only be fitted in patients with all or most of their own teeth.

A Cochrane review found that use of a mandibular advancement device improved subjective sleepiness and sleep disordered breathing in people with OSAS, compared to control. Several studies have also reported significant decreases in blood pressure in the order of 2 – 3 mmHg following four to ten weeks of treatment with a mandibular advancement device.
Treatment with a mandibular advancement device appears to be more successful in people with milder forms of OSAS, females, younger or leaner people, or people with supine-dependent sleep apnoea.

Mandibular advancement devices can be purchased from some community pharmacies and individually adjusted by a dentist, or custom-made by dentists or orthodontists. Custom-fitted devices are often more effective and better tolerated than more generic devices. If the degree of advancement is too small then the device will not be effective, and if it is too large, adverse effects are increased.

Tongue-retaining devices are designed to widen the upper airway by pulling the tongue forward by suction. There is evidence that these devices may be as effective as mandibular advancement devices if worn, however, they appear to be poorly tolerated by patients.

Pharmacological treatment of obstructive sleep apnoea

The use of medicines for the treatment of obstructive sleep apnoea is controversial because they can mask diagnostically useful symptoms and reduce adherence to CPAP treatment. Modafinil, a respiratory stimulant, is licensed in New Zealand for the treatment of obstructive sleep apnoea, although it is only subsidised under Special Authority for the treatment of narcolepsy. Modafinil may be considered in limited circumstances only, and usually after consultation with a respiratory physician.

Surgical treatment of obstructive sleep apnoea

Surgery may be appropriate for the treatment of OSAS in patients who have clear upper airway anatomical abnormalities, such as enlarged tonsils. Other patients are less likely to benefit from upper airway surgery, especially if obesity or other comorbidities are present.

ACKNOWLEDGEMENT: Thank you to Dr Michael Hlavac, Respiratory and Sleep Physician, Canterbury Respiratory Services, Canterbury DHB for expert guidance in developing this article.
References


Sleep disturbances: MANAGING PARASOMNIA S in general practice
Parasomnias are a broad group of disorders associated with unusual behaviour when sleeping, and at sleep onset and waking. The distinct conditions that make up the spectrum of parasomnias are classified predominantly into rapid eye movement (REM) and non-REM parasomnias, based on when they occur during sleep. Most people do not seek medical attention for sleep disorders, and many parasomnias cease over time, but for those people who do present to primary care, treatment options include environmental, psychological, physiological and, in severe cases, pharmacological management.

What are parasomnias?

A sleep disorder is defined as the medical dysfunction of an individual’s sleep pattern. Parasomnias are a sub-category of sleep disorder. They involve abnormal and unnatural movements, behaviours, emotions, perceptions and dreams that occur while falling asleep, during sleep, between sleep stages or upon waking.

Most people experience a parasomnia during their lifetime. A large Canadian study found that 88% of children manifested at least one parasomnia between age five months and six years.1 The incidence of parasomnias begins to decline after age 25 years. Almost all adults who experience parasomnias report a history of parasomnias during childhood.2

The term parasomnia refers to a large number of individual conditions, each with a different aetiology and epidemiology. In general, parasomnias can occur during non-rapid eye movement (non-REM) and rapid eye movement (REM) sleep and are grouped based on the stage of sleep in which they occur (see “The architecture of sleep”). The most common non-REM parasomnias are bruxism (teeth grinding), somnambulism (sleep walking), confusional arousals and sleep terrors. These generally occur in the first third of the night, when non-REM sleep is deepest. The most common REM parasomnias are nightmares, REM behaviour disorder and recurrent sleep paralysis.

General principles for managing a parasomnia

Management of parasomnias consists of identifying and resolving any underlying causes, providing reassurance and advice on optimal sleeping practices (sleep hygiene), and where necessary, modification of the sleeping environment. In severe cases, pharmacological treatment may be considered.

Exclusion of underlying causes may include investigation of:

- Use of medicines with CNS-related adverse effects, e.g. sedative hypnotics, SSRIs, beta-blockers and tricyclic antidepressants
- Use of non-pharmacological drugs with CNS-related adverse effects, e.g. caffeine, nicotine, alcohol, illicit drugs
- Anxiety or stress
- Depression or other mental illness
- Dementia or confusion in older people
- Other sleep disorders, e.g. restless leg syndrome, sleep apnoea, narcolepsy

Reassurance that parasomnias are common, usually without any specific cause and generally resolve over time may be
helpful. Household members should be advised that during parasomnia episodes, the person should not be woken as this may increase disturbance or lead to violent behaviour. If they have left their bed, the person should be gently redirected back to bed without waking, or if there is a history of violence, observed but left alone.

Sleep hygiene is the term used to describe a set of structured practices and habits that can help to maximise the quality and duration of sleep, and therefore minimise the occurrence of parasomnias. Sleep hygiene advice includes:

- Go to bed when sleepy, and get up at the same time each day
- Avoid daytime napping (except in young children), especially after 2 pm
- Avoid excessive light exposure prior to bed, e.g. computer screens, cell phones
- Ensure that sleep and sex are the only uses of the bed
- Get regular exercise, ideally mid to late afternoon
- Limit caffeine, alcohol and tobacco intake, particularly at night
- Have a hot drink, e.g. milk, prior to bed
- Avoid doing school-work or work prior to bed

Get out of bed if sleep onset does not occur within 20 minutes, perform a relaxing activity such as listening to music or reading for a short time and then return to bed.

Making the sleep environment safe may be necessary if the parasomnia behaviour involves leaving the bed. For example, place locks on second story windows, remove furniture, including mats and electrical cords, from around the bed, secure dangerous items such as knives or matches and secure exits to prevent wandering.

Scheduled waking may help to reduce the incidence of episodes of non-REM parasomnias such as somnambulism (sleep walking). The patient is gently and briefly woken 15 – 30 minutes prior to the normal episode time. The procedure is repeated nightly for up to one month, and then a trial without waking is done to assess whether there is a continued response.

Pharmacological treatment (Table 1) may be considered when parasomnias become frequent, cause extreme anxiety or there is potential for harm to the person or household members. The use of medicines to treat parasomnias is complex and rarely evidence based. There are no medicines currently approved

Table 1: Pharmacological treatment options for parasomnias in adults

<table>
<thead>
<tr>
<th>Medicine group</th>
<th>Medicine and dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepines</td>
<td>Clonazepam 1 mg daily, prior to sleeping, titrated up if required.</td>
<td>Clonazepam is the first-line choice as it has the strongest evidence base and a well known risk profile; however, it may be no more effective than any other benzodiazepine.</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Amitriptyline or nortriptyline, 10 mg daily prior to sleeping, titrated up if required.</td>
<td>If benzodiazepines are not effective or not tolerated, tricyclic antidepressants can be trialled.</td>
</tr>
<tr>
<td>Melatonin</td>
<td>Melatonin 2 – 12 mg daily, several hours prior to sleeping.</td>
<td>An alternative first-line treatment for REM parasomnias. Where patients have a risk of falls, melatonin should be used in preference to clonazepam. Patients should be started on 2 – 3 mg and titrated up if required. Melatonin is not subsidised, therefore the cost should be discussed with the patient before prescribing. Melatonin is supplied under Section 29, therefore availability may vary, check with your local pharmacy.</td>
</tr>
</tbody>
</table>
for use for parasomnias in New Zealand. Medicine should only be prescribed after exclusion of reversible underlying causes and all non-pharmacological options have been trialled. Pharmacological treatment is rarely recommended for children with parasomnias, and at present, the evidence is limited. Where pharmacological treatment is considered for a child, it should be discussed first with a paediatrician, sleep physician or psychiatrist.

**Psychotherapy**, particularly relaxation and cognitive behaviour therapy, where available, may be useful for some people with parasomnias.

**Referral** to a sleep physician is recommended if treatment is ineffective, the risk of harm is significant, the symptoms are atypical or the diagnosis is unclear.

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**Non-REM parasomnias**

**Somnambulism**

Somnambulism (sleep walking) is a series of behaviours that occur during sleep, such as changes in body position, gesturing with the hand, playing with the sheets, sitting up in bed or resting on the knees. These behaviours usually culminate in the person leaving the bed and moving around with an altered state of consciousness and impaired judgment, while still sleeping. Behaviours are often complex, co-ordinated and semi-purposeful, such as getting dressed or rearranging furniture. Rarer reports have described people driving, using firearms and performing physical assaults.

During episodes of somnambulism the person may be communicative, and is often receptive to commands. Episodes

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**The architecture of sleep**

Sleep occurs in a complex cycle, which is essential for physiological regulation, function and overall health. An individual’s sleep architecture, i.e. the structure and pattern of their sleep, can have a significant effect on their quality of life, day-time function and health.

The 24-hour sleep cycle is divided into three broad stages; non-rapid eye movement (non-REM), rapid eye movement (REM) and wakefulness. Sleep duration is the total time in a 24 hour period that a person sleeps, and is divided into non-REM and REM sleep stages (Figure 1). Non-REM sleep is further divided into stages, with “deepest” sleep occurring in Stage Four.

Quality of sleep is dependent on sleep duration, along with time of sleep onset and length of time spent in each stage of sleep.

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**Figure 1:** Human sleep architecture, showing deep sleep (Stage 4) early in the night and multiple REM stages
may last for more than 30 minutes, and usually end with the person returning to bed and resuming normal sleep.

Somnambulism occurs in up to 17% of children, and between 1–4% of adults. There is evidence that a genetic component (HLA gene DQB1) may contribute in some cases.

Treatment:
Identify and eliminate any underlying trigger, most commonly stress, fatigue or febrile illness, and medicines that are known to cause sleep walking, e.g. zopiclone or antihistamines. Intervention includes advice on sleep hygiene and changes to the sleep environment to make it safer. Consider a trial of scheduled waking (Page 18).

Where there is a risk of harm to the person or household members, pharmacological intervention with benzodiazepines or tricyclic antidepressants may be considered in adults.

Confusional arousals
Confusional arousals are partial awakenings with impaired consciousness and memory, that can occur during deep sleep or upon attempted waking. Episodes typically last less than five minutes, and in adults may be accompanied with unusual, violent or sexual behaviours and vocalisations. In adults, confusional arousals may be an indication of depression or other mental illness.

Confusional arousals have a population prevalence of approximately 3%, with no reported differences between genders.

Treatment:
Identify and manage any underlying cause such as sleep apnoea, periodic limb movements in sleep or a mental illness. Provide advice on sleep hygiene. Rarely, pharmacological intervention with benzodiazepines or tricyclic antidepressants can be considered in adults.

Confusional arousals which occur in children are not of clinical concern and generally do not require further investigation.

Sleep terrors
Sleep or night terrors are one of the most extreme and upsetting forms of parasomnia. Sleep terrors are characterised by intense fear, motor agitation, vocalisation and high levels of autonomic activity, e.g. profuse sweating, mydriasis, tachycardia and tachypnoea. Episodes generally last no more than two to three minutes, and end with either spontaneous return to normal sleep or waking with no memory of the incident.

Sleep terrors occur in approximately 6.5% of children and <1% of adults, with no reported differences between genders. It is not known what causes sleep terrors but they are rarely associated with any significant psychological illness.

Treatment:
Identify and manage any potential underlying triggers, e.g. fatigue, stress, anxiety or febrile illness. Where a trigger cannot be identified provide reassurance and advice on good sleep hygiene. A trial of scheduled waking may be useful.

Sleep talking
Sleep talking (somniloquy) is very common, particularly in children. It can occur in both REM and non-REM phases of sleep. Vocalisations may be loud, and range from simple sounds to complex speeches. In most people sleep talking is benign and not associated with serious psychopathology or any underlying issue. However, sleep talking can be upsetting or disruptive for a bed partner. Febrile illness can increase the likelihood of sleep talking. Stress management and relaxation techniques prior to bedtime may be helpful to reduce sleep talking.

At least some form of vocalisation is seen in most other parasomnias, therefore it is important to distinguish between simple sleep talking, and vocalisation accompanied by features of another parasomnia.
Bruxism

Bruxism (teeth grinding) is a common movement disorder in which a person grinds or clenches their teeth repetitively while asleep. Signs and symptoms include abnormal wear of the teeth, periodontal tissue damage and pain.

Bruxism is most often reported in adults, with a prevalence of approximately 20%, and no difference between genders. Bruxism occurs in 14% – 18% of children, although most infants exhibit some teeth grinding behaviours soon after incisor eruption. There is an increased prevalence of bruxism among children with cerebral palsy and intellectual disabilities.

Treatment:
Referral to a dentist is required where bruxism is causing significant wear to teeth.

As stress may be a contributing factor, potential causes should be explored and eliminated where possible.

Provide advice on sleep hygiene. Occlusal splints or devices may be trialled, but evidence suggests that they only temporarily reduce bruxism, without addressing the cause or reducing long-term recurrence. Occlusal splints should not be used by children. Physiotherapy can be useful for resulting jaw or muscle pain and fatigue. Jaw muscles can be stretched by opening the mouth wide, and repeating this movement ten times, twice daily. Generally, pharmacological management of bruxism is not indicated.

REM parasomnias

Nightmares

Nightmares are the most common REM parasomnia. They are defined as recurrent episodes of awakening from sleep or naps with detailed recall of dreams involving distressing or life threatening events. There is no confusion on waking. There is often a significant impact on the person's waking state, reduced daytime function and reluctance to return to sleep. Awakenings generally occur during the second half of the sleep period. Recurrent dreams are often associated with some underlying psychopathology such as post traumatic nightmares.

Diagnostic criteria and definitions differ in the literature and prevalence is difficult to quantify, but it is estimated that recurrent, problematic nightmares occur in 4 – 8% of people.
Treatment:
Treatment for recurrent nightmares usually involves cognitive behavioural therapies, including systematic desensitisation and relaxation techniques, and imagery rehearsal therapy. Referral to a psychologist may be required, particularly if dreams are related to a real life traumatic event.

REM sleep behaviour disorder
REM sleep behaviour disorder is the intermittent loss of REM-sleep muscle atonia (i.e. protective muscle paralysis), which results in acting out dreams. Common behaviours include punching, kicking, leaping and running from the bed during dream enactment.

Episodes usually occur after at least 90 minutes of sleep, once the person has entered REM sleep, and usually in the later one-third of the night. They may be very frequent, occurring up to four times per night, on consecutive nights.

REM sleep behaviour disorder has a population prevalence of 0.5 – 2% and is most commonly seen in adult males, with prevalence increasing with age. REM sleep behaviour disorder is more common in people with Parkinson’s disease and Lewy body dementia. In addition, people with idiopathic REM sleep behaviour disorder have a significantly increased risk of developing Parkinson’s disease and Lewy body dementia.

Treatment:
All patients with suspected REM behaviour disorder should ideally be referred for an overnight sleep study (polysomnography) in a sleep clinic. The priority for most publicly funded sleep clinics is investigating patients with sleep apnoea, therefore patients with suspected parasomnias may have to be referred to a private sleep clinic. A detailed history should be taken to help exclude other diagnoses. Making the sleeping environment safe is important for people with REM sleep behaviour disorder. As the risk of injury to the person and household members can be high, medicines are usually considered, along with standard sleep hygiene advice. Clonazepam and melatonin are the most commonly used medicines for REM sleep behaviour disorder (see Page 18 for recommended doses).

Table 2: The differentiation of parasomnias from nocturnal frontal lobe epilepsy

<table>
<thead>
<tr>
<th></th>
<th>Non-REM Parasomnia</th>
<th>REM Parasomnia</th>
<th>Frontal Lobe Seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Usual age at onset</strong></td>
<td>Childhood</td>
<td>Older adults</td>
<td>Any age, most often between age 9 – 20 years</td>
</tr>
<tr>
<td><strong>Gender bias</strong></td>
<td>None</td>
<td>More common in males</td>
<td>May be more common in males</td>
</tr>
<tr>
<td><strong>Occurrence during the night</strong></td>
<td>First third</td>
<td>At least 90 minutes after sleep onset</td>
<td>Most frequently between 2 am and waking</td>
</tr>
<tr>
<td><strong>Episodes per night</strong></td>
<td>Usually one</td>
<td>One to several</td>
<td>Several</td>
</tr>
<tr>
<td><strong>Episode duration</strong></td>
<td>1-30 minutes</td>
<td>1-2 minutes</td>
<td>Seconds to one minute</td>
</tr>
<tr>
<td><strong>Episode frequency</strong></td>
<td>Sporadic</td>
<td>Sporadic</td>
<td>Almost nightly</td>
</tr>
<tr>
<td><strong>Episode amnesia</strong></td>
<td>Often total</td>
<td>Occasionally total</td>
<td>No amnesia</td>
</tr>
<tr>
<td><strong>Stereotyped movement</strong></td>
<td>Absent</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td><strong>Autonomic activity</strong></td>
<td>Present</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td><strong>Evolution</strong></td>
<td>Tend to disappear</td>
<td>Rare remission</td>
<td>May increase in frequency</td>
</tr>
</tbody>
</table>
Recurrent sleep paralysis

Sleep paralysis is a common condition where complete muscle atonia (i.e. paralysis) accompanied by feelings of intense fear is experienced in a conscious person (i.e. awake, not dreaming), at the transition from wakefulness to REM sleep or during waking from REM sleep.

Recurrent sleep paralysis has a life-time prevalence of approximately 10 – 20%, with as many as 50% of people experiencing an episode of sleep paralysis at least once. It is approximately twice as common in females as in males. It is associated with several risk factors, including narcolepsy, migraine, anxiety, obstructive sleep apnoea and exhaustion.

Treatment:
If episodes are frequent, ask about any history which may suggest signs of narcolepsy (see “Narcolepsy”). Assess for any other underlying cause such as migraine, anxiety, exhaustion or sleep apnoea. If no underlying cause is found, provide advice on good sleep hygiene and reassurance that the condition is not harmful and will cease with time. If episodes are persistent, severe or causing or worsening anxiety, the use of tricyclic antidepressants at bed-time may be beneficial (see Page 18 for recommended doses).

A diagnosis not to be missed: differentiating parasomnias from nocturnal frontal lobe epilepsy

In some people, the signs and symptoms of nocturnal frontal lobe epilepsy may mimic that of a parasomnia, therefore it is essential not to miss this diagnosis. Table 2 lists features that may help differentiate between non-REM and REM parasomnias and frontal lobe seizure.

Frontal lobe epilepsy usually begins between age 9 – 20 years. Episodes are characterised by repetitive behaviours of short duration (often less than 30 seconds) and asymmetric, abnormal body movements, such as dystonic and dyskinetic postures. Grimacing and vocalisation may be present. Tongue biting and urinary incontinence are rare, but their presence significantly increases the likelihood of a diagnosis of nocturnal seizures rather than a parasomnia.

Parasomnias, in contrast, appear from an earlier age in children, and in adults are usually preceded by a history of childhood parasomnias. Parasomnic episodes have a longer duration and, with the exception of REM behaviour disorder, rarely have same-night recurrence, and have a decreasing frequency or cessation after puberty for most people.

Narcolepsy

Narcolepsy is a sleep disorder characterised by excessive sleepiness and daytime sleep attacks. The cause of narcolepsy is unknown but it has been linked to reduced amounts of orexin, a protein in the brain (also known as hypocretin), and may be autoimmune or genetic (familial) in origin.

Symptoms usually first occur between age 15 – 30 years, and include:
- Periods of extreme drowsiness during the day, with a strong urge to sleep, often followed by a short “sleep attack” (lasting approximately 15 minutes)
- Visual and auditory hallucinations between sleep and wakefulness
- Sleep paralysis
- Cataplexy (sudden loss of muscle tone), which can be triggered by strong emotions, e.g. laughter or anger, usually lasting for less than 30 seconds, but in severe cases, paralysis may last for up to several minutes

A patient with suspected narcolepsy should be referred to a sleep specialist for further assessment, including a sleep study (polysomnography).
**References**


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**ACKNOWLEDGEMENT:** Thank you to Dr Alex Bartle, Sleep Physician, Director Sleep Well Clinics, New Zealand for expert guidance in developing this article.
What are the changes?

1. Azithromycin granules for oral liquid (40 mg/mL and 200 mg/5mL are now fully subsidised, with no requirement for endorsement of the prescription (from 1 November, 2012).

2. As of 1 December, 2012, a 250 mg azithromycin tablet will be available, fully subsidised, in addition to the current 500 mg tablet. This is because the 500 mg tablet is unscored and doses may be inaccurate if the tablets are broken.

3. A restriction on the length of time azithromycin is able to be prescribed will now apply for all formulations. Azithromycin will be able to be prescribed for a maximum of five days and for longer periods only if specific endorsement criteria apply (see below).

Some restrictions on funding are still in place

The following funding restriction will apply to all community dispensions of azithromycin 250 and 500 mg tablets:

- A maximum of five days treatment per prescription; which can be waived by endorsement for patients who have:
  - Received a lung transplant and require treatment or prophylaxis for bronchiolitis obliterans syndrome*; or
  - Cystic fibrosis and chronic infection with Pseudomonas aeruginosa or Pseudomonas-related gram-negative organisms*
- A maximum of eight 500 mg tablets will continue to be available on PSO

* Currently unapproved indications

The recommended indications for azithromycin remain the same

Recommended first-line indications for azithromycin are:

Chlamydia infections – Adults: 1 g stat

Infants born to mothers who have chlamydia are at increased risk of pneumonia and conjunctivitis. Treatment with azithromycin suspension is appropriate if the infant has laboratory proven neonatal chlamydia conjunctivitis or pneumonia. The dose should be discussed with a paediatrician.

Acute non-specific urethritis – Adults: 1 g stat

Pertussis (treatment and prophylaxis) – Children: 10 mg/kg on day one, followed by 5mg/kg/day for days two to five (five days total treatment). For children weighing >45 kg, dose as per adults. Erythromycin is an alternative to azithromycin in children aged over one year.

Erythromycin is also the current recommended treatment and prophylaxis for pertussis in adults. Azithromycin is an alternative: 500 mg on day one, followed by 250 mg on days two to five.

N.B. Previous guidance has given a different dosing regimen for azithromycin in children for pertussis, depending on age (under or over age six months). United States, United Kingdom and Australian guidelines differ in their advice. The consensus in New Zealand is now to use the same regimen in children, regardless of age.

Update on azithromycin
new prescriber information and availability

Recommended first-line indications for azithromycin are:

Chlamydia infections – Adults: 1 g stat

Infants born to mothers who have chlamydia are at increased risk of pneumonia and conjunctivitis. Treatment with azithromycin suspension is appropriate if the infant has laboratory proven neonatal chlamydia conjunctivitis or pneumonia. The dose should be discussed with a paediatrician.

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Recommended second-line indications for azithromycin include:

- Pelvic inflammatory disease, as an alternative to doxycycline, when chlamydia is present – 1 g stat, repeated in seven days + ceftriaxone 500 mg IM stat + metronidazole 400 mg, twice daily, for two weeks

**Ensuring appropriate use of azithromycin**

PHARMAC’s proposal to remove the prescribing restrictions on azithromycin was initially outlined in July 2012. Feedback on this proposal, however, raised concerns that the removal of all restrictions would result in inappropriate prescribing of azithromycin. In particular, there were concerns that the medicine would be used for its anti-inflammatory properties, that it would be used for the treatment of conditions for which other antibiotics are effective and more appropriate, or as a long-term prophylactic in chronic obstructive pulmonary disease (COPD). It was thought that the widened access to azithromycin would increase the prevalence of azithromycin-resistant micro-organisms in New Zealand. There were also questions raised about the safety of the use of azithromycin due to recent evidence linking azithromycin with an increase in cardiovascular mortality.¹

In response to this feedback, PHARMAC altered the proposal allowing azithromycin to be funded without restriction and re-issued it with the restrictions as outlined.

**Prescribing notes for azithromycin**

**Appropriateness of the indication**

The recommended indications for the use of azithromycin remain the same. Azithromycin is not recommended for use in the majority of patients with upper or lower respiratory tract infections such as otitis media, sore throat or community-acquired pneumonia.

**Anti-inflammatory properties in long-term conditions**

Macrolide antibiotics, such as azithromycin, have immunomodulatory and anti-inflammatory effects in addition to their antimicrobial activity and in patients with some conditions, e.g. cystic fibrosis, this can be beneficial. Azithromycin has been subsidised since 1 July, 2009 for use in patients with cystic fibrosis and chronic infection. There may be a role for azithromycin in patients with non-cystic fibrosis bronchiectasis. The evidence for this is currently under review and the indication will be widened if appropriate.

**Long-term prophylaxis in patients with COPD**

There is increasing evidence that the long-term use of azithromycin may decrease the frequency of exacerbations in people with COPD and improve their quality of life. However, concerns about adverse effects and antibiotic resistance, mean that routine use is not recommended. In a recent study of the use of azithromycin in people with COPD, approximately 5% of participants experienced a reduction in hearing after use of azithromycin, which was not always reversed on cessation.² Significant concerns were also raised regarding resistance to macrolides. The authors acknowledge that there was an increase in the incidence of colonisation with macrolide-resistant organisms but that the significance of this for the patient, their families and the community is unknown.²

**Antibiotic resistance**

Widened access and increasing use of azithromycin in other countries have contributed to an increasing incidence of macrolide-resistant organisms.³ Concerns have been raised that a similar situation will arise in New Zealand. It is therefore important that azithromycin is only prescribed for the clinical situations it is indicated for. ESR will be monitoring resistance data in New Zealand.

**Azithromycin may be linked to an increased risk of cardiovascular death**

A large retrospective cohort study found that a five day course of azithromycin was associated with a small increase in the risk of cardiovascular death when compared to the risk in patients who took no antibiotics or other antibiotics, e.g. amoxicillin.¹ Macrolide antibiotics, particularly erythromycin and clarithromycin have been associated with prolongation of the QT interval and there is increasing evidence that azithromycin may also be proarrhythmic.⁴ Although there has been criticism of the study and further research is required, the authors conclude that the key factors that need to be considered when prescribing azithromycin are the patient’s baseline cardiovascular risk and the appropriateness of the indication for which azithromycin is prescribed.¹, ⁴

For more information on the changes to azithromycin, see: “Approval of proposal to amend the restrictions applying to azithromycin and list Apotex’s brand of azithromycin 250 mg tablets”, PHARMAC, Oct 2012; Available from [www.pharmac.govt.nz/2012/10/19/AzithromycinNotification.pdf](http://www.pharmac.govt.nz/2012/10/19/AzithromycinNotification.pdf)

For more information on the use of azithromycin, see: “The appropriate use of macrolides”, BPJ 44 (May, 2012).
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References
When and how to use a syringe driver in palliative care
Syringe drivers are often required to provide medicines for symptom management in patients who are terminally ill. They allow continuous subcutaneous administration of medicines to enable effective symptom control when medicines given by other routes are inappropriate or no longer effective. With guidance and support from the local hospice or district nursing services, General Practitioners can arrange a syringe driver infusion for a patient in their home or in a residential care facility, prescribe and monitor the appropriate mix of medicines and manage breakthrough symptoms.

What is a syringe driver?

A syringe driver is a small, portable, battery operated device that administers medicines subcutaneously over a selected time period, usually 24 hours. Medicines are drawn up into a syringe that is then attached to the driver, which is set to move the plunger of the syringe forward at an accurately controlled rate. Syringe drivers can be used either short-term or long-term, for patients who are ambulatory and those who are confined to bed. Syringe drivers can be placed into a carry bag or pouch when a patient is mobile or be tucked under a pillow if the patient is bed-bound.

Indications for use of a syringe driver

Continuous subcutaneous administration of medicines using a syringe driver often becomes necessary for the control of symptoms during palliative care. A syringe driver is useful when the oral route of administration is not possible and repeated subcutaneous doses are inappropriate, ineffective or impractical. Although medicines can also be administered by other routes, such as rectal or sublingual, a further advantage of a continuous subcutaneous infusion is that any peaks and troughs of intermittent delivery methods are avoided (Table 1).

The Niki T34 is used in a community setting

The lockable, battery operated, Niki T34 syringe driver is the current device available in New Zealand for the continuous subcutaneous administration of medicines in a community setting. The Graseby syringe driver has been gradually phased out of use as it was not tamper-proof. Concerns were also raised by the Health and Disability Commissioner after a number of cases occurred due to errors with syringe driver use.¹ As a result, a recommendation was made that there be consistency in the type of syringe driver used throughout New Zealand. Initially the preferred replacement option was the AD Ambulatory Syringe Driver, however, the company involved was unable to supply and support these drivers and a further decision was made so that by 30 June, 2011, the Niki T34 syringe driver was used exclusively.²
Consider using a syringe driver when:3

- The patient is unable to take medicines by mouth due to nausea and vomiting, severe oral lesions, e.g. mucosal ulceration, dysphagia, weakness, sedation or coma
- There is poor absorption of oral medicines
- Pain is not able to be controlled using orally administered medicines
- There is a malignant bowel obstruction and further surgery is inappropriate (therefore avoiding the need for an intravenous infusion or the insertion of a nasogastric tube)
- The patient does not wish to take regular medicine by mouth

**Table 1: Advantages and disadvantages of using a syringe driver**

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>The ability to gain effective symptom control due to steady plasma drug concentrations without peaks and troughs</td>
<td>Medicine requirements must be anticipated for a 24 hour period and can result in a loss of flexibility in dosing</td>
</tr>
<tr>
<td>Allows management of multiple symptoms through the use of combinations of medicines given via a single route</td>
<td>Medicines given by other routes (including “as needed” subcutaneous injections) may be required to manage the patients symptoms for the initial four hours of the syringe driver infusion while the medicines reach a plasma concentration that provides effective symptom control</td>
</tr>
<tr>
<td>The single route of administration minimises the need for repeated injections or multiple oral medicines</td>
<td>An increase in the patients symptoms may require additional injections for relief</td>
</tr>
<tr>
<td>Subcutaneous administration of medicines is more comfortable for the patient than intramuscular injections (particularly if the patient is cachexic) and is simpler and less invasive than medicines given intravenously</td>
<td>Local reactions such as pain, inflammation or infection can cause discomfort and interfere with the delivery and absorption of the medicines</td>
</tr>
<tr>
<td>The ability for patients who are still mobile to remain so, and once set up enables more independence</td>
<td>Patients may see the use of a syringe driver as a final step before death and find its use disconcerting and obtrusive</td>
</tr>
<tr>
<td></td>
<td>The patients symptoms and effectiveness of the infusion must still be reassessed regularly</td>
</tr>
</tbody>
</table>

**Talking about syringe drivers with patients and family/whānau**

Initiating use of a syringe driver in a patient during palliative care may represent a significant and unwelcome milestone for the patient and their family/whānau, because syringe drivers are often required when a patient is close to death. The goals of administering medicines via a syringe driver therefore need to be discussed with the patient and family and any concerns addressed. A syringe driver simply provides an alternative route for the administration of medicines. For example, a patient with severe nausea and vomiting that temporarily prevents the use of oral medicines may need a syringe driver to gain control of symptoms. It may be possible to revert back to the use of oral medicines once control of the nausea and vomiting is achieved.4

Topics of discussion with the patient and family/whānau may include:

- Any past experience they have had with syringe drivers
- The stage of illness they are at and what using a syringe driver means for them for the future, e.g. prognosis
- Reassurance that syringe drivers do not always mean that death is imminent
- Explanation that a syringe driver allows the symptoms associated with the process of dying to be managed, but does not speed up the process of dying
- Addressing any fears or anxieties about the syringe driver, including the medicines used, e.g. opioids
- Advance care planning options and specific advance care directives
Practical aspects of how the syringe driver functions also need to be discussed with the patient and their family/whānau. In many cases, it will be the family who become aware of any issues with the device itself or that the medicines are not controlling the patient’s symptoms.

Some of the practical issues that may need to be addressed include:
- Care of the syringe driver once in use
- The safety aspects of the syringe driver
- What to do and where to get advice if the syringe driver is not working properly, or symptoms are not controlled, e.g. who to call if an alarm sounds, ensuring that a spare battery is available
- Ways to carry the infusion device to minimise its intrusion in daily life, e.g. while showering
- The potential need to administer additional medicine via other routes, e.g. at initiation, for breakthrough symptoms

Arranging a syringe driver for a patient
Hospice or district nursing services can provide equipment and certified staff who can work with General Practitioners, patients and their families/whānau. Many patients will also be under the care of a palliative care physician. It is essential that there is good communication between the people who are providing care and support for the patient and their family (this also includes community pharmacy). Many residential aged care facilities have syringe drivers on site and staff trained in their use.

Hospice New Zealand offers a training programme on managing syringe drivers in primary care. For further information see: www.hospice.org.nz

Most symptoms can be controlled with a continuous subcutaneous infusion
In a palliative care setting, subcutaneous administration of medicines given via a syringe driver is useful for managing symptoms such as pain, nausea, anxiety and restlessness. Injectable forms of medicines to control symptoms can be given alone, or mixed together in a syringe depending on their physical and chemical compatibility and the diluents used (over page).

Choice of medicine and prescribing
In palliative care, medicines may be prescribed for unapproved indications, be administered by an unapproved route or given in doses not seen in routine day-to-day practice. Most medicines can be used in a subcutaneous infusion, however, chlorpromazine, prochlorperazine and diazepam are contraindicated as they can cause skin reactions at the injection site.

Infusions for administration via continuous subcutaneous infusion using a syringe driver should be prescribed to run over 24 hours, although medicines mixed together may be pharmaceutically compatible and stable for longer than this.

The patient should ideally be reviewed every day so that medicine doses can be adjusted according to their needs.

When prescribing consider:
- The patient’s medicine requirements for 24 hours
- The doses that may be required for breakthrough symptoms – these need to be available for immediate use
- The choice of diluent
- The compatibility of the medicines required to manage symptoms (Table 2, over page). In general, avoid combining more than three medicines in one syringe (occasionally more than one syringe driver is required)

Choice of diluent
The choice of diluent for the infusion solution varies according to local guidelines as there is evidence for and against the two most commonly used diluents – sterile water (water for injection) and normal saline (NaCl 0.9%). In general, sterile water is used.

Sterile water is compatible with most medicines (with some exceptions, e.g. levomepromazine, ondansetron and octreotide which should be diluted with normal saline) and unlikely to cause precipitation of medicines, but it is hypotonic and may be associated with pain at the infusion site. However, in practice, pain is not that common because of the slow rate of infusion.

Normal saline is also compatible with most medicines (with some exceptions, e.g. cyclizine which should be diluted with sterile water) and may be less irritating at the insertion site because it is isotonic, however, the likelihood of precipitation increases, particularly when more than one medicine is used.

Compatibility of medicines
When more than one medicine is used in an infusion solution there is a risk that they may not be compatible, either chemically or physically. Increasing the number of medicines in the
Table 2. Compatibility of medicines for syringe driver infusions commonly prescribed in general practice (Adapted from Palliative Care Handbook 2012).†

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Morphine</th>
<th>Oxycodone</th>
<th>Fentanyl</th>
<th>Methadone</th>
<th>Metoclopramide</th>
<th>Cyclizine</th>
<th>Haloperidol</th>
<th>Methotrimeprazine</th>
<th>Midazolam</th>
<th>Clonazepam</th>
<th>Hyoscine butylbromide</th>
<th>Dexamethasone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>–</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y/SI</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y/?</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>NA</td>
<td>–</td>
<td>NA</td>
<td>NA</td>
<td>Y</td>
<td>SI</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>NA</td>
<td>NA</td>
<td>–</td>
<td>NA</td>
<td>Y</td>
<td>SI</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>?</td>
<td>Y</td>
<td>?</td>
</tr>
<tr>
<td>Methadone</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>–</td>
<td>Y</td>
<td>?</td>
<td>Y</td>
<td>Y</td>
<td>Y/?</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>–</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Cyclizine†</td>
<td>Y</td>
<td>SI</td>
<td>SI</td>
<td>?</td>
<td>Y</td>
<td>–</td>
<td>Y</td>
<td>Y</td>
<td>SI</td>
<td>SI</td>
<td>SI</td>
<td>SI</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Y/SI</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>–</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>SI</td>
</tr>
<tr>
<td>Levomepromazine (Methotrimeprazine)</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>–</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>SI</td>
</tr>
<tr>
<td>Midazolam</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>SI</td>
<td>Y</td>
<td>Y</td>
<td>–</td>
<td>Y</td>
<td>Y</td>
<td>SI</td>
<td></td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Y</td>
<td>Y</td>
<td>?</td>
<td>Y</td>
<td>Y</td>
<td>SI</td>
<td>Y</td>
<td>Y</td>
<td>–</td>
<td>Y</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>Hyoscine butylbromide (Buscopan)</td>
<td>Y/?</td>
<td>Y</td>
<td>Y</td>
<td>?</td>
<td>Y</td>
<td>SI</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone†</td>
<td>Y</td>
<td>Y</td>
<td>?</td>
<td>Y</td>
<td>Y</td>
<td>SI</td>
<td>SI</td>
<td>SI</td>
<td>SI</td>
<td>Y</td>
<td>Y</td>
<td>–</td>
</tr>
</tbody>
</table>

**Y** = Compatible  **SI** = Sometimes incompatible (usually at higher doses)  **NA** = Not usually used together  **?** = unknown

† May crystallize, dilute well
‡ 0.5 to 1mg dexamethasone added to a syringe driver solution may reduce the risk of irritation at the subcutaneous insertion site

If more than two medicines are to be mixed in an infusion, refer to The Palliative Care Handbook 2012 or contact your local hospice for commonly used combinations and additional compatibility information.
solution increases the risk of problems with the combinations. Physical incompatibility usually results in changes in the solution that can be observed such as discolouration, clouding or precipitation of crystals or particles. However, it is important to refer to compatibility tables because a solution can remain clear even if the medicines are chemically incompatible.

Precipitation may occur as a result of a reaction between medicines in a syringe. The risk of precipitation can be minimised by using sterile water as the diluent and by maximising the total volume of the solution in the syringe, i.e. making the solution as dilute as possible. 7

Once mixed, syringes should be observed for any signs of precipitation or discolouration. Provided that doses are within normal ranges, Table 2 shows which injectable medicines are expected to be compatible in a 24-hour syringe driver solution.

Prescribing the medicines for the syringe driver
Convert the patient’s previous 24-hour oral medicine requirements (including regular and “as needed” doses) to the equivalent subcutaneous dose.

Usual starting doses for subcutaneous infusion for commonly used medicines are:
- Morphine – use half the total 24 hour oral dose
- Oxycodone – use half the total 24 hour oral dose
- Metoclopramide, cyclizine and hyoscine hydrobromide (the injectable hyoscine salt Buscopan) – same as the oral dose
- Haloperidol – antiemetic dose is 1 – 2 mg for 24 hours
- Midazolam – 5 – 40 mg over 24 hours

For patients who have not been on opioid medicine for analgesia, an example of an initial starting dose would be 10 mg morphine subcutaneously over 24 hours. 3

Prescribe the doses of the subcutaneous medicines to cover a 24-hour period. Check the compatibilities of the medicines in the syringe using the chart in The Palliative Care Handbook 2012 or Table 2 and decide on the volume to infuse, stating the diluents. A maximum of 24 mL solution in a 30 mL syringe is appropriate for the Niki T34 syringe pump. Smaller syringes, e.g. 10 mL and 20 mL, can also be used, but they should be filled to a maximum of 8 mL and 18 mL respectively. A luer-lock syringe should always be used to avoid any risk of disconnection.

Larger volume syringes should be used for medicines that will require more ampoules to be combined to achieve the total daily dose, e.g. metoclopramide, oxycodone and fentanyl, or medicines that are potentially irritant when given subcutaneously, e.g. cyclizine, methadone and high doses of dexamethasone.

The first syringe of a new prescription will lose some of the solution when the line is primed, therefore the infusion will not run for a full 24 hours. An initial subcutaneous injection may also be required as a loading dose to manage the patient’s symptoms for the initial two to four hours of syringe driver use until the medicines in the infusion reach effective blood plasma levels. When an infusion is due to be changed, a delay of an hour or two should not cause problems if the patient’s symptoms are well controlled. This can be a concern for patients and families if the clinicians or nurses visit is delayed.

Hospices and residential aged care facilities are likely to have standardised prescribing and administration charts for syringe driver prescriptions. Similar documentation is recommended for patients who are receiving care at home.

An example of a prescription chart for documenting medicines given via syringe driver is available at: http://palcare.streamliners.co.nz click on “forms”. The individual medicines to go in the syringe can be prescribed on a standard prescription for a community pharmacy. Indicate the prescription is for a syringe driver. State the dose and diluents, and remember a triplicate controlled drug prescription for any opioids. Some community pharmacies provide a service for compounding medicine solutions in daily subcutaneous syringes.

Administration instructions do not need to include the rate of infusion, just the infusion duration (usually 24 hours). This is because the Niki T34 syringe driver simplifies administration by detecting the syringe size and volume of medicine, and sets the rate to deliver the infusion over the required time period, e.g. 18 mL in a 20 mL syringe will deliver at 0.75 mL per hour for a 24-hour period.

Controlled drugs that are no longer required for a patient can be returned to the pharmacy or general practice for safe disposal.

Starting the infusion
In most cases, a healthcare professional trained in the use of syringe drivers, e.g. a hospice nurse, district nurse or residential aged care facility nurse, will assist with setting up the continuous subcutaneous infusion.
A step by step guide for operating the Niki T34 is available from the manufacturer, REM Systems. Instructions are also available online from many hospices.

Selection of the infusion site

Plastic cannulae are recommended, although metal butterfly needles can be used. The preferred sites for insertion of the cannula for a continuous subcutaneous infusion are:

- The anterior chest wall
- The anterior abdominal wall
- The anterior aspect of the upper arms
- The anterior aspect of the thighs

These sites are preferred because they are accessible, both for initial insertion and for monitoring, and they are rarely oedematous. The choice of site may be influenced by a number of factors including patient preference, their level of mobility and the patient’s condition, e.g. if they are cachexic the abdomen may be the most suitable site, the upper arm should be avoided if the patient is bed-bound and requires regular turning and anterior sites may not be suitable for patients who are agitated as they may dislodge the cannula – a posterior site over the scapula may be preferable.

Inappropriate sites include:

- Lymphoedematous or ascitic areas – as absorption will be reduced and there is an increased risk of infection and leakage
- Areas of skin that are scarred, broken, inflamed, infected or hairy
- Skin folds or skin over bony prominences or near joints
- The anterior chest wall in patients who are very cachexic – there is a small risk of pneumothorax
- The upper abdomen in a patient with an enlarged liver – there is a small risk of puncturing the liver capsule
- Skin that has been irradiated within the last six weeks
- Any area that has a tumour

Minimising reactions at the site of insertion

A number of factors influence the longevity of the insertion site. These include the site selected, the type of cannulae used and the medicine being given. If problems arise with an infusion site the patient may have localised discomfort, or there may be reduced absorption of the medicine and a loss of symptom control. As a general guide, plastic cannulae can stay in place for up to a week or more, whereas metal cannulae remain viable for approximately 72 hours. Provided there is no evidence of a site reaction, it is reasonable to only change a site when it becomes necessary, e.g. due to pain, swelling or inflammation.

Techniques that may help to prolong the usefulness of a site and to minimise reactions include:

- Make the solution as dilute as possible – use a larger syringe
- When possible, select a solution that is close to physiological tonicity – sterile water is hypotonic, normal saline is isotonic, and solutions with high concentrations of some medicines become hypertonic
- Use plastic cannulae as they cause less site irritation than metal cannulae
- In a patient who has been prone to site problems, consider rotation of the site of infusion before any localised reactions develop
- Avoid oedematous areas when selecting the site for infusion
- Use 0.5 – 1 mg of dexamethasone in the syringe driver solution to reduce site reactions, particularly if the medicines used are known to be irritant, e.g. methadone
- Consider the use of heparinoid (Hirudoid) cream (not subsidised) on inflamed sites if there is no infection present

Monitoring the infusion

Patients being cared for at home should ideally have a daily visit from a health professional for review of symptom control and monitoring of the infusion. This should occur at least every four hours when patients are in a hospice or residential aged care facility.

A check should be made of the:

- Cannula site – for redness, swelling, leakage or cannula blockage or displacement
- Tubing – for kinks or knots in the tubing
- Syringe – for precipitation or crystallisation, discolouration of solution
- Syringe driver – to ensure that the syringe remains in the correct position, that the infusion is running at the correct rate and the syringe driver battery has enough power to last until the next check

Managing breakthrough symptoms

First check that the medicines are being delivered effectively via the syringe driver.

Breakthrough pain can be treated with additional subcutaneous doses of the opioid being used (usually morphine). If possible,
Doses should be given through a side port in the syringe driver cannula line to minimise patient distress. This can be given as often as required to relieve breakthrough pain. Doses can be prescribed in a flexible manner to achieve good symptom control, e.g. 2.5 mg morphine as required every 15 minutes up to a total of three doses over 60 minutes.

Extra doses of antiemetics and other medicines in the syringe can also be given subcutaneously at the usual dose. If supplementary doses are required regularly for breakthrough symptoms, include these doses when calculating the amount of medicine needed for the subsequent 24 hour period. If the patient’s symptoms remain uncontrolled despite an increase in dose, consider an alternative medicine (e.g. because nausea may have many underlying causes it may be relieved by different medicines) and consider a discussion with a palliative care physician. Also consider other methods to relieve a patient’s distress – sometimes taking the time to sit and listen can be as effective as administering a medicine.

Further resources

General Practitioners and other carers can access 24-hour telephone help from their nearest hospice: www.hospice.org.nz/find-your-local-hospice-service


References


Acknowledgement

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Initiating interventions in people with intermediate hyperglycaemia ("pre-diabetes")

Intermediate hyperglycaemia is a state of raised glycaemic levels in a person without diabetes. It is an independent risk-factor for type 2 diabetes and cardiovascular disease. The primary aim of management of intermediate hyperglycaemia is to prevent progression to diabetes. Intervention involves structured lifestyle changes, and for people with a high risk of progression to diabetes who do not achieve normoglycaemia, treatment with metformin.
What constitutes intermediate hyperglycaemia?

Diabetes is diagnosed with an HbA1c level of 50 mmol/mol or greater (and, if measured, a fasting blood glucose ≥7.0 mmol/L). This is the glycaemic level at which the incidence of moderate diabetic retinopathy begins to rise exponentially. In an asymptomatic person, a result greater than 50 mmol/mol should be repeated to confirm the diagnosis.

Intermediate hyperglycaemia is a biochemical state in which a person has glucose levels above the normal range, but does not yet meet the criteria for a diagnosis of diabetes. In New Zealand intermediate hyperglycaemia is defined as an HbA1c level of 41 – 49 mmol/mol (and, if measured, a fasting blood glucose of 6.1 – 6.9 mmol/L).

Unlike diabetes, repeat testing is not required to confirm intermediate hyperglycaemia. A single HbA1c result between 41 – 49 mmol/mol in a person who is not acutely ill or who does not have a condition that may affect HbA1c levels is sufficient. HbA1c should then be monitored every six to 12 months, unless there are intervening symptoms.

HbA1c is most frequently requested in the context of a cardiovascular disease (CVD) risk assessment. If a person is identified as having intermediate hyperglycaemia, and they are in the targeted age range, they should have a full CVD risk assessment, including investigation of lipid levels, if this was not done at the same time as the HbA1c test.

In New Zealand, normoglycaemia is defined as an HbA1c level below 40 mmol/mol (and, if measured, a fasting blood glucose ≤6.0 mmol/L).

For further information on the use of HbA1c to diagnose diabetes, see: “The new role of HbA1c in diagnosing type 2 diabetes”, BPJ 42 (Feb, 2012) and “Understanding the new HbA1c units for the diagnosis of Type 2 diabetes”, Braatvedt G et al, NZMJ 2012;125(1362).

What’s in a name? Intermediate hyperglycaemia versus pre-diabetes

The term pre-diabetes is controversial: in 1980 the World Health Organisation (WHO) recommended against its use as not all people with borderline glycaemic levels progress to diabetes. In 2006 the WHO again discouraged the use of the term pre-diabetes and instead suggested “intermediate hyperglycaemia” to signify impaired fasting glucose (IFG) and impaired glucose tolerance (IGT). The 2012 NICE guidelines (United Kingdom) refer to “increased risk of type 2 diabetes” rather than pre-diabetes.

Intermediate hyperglycaemia is an independent risk-factor for diabetes

Approximately 5 – 10% of people with intermediate hyperglycaemia progress to diabetes every year, but 5 – 10% will revert back to normoglycaemia. However, in the long-term, up to 70% of people with intermediate hyperglycaemia will eventually develop type 2 diabetes. This represents a relative risk for type 2 diabetes six times greater for people with intermediate hyperglycaemia than those with normoglycaemia.

Intermediate hyperglycaemia should be viewed as a continuous scale rather than a discrete variable, i.e. those at the higher end of the 41 – 49 mmol/mol range have a much greater risk of developing diabetes than those at the lower end. The risk of having a high glycaemic level remains, even for people who have undergone proven prevention such as bariatric surgery.

In addition, other factors play an important part in assessing an individual’s risk of progressing to diabetes, including:
- Age
- Weight and BMI
- Physical activity
- Diet
- Ethnicity – Māori, Pacific and South-Asian people have an increased risk of diabetes

*For example high red blood cell turnover, iron or B12 supplementation or recent blood transfusion can falsely lower HbA1c levels and severe anaemia, B12 or folate deficiency, chronic alcoholism, chronic renal failure or certain haemoglobinopathies can falsely raise HbA1c levels.*
Smoking status – three-fold increase in risk of progression to diabetes
Family history of diabetes
Increased blood pressure
Increased lipid levels
Certain conditions, such as polycystic ovary syndrome (see sidebar)

There are a number of tools for assessing who is at risk of developing diabetes, and helping to determine the pre-test probability of a diagnosis in people who have not had a recent HbA1c test. The most practical tools incorporate information readily available to primary care and have a high specificity for future diabetes progression.9 These prediction tools have not been validated in high risk ethnicities in New Zealand, therefore a single tool cannot be recommended above any other for this population. However, viewing the patient’s risk in light of the above risk factors is likely to be beneficial in assessing the likelihood of progression to diabetes.

Many vascular complications begin before HbA1c reaches “diabetic” levels

While diabetes is defined by the threshold where the prevalence of moderate diabetic retinopathy begins to increase exponentially, many of the underlying pathophysiological processes associated with diabetes begin during the intermediate hyperglycaemic stage. This includes nephropathy, chronic kidney disease, neuropathy, retinopathy, cardiovascular disease and overall mortality.10 Similarly, increased vascular risk remains even in people with diabetes who have achieved target glycaemic levels below the diagnostic threshold for diabetes.11

Early management is particularly important among high-risk groups as complications develop earlier, often before a diagnosis of diabetes is made, although this could be a result of either lower testing rates (meaning longer unmanaged time with hyperglycaemia) or a greater actual risk. For example, in a New Zealand study of 4269 Māori, of the participants identified as having clinical diabetes, 29.6% already had established microalbuminuria, and 7.7% albuminuria, at diagnosis.12

Management of intermediate hyperglycaemia reduces progression to diabetes

The identification and management of people with intermediate hyperglycaemia should be viewed as an opportunity to halt progression to diabetes and to reduce the risk of diabetes related complications. Intervention with lifestyle changes, and initiation of metformin where appropriate, can reduce the number of people progressing to clinical diabetes by 30 – 60%.6, 13 Treatment is considered to be both safe and cost-effective.13–15

The Diabetes Prevention Program, a large United States study of early prevention, found that 5% of people in the lifestyle intervention group and 7.8% of people in the metformin group (no lifestyle changes) developed clinical diabetes each year, compared to 11% of those in the placebo group (Figure 1).6 Lifestyle intervention was more advantageous than metformin in people aged over 60 years and those with a lower body-mass index.9 People who achieved even one normoglycaemic result during the study period had a significantly lower long-term risk of progressing to diabetes.16

In the Diabetes Prevention Program, women with a history of gestational diabetes and current intermediate hyperglycaemia showed significant benefit from both lifestyle intervention and metformin. Each intervention reduced the relative risk of progression to diabetes by approximately 50% compared with the placebo group. In contrast, this reduction was 49% for lifestyle and 14% for metformin in women without a history of gestational diabetes.17

Overall, it is estimated that the number of people with intermediate hyperglycaemia who need to be treated for three years in order to prevent one case of diabetes is 6.9 for lifestyle intervention and 13.9 for metformin.6

Treatment goal: agree on a target HbA1c level

There is no defined treatment target in people with intermediate hyperglycaemia, therefore a target should be individually agreed upon between the patient and the doctor. Ideally the goal of treatment should be regression to normoglycaemia, in which case an HbA1c target of < 40 mmol/mol should be aimed for, as this is associated with significant reductions in long-term diabetes risk.15 However, for many people delaying and slowing the progression to diabetes is a more realistic target and is still likely to be beneficial.

Repeat testing of HbA1c is recommended every 6 – 12 months, unless there are intervening symptoms.20

N.B It is critical that HbA1c level targets are not the only goal set, weight loss and exercise goals should be part of the treatment process.
Lifestyle intervention for everyone
Most people with raised glycaemic levels will benefit from advice on an intensive programme of lifestyle changes. The two most important modifiable risk factors for diabetes development are obesity and physical inactivity. Target goals should be set for weight, weekly physical activity level and diet, e.g. fat intake, fibre intake and total kilojoules.

Key advice includes encouraging people to:
- Undertake a minimum of 150 minutes of “moderate intensity” physical activity per week
- Gradually lose weight to reach and maintain a BMI within the healthy range
- Increase consumption of whole grains, vegetables and other foods that are high in dietary fibre
- Reduce the total amount of fat in their diet
- Eat less saturated fat

In the Finnish Diabetes Prevention study, achievement of lifestyle intervention goals resulted in a reduction of 58% in the risk of progression to diabetes. Achieving each individual goal (e.g. exercise, reducing fat in the diet) was independently associated with reduced risk of progression to diabetes. For example, a 5% reduction in weight significantly reduced the overall risk of developing diabetes (odds ratio of 0.3 compared to no weight loss). In the Diabetes Prevention Program study population, it was found that even a small weight loss, e.g. 1 kg, resulted in a significant reduction in the risk of progression to diabetes.

Some practices may consider addressing lifestyle interventions with patients in a group setting. Key components of a successful programme include:
- Participants meet at least eight times over 9-18 months
- Participants have at least 16 hours of educational time, either in the group or on a one-to-one basis
- Follow-up sessions should be offered regularly, e.g. every three months, for at least two years after the programme
- Behavioural change techniques should be used in conjunction with diet and exercise advice, e.g. setting short and long-term goals, identifying triggers

Referral to a dietitian for further advice and guidance is likely to be beneficial, although waiting times for publically funded services and the cost of private services may be an issue for some people.

For further information on lifestyle interventions see: “Addressing weight issues in young people and families in New Zealand”. BPJ 45 (Aug, 2012) and “Promoting healthy lifestyles for Pacific peoples” BPJ 32 (Nov, 2010).

Add metformin if lifestyle intervention is insufficient
After approximately six months of lifestyle intervention, people who do not show glycaemic improvement, gain weight or are unable to adhere to recommendations may be offered metformin as an adjunct to lifestyle intervention.
In addition, most women with polycystic ovary syndrome and raised glycaemic levels are likely to benefit from a trial with metformin (see “The role of metformin in women with polycystic ovary syndrome”).19 Women with a history of gestational diabetes and current intermediate hyperglycaemia are also likely to particularly benefit from metformin.17

Because the benefits of metformin are not maintained after cessation, it is important that diet and lifestyle management is continued during metformin treatment in order to address and improve the underlying obesogenic behaviours that contribute to intermediate hyperglycaemia and diabetes. Long-term primary prevention can then be maintained even after medicine cessation.

How to prescribe metformin for intermediate hyperglycaemia

Intermediate hyperglycaemia is not an approved use for metformin, but it can be prescribed fully subsidised for this indication and there is strong clinical evidence to justify its use.

Metformin can be commenced at a low dose, e.g. 500 mg once daily, and increased gradually, e.g. over several weeks, as tolerated to a maximum of 2 g daily if required.4

Lactic acidosis has been reported in people taking metformin who have reduced renal function. Although the risk may be overstated, at present it is recommended that the dose of metformin should be reduced if renal function deteriorates, and people who decline to an eGFR < 30 mL/min/1.73m² or are at risk of rapid decline in renal function should cease treatment.1 A Cochrane review of 96,295 patients found no incidences of lactic acidosis in people taking metformin, even in those who had a contraindication to metformin, such as renal insufficiency.23

Consider a maximum daily dose of 1 g metformin in patients with eGFR 30–60 mL/min/1.73m². However, in patients who are obese, eGFR may be an underestimate of their true creatinine clearance, and this group is likely to benefit most from metformin. Therefore metformin doses may not have to be reduced in obese patients with eGFR in the 45–60 mL/min/1.73m² range. If required, consider using the Cockcroft-Gault equation to calculate a more accurate value for creatinine clearance in these patients.

As metformin is primarily cleared by the kidneys, all patients taking metformin should have their renal function monitored annually and more frequently if clinically indicated.
Compliance and adverse effects of metformin need to be monitored

Metformin is generally well tolerated. The most common reported adverse effect is gastrointestinal disturbance. Other adverse effects include anorexia, nausea, taste disturbance and decreased vitamin-B12 absorption. Regularly follow-up to ensure that metformin is being taken as prescribed and that adverse effects are not affecting adherence.

Metformin may need to be continued long-term

Metformin should be given initially for six to 12 months. For many people metformin will need to be continued long-term. If no effect is seen with metformin, consider stopping the medicine, but continue with lifestyle interventions. If, despite metformin treatment, the patient progresses to diabetes, other medicines, e.g. sulphonylureas or insulin, may need to be added if glycaemic control cannot be achieved with metformin alone.

ACKNOWLEDGEMENT: Thank you to Dr Brandon Orr-Walker, Endocrinologist, Middlemore Hospital, Auckland and Dr Kirsten Coppell, Senior Research Fellow, Edgar National Centre for Diabetes Research, Dunedin School of Medicine, University of Otago for expert guidance in developing this article.

References

Are you getting the most you can from the New Zealand Formulary?

Resources for getting started

The NZF offers several downloadable resources for understanding how to use the formulary and for teaching others. These are available from: www.nzformulary.org

**Getting started**

Although the NZF has been developed to be logical and intuitive for users, a few minutes spent finding out more about its features will enhance your ability to find the information you seek within the website.

Enter www.nzformulary.org and click on “User Information”.

**Tutorial videos**

The full NZF tutorial video plays for approximately 12 minutes. Shorter video excerpts show examples of how to search and navigate within the online NZF, how monographs are laid out and how to use the interactions function for best results.

Before viewing the tutorial video, ensure there is a video player programme installed on the computer/device you are using. The video can be expanded to fill the screen by clicking on the white arrows 🔄 at the top right corner of the black side bar strip.

The “Guidance on medicines use” section at the front of the formulary is also explained in the tutorial. This section contains expert-reviewed, general and specialised information under headings such as:

- Drugs in sport
- Excipients
- Māori health
- Drugs and driving
- Prescribing in dental practice
- Prescribing in hepatic impairment

Links to websites of New Zealand healthcare groups and professional organisations, and regulatory websites also appear in this section and throughout the NZF.

The section titled “Calculators” enables you to enter specific patient information to calculate body mass index, body surface area, creatinine clearance, height conversion (feet to metres) and pregnancy due dates.

**Presentation slides for users**

The NZF tutorial slide show presents the main features of the NZF website in a format that can be viewed at the users own pace with simple, clear instructions.
Frequently Asked Questions

A look at “Frequently asked questions” is a quick way of learning about some very useful features of the NZF, e.g. how to install the NZF icon on your MedTech Toolbar.

A commonly asked question is: When will there be an NZF app? The NZF team are currently investigating the development of an iPhone/iPad and android portable application.

In the meantime, the NZF eBook can be used on mobile devices. An eBook can be downloaded from the opening page of the NZF website. It is important to register to receive notifications of e-book updates.

Internet Explorer Compatibility

Some issues with display of the left hand navigation menu have been reported for older Internet Explorer browsers. This issue is being investigated and a solution is being developed. If you are using an IE6, IE7 or IE8 browser and experiencing issues please consider upgrading to a later version of Internet Explorer or an alternative browser such as Firefox or Chrome.

Feedback to the NZF

Feedback is monitored daily and all suggestions for changes and improvements to the NZF are considered by the production team. This includes both technological and content enhancements.

Continued feedback is welcome; use the “Feedback” tab alongside the “Search” and “Browse” tabs at the top of each page of the online version of NZ. Include a contact email address to ensure you receive a personal reply.

The bestpractice CVD Quick Screen module is designed for speed — only data essential to the Framingham equation is required and much of this can be pre-populated from the PMS. The result — a CVD Risk determined in seconds.

Features include:

- Faster CVD Risk calculation
- Heart Forecast tool integration
- Saves a copy in the PMS
- PPP compliant
- Handles non-fasting bloods

See www.bestpractice.net.nz for more information about this and other bestpractice modules. Simply click the “All about modules” link on the Features tab.
CORRESPONDENCE

Recommended ceftriaxone dose for gonorrhoea now 500 mg IM stat

Dear Editor,

I am writing regarding the treatment guideline for gonorrhoea which you recommend as ceftriaxone 250 mg stat (“Antibiotic choices for common infections”, bpac® 2011). Best practice guidelines on the Sexual Health Society website recommend ceftriaxone 500 mg. This was reiterated by doctors from Auckland Sexual Health, at a recent conference. I understand that 250 mg is acceptable but we mostly use 1 g vials, so it is easier and more accurate to reduce by half to 500 mg.

Jody Macdonald, Clinical Nurse Specialist
Palmerston North

The New Zealand Sexual Health Society has recently changed its recommendation for gonorrhoea treatment from 250 mg ceftriaxone IM stat (in 2009),¹ to 500mg IM stat (in 2012),² given with azithromycin 1 g stat to cover concurrent chlamydia infection. This increase in dose has been recommended to overcome emerging resistance of *Neisseria gonorrhoeae* to cephalosporins.³ It should be noted that 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.⁴ Ceftriaxone is available in 500 mg and 1 g formulations for injection.

There is an update of recommendations for the treatment of sexual health conditions scheduled for Best Practice Journal in 2013. This will include the following recommendations where ceftriaxone is part of the treatment regimen:

- **Gonorrhoea – ceftriaxone 500 mg IM, stat + azithromycin 1 g stat**
- **Pelvic inflammatory disease – ceftriaxone 500 mg IM, stat + doxycycline 100 mg, twice daily, for two weeks (or azithromycin 1 g stat, repeated in seven days) + metronidazole 400 mg, twice daily, for two weeks**
- **Acute non-specific urethritis (with purulent discharge) - ceftriaxone 500 mg IM, stat + azithromycin 1 g stat**
- **Epididymo-orchitis (STI pathogens suspected) - ceftriaxone 500 mg IM, stat + doxycycline 100 mg, twice daily, for at least two weeks**

References


The role of digital rectal examination in prostate cancer follow-up

Dear Editor,

I am a little confused over a point made in your latest Best Tests (Oct, 2012). I am sure I heard Dr Costello tell us on several occasions at the GP CME conference in Dunedin in August 2012, that 6 – 12 monthly DRE was still necessary in prostate cancer follow-up, no matter what the grade as there is a risk of the cancer undifferentiating which makes PSA unreliable.

Dr Phil White, General Practitioner
Dunedin

Dr Costello provided expert guidance in the development of our article: “Following up prostate cancer in primary care”, Best Tests (Oct, 2012). Most guidelines recommend that routine digital rectal examination (DRE) is generally not necessary in men where regular PSA testing indicates no change from baseline (but would be indicated if change occurred). DRE is not very useful after radical prostatectomy because early local recurrence is not usually able to be felt. After radical radiotherapy, it may be difficult to distinguish between scar tissue and residual or recurrent cancer. Therefore, DRE is regarded as being of limited clinical value in these situations. The exception is in men who have had high grade prostate cancers, i.e. Gleasons 9 and 10, where DRE may be of more value as PSA may not be representative. This is an area of some disagreement, however, and guidelines do vary.
There is some evidence that adding DRE to regular PSA testing for a small subset of patients with poorly differentiated, high Gleason score prostate cancers may reduce prostate cancer related death. Routine DRE is not, however, necessary as part of follow up in all men with prostate cancer. It is recognised that poorly differentiated prostate cells leak PSA at a lower rate than well differentiated cancer cells. De-differentiation (the change of cancer cells to a poorly differentiated state) may lead to a slower rise in PSA level than the disease level might indicate. There have been cases studies illustrating the progression to metastatic disease without an elevation in PSA level. It is estimated that the incidence of developing metastatic prostate cancer following radical prostatectomy, without a rise in PSA, is of the order of 2.3 – 2.6%. It is also recognised that small cell prostatic cancer is not associated with PSA expression.

It should be noted that there is a small potential for radical radiotherapy to induce rectal cancer after a period of years, therefore, there should be increased vigilance for this.

New Zealand-specific guidelines are likely to be produced soon as the Prostate Cancer Taskforce has now released a working consultation document, so recommendations may change in the future.

ACKNOWLEDGEMENT: Thank you to Dr Shaun Costello, Radiation Oncologist, Clinical Director Southern Cancer Network for expert guidance in developing this response.

References
1. Hattangadi J, Chen M, D’Amico A. Early detection of high-grade prostate cancer using digital rectal examination (DRE) in men with a prostate-specific antigen level of <2.5 ng/mL and the risk of death. BJU Int 2012;[Epub ahead of print].

Heterophile antibody vs EBV serology testing for glandular fever: Best Tests (Oct 2012)

Dear Editor,
A few months ago I was advised by the local lab not to order Paul-Bunnell or Monospot, i.e. heterophile antibodies, to aid glandular fever diagnosis because of its inaccuracy and they advised EBV serology instead. I am pretty certain there were no particular features about the patient in question.

Dr Phil White, General Practitioner Dunedin

Firstly, if the patient has clear clinical features suggesting glandular fever, and no other complications, testing may not be necessary at all.

Heterophile antibody testing, most commonly with the Monospot test, is highly accurate in a person with symptomatic, suspected glandular fever when interpreted in conjunction with a full blood count. In a typical, symptomatic patient, heterophile antibodies have a high sensitivity and specificity. The exception to this is in the first week of illness; if the patient has only recently developed symptoms then the sensitivity is lower and false-negatives will occur in approximately 25% of people. In this case EBV serology may be more appropriate. In addition, false-positives can occur in people with other conditions, such as HIV.

When taken in the context of the atypical antibody film from the full blood count, the results of a Monospot are sufficiently accurate for most immunocompetent people (excluding pregnant women and young children). As glandular fever is not a notifiable disease, is generally uncomplicated and has a life-time prevalence of 90%, more accurate testing (i.e. EBV serology) is probably not necessary.

That being said, laboratories are not standardised across New Zealand and individual requirements and recommendations differ. While New Zealand and international guidance would indicate that heterophile testing plus atypical antibodies is sufficient, if your local laboratory requires EBV serology, it is best to adhere to their recommendations.