

Symptoms 1 - Pain
Module - 3
Facilitator Guidelines

General Points

- The modules have been developed for presentation by facilitator(s) who are acute hospital-based clinicians, though not necessarily practicing specialist palliative care.
- The modules have been designed as a group (of six), though are independent of each other and can be delivered individually, or out of sequence.
- The target audience is junior medical staff, post graduate years 2-4 of all training streams.
- It is envisaged that each module will take about an hour in total (including discussion time).
- Technical requirements include a computer and data projector, able to run PowerPoint. It is suggested that pre-reading be distributed, electronically or by hard copy prior to the presentation.
- It is hoped that the presentation will stimulate discussion amongst the group and sharing of clinical experiences. Appropriate facilitation and management of these discussions is an essential role of the facilitator.
- The presentations aim to enable attainment of the objectives outlined below.
- There is an accompanying evaluation form, based on the stated objectives.
- It is recommended that facilitators familiarise themselves with the material prior to presenting it and contact the authors or local palliative care consult service with any questions.

Module Summary

Unrelieved pain at the end of life is not only widely feared, but is an unfortunately an all too common reality. It is also usually easily managed by relatively simple techniques, which can be readily employed by non-specialists. It is the lack of knowledge and skills about the assessment and treatment of pain, which this module aims to address.

Objectives

Knowledge:

- Build on methods of pain classification and assessment, particularly using a ‘mechanistic framework’ to guide description and management.
- Consider the opioid myths and be aware of the evidence dispelling them.
- Prescribe opioids safely and effectively, particularly with:
 - awareness of side effects (including withdrawal)
 - appropriate choice of drug, route and calculation of dose equivalents
- List (non-opioid) co-analgesic drug classes, and be aware of their role and which have utility for certain mechanisms of pain.
- Be aware of the utility of non-drug options.
- Understand the distinction between cancer pain and non-malignant chronic pain and the need for a different approach.
- Recognise what may constitute ‘difficult’ pain and know when and how to refer for specialist advice and involvement.
- Be aware of opioid induced neurotoxicity and have a basic approach to its management.

Attitudes:

- Appreciate the immense burden and suffering of severe pain and approach the management of the patient and family with compassion, respect and professionalism.

Skills:

- Use a mechanistic model of pain assessment and management.
- Prescribe drugs appropriately and safely for the management of most cancer pain, with clear guidelines for when referral for specialist input is required.
- Be able to communicate with patients and their families about opioid myths, providing evidence to reassure where appropriate and ensure good analgesia and compliance with management.

Pre-Reading

- Forbes K and Huxtable R **Clarifying the data on double effect** *Palliative Medicine* 2006;20(4):395-6 (see attached)

Handouts

- Calvary Healthcare Bethlehem **Opioid Conversion Chart** 2007 Available from URL: <http://www.bethlehem.org.au/OpioidConversionChart2007.pdf> (see attached)

PowerPoint Presentation - notes

SLIDE 1

SLIDE 2

- Everyone will be familiar with the international association for the study of pain definition.
- Pain is a complex experience, and even this well researched and long-considered definition has shortcomings.
- In its defence it does acknowledge that pain is both a sensory but also very much an emotional experience. The final sentence is also critical.

SLIDE 3

- While it is not the intention to become bogged down in definition, there are many other thoughts about pain that affect our patients' experience and our clinical management of their pain.
- Dame Cicely Saunders, the founder of the hospice movement, at a similar time to the development of the IASP definition stressed the multi-dimensional nature of pain, well beyond the mere physicality. She used pain figuratively such as when she noted that "mental distress may perhaps be the most intractable pain of all", emphasising the link between mental suffering and pain. She also developed a concept of 'total pain' that came to include the entire illness: physical symptoms, mental distress, social problems, and spiritual needs.
- This use of the term 'pain' is understandably problematic for some, with confusion about whether 'total pain' refers to pain or other forms of suffering. For this reason, the term 'total suffering' is used in this pictorial representation though this should not detract from the concept.
- These factors are clinically relevant to our care of suffering patients, as they may reinforce or exacerbate pain, or indeed be the primary cause of pain and suffering.

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- Cancer pain is not surprisingly the best studied and therefore provides us with much of our knowledge about pain at the end of life.
- The prevalence of pain in this population has remained fairly static over many decades, despite new systemic opiates and advances in directed cancer therapies.
- Despite recognition of its importance, as the '5th vital sign' it is very much under recognised and undertreated.
- This data is from Cleeland and colleagues (published in NEJM) who undertook a survey of patients with metastatic cancer attending specialist out patient clinics

SLIDE 5

- Our main focus is the 80-90% that can be managed through relatively simple means. An awareness and approach to the 'difficult' and 'intractable' is also important, particularly in acute hospital practice.

SLIDE 6

- So far, it seems pain at the end of life can mostly be managed with relatively simple techniques, yet we are failing to do so.
- Sun and colleagues tried to establish the barriers in their survey of 83 medical oncology outpatients with moderate to severe pain.
- Patient barriers are perhaps not surprising, except perhaps the last item: which was more specifically a fear of distracting their doctors from cancer-specific

treatment (this was a firmly held belief of those having chemotherapy). This would hopefully be very much contrary to our views, which would value good symptom control during disease specific treatment.

- The professional barriers are highlighted, since they are our main focus and the reason we are here. The most startling amongst this list is the failure to assess the patient's pain, in study only 7.8% were asked about pain despite having cancer diagnoses and qualifying for the study because of moderate to severe pain.

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- Once recognising that pain is present, the most essential principle is to make thorough assessment. This cannot be over emphasised and should involve a detailed history, examination and usually investigations.
- Each pain should be assessed separately and thoroughly with thought given to the mechanisms causing the pain.
- This will then guide 'type specific treatment'.
- Reassessment is another essential principle, and includes reassessment of the patient as a whole, the pain(s) and the management approach.

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- These are the basic pain questions and should be familiar to you all.

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- The last point requires particular mention.

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- The basic pain questions suggest looking for 'intercurrent stressors' or 'other factors' affecting the pain response. We have already spoken about the many factors that connect pain and suffering, most particularly in patients with chronic pain.
- Therefore consideration of psychological influences on the pain experience for an individual is essential.
- I am sure we all have patient examples that reflect each of these and led to a very different pain experience for the individual patient.
- Certainly exploring the patients perceived meaning of the pain is valuable and often therapeutic, such as explaining that the pain is post thoracotomy neuralgia rather than recurrent disease.

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- It is important however to be careful and remember that our assessment of a patients psychological state is also greatly influenced by the pain experience. While these factors should be noted in our assessment, it is essential to reassess their influence after our thorough assessment and most importantly successful management of the pain.
- Not only is it essential to our therapeutic relationship, but even the IASP definition recognises that pain is subjective, so always believe the patient.

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- The aim of our thorough assessment is to categorise the pain. This allows us to:
 - Communicate with the patient
 - Communicate with colleagues
 - Clearly document, often multiple pains
 - Consider the mechanism, which will guide examination and investigation and ultimately treatment

- Temporal categorisation is important, particularly in the non-malignant setting. In the absence of malignancy (which usually has both) acute pain is usually self-limited and responds to treatment with management of the precipitant and analgesia. This contrasts with chronic pain, which is associated with adaptation of the autonomic nervous system and significant changes in personality, lifestyle and function. Chronic pain needs to be identified because it requires a very different approach.
- The neurophysiologic categorisation is also helpful and we will discuss their clinical utility in more detail.

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- This list is by no means exhaustive, but gives some examples to help you use the categories.
- Nociceptor activation occurs in cutaneous and deep musculoskeletal tissues.
- Visceral pain from infiltration, compression, distension or stretching of thoracic and abdominal viscera.

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- Neuropathic pain is from tumour compression or infiltration, usually of the peripheral nerves or spinal cord. Surgery, radiotherapy and chemotherapy are also important causes of neuropathic pain.
- There is no universally accepted pain classification measure, which can accurately predict the complexity of pain management, particularly for patients with cancer pain that is difficult to treat. In an effort to address this gap a group in Edmonton developed, through various revisions the Edmonton Classification System – Cancer Pain (ECS-CP). *The complete tool is available for further reading (in the references section of these notes, Fasinger et al. 2006).*

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- Non-opioid analgesics include paracetamol and NSAIDs
- Adjuvant analgesics are drugs that have primary indications other than pain. The term can be a little misleading, since they can be used alone (not adjuvant to any other therapy).
- The term, ‘co-analgesics’ is often used synonymously, but relates more specifically to drugs that are co-administered with a primary analgesic to:
 - Enhance analgesia
 - Treat pain refractory to the primary analgesic
 - Allow reduction of the primary analgesic to limit side effects
- Adjuvants will be discussed in more detail.

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- The more complex the pain, the more important to approach management in a multidimensional and integrated fashion.

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- Opioids are the cornerstone of analgesia in palliative medicine, and therefore will be discussed first.
- Opioid myths, as we have discussed are barriers to good pain relief at the end of the life, both at the level of patients but also health professionals. Therefore dispelling opioid myths is an essential task for us, and indeed a vital therapeutic task.

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- Morita and colleagues performed a well-designed study, which is one of many dispelling this very common myth. Indeed the safety of morphine is so well established, that it is hardly ever used where euthanasia is legal.
- Concerns about addiction are usually more prevalent in our patients, but this large study suggests that this too is a myth.

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- This first myth is again often a concern of our patients, and should be reassured. Opioids are used by the living and good analgesia equates to better function and quality of life.
- Opioids are poor sedatives and should not be used for this purpose. Warning patients of an initial but self-limiting increase in drowsiness on initiation or dose escalation may be appropriate.
- This leads to the issue of driving. This myth, particularly when it is an unacknowledged fear is very significant as quality of life and driving are very much interlinked. Because of the initial sedative effects, driving should be avoided at initiation or dose escalation, but can be resumed once patient and doctor are satisfied these effects have worn off. There have been several studies supporting this advice, including that of Vainio and colleagues published in the Lancet of cancer patients on long-term stable morphine therapy that showed the effects on driving were minimal.
- Opioids can cause nausea through central and peripheral mechanisms. However it is by no means universal, usually transitory and easily controlled. Indeed the routine administration of an anti-emetic is not necessary (though patients should be informed and aware of how to access them). The exception is patients with a history of severe opioid induced nausea and vomiting.

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- Opioids can be safely used in the elderly, following the usual principles. In fact there is evidence (Auret and Shug) that opioids are underutilised in this group and as a consequence there is unnecessary disability and poor quality of life.
- There are many preparations and assuming an intact gastrointestinal system, no reason for choosing injectable opioids over oral preparations.
- Codeine is much less potent than morphine, is poorly orally bioavailable and has only weak analgesic effects; this is compounded by the prevalence of poor metabolisers who are unable to transform it to morphine (the active compound). Consequently it is a poor analgesic option, though has excellent constipating effects, which are probably its main use. For this reason, the old-fashioned panadol/panadeine/panadeine forte analgesia is not appropriate.

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- Now we are comfortable with opioids, we need to choose one. There are an ever increasing variety of preparations available, so what is needed is some familiarity with the basic options and an awareness that others exist for more complex situations
- Obviously, as with any drug choice, take into consideration previous experience and effects (good and bad).
- There are also some concerns about co-existing diseases and particularly renal failure and morphine in particular. While there are no clear guidelines, it is generally agreed that 'prn' doses are fine, though if a long

acting preparation is required an alternative is preferable. This would be worth discussing with the palliative care team on a case-by-case basis.

- The major factor is often the preparation...

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- There are many different preparations. Intentionally no trade names have been used, but these add to the complexity. Certainly when you are unfamiliar it is worth checking that the trade name is actually the preparation you are expecting.
- Those that you are probably prescribing regularly, and should be familiar with, are:
 - Morphine: ms (morphine sulfate) contin SR, is the long acting preparation, morphine mixture (ordine) is the short acting preparation most commonly used as break through / rescue.
 - Oxycodone: is a semi-synthetic opioid. Oxycontin SR, is the long acting preparation, endone or oxynorm are the trade names for the short acting preparations.
- Note that morphine and oxycodone are actually different opioids, and if you refer to your conversion charts, despite popular opinion are not interchangeable and actually not equal in potency.
- Others to be aware of are:
 - Buprenorphine patches, the trade name is norspan and they are a 7 day patch, marketed to general practice and increasing in their prevalence, particularly in the elderly with osteoarthritis. It should be noted that their place in the treatment of cancer pain is very limited.
 - Fentanyl patches, trade name durogesic, are 3 day patches more appropriate for cancer pain. The main errors in their usage relate to inappropriate titration (refer to your conversion charts) and inappropriate breakthroughs. The later is either because of inappropriate dose, largely relating to a lack of familiarity, or inappropriate drug. The later because generally fentanyl is not a good breakthrough drug (lipophilic, short duration of action).
 - Hydromorphone has a similar chemical structure to morphine, but is five times more potent. This can be useful for patients on high doses, particularly parenterally.
 - Methadone is very useful in palliative care and the management of difficult pain syndromes. It has complex pharmacokinetics; and commencement and titration should be undertaken by clinicians experienced with its use, usually in conjunction with the palliative care service.
 - Pethidine is not mentioned, as it has essentially no role in chronic cancer pain.
- Care needs to be taken with rotating between preparations with different pharmacokinetics. Equally an understanding of the transdermal system is important when starting patches de novo, because there is a significant delay in analgesia that makes them inappropriate for unstable pain and patients need to be warned and have alternatives available.

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- In hospital, often a parenteral option for breakthroughs is desirable; again a number of different opioids are available. Ideally, and where possible the

same opioid should be used, to ease titration and clarify any issues about side effects or intolerance.

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- An example that is very common around the hospital, have a go and refer to your conversion chart.

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- Subcutaneous oxycodone, while available is not readily so (depending on your hospital). Equally morphine is less expensive, far more familiar on the wards and therefore a better choice. True allergy is extremely rare, so get a detailed history and discuss the case with a senior or the palliative care service before embarking on a complex rotation to an opioid ward staff will be less comfortable with.
- Oxycodone is about 50% more potent than morphine, so that converting a total daily dose of oral oxycodone 60mg, is the equivalent of 90mg of oral morphine. To then convert to subcutaneous morphine, a factor of 2 or 3 is used, while both are reasonable, Mary's pain has been stable and so the more conservative figure is probably better.
- Ensuring clear instructions and adequate breakthroughs is essential.

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- Consideration of route is essential; if the patient cannot absorb it they won't have good pain control.
- Commencing in an opioid naïve patient, the safest option is to prescribe a short acting preparation and review in a day or two. Using the average 24 hour usage an appropriate long acting dose can be commenced. Errors come with lack of familiarity and failing to reference conversions –
 - eg. a doctor from St. Elsewhere's commences a 25mcg/hr fentanyl patch in an elderly opioid naïve patient. They present sedated and delirious 12 hours later. What dose, in oral morphine equivalent was prescribed?
 - Answer = 60mg / 24 hours (a huge starting dose, even for a young person!)
- The myths need to be actively dispelled and the patient and family engaged and willing. If not, they won't take the drug and won't have their pain relieved.

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- Warning about adverse events, particularly self-limiting ones, is important to ensure compliance (and that if the drug doesn't suit an alternative is found in a timely fashion).
- Remind yourself, and the patient, that overdose is extremely rare, though very avoidable with careful and thoughtful prescribing and patient education.

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- A useful concept to illustrate this important point about opioid safety and dosing, is the (familiar) notion of therapeutic range.
- Below the therapeutic range is ineffective dosing, with ineffective symptom management, which we clearly want to avoid.
- Above the therapeutic range is toxicity, and for opioids, as with most other drugs, there are predictable dose related side effects. Such as those we warn patients about and 'look out for' when commencing or adjusting the

dose. For instance mild cognitive effects, such as inattention, and then delirium will occur relatively early within this toxic range and are useful warning signs. They occur well before any (of the extremely rare) life threatening side effects such as respiratory depression, and therefore allow us to review the drug and its' dosing early. In this way we can be reassured that with careful monitoring and proportional dose adjustment opioids are safe and effective.

- This concept of therapeutic range is identical to that for many drugs which we use everyday, albeit with caution and knowledge.

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- We have already defined adjuvants or co-analgesics
- Opioids should be first line and other drugs should only be added once opioid therapy is optimised
 - ie. further escalation is not effective or limited by side effects

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- If despite your assessment (and reassessment) and employing the strategies we have discussed, the pain persists you might be dealing with the 10-20% of 'difficult' cancer pain
- 'Difficult' pain is very rarely an 'all or nothing effect' - hence the terminology 'poorly responsive' versus 'resistant'.
- Opioid irrelevant pain describes pain that is of a mechanism not expected to be responsive, eg. psychological distress

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- These are some examples; neuropathic pain is highlighted because it is the prototype of these 'difficult pains'.

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- Persistent or poorly controlled pain should prompt a thorough reassessment
- We will discuss factors influencing opioid responsiveness in more detail in the following slide.
- The benefits of involving others, particularly the multi-disciplinary team and possible the palliative care service, early, cannot be over emphasised.

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- This list should serve as 'red flags' during your assessment of a patients' pain and are particularly useful to reconsider if pain fails to respond.
- The type of pain is very important, particularly the mechanism. We know that neuropathic pain can be particularly unresponsive, though not inherently resistant (so opioid titration should always be tried).
- Transitory pains, such as that of bony metastases on movement, can be 'difficult' because the dose of opioid required to control the episodes may lead to unacceptable side effects at rest.
- Tolerance describes dose escalation in the absence of any other causes (eg progressive disease).
- Progression of disease is an important and not to be missed reason for poorly responsive pain. Equally if pain is managed by another treatment, eg. radiotherapy, nerve block, patients can experience serious side effects if their opioids are not adjusted expectantly.

- Individual factors are clearly very important as we discussed earlier, since the experience of pain is complex and has affective dimension. Screening for psychological distress, and particularly anxiety, depression and delirium is very important.
- Morphine metabolites are an area receiving increasing attention. While morphine-6-glucuronide is thought to contribute to the analgesic effect, M3G is thought to be less helpful. While there is some contention, M3G is thought to functionally antagonise the analgesic effects of morphine, and contribute to opioid induced hyperalgesia.
- The route of administration is very important, for the obvious concerns about absorption and compliance we have already discussed. There is also some data suggesting that metabolite accumulation varies with the route, which has led to some experts to consider alternative routes in selected patients.

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- Approaches include adjuvant agents, as we have discussed
- Another strategy is to aggressively manage side effects to open the therapeutic window and allow more effective opioid doses.
- Drugs that enhance opioid analgesia, such as NMDA antagonists (ketamine) would require specialist referral.
- Switching the opioid and/or the route may be helpful, again choice of opioid and the mechanics of rotating may well best be managed with specialist referral
- Other measures and treatments should be considered, hence the benefits of early referral to specialist services and the multi-disciplinary team. Often all these approaches are worked on in series or concurrently.

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- This syndrome has been long recognised, indeed in 1880 Rosbach wrote, “when dependence on opioids finally becomes an illness of itself, opposite effects like restlessness, sleep disturbance, hyperesthesia, neuralgia and irritability become manifest.”
- While we are loathe to create fear (and perhaps even another myth) about opioids, this syndrome does exist and an awareness of it is important.

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- Rotating to another opioid is a well-established, safe and reliable technique to decrease neurotoxicity while maintaining analgesia. There is no ‘ideal’ or particular opioid to switch too, though methadone finds ever-increasing favour.
- While there is evidence that dose reduction/discontinuation works (proving causality) it is rarely practical in patients with advanced cancer.
- The active metabolites of morphine are water soluble, therefore accumulating in patients with renal failure or volume depletion. This can mean a difficult balance, particularly in terminal care. Bruera and colleagues found that a policy of hydration (usually 1-1.5 L subcutaneously daily) resulted in rapid decreases in the level of sedation, and myoclonus and a trend toward a decreased level of hallucinations.
- After opioid rotation, approximately 10% will continue to suffer significant sedation. Obviously psychostimulants (eg. Methylphenidate) can promote hallucinations, delirium or psychosis and so should be used with care and caution in this population.

- Neuroleptics such as haloperidol are useful for the symptomatic management, specifically of agitated delirium and hallucinations. Other medications such as baclofen, benzodiazepines and barbiturates have a role in managing the myoclonus. Care should be taken with benzodiazepines, which are known to worsen delirium.
- Seeking advice is important, and this would be a very appropriate reason to refer to the palliative care team.
- Prevention is as always our ideal. Again the concept of a thorough 'multidimensional' pain assessment is reinforced, so that all the factors contributing to the pain are considered and addressed, therefore reducing the potential for 'overtreatment'. Equally though we must not become unduly paranoid and remember the figures presented at the beginning, that we largely under-recognise and under treat pain in this population.
- Delirium is very common, affecting up to 80% of people near death. It is often a missed diagnosis and can be mistaken for increased pain and suffering. This leads to escalation of opioids, often with worsening symptoms. MMSE and MDAS (memorial delirium assessment scale) are useful tools, but a high index of suspicion is essential. Reversible causes are only present in about 50% of terminally ill patients, though consideration and assessment are important so as to allow appropriate symptomatic and pharmacological treatment.
- The main drug interaction is benzodiazepines.
- Neuropathic pain, as we know, is an independent predictor of poor pain control, but also necessitates the use of adjuvants, many of which have neurotoxic side effects. Incident pain is another poor predictor, as we have discussed, and a problem because the doses required to maintain comfort at rest are insufficient on movement, and with escalation side effects are likely.
- Substance abuse suggests maladaptive coping strategies, which often leads to worsening expression of symptomatology, which may be misinterpreted as nociception.
- A thorough assessment (and reassessment) should help avoid escalation, particularly while focussing on other non-drug options for management.

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- The 'take home' messages.

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