

Cancer Care Ontario

Action Cancer Ontario

**Symptom
Management
Pocket Guides:**

DELIRIUM

August 2010

DYSPNEA NAUSEA & VOMITING PAIN

August 2010



Ontario
Cancer Care Ontario

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Considerations

- The underlying etiology needs to be identified in order to intervene.

- Delirium may interfere with the patient's ability to report other symptom experiences.
- Provide explanation and reassure the family that the symptoms of delirium will fluctuate, are caused by the illness, are not within the patient's control, and the patient is not going 'insane'.
- Some hallucinations, nightmares, and misperceptions may reflect unresolved fears, anxiety or spiritual passage.
- Include the family in decision making, emphasizing the shared goals of care; support caregivers.

- Correct reversible factors – infection, constipation, pain, withdrawal, drug toxicity.
- Review medications; consider opioid rotation to reverse opioid neurotoxicity; discontinue unnecessary drugs or prolong dosing interval for necessary drugs.
 - Anticipate the need to change treatment options if agitation develops, particularly in cases where patient, family and staff safety may become threatened.
 - Misinterpreting symptoms of agitation/ restlessness, moaning and/or grimacing as poorly controlled pain, with subsequent

administration of more opioids, can potentially aggravate the symptom and cause opioid neurotoxicity.

Assessment

- Ongoing comprehensive assessment is the foundation of effective management of delirium and restlessness including interview, physical assessment, medication review, medical and surgical review, psychosocial review, review of physical environment and appropriate diagnostics.

- Delirium may interfere with optimal pain and symptom expression (self-reporting), assessment and management.
- In situations where a patient is not able to complete an assessment by self reporting, then the health professional and/or the caregiver may act as a surrogate.

Diagnosis

- Identifying the underlying etiology of the delirium or restlessness is essential in determining the interventions required.

- The causes of delirium are usually multi-factorial (See table below, adapted from Capital Health).
- Determining the underlying etiology, education/reassuring the patient/family and treating the symptoms should occur simultaneously.

D	Drugs, drugs, drugs, dehydration, depression
E	Electrolyte, endocrine dysfunction (thyroid, adrenal), ETOH (alcohol) and/or drug use, abuse or withdrawal
L	Liver failure
I	Infection (urinary tract infection, pneumonia, sepsis)
R	Respiratory problems (hypoxia), retention of urine or stool (constipation)
I	Increased intracranial pressure;
U	Uremia (renal failure), under treated pain
M	Metabolic disease, metastasis to brain, medication errors/omissions, malnutrition (thiamine, folate or B12 deficiency)

Non-Pharmacological Treatment

- Report hallucinations that become threatening.
- Instruct the family to provide gentle, repeated reassurance and avoid arguing with the patient.
- Watch for the “sun downing” effect (nocturnal confusion) , as it may be the first symptom of early delirium.
- Provide a calm, quiet environment and help the patient reorient to time, place and person (visible clock,

calendar, well known or familiar objects).

- Presence of a well known family member is preferred.
- Provide a well lit, quiet environment. Provide night light.
- To prevent over-stimulation, keep visitors to a minimum, and minimize staff changes and room changes.
- Correct reversible factors – dehydration, nutrition, alteration in visual or auditory acuity (provide aids), sleep deprivation.
- Avoid the use of physical restraints and other

impediments to ambulation.
Avoid catheterization unless urinary retention is present.

- Encourage activity if patient is physically able.
- When mildly restless provide observation and relaxation techniques (massage, tub baths, gentle music) as applicable.
- Encourage the family to be present in a calming way.

Pharmacological Treatment

- Review medications; consider opioid rotation to reverse opioid neurotoxicity
- Consider psychotropic drugs for patients developing “sun downing” effect (confusion in the evening).
- Anticipate the need to change treatment options if agitation develops – particularly in cases where patient, family and staff safety may become threatened.
- Benzodiazepines may paradoxically excite some patients and should be avoided unless the source of delirium is alcohol or sedative drug

- withdrawal, or when severe agitation is not controlled by the neuroleptic.
- If patient has known or suspected brain metastases a trial of corticosteroids is worthwhile.
 - Dexamethasone 16 - 32 mg po daily in the morning may be used (*Suggestion is based on expert opinion and doses may vary from region to region*).
 - Misinterpreting symptoms of agitation/ restlessness, moaning and/or grimacing as poorly controlled pain, with subsequent administration of more opioids, can potentially aggravate the symptom and cause opioid neurotoxicity.
 - Titrate starting dose to optimal effect.

Mild Delirium

- Orient patient as per non-pharmacological recommendations.

Pharmacological

- Haloperidol is the gold standard for management of delirium.
- If titration with haloperidol is not effective consider using methotrimeprazine.
- Haloperidol 0.5-1 mg po / subcut bid-tid
- Alternate agents:
 - Risperidone 0.5-1 mg po bid
 - Olanzapine 2.5–15 mg po daily

- Quetiapine fumarate 50-100 mg po bid
- Methotrimeprazine 5-12.5 mg po OR 6.25-12.5 mg subcut q4-6h prn
- Chlorpromazine 25-50 mg po q4-6h prn

Moderate Delirium

Pharmacological

- Haloperidol 0.5-2 mg subcut q1h prn until episode under control; may require a starting dose of 5 mg subcut
- Alternate agents:

- Risperidone 0.5-1 mg po bid
- Olanzapine 2.5-15 mg po daily
- Quetiapine fumarate 50-100 mg po bid
- Benzodiazepines may paradoxically excite some patients and should be avoided unless the source of delirium is alcohol or sedative drug withdrawal, or when severe agitation is not controlled by the neuroleptic

Severe Delirium

- Titrate starting dose(s) to optimal effect.

- If agitation is refractory to high doses of neuroleptics, (as outlined in moderate delirium) consider adding lorazepam
0.5-2 mg subcut q4-6h prn or midazolam
2.5-5 mg subcut q1-2h prn in conjunction with the neuroleptic.

Alternate agents to consider:

- Methotrimeprazine 12.5–25 mg subcut q8-12h and q1h prn OR
- Chlorpromazine 25-50 mg po/subcut q4-6h prn.
- If above not effective consider:
 - Haloperidol 10 mg subcut.
Typically, in palliative care the

maximum dose of haloperidol
is 20 mg/day OR

- Methotrimeprazine 25-50 mg
subcut
q6-8h and q1h prn.

Adverse Effects of Medications Used to Treat Delirium

- Extrapiramidal side effects (EPS)
are common adverse events of
neuroleptics, with the newer
atypical neuroleptics having a
lower risk of EPS than the older
typical neuroleptics.
- Potentially all dopamine
antagonists can cause EPS, to

varying degrees, due to the D2 central antagonist actions.

- Manifestations of EPS are usually dose dependent. Extrapyrimal side effects may include: acute dystonia, akathisia, and Parkinson-like signs/symptoms.
- Akathisia and acute dystonias tend to resolve with discontinuation of the offending drug.
- For the treatment of mild cases one should consider discontinuation of the drug or switching to a less antidopaminergic agent if possible.
- If pharmacologic management is needed, then consider benztropine

(1st line) 1-2 mg po/subcut bid (or 2mg IM/IV for acute dystonic reactions). Alternative medications include biperiden 2 mg po bid or diphenhydramine 25-50 mg po/subcut bid to qid (or 25-50 mg IV/IM for acute dystonia).

Selected References

- 1) Fraser Health. Hospice Palliative Care Program Symptom Guidelines: Delirium/Restlessness. Fraser Health Website, 2006. Accessed: August 2008. Available from:
<http://www.fraserhealth.ca/media/07FHSymptomGuidelinesDelirium.pdf>
- 2) Common Questions by Capital Health, Regional Palliative Care Program Edmonton, 3rd Edition, 2006, Pg. 60.
- 3) Adapted with permission from the National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology Palliative Care. V.2.2011. Website:
http://www.nccn.org/professionals/physician_gls/f_guidelines.asp

For full references and more information please refer to [CCO's Symptom Management Guide-to-Practice: Delirium](#) document.

Disclaimer:

Care has been taken by Cancer Care Ontario's Symptom Management Group in the preparation of the information contained in this pocket guide.

Nonetheless, any person seeking to apply or consult the pocket guide is expected to use independent clinical judgment and skills in the context of individual clinical circumstances or seek out the supervision of a qualified specialist clinician.

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Considerations

- Because dyspnea is subjective, the patient's self report of symptoms should be acknowledged and accepted.
- Identify and treat common exacerbating medical conditions underlying dyspnea or shortness of

breath, e.g. COPD, CHF, pneumonia (link to table in guide).

- Evaluate impact of anxiety and fear on dyspnea and treat appropriately.
- Use **Edmonton Symptom Assessment System (ESAS)** and **Oxygen Cost Diagram (OCD)** (See OCD) to measure outcome.

Non-Pharmacological Treatments

- Ambient air flow can be achieved by opening a window, using a fan,

or administering air through nasal prongs.

- Cool temperatures can be applied to the brow or upper cheek bones by applying a cool cloth or opening a window to let cooler air in.
- A program of **cognitive behavioural interventions** involving the following 6 interventions for a time period of 3 to 8 weeks is recommended:
 - 1) Assessment of breathlessness – what improves and what worsens it
 - 2) Provision of information and support for patients and

- families in the management of breathlessness
- 3) Exploration of the significance of breathlessness with patients, their disease, and their future
 - 4) Instruction on breathing control, relaxation and distraction techniques and breathing exercises
 - 5) Goal setting to enhance breathing and relaxation techniques as well as to enhance function, enable participation in social activities and develop coping skills

- 6) Identification of early signs of problems that need medical or pharmacotherapy intervention

These suggestions should be taught as preventative strategies, when patients are not dyspneic, and regular practice should be encouraged.

Pharmacological Treatments

Mild Dyspnea ESAS 1 to 3

- **Supplemental oxygen is recommended for hypoxic patients experiencing dyspnea.**

- **Supplemental oxygen is not recommended for non-hypoxic, dyspneic patients.**

Non-hypoxic Patients (>90% O₂ saturation)¹

For patients with PPS 100% - 10%:

Use a fan or humidified ambient air via nasal prongs (as per patient preference and availability). This is not covered by the Ontario Ministry of Health and Long-Term Care (MOHLTC)

¹ $\leq 88\%$ oxygen saturation at rest or on exertion is the threshold for MOHLTC approval of funding for home oxygen for palliative care patients beyond 3 months; for some patients $\leq 90\%$ oxygen saturation may be a more appropriate threshold for introducing home oxygen therapy.

- If effective and tolerated, then utilize one or the other.
- If not effective or not tolerated, consider a trial of humidified, supplemental oxygen via nasal prongs – assess benefits over a few days and discontinue if no benefit reported for dyspnea (covered by MOHLTC on the Home Oxygen program for up to 3 months if the “palliative care” indication is used).

Hypoxic Patients ($\leq 90\%$ O_2 saturation at rest or on exertion)

For Patients with PPS 100% - 10%:

Use humidified, supplemental oxygen via nasal prongs, continuously or as-needed, at flow rates between 1 and 7 litres per minute, aiming for oxygen saturations over 90% or improvement in dyspnea at tolerated flow rates.

- Continue this therapy if it is effective at improving dyspnea and is tolerated.
- If dyspnea and low oxygen saturation persist despite maximum-tolerated flow of humidified, oxygen by nasal prongs, consider offering a trial of supplemental oxygen by oxymizer (nasal cannulae with reservoir), ventimask or non-rebreathing mask to deliver a more predictable

fraction of inspired oxygen to the lungs. If this is not tolerated, the patient can return to the best-tolerated flow of humidified oxygen by nasal prongs or discontinue supplemental oxygen altogether.

- **Systemic opioids, by the oral or parenteral routes, can be used to manage dyspnea in advanced cancer patients.**

For patients with PPS 100-10%:

Other pharmacological treatments are not generally needed for patients with mild dyspnea, regardless of their PPS; however, systemic opioids (oral or

parenteral) may be considered if non-pharmacological approaches result in inadequate relief of dyspnea.

- Consider systemic opioids for mild, continuous dyspnea, not for dyspnea that is mild and intermittent (eg. on exertion) since any benefit is limited by the time to onset of effect.
- If systemic opioids are considered, weigh their potential risks and benefits and reassess the severity of the dyspnea and the effect the dyspnea has on the patient's function.
- If the patient is already taking a systemic opioid for another indication, such as pain

- titrate the dose of the same opioid, if it is well-tolerated, to improve the dyspnea
- switch to an alternate opioid, if the current opioid is not tolerated, and titrate it to improve the dyspnea
- If the patient is opioid naïve, introduce an opioid to treat the dyspnea.

Properly titrated, systemic opioids do not produce respiratory depression.

Moderate Dyspnea ESAS 4

to 6

For Patients with PPS 100% - 10%:

Non Opioids

- May use benzodiazepines for anxiety.
- There is no evidence for the use of systemic corticosteroids

Systemic Opioids

For opioid-naïve patients:

- Morphine (or equivalent dose of alternate immediate-release opioid) 5mg po q4h regularly and 2.5mg po q2h PRN for breakthrough dyspnea

- If the oral route is not available or reliable, morphine 3 mg subcut q4h regularly and 1.5 mg subcut q1h PRN for breakthrough dyspnea.

For patients already taking systemic opioids:

- Increase the patient's regular dose by 25%, guided by the total breakthrough doses used in the previous 24 hours
- The breakthrough dose is 10% of the total 24-hour regular opioid dose, using the same opioid by the same route.
 - oral breakthrough doses q2 hrs as needed

- subcutaneous breakthrough doses q1hr as needed, due to more rapid peak effect.
- Do not use nebulized opioids, nebulized furosemide, nebulized lidocaine or benzodiazepines.

For Patients with PPS 100% - 20%

- If patient has or may have COPD, consider a 5-day trial of a corticosteroid
 - Dexamethasone 8 mg/day po or subcut or IV
 - Prednisone 50 mg/day po
 - Discontinue corticosteroid if there is no obvious benefit after 5 days

- If the patient does not have COPD, but has known or suspected lung involvement by the cancer, weigh the risks before commencing a 5-day trial
 - Other potential benefits, such as for appetite stimulation or pain management, may justify a 5-day trial of a corticosteroid
- Do not start prophylactic gastric mucosal protection therapy during a 5-day trial of a corticosteroid, but consider such therapy if the corticosteroid is continued past the trial
- Prochlorperazine is not recommended as a therapy for managing dyspnea.

- No comparative trials are available to support or refute the use of other phenothiazines, such as chlorpromazine and methotrimeprazine.

For Patients with PPS 30% - 10%:

- Consider a trial of chlorpromazine or methotrimeprazine, if dyspnea persists despite other therapies
 - Methotrimeprazine 2.5-10 mg po or subcut q6-8h regularly or as needed
 - Chlorpromazine 7.5-25 mg po q6-8h regularly or as needed
- Anxiety, nausea or agitation, may justify a trial of chlorpromazine or methotrimeprazine

Severe Dyspnea ESAS 7 to 10

For Patients with PPS 100% - 10%:

Systemic Opioids

For opioid-naïve patients:

- Give a subcut bolus of morphine 2.5 mg (or an equivalent dose of an alternate opioid).
 - If tolerated, repeat dose every 30 minutes if needed.
 - Consider doubling dose if 2 doses fail to produce an adequate

reduction in dyspnea and are tolerated

- Monitor the patient's respiratory rate closely, since the time to peak effect of a sc dose of morphine may be longer than 30 minutes
- If intravenous access is available, consider giving an IV bolus of morphine 2.5 mg (or an equivalent dose of an alternate opioid) to achieve a more rapid effect.
 - If tolerated, repeat dose every 30 minutes if needed.
 - Consider doubling dose if 2 doses fail to produce an adequate reduction in dyspnea and are tolerated

- Monitor the patient's respiratory rate closely, since IV boluses of morphine result in faster and higher peak effects.
- Start a regular dose of an immediate-release opioid, guided by the bolus doses used
 - For the breakthrough opioid dose, consider using the subcut route initially for severe dyspnea until the symptom comes under control.

For patients already taking systemic opioids:

- Follow the same suggestions as above for opioid naïve patients, with the following changes.

- Give a subcut bolus of the patient's current opioid using a dose equal to 10% of the regular, 24-hour, parenteral-dose-equivalent of the patient's current opioid (a parenteral dose is equivalent to half the oral dose)
- Consider giving an IV bolus of the patient's current opioid, using a dose equal to 10% of the regular, 24-hour, parenteral-dose-equivalent of the patient's current opioid
- Increase the regular opioid dose by 25%, guided by the bolus doses used

Phenothiazines

- Consider a trial of chlorpromazine or methotrimeprazine, if severe dyspnea persists despite other therapies.
- Methotrimeprazine 2.5-10 mg po or subcut q6-8h regularly or as needed
- Chlorpromazine 7.5-25 mg po or IV q6-8h regularly or as needed
- Consider benzodiazepine for co-existing anxiety

Titration Guide

General principles:

1. Calculate the total opioid dose taken by the patient in 24 h (regular q4h dose x 6 **PLUS** the total number of breakthrough doses given x breakthrough dose).
2. Divide this 24 h total by 6 for the equivalent q4h dose.
3. Divide the newly calculated q4h dose by 2 for the breakthrough dose.
4. Use clinical judgment regarding symptom control as to whether to round up or down the obtained result (both breakthrough and regular dosing). Remember to consider available doses (in the case of PO medications especially).
5. If the patient is very symptomatic, a review of how many breakthrough doses have been given in the past few hours might be more representative of his/her needs.

Example:

A patient is ordered morphine 20 mg q4h PO and 10 mg PO q2h PRN, and has taken 3 breakthrough doses in the past 24 h.

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1. Add up the amount of morphine taken in the past 24 h:
6 x 20 mg of regular dosing, plus 3 x 10 mg PRN doses

Conversion Guide

(To convert from long-acting preparations to short-acting preparations)

General principles in converting from sustained release to immediate release preparations (for the same drug):

1. Add up the total amount of opioid used in the past 24 h, including breakthrough dosing.
2. Divide this total by 6 to obtain equivalent q4h dosing.
3. Divide the q4h dose by 2 to obtain breakthrough dosing.
4. Use clinical judgment to adjust this dose up or down depending on symptom control.
5. Consider available tablet sizes when calculating doses.

Example:

A patient is ordered a sustained release morphine

preparation at a dose of 60 mg PO q12h, with 20 mg PO q4h for breakthrough, and has taken 4 breakthrough doses in 24 h.

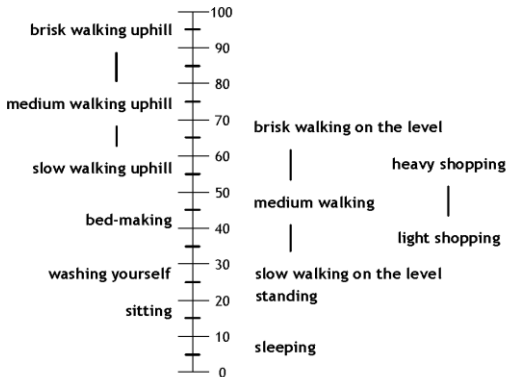
1. Add up the amount of opioid taken in 24 h: 2 x 60 mg of sustained release morphine plus 4 x 20 mg of breakthrough is 200 mg of morphine in 24 h
2. Divide this total by 6 to obtain the equivalent q4h dosing: 200 divided by 6 is approximately 33 mg PO q4h
3. Divide this q4h dose by 2 for the breakthrough dose 33 mg divided by 2 is 16.5 mg

If the patient had reasonable symptom control with the previous regimen, then a reasonable order would be: 30 mg PO q4h and 15 mg q1 - 2h PO PRN

Oxygen Cost Diagram (OCD)

The *Oxygen Cost Diagram* is a 100 mm vertical lines along which every day activities are placed which correspond to different activity levels and oxygen cost. The activities range from “brisk walking uphill” to “sleeping”. Patients are asked to mark the activity that will make them breathless. McGavin et al found that the patient’s ratings of their breathlessness with this scale were correlated $r = 0.68$ ($p < 0.001$) with the 12 minute walking test. (McGavin et al, 1978) Others have found that the OCD correlated significantly with lung function and respiratory muscle strength. (Mahler et al, 1988)

Oxygen-Cost Diagram



EQUIANALGESIC CONVERSION TABLE			
DRUG	SC	PO	Ratio
Morphine	10 mg	20 mg	
Codeine	120 mg	200 mg	12:1 (PO codeine to PO morphine)
Oxycodone	N/A	10 - 15 mg	1:2 (PO oxycodone to PO morphine)
Hydro-morphone	2 mg	4 mg	1:5 (PO hydromorphone to PO morphine)

Selected References

- 1) Fraser Health (2009) ‘Hospice Palliative Care Program Symptom Guidelines: Dyspnea’ Fraser Health Website [Internet]. Available from: <http://www.fraserhealth.ca/Services/HomeandCommunityCare/HospicePalliativeCare/Documents/Dyspnea.pdf> (Accessed: 23 July 2009).
- 2) Oncology Nursing Society (2008) ‘Putting Evidence Into Practice: Evidence-Based Interventions for Cancer-Related Dyspnea’ Oncology Nursing Society Website [Internet]. Available from: <http://ons.metapress.com/content/c21324512r838824/>.

- 3) Viola, R., Kiteley, C., Lloyd, N., Mackay, J. A., Wilson, J., Wong, R. and the Supportive Care Guidelines Group (2006) ‘The Management of Dyspnea in Cancer Patients: A Clinical Practice Guideline’ Program in Evidence Based Care Series 13-5, Cancer Care Ontario.

For full references and more information please refer to [CCO’s Symptom Management Guide-to-Practice: Dyspnea](#) document.

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NAUSEA & VOMITING

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Assessment

- Comprehensive assessment includes: interview, physical assessment, nutrition assessment, medication review, medical and surgical review, psychosocial and physical environment review and appropriate diagnostics.

Diagnosis

- Nausea and vomiting is common and has multiple etiologies, several of which may be present at the same time, hence identifying the underlying causes is essential.

Non-Pharmacological Treatments

- **Providing information and education is recommended as it**

is fundamental to enhance the patient and family's ability to cope.

- Consult with the inter-professional team members (e.g., social worker, spiritual practitioner, physiotherapist, occupational therapist, counselor for psychosocial care and anxiety reduction).
- Explain to the patient/family what is understood about the multiple triggers of nausea and/or vomiting and that it may take a number of strategies to make a difference

Consult with a Clinical Dietitian and have them provide dietary/nutritional advice

- Limit spicy, fatty and excessively salty or sweet foods, foods with strong odours and foods not well tolerated.
- Use small, frequent, bland meals and snacks throughout the day. Suggest small amounts of food every few hours. (Hunger can make feelings of nausea stronger).
- Hard candies, such as peppermints or lemon drops may be helpful.
- Sip water and other fluids (fruit juice, flat pop, sports drinks, broth and herbal teas such as ginger tea) and suck on ice chips, popsicles or

frozen fruit. It is important to try and drink fluids throughout the day even when not feeling thirsty.

- Limit the use of caffeine, including colas and other caffeinated soft drinks, such as coffee drinks, and tea (both hot and cold).
- Reduce meal size when gastric distension is a factor.
- Ingest liquids and solids separately. It is often helpful to drink fluids after and/or in between meals.
- Consume food/liquids cold or at room temperature to decrease odours.

- Sit upright or recline with head elevated for 30-60 minutes after meals.
- If vomiting, limit all food and drink until vomiting stops; wait for 30-60 minutes after vomiting, then initiate sips of clear fluid.
- When clear fluids are tolerated, add dry starchy foods (crackers, dry toast, dry cereal, pretzels)
- When starchy foods are tolerated, increase diet to include protein rich foods (eggs, chicken, fish) and lastly incorporate dairy products into the diet.

Environmental modification (where possible)

- Eliminate strong smells and sights.
- Optimize oral hygiene, especially after episodes of vomiting. Rinse with ½ tsp baking soda, ½ tsp salt in 2 cups water.
- Try rinsing mouth before eating to remove thick oral mucus and help clean and moisten mouth.
- Wear loose clothing.
- If possible try to create a peaceful eating place with a relaxed, calm atmosphere. A well ventilated room may also be helpful.

Complementary Therapies

- Acupuncture or acupressure points.
- Visualization, hypnosis, distraction.

Pharmacological Treatments

- Selection of antiemetics should be based on the most likely etiology of nausea and vomiting and site of action of medication.
- Any unnecessary medications that may be contributing to nausea and vomiting should be discontinued.
- Constipation may be a factor contributing to nausea and vomiting and requires treatment.
- It is necessary to rule out bowel obstruction and if present, appropriate treatment should be undertaken.

Choosing an antiemetic

- Metoclopramide is recommended as the drug of first choice to control chronic nausea/vomiting in patients with advanced cancer.
- Titrate metoclopramide to maximum benefit and tolerance. If not effective add/switch to another dopamine antagonist (e.g. haloperidol).
- Domperidone may be substituted for patients who can swallow medications and who have difficulties with extrapyramidal reactions.
- Titrate antiemetics to their full dose, unless patient develops undesirable effects, before adding another drug.
- If nausea is not controlled with a specific antiemetic within 48h, add

another antiemetic from another group, but do not stop the initial agent.

- Consider combinations but monitor overlapping toxicities.
- Use regular dosing of antiemetics if experiencing constant nausea and/or vomiting.
- **For persistent nausea and/or vomiting antiemetics should be prescribed on a regular dosing schedule with a breakthrough dose available.**
- All medications need to be individually titrated to the smallest effective dose or until undesirable side effects occur.

Treatment and Management

1. Treat the cause, if possible.
2. Symptomatic management:
 - Fluid and electrolyte replacement as appropriate.
 - Nutritional advice – consider making patient NPO if obstructed or until emesis has resolved for several hours; if not obstructed, change diet as appropriate, depending on the cause of nausea.
 - Treat gastrointestinal obstruction (may need to consider interventions such as nasogastric tube (NGT), venting gastrostomy tube (PEG), stents, ostomies, possible surgical resection).
 - Pharmacological treatment of symptoms.

Pharmacological Treatment of Symptoms: Step 1

The choice of antiemetic depends on the cause and the receptors and neurotransmitters involved:

- **For delayed gastric emptying or abdominal causes (excluding bowel obstruction, see above):**
 - Metoclopramide 5-20 mg po/subcut/IV q6h (or tid AC meals plus qhs); may be used q4h if needed; 40-100 mg/24 h subcut/IV continuous infusion.
 - Alternative (if metoclopramide is not well tolerated):
domperidone 5-20 mg po q6h

(or tid AC meals plus qhs);
causes less extrapyramidal side
effects than metoclopramide.

- **For patients treated with palliative radiotherapy:**
 - For symptoms that occur within 24 hours of administration of radiotherapy: Ondansetron 8 mg po/subcut/IV q8 – 24h; Granisetron 1 mg po q12h or 1 mg IV once daily
 - For anticipatory nausea or vomiting: lorazepam 1-2 mg po/sl/IV/subcut

- The above agents are also best given prior to radiation for optimal effect.

- **For opioid-induced nausea:**
 - Metoclopramide 10-20 mg po/subcut/IV q6h
 - Alternative: haloperidol 0.5-2.5 mg po/subcut q12h

- **For other chemical/metabolic causes:**
 - Haloperidol 0.5-2.5 mg po/subcut q12h
 - Alternative: metoclopramide 10-20 mg po/subcut/IV q6h

- **For brain metastases:**

- Dexamethasone 4-8 mg po/subcut/IV bid (0800 and 1300 h); for brain metastases that do not respond to dexamethasone or for leptomeningeal carcinomatosis:
- Haloperidol 1-2 mg po/subcut q12h

- **For vestibular causes:**
 - Scopolamine (transdermal patch) one or two 1.5 mg patches q72h
 - Alternate: Dimenhydrinate 25-50 mg po/ subcut/IV q4h

- **If psychogenic factors play a role:**
 - Oxazepam 10 mg po tid or lorazepam 1-2 mg po/sl/subcut/IV tid

- Psychological techniques (particularly for chemotherapy-induced nausea and vomiting)

Pharmacological Treatment of Symptoms: Step 2

A combination of different antiemetics is required in approximately 30% of cases. Combination therapy is only beneficial if different neurotransmitters are targeted.

If the response to monotherapy is inadequate, the following combinations may be considered:

- Metoclopramide po/subcut/IV + dexamethasone po/subcut/IV.
- Haloperidol po/subcut + dexamethasone po/subcut/IV.

Pharmacological Treatment of Symptoms: Step 3

If dexamethasone combined with either metoclopramide or haloperidol yields insufficient results, the following approaches may be considered:

- Serotonin (5HT₃) antagonists (ondansetron 4 - 8 mg po/subcut/IV q8-12h; granisetron 1 mg po q12h/1mg IV once daily; or dolasetron 100 mg po/IV once daily); in principle, combine with dexamethasone 4 mg po/subcut/IV

once daily. Disadvantages of the serotonin antagonists: high costs; side effects include constipation, headaches.

- Methotrimeprazine monotherapy using a starting dose of 5 – 10 mg po q8h PRN or 6.25-12.5 mg subcut q8h PRN. Increase as needed to maximum of 25 mg per dose.
- Olanzapine monotherapy 2.5 – 5 mg po/sl/subcut once daily or bid.

Diphenhydramine may be used for the treatment of akathesias secondary to increased doses of metoclopramide.

Selected References

- 1) Cancer Care Nova Scotia. Guidelines for the Management of Nausea and Vomiting In Cancer Patients, Jan 2004.
- 2) Fraser Health. Hospice Palliative Care Program Symptom Guidelines. Fraser Health, 2006.
- 3) Editorial Board Palliative Care: Practice Guidelines. Nausea and vomiting. Utrecht, The Netherlands: Association of Comprehensive Cancer Centres (ACCC), National Guideline Clearinghouse, 2006.
- 4) Adapted with permission from the National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology Palliative Care.

V.2.2011. Website:

http://www.nccn.org/professionals/physician_gls/f_guidelines.asp

For full references and more information please refer to [CCO's Symptom Management Guide-to-Practice: Nausea & Vomiting](#) document.

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Assessment

- Prior to treatment an accurate assessment should be done to

- determine the cause(s), type(s) and severity of pain and its impact.
- A comprehensive assessment of pain should consider the following domains:
 - physical effects/manifestations of pain
 - functional effects (interference with activities of daily living)
 - spiritual aspects
 - psychosocial factors (level of anxiety, mood) cultural influences, fears, effects on interpersonal relationships, factors affecting pain tolerance.
 - Self assessment pain scales should be used by patients with no cognitive impairment.

- Observational pain rating scales should be used in patients who cannot complete a self assessment scale.
- The frequency of the review depends upon the severity of the pain and associated distress.

General Principles of Cancer Pain Assessment

1. Perform an adequate pain history.
2. Use tools valid for the patient's age and cognitive abilities, with additional attention to the language needs of the patient (e.g.,

Brief Pain Inventory (BPI),
Edmonton Symptom
Assessment System (ESAS),
Palliative Performance Scale
(PPS)).

3. Record medications currently taken as well as those used in the past, including efficacy and any adverse effect.
4. Classify the pain – nociceptive, neuropathic or mixed?
5. Consider common cancer pain syndromes while conducting the history and physical examination.

6. Assess for functional impairment and the need for safety measures.
7. Incorporate a psychosocial evaluation into the assessment, including determination of the patient's/family's goals of care
8. Use a pain diary to track the effectiveness of therapies and evaluate changes in pain.
9. Review current diagnostic tests for clues to the origin of the pain. Order a diagnostic test (e.g., MRI, CT, laboratory testing) when warranted for new pain or increasing pain, and only if it

will contribute to the treatment plan.

10. Evaluate for the presence of other symptoms, as pain is highly correlated with fatigue, constipation, mood disturbances, and other symptoms.
11. Assess for risk if opioids are being considered.

Non-Pharmacological Treatment

Radiation Therapy

- All patients with pain from bone metastases which is proving

difficult to control by pharmacological means should be referred to a radiation oncologist for consideration of external beam radiotherapy

Vertebroplasty

- Vertebroplasty or percutaneous cementoplasty should be considered in patients with pharmacologically difficult to control bone pain from malignant vertebral collapse or pelvic metastases.

Surgery

- Removal of tumours or stabilization of bones may remove localized pain.

Anesthetic Interventions

- Interventions such as coeliac plexus block and neuraxial opioids should be considered to improve pain control and quality of life in patients with difficult to control cancer pain.

Other Therapies

- Consider role for physiotherapy or occupational therapy

- Complementary therapies (e.g. massage, aromatherapy, music therapy, acupuncture, transcutaneous electrical nerve stimulation, reflexology, Reiki, hypnotherapy) may be considered.

Psycho-social-spiritual interventions

- Psycho-social-spiritual interventions (patient education, counseling, recreational activities, relaxation therapy imagery, social interaction, spiritual counseling) should be considered.

Pharmacological Treatment

General Principles in Using Adjuvants

- The type and cause of the pain will influence the choice of adjuvant analgesic (e.g. nociceptive, neuropathic, bone metastases).
- The choice of antidepressant or anticonvulsant should be based on concomitant disease, drug therapy and drug side effects and interactions.
- Patients with neuropathic pain should be given either a tricyclic antidepressant (eg amitriptyline,

desipramine, nortriptyline or imipramine) or an anticonvulsant (eg gabapentin or pregabalin) with careful monitoring for adverse effects.

- Cannabinoids may have a role in refractory pain, particularly refractory neuropathic pain.

General Principles in Using Opioids

1. Educate the patient and/or family about the use of opioids and the expected outcomes.
2. Anticipate adverse effects like sedation and educate patients about the fact that they will

- quickly tolerate most adverse effects except for constipation.
3. In opioid-naïve patients and the frail elderly, start low and go slow with titration. Transdermal fentanyl is **not** recommended in opioid-naïve patients.
 4. In patients already on opioids, titrate them fairly quickly to the point where they are getting adequate pain control without intolerable adverse effects.
 5. Immediate release or sustained release products can both be used for titration and maintenance.

6. Give opioids regularly, around the clock for constant pain, not ‘as required’.
7. Always prescribe breakthrough doses.
8. Prevent adverse effects e.g., for constipation prescribe laxatives right from the initiation of therapy and decide on a plan for the management of constipation.
9. Monitor patients closely as you are titrating opioids.
10. Use universal precautions where a risk for abuse is identified.
11. Specialist pain or palliative care advice should be considered for the appropriate

choice, dosage and route of opioids in patients with reduced kidney function or in patients with difficulty to control pain.

- All patients with moderate to severe cancer pain, regardless of etiology, should receive a trial of opioid analgesia.
- In the presence of reduced kidney function all opioids should be used with caution and at reduced doses and/or frequency.
- Fentanyl, methadone and oxycodone are the safest opioids of choice in patients with chronic kidney disease.

- Methadone requires an experienced prescriber.
- **Check for significant drug interactions before prescribing any drug to a patient on methadone.**
- When using a transmucosal fentanyl formulation for breakthrough pain the effective dose should be found by upward titration independent of the regular opioid dose.
- For those with stabilized severe pain and on a stable opioid dose or those with swallowing difficulties or intractable nausea and vomiting, fentanyl transdermal patches may be appropriate.

Adverse Effects of Opioids

- Many opioid-naïve patients will develop nausea or vomiting when starting opioids, tolerance usually occurs within 5-10 days. Patients commencing an opioid for moderate to severe pain should have access to an antiemetic to be taken if required.
- The majority of patients taking opioids will develop constipation. Little or no tolerance develops. The commonest prophylactic treatment for preventing opioid-induced constipation is a combination of

stimulant (senna or bisacodyl) and osmotic laxatives (lactulose or PEG 3350)

Patient Education should include:

- Taking routine and breakthrough analgesics, adverse effect management, non pharmacologic measures that can be used in conjunction with pharmacologic treatment.

Mild Pain ESAS 1 to 3

TREATMENT WITH NON-OPIOIDS

Acetaminophen and NSAIDS

- Acetaminophen and NSAIDS including COX-2 inhibitors should be considered at the lowest effective dose.
- The need for ongoing or long term treatment should be reviewed periodically, if no significant response in one week drugs should be stopped.
- Long term use of NSAIDs should require gastric mucosa protection.

Bisphosphonates

- There is insufficient evidence to recommend bisphosphonates for

first line therapy for pain management.

TREATMENT WITH OPIOIDS

- For mild to moderate pain, weak opioids such as codeine or tramadol could be given in combination with a non-opioid analgesic.
- If pain is not controlled with these combinations go to “Moderate Pain” re: initiation and treatment with opioids

Moderate Pain ESAS 4 to 6

TREATMENT WITH OPIOIDS

- If the person is opioid naïve:
 - Morphine starting dose is usually 5mg Q4h with 2.5-5mg Q1H PRN for breakthrough pain. For elderly or debilitated patients consider a starting dose of 2.5mg Q4h.
 - Hydromorphone starting dose is 1mg Q4h with 0.5-1mg Q1h PRN for breakthrough pain. For elderly or debilitated

patients consider a starting dose of 0.5 mg Q4h.

- Oxycodone starting dose is 2.5 mg or one half tablet Q4H with 2.5 mg or one half tablet Q2H PRN for breakthrough. (The lowest dose oxycodone tablets available, either in combination with acetaminophen or alone, contain 5mg of oxycodone, equivalent to ~5-10mg of morphine).
- If the person is taking an opioid:
 - As an immediate release preparation with q4h dosing,

increase the regular and breakthrough doses by 25%.

- As a sustained release opioid, increase this dose by 25%.
Change the breakthrough dose to 10% of the regular 24h dose, either q1-2h PRN PO or q30 min PRN subcut.
- Patients with stable pain and analgesic usage, receiving oral morphine, oxycodone or hydromorphone should have the drug converted to a sustained or controlled release formulation given q12h for ease of administration. The short acting breakthrough dose is usually 10% of the

- total daily dose.
- The frequency of breakthrough doses for oral opioids is Q1-2h PRN. After conversion to a long acting preparation, if pain is not well controlled, reassess the patient and consider why multiple breakthrough doses are being used and the effectiveness of the breakthrough doses.
 - If indicated after proper assessment, the daily dose can be titrated by adding 20 to 30% of the breakthrough doses used in the preceding 24 hrs to the daily sustained

- release formulation.
- Make frequent assessments and adjustments to the opioid dose until the pain is better controlled.

Severe Pain ESAS 7 to 10

TREATMENT WITH STRONG OPIOIDS

- **If the person is opioid naïve:**
Oral: Morphine 5-10 mg PO q4h and 5mg PO q1h PRN **OR**
hydromorphone 1.0-2.0 mg PO q4h and 1.0 mg PO q1h PRN **OR**

Subcutaneous: Morphine 2.5 - 5 mg subcut q4h & 2.5 mg subcut q30min PRN **OR** hydromorphone 0.5 - 1.0 mg subcut q4h & 0.5 mg subcut q30min PRN.

- **If the patient is taking an opioid** with q4h dosing, increase the regular and breakthrough doses by 25%. Change frequency of the breakthrough to q1h PRN if PO and q30min PRN if subcut.
- If the patient is taking a sustained release opioid, increase this dose by 25%. Change the breakthrough dose to 10-15% of the regular 24h dose, either q1h PRN PO or q30 min PRN subcut.

- Titrate the dose every 24h to reflect the previous 24h total dose received
- If unmanageable opioid-limiting adverse effects are present (e.g. nausea, drowsiness, myoclonus), consider switching to another opioid and re-titrate or consult palliative care.
- For patients with severe uncontrolled pain consider switching back to an equivalent daily dose of immediate release morphine to allow more rapid titration of dose or switch to a sc preparation/infusion.
- Meperidine and pentazocine should generally not be used in cancer patients with chronic or acute pain.

- If there is difficulty getting the pain under control consider a consultation to palliative care.

Severe Pain Crisis

1. A severe pain crisis requires prompt use of analgesics, adjuvant therapies, reassurance and a calm atmosphere.
2. **Consider a consultation to palliative care or a cancer pain specialist.**
3. If IV access is present, and the person is **opioid naïve**

give stat morphine 5-10 mg
IV q10min until pain is
relieved; if the person is **on
opioids** give the po PRN dose
IV q10min until pain is
relieved. Monitor carefully.

4. If no IV access available, and the person is **opioid naïve** give stat morphine 5-10 mg subcut q20-30min until pain is relieved; if the person is on opioids give the po PRN dose subcut q20-30min until pain is relieved.
5. Titrate dose by 25% every 1 - 2 doses until pain is relieved.
6. When pain is controlled: If the patient is taking a

sustained release opioid increase this dose by 25% and change to q4h dosing po or subcut. **Do Not** try to manage a severe pain crisis with a long-acting opioid. Change the breakthrough dose to half of the regular dose, either q1h PRN PO or q30 min PRN subcut.

CONVERSION RATIOS

- It should be noted that these conversion ratios, based on available evidence, are conservative in the direction specified; if converting in

the reverse direction, a reduction in dose of one third should be used following conversion, or specialist advice sought.

Drug	Approximate Equivalent Dose ^a	
	Parenteral	Oral
Codeine	120	200
Fentanyl	0.1-02	n/a ^b
Morphine	10	20-30 ^c
Hydromorphone	2	4-6
Oxycodone	n/a	30
Pethidine (Meperidine)	75	300
Sufentanil	0.01-0.04	n/a ^b

Tramadol	d	d
Methadone	e	e

- a. From single dose studies using immediate-release dosage forms. These approximate analgesic equivalences should be used only as a guide for estimating equivalent doses when switching from one opioid to another. Additional references should be consulted to verify appropriate dosing of individual agents.
- b. Route of administration not applicable.
- c. With repeated dosing.
- d. Tramadol's precise analgesic potency relative to morphine is not established. Consult the product monograph for dosing recommendations.
- e. For methadone, see [Guide-to-Practice: Pain](#)

Conversion doses from oral morphine to transdermal fentanyl

Oral 24-hour morphine (mg/day)	Transdermal Fentanyl (mcg/h)
<90	25
90 – 134	37 (if available, otherwise 25)
135 – 189	50
190 – 224	62 (if available, otherwise 50)
225 – 314	75
315 – 404	100

405 – 494	125
495 – 584	150
585 – 674	175
675 – 764	200
765 – 854	225
855 – 944	250
945 – 1034	275
1035 – 1124	300

TITRATION GUIDE

General principles:

6. Calculate the total opioid dose taken by the patient in 24 h (regular q4h dose x 6 **PLUS** the total number of breakthrough doses given x breakthrough dose).
7. Divide this 24 h total by 6 for the equivalent q4h dose.
8. Divide the newly calculated q4h dose by 2 for the breakthrough dose.
9. Use clinical judgment regarding symptom control as to whether to round up or down the obtained result (both breakthrough and regular dosing). Remember to consider available dosage forms (in the case of PO medications especially).
10. If the patient is very symptomatic a review of how many breakthrough doses have been given in the past few hours

might be more representative of his/her needs.

Example:

A patient is ordered morphine 20 mg q4h PO and 10 mg PO q2h PRN, and has taken 3 breakthrough doses in the past 24 h.

1. Add up the amount of morphine taken in the past 24 h:
6 x 20 mg of regular dosing, plus 3 x 10 mg PRN doses equals a total of 150 mg morphine in 24 hours
2. Divide this total by 6 to obtain the new q4h dose:
150 divided by 6 = 25 mg q4h
3. Divide the newly calculated q4h dose by 2 to obtain the new breakthrough dose:
25 mg divided by 2 = 12.5 mg q1 - 2h PRN

4. If this dose provided reasonable symptom control, then order 25 mg PO q4h, with 12.5 mg PO q1 - 2h PRN. (It would also be reasonable to order 10 mg or 15 mg PO q2h for breakthrough.)

CONVERSION GUIDE

(To convert from long-acting preparations to short-acting preparations)

General principles in converting from *sustained release* to *immediate release* formulations (for the same drug):

1. Add up the total amount of opioid used in the past 24 h, including breakthrough dosing.
2. Divide this total by 6 to obtain equivalent q4h dosing.
3. Divide the q4h dose by 2 to obtain breakthrough dosing.
4. Use clinical judgment to adjust this dose up or down depending on symptom control.
5. Consider available tablet sizes when calculating doses.

Example:

A patient is ordered a long-acting morphine preparation at a dose of 60 mg PO q12h, with 20 mg PO q4h for breakthrough, and has taken 4 breakthrough doses in 24 h.

Selected References:

- 1.Scottish Intercollegiate Guidelines Network SIGN 106, ‘Control of Cancer Pain in Adults with Cancer: A National Clinical Guideline’ November 2008.

For full references and more information please refer to [CCO’s Symptom Management Guide-to-Practice: Pain](#) document.

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Notes:

Edmonton Symptom Assessment System (ESAS)

Edmonton Symptom Assessment System (ESAS)

Please circle the number that best describes:

No pain 0 1 2 3 4 5 6 7 8 9 10 Worst possible pain

Not tired 0 1 2 3 4 5 6 7 8 9 10 Worst possible tiredness

Not nauseated 0 1 2 3 4 5 6 7 8 9 10 Worst possible nausea

Not depressed 0 1 2 3 4 5 6 7 8 9 10 Worst possible depression

Not anxious 0 1 2 3 4 5 6 7 8 9 10 Worst possible anxiety

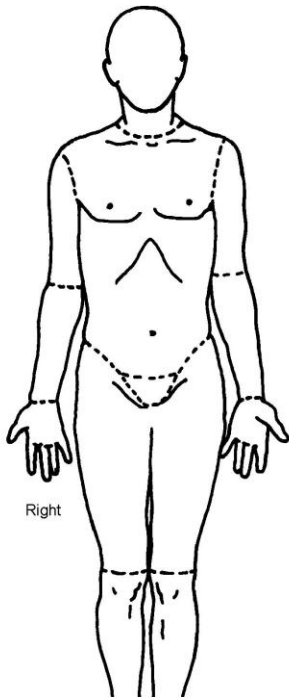
Not drowsy 0 1 2 3 4 5 6 7 8 9 10 Worst possible drowsiness

Best appetite 0 1 2 3 4 5 6 7 8 9 10 Worst possible appetite

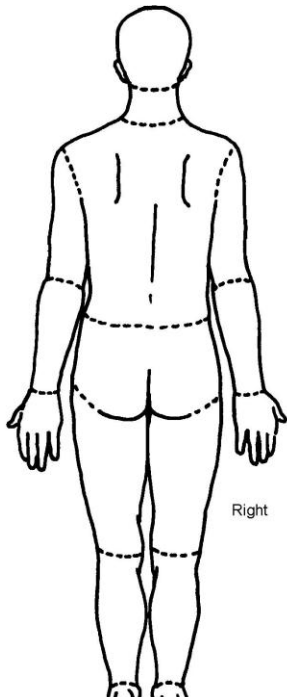
Best feeling of wellbeing 0 1 2 3 4 5 6 7 8 9 10 Worst possible feeling of wellbeing

No shortness of 0 1 2 3 4 5 6 7 8 9 10 Worst possible

Please mark on these pictures where it is you hurt.



Right



Right

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