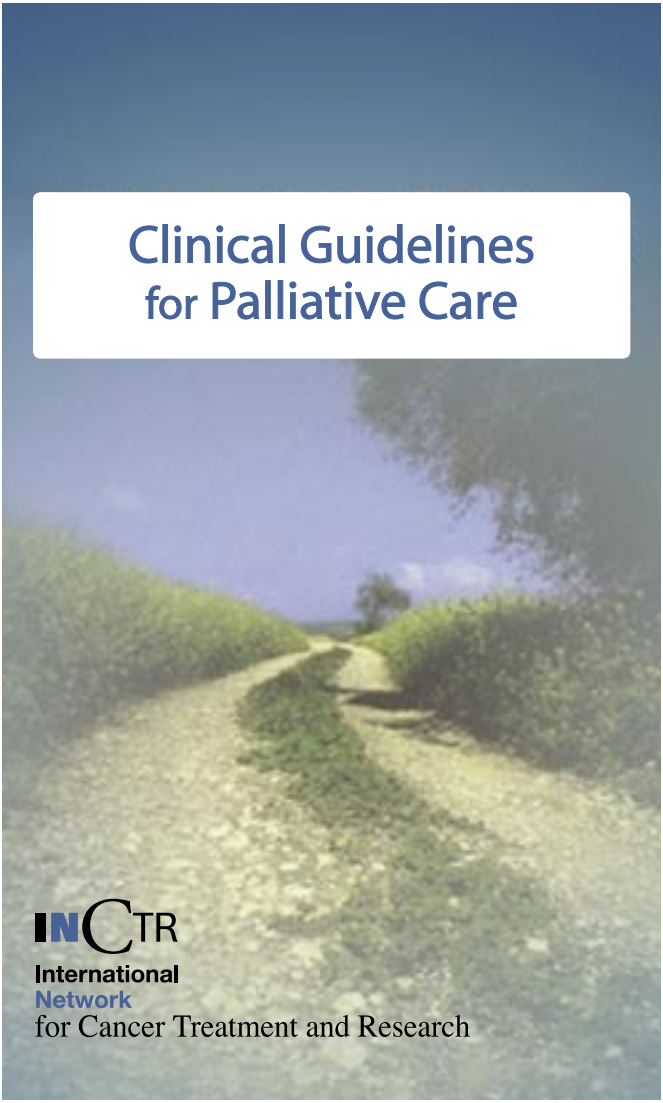
Clinical Guidelines for Palliative Care



INCTR
International
Network
for Cancer Treatment and Research

INCTR

INCTR is a non-profit organization whose founder members are the International Union against Cancer and the Institut Pasteur, Brussels. The goals of the organization are to assist in controlling cancer in developing countries through the development of infrastructure for cancer treatment and research. INCTR emphasizes international collaboration and works to improve communication among the wide range of professionals and volunteers working to control cancer throughout the world.

PAX (Palliative Access) PROGRAM

The aim of the PAX Program is to improve the delivery of good quality palliative care in resource poor areas. Our strategies are threefold: collaborative efforts to develop Regional Palliative Care Centres at various key institutions, the provision of expert consulting and advisory services to national and regional governments, and the promotion of good generalist palliative care practice amongst oncology and other professionals through clinical guidelines, workshops and other means.

Endorsing Agencies

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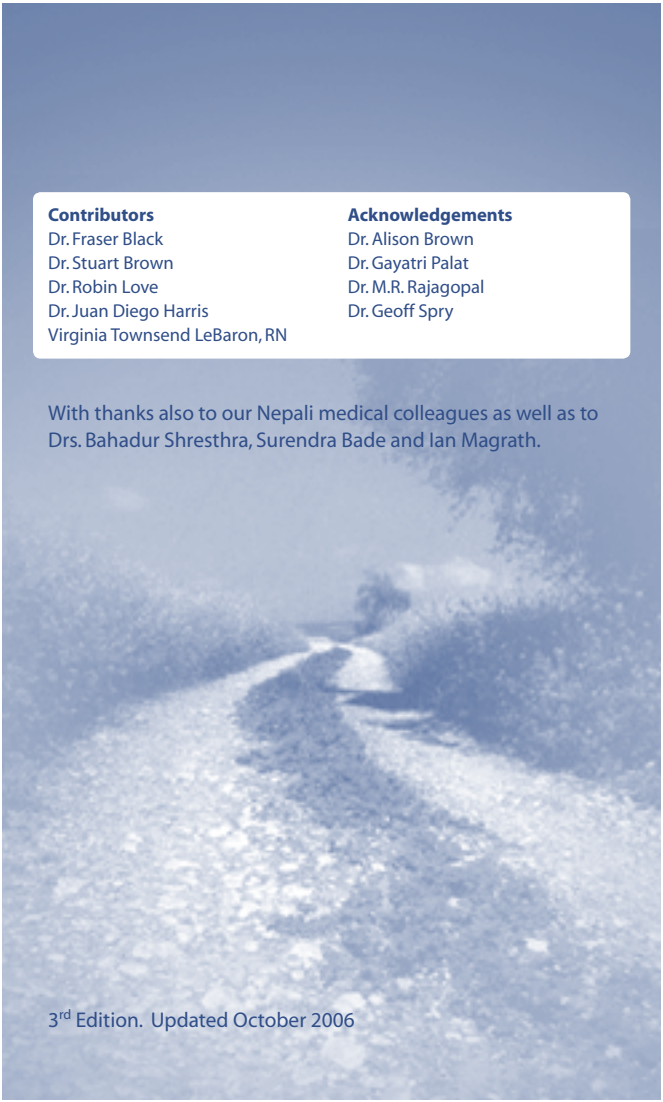

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The burden of investigation and treatment should always be weighed against the prognosis, the likely benefit of treatment and the patient's wishes. In other words: "Will the investigation change the management?"

Since the material in this handbook is abbreviated it should be interpreted in the context of other materials and textbooks.

Clinical judgment should be exercised at all times.

Anorexia and Cachexia

KEYPOINTS

- Cancer can often cause a lack of appetite (anorexia) and weight loss (cachexia) with muscle wasting
- This is often accompanied by fatigue
- The process of anorexia/cachexia is complex and involves numerous metabolic changes
- Anorexia/cachexia is present in up to 80% of patients with cancer

ASSESSMENT

see comment on page 4

- A good history and clinical assessment is important to try and identify the underlying cause of the anorexia/cachexia
  - Assess appetite
  - Assess ability/difficulty in swallowing and chewing
  - Identify any other symptoms such as pain, constipation, depression, or nausea and vomiting that may be causing decreased appetite
  - Examine the mouth for any sores, lesions or infection
- Investigations to consider may include:
  - Body weight
- Treatable causes of anorexia/cachexia include:

- Ongoing pain
- Nausea and vomiting
- Depression
- Oral problems
  - Dry mouth
  - Mucositis secondary to chemotherapy
  - Thrush/candidiasis
  - Oral herpes
- Gastrointestinal motility problems
  - Reflux oesophagitis
  - Gastric stasis
  - Constipation

MANAGEMENT

Consider treatment of the underlying cause if one is identifiable ***Consider if patient is well enough to benefit***

NONPHARMACOLOGIC APPROACHES

- Patient and family education
- Eliminate dietary restrictions
- Encourage patient to eat their favourite foods

PHARMACOLOGIC APPROACHES

- Ensure good pain and nausea/vomiting control, treat constipation
- Stimulate appetite
  - **Megestrol acetate 40-240 mg up to four times a day PO or 800 mg PO QD**
  - **Dexamethasone 4-8 mg qAM PO**

PALLIATIVE TIPS

- Despite the appearance of malnutrition, anorexia/ cachexia is usually NOT simply reversed with improved nutrition
- Aggressive feeding can often make symptoms such as nausea, vomiting and pain worse
- Educating the family that wasting is a part of the disease process and not the result of the family not providing enough nutrition for the patient is important
- Anorexia can cause significant anxiety and distress for family members and caregivers who may not understand that loss of appetite is a common symptom of dying
- There is no evidence that providing nutritional support either enterally or parenterally improves morbidity or mortality in terminally ill patients

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Ascites

KEYPOINTS

- Ascites is reported in 15-50% of patients with malignancy
- 10% of all cases of ascites are from malignancy. Non-malignant ascites may also be seen in cancer patients (from other causes), and non-cancer palliative patients may have ascites (cirrhosis, CHF, tuberculosis etc)
- Ascites is common in ovarian, breast and GI malignancies (30% of ovarian cancer patients develop ascites)
- The prognosis is poor so the goal is usually comfort with minimal disturbance (exception is ovarian cancer which may still have a moderate prognosis)

ASSESSMENT

see comment on page 4

- Clinical features include abdominal swelling, bloating, weight gain, reflux, and dyspnea
- Exam may reveal increased abdominal girth, bulging flanks, shifting dullness
- Investigations to consider are ultrasound, diagnostic paracentesis (cytology, albumin, bacterial culture), serum electrolytes and albumin
- Malignant ascites may be caused by liver disease/ metastases leading to portal hypertension, intra-abdominal metastases/peritoneal seeding, lymphatic obstruction and leakage (chylous ascites), or a combination of these

MANAGEMENT

- Consider treatment of the primary tumour (particularly with ovarian cancer), but usually the cancer is advanced and the prognosis is poor
- Diuretics can be helpful in some patients with ascites. Serum electrolytes (Na, K) may need to be followed. Diuretics are unlikely to be helpful in chylous ascites (accumulation of lymph in the peritoneal cavity characterized by increased triglyceride concentrations)
- Paracentesis is best for immediate symptom relief, if the ascites does not respond to diuretics and for chylous ascites

Pharmacologic Management

- Spironolactone starting with 50 mg/day and increasing up to 400 mg/day if required
- Furosemide starting at 40 mg/day and increasing up to 160 mg/day if required

- Paracentesis
  - This is a simple procedure that can be done at the bedside or with ultrasound guidance (recommended if there is diagnostic uncertainty, possible loculations or uncertainty about catheter placement due to tumor masses)
  - Remove the drain after 6 hours, after 5 liters have drained or when the drainage has stopped
  - A small number of patients (<5%) may deteriorate rapidly after paracentesis. Sepsis and catheter blockage are other complications
- Intravenous fluids and albumin infusions are not

routinely required (unless hypotensive, dehydrated, or severe renal impairment)

PITFALLS/CONCERNS

⚖ ***In patients in the final terminal phase – ie. hours to days, it would be inappropriate to drain the ascites (treatment should be as least invasive as possible)***

⚖ ***In patients in the final terminal phase – ie. hours to days symptomatic relief through pharmacologic and other means would be preferred***

PALLIATIVE TIPS

- Drain for symptomatic relief, not just because the fluid is there
- If the drain site keeps leaking afterwards, an ostomy bag over the site is helpful in containing the fluid
- **Some patients who rapidly re-accumulate fluid despite high dose diuretics may benefit from an indwelling catheter. If the prognosis is many weeks, consider a tunneled catheter to reduce infection risk**
- Patients with ascites from cirrhosis may benefit from sodium restriction. The benefit of this must be weighed against unnecessary discomfort from dietary restriction
- **Octreotide** may be useful in controlling ascites

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APPENDIX: METHOD OF PARACENTESIS

If there is substantial ascites (tense abdomen), it is probably safe to proceed without ultrasound

With patient semi-recumbent and with an empty bladder, choose a puncture site below the umbilicus in the midline or the LLQ at the anterior axillary line below the level of percussible dullness

Using sterile technique, prep the skin with antiseptic and infiltrate local anaesthetic

Retract the skin inferiorly; insert a 14-16 g needle or catheter that is attached to a drainage tube (IV extension tube)

Gravity drain to dryness or a total of 5-6 liters into a container

Withdraw the needle allowing the skin to return to the original position (creates a Z-track and lowers the post procedure leakage)

Constipation

KEYPOINTS

- Prevention is the most important part of treatment
- Constipation is defined as the infrequent and difficult passage of hard stools
- Constipation may be related to the disease, the treatment or may be unrelated
- The prevalence of constipation in palliative care patients is 29-86%
- Constipation can be a distressing symptom for patients and cause other problems such as nausea and vomiting, abdominal pain, or if left untreated, bowel obstruction
- Preventing and relieving constipation can improve quality of life

ASSESSMENT

see comment on page 4

- Taking a thorough history and performing a good clinical assessment (including rectal exam to assess for the presence of hard stool in the vault and rule out impaction) is important to try and identify the underlying cause(s) of the constipation
- Causes of constipation can include: opioids or other medications, dehydration, mechanical obstruction, immobility, emotional stress, decreased oral intake, and electrolyte imbalances

- Investigations to consider may include:
  - Abdominal x-ray to assess bowel gas pattern and rule out ileus or bowel obstruction

MANAGEMENT

- Mild constipation
  - ***If possible***
    - Increase fluids
    - Increase fibre ***(if not accompanied by increase in fluids may make constipation worse)***
    - Increase activity

- Mild or moderate or when initiating opioids
  - As above + stool softener i.e.
    - **Docusate 100 mg bid PO** as well as a peristaltic agent:
    - **Bisacodyl 5 mg bid PO or**
    - **Senna two tabs PO at HS, increase to bid if necessary PO**

- No stool for 3 days and stool in rectum
  - As above +
  - **Lactulose or sorbitol 70% 15-30-cc PO/BID,** or can be given q3-4 hours until patient has a bowel movement in cases of significant constipation
  - Glycerine and dulcolax suppositories
  - Fleet or saline enema if suppositories not effective

- Constipated stool in rectum
  - Disimpaction if indicated (use oil retention enema) before and after disimpaction

PITFALLS/CONCERNS

⚖ ***In patients in the final terminal phase – ie. hours to days, it may be inappropriate to treat obstruction or constipation***

PALLIATIVE TIPS

- Bowel regimens should be individualized and titrated to patient response
- A bowel regimen should be initiated at the time opioids are started and should be continued for as long as the patient takes opioids
- Urinary retention, nausea and vomiting, terminal restlessness, and other symptoms can sometimes be relieved by treating constipation

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Cough

KEYPOINTS

- Cough may be related to the disease, the treatment or may be unrelated
- Cough can be a distressing symptom for the patient and interfere with sleep
- Using cough suppressants (e.g. **codeine, morphine**) can bring symptomatic relief and improve quality of life

ASSESSMENT

see comment on page 4

- A good clinical assessment is important to try and identify the underlying cause of the cough (e.g. pneumonia, CHF, pleural effusion, asthma, etc)
- Investigations to consider may include:
  - Chest x-ray to assess possible chest disease

MANAGEMENT

- Consider treatment of the underlying cause (e.g. oncological treatment of tumour, draining of pleural effusion, treatment of infection, gastroreflux disease)
   ***Consider if patient is well enough to benefit***
- Simple measures such as moist inhalations or **nebulized 0.9% saline** can be helpful
- **Simple cough suppressant** may be tried

- A weak opioid such as **codeine 15-30 mg q4h PO** or **Dextromethorphan 30 mg (or higher doses) q4h PO** can be used to suppress cough
- **Morphine** should be used if the cough is not suppressed by **codeine** or other means.
  The initial starting dose will depend on the patient's previous exposure to opioids
  - A dose of **Morphine 2.5 mg regularly q4h PO (or 1 to 2 mg SC/IV)** and a breakthrough or rescue dose every hour, as required (see Appendix 1) is suitable for an opioid-naive patient
  - A dose of **Morphine 5-10 mg regularly q4h PO (or 2.5 - 5 mg q4h SC/IV)** and a breakthrough or rescue dose every hour, as required (see Appendix 1) should be used for patients who have already been on **codeine**
  - For a patient already on morphine an increase in the dose by 20% may improve the cough
- Also consider a trial of **Dexamethasone 8 mg qAM PO**
- Inhaled corticosteroids or sodium cromoglycate may be helpful
- For refractory symptoms consider nebulized local anaesthetics such as **lignocaine/lidocaine 5 ml of 2% solution (without adrenaline) prn**
- If tenacious secretions are difficult to clear with coughing:
  - Consider using **moist inhalations**
  - **Nebulized hypertonic saline** can be effective
  - Try **normal saline** if this is not available

PITFALLS/CONCERNS

⚖ ***In patients in the final terminal phase – ie. hours to days, antibiotics will make little difference to the course of events***

PALLIATIVE TIPS

- A bedtime dose of **Codeine or Morphine** can help suppress the cough and allow for an undisturbed sleep

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Delirium and Hallucinations

KEYPOINTS

- Delirium (with or without hallucinations) is commonly experienced by patients with advanced illnesses
- Possible causes are many, may be multifactorial and difficult to determine in about 50% of cases
- Delirium or confusion can be caused by the opioids themselves, and/or the accumulation of opioid neurotoxic metabolites

ASSESSMENT

see comment on page 4

Non opioid causes include:

- Dehydration*
- Hepatic and renal failure*
- Urinary retention
- Infection e.g. urine infection
- Constipation
- Brain metastasis
- Biochemical imbalances,
  i.e. hypercalcemia, hyponatremia

Medications,
i.e. tricyclics, steroids, **benzodiazepines**

** possibly caused by accumulation of opioids and their metabolites*

MANAGEMENT

Consider if cause of delirium identifiable and if patient well enough for intervention

- Discontinue drugs that may be causing the delirium (such as anticholinergics, etc)
- A trial of hydration if the patient's condition would tolerate this. (May help correct electrolyte disturbances and may diminish opioid toxic metabolite accumulation)
- Correct electrolyte imbalance; hypercalcemia may respond to hydration and/or to biphosphonates such as **pamidronate 60-90 mg (single dose) IV**

PHARMACOLOGIC MANAGEMENT

If symptoms persist, pharmacological management includes:

(1) Neuroleptics

- Haloperidol is commonly used. Chlorpromazine may be more effective in cases of severe agitation

NEUROLEPTICS		via
Haloperidol	0.5-5 mg bid + q4h prn	PO/SC/IV/PR
Chlorpromazine	15-50 mg bid prn	PO/IV
Risperidone	0.5-4 mg bid	PO
Olanzepine	2.5 mg qhs-10 mg bid	PO

(2) **Benzodiazepines**

- **Lorazepam** or midazolam can also be used in situations where there is considerable agitation. It should be noted however that **benzodiazepines** can sometimes make confusion worse and should not be used alone for the treatment of delirium

BENZODIAZEPINES		via
Lorazepam	0.5-2 mg bid + q1h prn	PO/SC/IV/PR
Midazolam	5-60 mg/24h via infusion	SC/IV

(3) Opioid rotation (if alternative opioids available)

- ***Opioid rotation (switching from one opioid to another) can be helpful for some patients who do not respond to the addition of neuroleptics or benzodiazepines. This is especially so in patients who may have renal failure in whom metabolites from morphine can accumulate. If an opioid rotation is done, establish the equianalgesic dose from an equianalgesic table, and start the new opioid at 50% of the equianalgesic dose.***
  This is to take into account that there is a large variability between individuals in response to various opioids

PALLIATIVE TIPS

❍ If opioids are suspected as the cause of delirium, it is important to realize the symptoms may disappear after a few days of stable dosing of the opioid

Thus, unless the symptoms are severe, it is recommended to treat them pharmacologically (e.g. as with a neuroleptic) initially, prior to deciding on changing the opioid

- The newer atypical antipsychotics such as Risperidone and Olanzapine can also be used effectively and offer the advantage of less antiparkinsonian/anticholinergic side effects

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Dyspnea

KEYPOINTS

- Dyspnea has a prevalence of 50% in people with any type of cancer (not just lung cancer)
- Dyspnea is moderate to severe in more than 28% of terminally ill cancer patients
- Opioids (e.g. **Morphine**) play an important and effective part in the management of dyspnea
- Dyspnea (like pain) is a subjective symptom and therefore it is important to ask the patient about their feelings of dyspnea rather than rely on clinical exam findings

ASSESSMENT

see comment on page 4

- A good clinical assessment is important to try and identify the underlying cause of the dyspnea (e.g. pneumonia, CHF, pleural effusion etc)
- Investigations to consider may include:
  - Chest x-ray to assess possible chest disease
  - CBC to rule out anaemia or infection
  - Oxygen saturation (not necessarily arterial blood gases) can sometimes be helpful

MANAGEMENT

- Consider treatment of the underlying cause

(e.g. oncological treatment of tumour, draining of pleural effusion, treatment of infection, COPD, CHF etc.)

Consider if patient is well enough to benefit

- Simple measures such as repositioning, opening a window or providing a fan and relaxation techniques can be very helpful
- Ensure patients do "not feel trapped" by being crowded by people and equipment
- Oxygen may or may not be helpful for dyspnea and is not necessary for all patients. For some patients it may make their feeling of dyspnea worse to have their face covered by an oxygen mask or nasal prongs. Treat the patient's symptoms, not the lab test (i.e. the oxygen saturation)
- Fresh air may be as helpful as oxygen for many patients
- **Morphine and other opioids** are an effective treatment for dyspnea. The initial starting dose will depend on the patient's previous exposure to opioids
  - A dose of **Morphine 2.5 mg regularly q4h PO (or 1 to 2 mg SC/IV)** and a breakthrough or rescue dose as required (see Appendix 1) is suitable for an opioid-naive patient
  - A dose of **Morphine 5-10 mg regularly q4h PO (or 2.5–5 mg q4h SC/IV)** and a breakthrough or rescue dose as required (see Appendix 1) should be used for patients who have already been on **codeine**
  - Patients who are already on strong opioids for pain will usually benefit from an increase in their regular dose
  - Titrate **Morphine** in the same way as for pain management - see guideline on pain (some patients may require high doses for dyspnea)

Benzodiazepines may be helpful with dyspnea and the associated anxiety

PITFALLS/CONCERNS

⚖ ***In patients in the final terminal phase – ie. hours to days, antibiotics will make little difference to the course of events even if infection is suspected***

Intubation is not appropriate for palliative care patients

PALLIATIVE TIPS

- Remember to ask the patient about their feelings of dyspnea – physical examination findings and our observations of tachypnea or perceived difficulty in breathing do not always correlate with the level of distress
- Educating the patient about dyspnea can reduce the anxiety that patients feel when short of breath
- Sedation may be needed in severe cases

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Hiccups

KEYPOINTS

- Hiccups (singultus) are repeated involuntary contractions of the diaphragm and respiratory muscles
- There are close to 100 different causes of hiccups - causes may be natural or drug-induced
- Gastrointestinal causes are the most common cause of hiccups
- Hiccups can be extremely distressing and can lead to fatigue and sleep disturbance
- Treatment options include both pharmacologic and non-pharmacologic approaches

ASSESSMENT

see comment on page 4

- A good clinical assessment is important to try and identify the underlying cause of the hiccups
- Finding the cause (if possible) can often help direct treatment
- Causes of hiccups include:
  - Gastric Distension or gastroesophageal reflux disease (GERD) – most common
    - Overload
    - Obstruction
    - Gastritis or esophagitis
  - Irritation of the diaphragm
- Hepatic and other tumours

- Infection or inflammation
- Ascites
  - Other problems involving the thorax or abdomen
- Pneumonia
- Pericarditis
- Pancreatitis
  - Due to medication
- Eg. corticosteroids
  - Metabolic problems
- Renal failure/uremia
- Hyponatremia
  - Intracranial disease
- Tumours - especially brain stem lesions
- Infection
  - Idiopathic (unknown cause)

MANAGEMENT

- Consider treatment of the underlying cause if one is identifiable ***Consider if patient is well enough to benefit***
  - Remove offending pharmacologic agents
  - Correct imbalances/infections if possible
- If due to gastric distension
  - Decrease gastric distension by encouraging smaller more frequent meals
  - Use a prokinetic drug such as **metoclopramide 10 mg qid PO, cisapride 10-20 mg bid PO or domperidone 10 mg qid PO**
  - **Simethicone/dimethicone containing agents 5 mls qid PO and prn** may help to decrease gas and distension

- If due to GERD provide treatment such as omeprazole 20 mg once a day PO
- If a cause can not be identified or corrected then general measures should be used
- General non-pharmacologic measures (many different measures have been suggested):
  - Pharyngeal stimulation
    - Eating 1-2 teaspoons of sugar or crushed ice
    - Lightly rubbing the midline of the soft palate for 1 minute
    - Long slow slips of water
  - Breath holding or rebreathing into a bag
  - Passage of a naso-gastric tube
  - Massage of external auditory canal
- General pharmacologic measures
  (many have been tried – little evidence of efficacy exists):
  - **Baclofen 5-10 mg tid PO** has been shown to be effective in intractable hiccups
  - **Chlorpromazine 10-25-50 mg qid PO**
  - **Nifedipine 10-20 mg bid to tid PO**
  - **Haloperidol 1-5 mg every 4-12 hours PO/SC**
  - **Anticonvulsants**
    - **Phenytoin 200-300 mg PO HS**
    - **Gabapentin 300 mg tid PO**
    - **Carbamazepine 100-200 mg bid PO**
    - **Clonazepam 0.5-1 mg bid PO**

PITFALLS/CONCERNS

- ***The same agents that are used to treat hiccups may also cause them !***

PALLIATIVE TIPS

- Gastric distension and gastroesophageal reflux disease (GERD) are the most common cause of hiccups and a trial of treatments as outlined above should be considered
- Combinations of agents is sometimes required for intractable hiccups. These would include combinations such as COB (cisapride, omeprazole and baclofen) or COG (cisapride, omeprazole, **Gabapentin**) or COBG (cisapride, omeprazole, baclofen, **Gabapentin**)

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Malignant Bowel Obstruction

KEYPOINTS

- Has been reported in 5-15% of cases of advanced cancer
- 5-40% of ovarian cancer and 5-24% of bowel cancer
- Signs and symptoms of bowel obstruction may not be 'classic' in advanced malignant disease
- May resolve spontaneously especially in early stages
- Oral administration of medications is unreliable
- The "goals of care" must be clear:
  "is this a patient that we would consider for surgery, oncological treaments or comfort only?"

ASSESSMENT

see comment on page 4

- Clinical features may include pain, nausea, vomiting, abdominal distension and reduced or absent passing of faeces or flatus
- Investigations to consider for diagnosis may include:
  - Abdominal x-rays to demonstrate fluid levels

  If surgical intervention is a possibility, consider imaging (CT or contrast plain films) to help define level of obstruction (gastrograffin is preferable as may be useful in restoring bowel function in some cases)

PHARMACOLOGICAL TREATMENT

- **Symptom management or possible reversal of bowel obstruction**
  - In many cases, reversal of the bowel obstruction or marked reduction in symptoms may be possible by using a combination of steroids, prokinetic, antiemetic and antisecretory drugs.
    A trial of **Dexamethasone 16 mg/day SC/IV, metoclopramide 10-30 mg qid SC/IV and haloperidol 1-2 mg sc/24h** is used for 3 to 5 days. Octreotide may be added or substituted for the metoclopramide
  - Hyoscine butylbromide can also reduce colic and secretions but is less effective

- **Pain Control**
  - Use of appropriate opioid analgesics such as **morphine SC/IV** as outlined in the section on pain is the mainstay of treatment
  - For colic add: **hyoscine butylbromide 20 mg q6h/prn SC or hyoscine hydrobromide 0.4 mg sc q4h prn**

- **Nausea and Vomiting**
  - **Haloperidol 2-4 mg/24hrs PO/SC/IV in divided doses**
  - **Metoclopramide 10-30 mg SC/IV qid or as infusion**
    (⚖ Metoclopramide may increase colic as it is a prokinetic agent and therefore should be monitored closely and discontinued if the patient experiences more pain)

- **Dexamethasone 16 mg/day SC/IV:** can be helpful to reduce nausea and vomiting, increase water and salt absorption form G.I. tract, reduce peritumoral oedema and alleviate obstruction. Give for a 5-day trial, reduce dose as tolerated or discontinue if not helpful
- **Octreotide 200 mcg-500 mcg in divided doses (bid or tid) SC or 300-1200 mcg/24hrs by SC infusion:** can be useful especially in cases where there is high volume emesis

NON-PHARMACOLOGICAL TREATMENT

- **Nasogastric tube** will relieve some patients especially with high level obstruction

  ⚖ ***This is usually reserved for patients with frequent or severe symptoms. Usually short term use only while waiting to see if pharmacological management is effective. If necessary for control of symptoms, conversion to a venting gastrostomy tube is beneficial***

- **By-pass surgeries and stenting** may be considered in selected patients depending on the nature of the obstruction, condition of the patient, prognosis and likely benefit

HYDRATION

- Administration daily of 1-1.5 L solution containing electrolytes (+/- glucose) IV or SC may be useful in maintaining electrolyte balance and preventing adverse effects such as opioid toxicity and delirium. Hydration may also cause some symptoms to worsen due to increased third spacing and edema

PITFALLS/CONCERNS

- ***In patients in the final terminal phase – ie. hours to days, invasive treatments should be minimized***
  - ***Prolonged use of nasogastric tubes can cause considerable distress as well as medical complications***
  - ***Hydration should be tailored to individual needs; beware of over-hydration***
  - ***If the bowel obstruction does reverse it may recurr at some point in the future***

PALLIATIVE TIPS

- Aggressive pharmacological management can be very effective in reversing obstruction and reducing gastrointestinal symptoms in inoperable bowel obstruction. A combination of drugs is usually necessary
- Treatment should be initiated early
- Hydration may be given by SC infusion (hypodermolysis) up to 80 cc/h
- In cases of partial obstruction with constipation; continue stool softeners (**docusate**) but stop stimulants (**Senna and Bisacodyl**) if colic is a problem. Try rectal measures such as suppositories

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Malignant Ulcers or Wounds

KEYPOINTS

- Malignant ulcers or wounds can be caused by direct invasion of the skin by a primary tumour or by metastasis to the skin
- These wounds can have both ulcerative and fungating features
- Odour and discharge are common problems with malignant wounds
- Pain, infection and bleeding can also occur
- The psychological distress to the patient or caregivers caused by these wounds should also be addressed
- These wounds rarely heal but the symptoms can usually be controlled with good assessment and management
- Malignant wounds occur in 5-10% of patient with metastatic disease, most commonly in breast cancer and melanoma

ASSESSMENT

see comment on page 4

- A clinical assessment is usually all that is required
- It is important to review the symptoms of odour, discharge, pain, bleeding and psychological impact when assessing the wound
- Swab cultures can sometimes be helpful to determine the need for antimicrobial treatment.

Local bacterial colonization of the wound is expected and should be treated with topical cleansing, debridement as appropriate, and antimicrobial creams. If there are signs of systemic infection, the use of oral or intravenous antibiotics may be considered

- Wound location, size, appearance, exudate, odor, condition of surrounding skin, and pain should all be assessed
- The potential for serious complications, such as hemorrhage, vessel compression, or airway obstruction should be evaluated and a plan developed for management

MANAGEMENT

- **Cleaning the wound**
  - Wound cleansing reduces odor by removing necrotic tissue and decreasing bacterial counts
  - Gentle irrigation of the wound with normal saline is helpful and can be done as often as needed
  - Good handwashing is very important in caring for malignant wounds
  - Local debridement can be performed by *very gently* scrubbing the necrotic areas with gauze saturated with saline or wound cleanser. This must be done carefully and gently to avoid bleeding or pain
  - Topical antimicrobial ointments or creams can be helpful

- **Exudate/Discharge**
  - The inflammation and edema of malignant wounds can cause significant exudate (drainage)

- Dressings should be selected that can best conceal the wound, absorb exudate and reduce odor
- Dressings are generally changed 1-2 times per day based on the amount of exudates and odor
- Menstrual pads can be especially effective because of their good absorption and availability

❍ **Odour control**

- Wound odor is caused from bacterial overgrowth and necrotic tissue
- Managing odor is extremely important for the well-being of the patient and family
- Wound cleaning and dressings for exudates/ discharge (as mentioned above) is important to reduce odor
- Metronidazole (orally or topically) can be very helpful
  - **Metronidazole 400 mg bid or tid PO/IV**
  - Metronidazole gel or injectable metronidazole can be "sprinkled" (not injected!) to the wound with each dressing change
  - Metronidazole capsules/tablets can also be broken and the powder contents sprinkled onto the wound with each dressing change
- Activated-charcoal dressings or a basket of charcoal placed under the bed or table can help absorb and reduce odor
- Peppermint or other oils placed in the room can be helpful. Incense may be helpful but strong perfumes can sometimes cause difficulties in breathing for patients or may induce nausea

- **Pain**
  - It is important to help control pain by using **Morphine** and other medications as mentioned in the section on pain (some malignant wounds can cause neuropathic pain)
  - Topical **Morphine** can be helpful for the wound for some patients. Injectable **Morphine** (e.g. 1 ampoule of 10mg/ml can be mixed in most gels that may be applied or simply "sprinkled" over the wound)
  - Dressing changes can be particularly painful. Giving a breakthrough or rescue dose of Morphine prior to the dressing change can often be helpful

- **Control of bleeding**
  - The viable tissue in a malignant wound may be very friable and bleed with minimal manipulation
  - Prevention is the best method to avoid bleeding. Care must be taken when removing dressings to avoid bleeding. Use warmed normal saline irrigation to moisten the dressing and prevent trauma during dressing changes. Use non-adherent dressings and moist wound products when possible
  - If bleeding does occur, apply direct pressure for 10-15 minutes. Local ice packs can also assist in controlling bleeding
  - Radiotherapy can be considered if appropriate for the patient and the tumour is thought to be radiosensitive
  - Haemostatic dressings or pressure dressings are sometimes required if the bleeding is severe
  - If a patient is at the end of life and having uncontrolled bleeding from a large wound, using dark towels/

blankets to mask the blood can decrease anxiety for the patient and family. Pain control and sedation with a benzodiazepine would be important considerations in this situation

PITFALLS/CONCERNS

- ***Ensure that the dressing used is not "too dry" and therefore causes more pain and bleeding at the time of dressing changes***
- **Perfumes used sometimes become associated with the unpleasant odour rather than "hide" the smell and do not necessarily help**
- **Healthcare providers can become "desensitized" to the smell and so must listen to the patient or family if they complain about the smell from the wound rather than rely on their observations**

PALLIATIVE TIPS

- It is very important to pay particular attention to the emotional impact of these wounds on the patient and family. Medical staff can help reduce social isolation that can often occur

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Nausea and Vomiting

KEYPOINTS

- A distressing symptom present in over 50% of patients with advanced cancer
- There are multiple receptors in the central nervous system, which are involved in the development of nausea. Blocking of these receptors forms the basis of antiemetic medications. These receptors are: dopaminergic, muscarinic, cholinergic, histaminic, and serotonergic
- The choice of antiemetic therapy should be based on what is the presumed underlying cause of the nausea
- Often multiple, concurrent medications from different classes may be required for effective control (e.g. metoclopramide and haloperidol, or prochlorperazine and **Dexamethasone**, etc)

ASSESSMENT

see comment on page 4

- Examination and investigation can be helpful in determining the underlying cause of the nausea/vomiting
- In addition to a (normally transient) side effect of initiating opioids, other causes of nausea/vomiting include severe constipation and impaction, bowel obstruction (malignant and non-malignant), chemotherapy, radiotherapy, metabolic abnormalities (e.g. hypercalcaemia), infection, and other medications

MANAGEMENT

- Management should be "mechanism based" and reflect the most likely underlying cause of the nausea and vomiting
  - For gastric stasis consider a prokinetic such as **Metoclopramide 10-20 mg q4-6h PO/SC/IV**
  - For opioid-induced nausea consider a prokinetic (see above) or a neuroleptic (see below)
  - For metabolic abnormalities or uremia consider a neuroleptic such as **Haloperidol 0.5-2 mg q6-12h PO/SC/IV, Metoclopramide 10-20 mg q4-6h PO/SC/IV** or **Prochlorperazine 10-20 mg q6h PO/IV** or **25 mg q6h PR.**
    These act as dopamine receptor antagonists at the chemoreceptor trigger zone (CTZ).
    Olanzapine 1.25-2.5 mg PO OD is a atypical neuroleptic which is both a dopamine and 5HT receptor antagonist
  - For gastric irriation consider stopping offending agent and adding an H2 blocker such as **Ranitidine 150 mg bid PO** or a proton pump inhibitor such as **Omeprazole 20 mg once a day PO**
  - For chemotherapy or radiation induced nausea consider HT3 receptor antagonists such as **Ondansetron 4-8 mg q8-12h PO/IV** and/or **Dexamethasone 4-20 mg qAM PO/IV/SC**
  - For motion induced nausea consider an anti-histamine such as **Dimenhydrinate 50–100mg q4-6h PO/IV**
  - For infection consider treatment with antibiotics

- For raised ICP (intracranial pressure) consider **Dexamethasone 4-20 mg qAM PO/IV/SC**
- For hypercalcemia consider treatment with hydration and bisphosphonates such as **pamidronate 60-90 mg (single dose) IV**
- For constipation see section on constipation
- For bowel obstruction see section on bowel obstruction
- For over eating re-educate patient and family to reduce intake

❍ If no resolution then consider an additional antiemetic agent that targets different receptors (prokinetic, neuroleptic, anti-histamine, HT3 receptor antagonist)

❍ If anxiety is thought to be a contributing factor to the nausea or vomiting then **Lorazepam 0.5-2 mg q4-6h PO/SC/PR** can be effective in control of nausea and vomiting in addition to other medications such as those mentioned above

❍ If no resolution then consider steroids i.e. **Dexamethasone 4-20 mg qAM PO/IV/SC**

Medications should be dosed **regularly** if nausea and vomiting are ongoing symptoms

PITFALLS/CONCERNS

❍ In the setting of complete bowel obstruction the use of prokinetic agents such as metoclopramide may result in increased pain and cramping and should be discontinued

PALLIATIVE TIPS

- For intractable nausea and vomiting, a multimodal approach combining antiemetics targeting different receptors is recommended (eg. haloperidol + dimenhydrinate + **Dexamethasone**)
- Similar to the setting of ongoing pain, ongoing nausea requires regular dosing of antiemetics rather than just prn!

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Pain

KEYPOINTS

- Pain in advanced cancer occurs about 70-90% of the time
- Almost all pain can be satisfactorily controlled using simple medication combinations
- The use of the World Health Organization (WHO) analgesic ladder (Appendix 2) is a helpful tool in treating pain
- The WHO method can be summarized in five phrases: "by mouth", "by the clock", "by the ladder", "for the individual" and "attention to detail."
- Paracetamol and NSAIDs can be used for mild pain
- Opioids such as **morphine** should be used in moderate to severe pain
- Remember to prevent or treat the side effects of morphine such as constipation and nausea/vomiting
- There is no "upper ceiling" dose to the amount of **morphine** that can be used. The right dose is the dose that works
- Neuropathic pain is common and is pain which is transmitted by a damaged nervous system
- Consider the use of adjuvant medications at all levels of the analgesic ladder (especially with neuropathic pain)

ASSESSMENT

see comment on page 4

- A good clinical assessment is important to try and identify

the underlying cause of the pain (e.g. tumour involvement, bone metastases, liver enlargement, etc)

- Listening to the patient describe their pain location, intensity, quality, "what makes it worse", "what makes it better", etc can tell a lot about what might be causing the pain and how best it might be treated
- The use of pain measurement scales such as the Visual Analogue Scale (VAS) or a "0-10" scale are important tools to use in assessing a patient's pain and the response to treatment
- The impact of pain on things such as function and sleep is important to ask about
- Investigations to consider may include
  - Radiologic investigations (e.g. x-ray) to determine if there is bony metastasis or tumour involvement
- Assess for the presence of neuropathic pain
  - Pain or discomfort resulting from injury to the peripheral or central nervous system
  - Pain is often described as "burning, stabbing or shooting"
  - Allodynia or hyperalgesia may be found on exam and suggests the presence of neuropathic pain
    - Allodynia – something that is usually not painful is now experienced as painful
    - Hyperalgesia – something that is a usually a little painful is now experienced as more painful

MANAGEMENT

- Consider treatment of the underlying cause (e.g. oncological treatment of tumour, radiation for bone metastasis etc.)

Consider if patient is well enough to benefit

- **See Appendix 2 for the use of the WHO analgesic ladder**
- The WHO method can be summarized in five phrases: "by mouth", "by the clock", "by the ladder", "for the individual" and "attention to detail"

FOR MILD PAIN

- **Paracetamol 650 mg-1 gm every 4 h or 1 gm every 6 h** (daily maximum 4 g/d)
  - Hepatotoxicity can occur at doses higher than this
  - Paracetamol can also be combined with NSAIDs
- NonSteroidal Anti-inflammatory Drugs (NSAIDs)
  - Produce an analgesic effect within 1 to 2 hours
  - Produce an anti-inflammatory effect within 2 to 3 weeks
  - Serious side-effects can occur with NSAIDS including:
    - Gastrointestinal (GI bleed)
    - Renal toxicity
    - Congestive heart failure
  - They should therefore be used with caution especially in patients at risk for GI or renal toxicities
  - If GI symptoms occur, the NSAID can be discontinued or the risk of GI toxicity can be reduced by the addition of a protective agent such as an H2 receptor antagonist **(eg. ranitidine), misoprostol** or **omeprazole**
  - Evidence to support efficacy or safety of one NSAID over another is lacking
  - Examples of NSAIDs include:
    - **Ibuprofen 200-400 mg PO tid**
    - **Diclofenac 50 mg PO/SC tid**
    - **Naproxen 250-500 mg PO/PR bid**

- **Ketorolac 10 mg PO qid or 10-30 mg SC tid**
- Multiple other NSAIDs exist

For moderate Pain

- A "weak" opioid such as **Codeine 30-60 mg q4h PO** or **Tramadol 50 mg PO qid** can be tried. **Codeine** is often combined with other agents such as paracetamol and thus maximum doses may be limited by the amount of paracetamol
- **Morphine** can also be used at this point and should definitely be used if the pain is not controlled by **Codeine** or other means
- Remember to consider he use of adjuvants along with the opioid

For severe Pain

- **Morphine** or another opioid should be started
- The initial starting dose will depend on the patient's previous exposure to opioids:
  - A dose of **Morphine 2.5 mg regularly q4h PO (or 1 to 2 mg SC/IV)** and a breakthrough or rescue dose every hour, as required (see Appendix 1) is suitable for an opioid-naive patient
  - A dose of **Morphine 5-10 mg regularly q4h PO (or 2.5–5 mg q4h SC/IV)** and a breakthrough or rescue dose every hour, as required (see Appendix 1) should be used for patients who have already been on **Codeine**
  - It is necessary over the next days to titrate the regular dose to achieve good control (more than 3 BTDs/day often means that the baseline **Morphine** is not enough)

- To determine the new dose, add the number of breakthroughs being used in a 24h period to the regular total daily dose. Then divide by 6 to determine the new q4h dose. Alternatively, you can also increase the total daily opioid dose by 25% to 50% depending on the severity of the patient's pain
- Remember that there is no "upper ceiling" dose to the amount of **morphine** that can be used. The right dose is the dose that works

❍ Alternative routes for **Morphine** include:
rectal, subcutaneous, buccal, intravenous and via a gastrostomy tube – **the oral route** for Morphine should be **the route of choice** in most cases.
The PO: SC **Morphine** ratio is 2:1
The PO: IV **Morphine** ratio is 2-3:1
e.g. 10 mg oral **Morphine** = 5 mg SC **Morphine**

❍ Be aware, educate patients/families about, prevent and treat the common side effects of Morphine:
- Constipation (prescribe laxatives/stool softeners when starting someone on **Morphine**, see section on constipation)
- Nausea (usually only temporary - ensure an antiemetic is available especially if just starting someone on **Morphine**)
- Excessive sedation or drowsiness (usually only temporary)

Adjuvants

❍ Adjuvants are medications or measures that provide relief to the patient in addition to the analgesic medications themselves

❍ They are often used in pain due to bone metastases and in neuropathic pain

- For bone pain consider:
  - NSAIDs, corticosteroids, radiotherapy
- For neuropathic pain consider:
  - Trial of antidepressant: start with low dose and increase every 3-5 days if tolerated (eg, **nortriptyline**, **amitriptyline** or **desipramine 10-150 mg PO od**) and/or
  - Trial of anticonvulsant: start with low dose and increase every 3-5 days if (eg, **gapabentin 100-200 mg pot id; carbamazepine100-400 mg PO bid**)

PITFALLS/CONCERNS

- ⚖ ***Meperidine if used on an ongoing basis will cause a build up of the metabolite (normeperidine) and may cause delirium and seizures – it should be avoided in the treatment of cancer pain***
- ***Never ever use a slow-release opioid as the breakthrough or rescue medication (use regular short-acting instead)***
- ***Serious side-effects can occur with NSAIDs – they should be used cautiously. An opioid such as morphine may be a more effective and safer option***

PALLIATIVE TIPS

- Treat pain promptly and aggressively!!!
- The WHO guidelines remind us that the "relief of psychological, social and spiritual problems is paramount. Attempting to relieve pain without addressing the patient's non-physical concerns is likely to lead to frustration and failure"

- Constant pain requires regular analgesia. Use "around-the-clock" dosing to treat and prevent pain
- Make sure to provide a breakthrough or rescue dose (BTD) in addition to the regular dose of **Morphine**
- Optimize the opioid by titrating up until pain improved
- The PO **Morphine** to SC/IV **Morphine** ratio is 2:1 e.g. 10 mg oral = 5 mg SC
- **Morphine** 10 mg PO = **Codeine** 100 mg PO
- Remember the use of adjuvants in the treament of pain (eg. Neuropathic pain)

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Pleural Effusion

KEYPOINTS

- Approximately half of all patients with metastatic cancer will develop a pleural effusion
- Lung and breast cancer are the most common causes of a malignant pleural effusion although it can occur in almost any type of cancer
- Patients may experience dyspnea, dull aching chest pain, or dry cough due to this fluid accumulation
- Thoracentesis (removal of the fluid) can be helpful in relieving dyspnea in some patients
- Pleurodesis (after thoracentesis and drainage) is sometimes used to try and prevent re-accumulation of the fluid
- Pleural effusion may be the first presenting sign of cancer, or suggestive of recurrent or advanced disease

ASSESSMENT

see comment on page 4

- A moderate to large pleural effusion can most often be diagnosed by clinical exam alone (decreased breath sounds and dullness to percussion)
- A good clinical assessment can also help to identify the underlying cause of the pleural effusion
- Pleural effusions can be caused by malignant or non-malignant processes

- Non-malignant processes include:
  - Congestive heart failure
  - Pneumonia
  - Low albumin (hypoalbuminemia)
  - Pulmonary embolus
  - Pancreatic disease
  - Interstitial lung disease
  - Ascites
- Investigations to consider may include:
  - Chest X-ray to assess extent of effusion and evidence of other diagnoses (eg. pneumonia)
    - If the fluid amount is > 200 to 300 mL it can usually be detected by Chest X-ray
    - Smaller amounts of fluid can sometimes be detected using ultrasound or a CT scan
- Analyses of the pleural fluid (if removed) may help in diagnosing the underlying cause of the effusion. Malignant pleural effusions are typically exudative but on rare occasion can be transudative

MANAGEMENT

- The management of **dyspnea** and **cough** are covered in other guidelines and should be followed if these symptoms are present
- A small effusion that is not causing the patient any distress does not normally need to be drained
- Pleural effusions can sometimes resolve on their own with effective treatment of the underlying disease, such as congestive heart failure
- Consider drainage of the pleural fluid (thoracentesis)

if the patient is highly symptomatic

Consider only if patient is well enough to benefit

- Risks and benefits of a thoracentesis should be explained to the patient before proceeding. These would include hemothorax, pneumothorax and infection

❍ THORACENTESIS procedure (adapted from Oxford handbook of Palliative Care [7]:

- The patient should be sitting, leaning forward on a bedside table
- Choose a point in the posterior chest wall, medial to the angle of the scapula, one intercostal space below the upper limit of dullness to percussion
- On insertion, be careful to avoid the inferior border of the rib
- Inject local anaesthetic. Wait for the area to be anaesthetized then advance the needle until pleural fluid is obtained
- Introduce a large bore IV cannula with a syringe attached until fluid is just obtained, then advance a further 0.5 – 1 cm to ensure that the cannula is in the pleural space
- Ask the patient to exhale against pursued lips (this will increase the intrathoracic pressure) and remove the metal trochar or needle and then attach a large syringe with a three-way tap
- Aspirate 50 ml at a time until:
  - Drainage complete or
  - Patient starts to cough or
  - Light-headedness or chest discomfort occurs
- Remove the cannula, having asked the patient to take

a breath, and immediately seal with an appropriate dressing

- Sometimes a chest tube is left in place while the fluid continues to drain
- Pleurodesis is sometimes carried out following thoracentesis and drainage. It is undertaken to try and prevent re-accumulation of the fluid
  - It occurs by inducing inflammation of the pleura by the introduction of a sclerosing agent administered by a chest tube or indwelling catheter into the chest cavity
  - Talc is the most effective sclerosing agent used for pleurodesis
  - Pleurodesis is not always effective and does have procedure related side-effects including increased pain
  - Patients should be evaluated on an individual basis when deciding whether or not to undergo pleurodesis. It should only be done if the patient has an expected survival of at least several months and is not debilitated

PITFALLS/CONCERNS

- ⚖ ***In patients in the final terminal phase – ie. hours to days, it would be inappropriate to drain a pleural effusion (treatment should be as least invasive as possible)***

- ⚖ ***In patients in the final terminal phase – ie. hours to days, symptomatic relief through pharmacologic and other means would be preferred***

PALLIATIVE TIPS

- The decision whether to repeatedly perform thoracentesis must be carefully weighed against the patient's wishes, available resources, the patient's ability to tolerate the procedure, the risks involved with repeated thoracentesis, the knowledge that the fluid will likely reaccumulate and the ability to symptomatically control dyspnea by other non-invasive means
- It is important to remember that malignant effusions usually recur and the fluid can re-accumulate in as little as four days. Serial thoracentesis may result in loculated fluid and worsening of symptoms
- Repeated thoracentesis, especially if the fluid rapidly reaccumulates, is usually not indicated

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Pruritus

KEYPOINTS

- Pruritus can be described as an unpleasant cutaneous sensation which produces the desire to scratch
- Pruritus is relatively uncommon in advanced disease but can be very unpleasant and difficult to treat
- General non-pharmacologic treatment can be very helpful

ASSESSMENT

- History should include the times at which the itching occurs (whether continuous and whether at night or day) its nature (burning, itching etc), location and relevant medication history
- Examination should include review of dryness of skin, possible presence of scabies, possible presence of jaundice

MANAGEMENT

General Measures

- Pruritus is often caused by dry skin, so a good first measure is a simple moisturiser cream
- Keep patient cool and use cool clothing
- Tepid (around 37 C) baths and showers (avoiding detergents), followed by gentle drying and application of moisturiser cream

- Keep nails short (filed not cut)
- Avoidance of alcohol and spicy foods

Topical Agents

- Menthol 1% and Camphor 1% compounded in aqueous cream can be used several times a day as needed

Cause Specific Therapy

- Cholestasis
  - Use general measures (see above)
  - HI and H2 receptor blockers likely to be ineffective
  - Place biliary stent (if possible and if patient's general condition warrants this.
    The burden of investigation and treatment should always be weighed against the prognosis, the likely benefit of treatment and the patient's wishes.
  - Rifampacin start at 75 mg PO once daily and increase to 150 mg bid PO
    If ineffective: add or substitute:
  - Cholestyramine 4 g 1-6 times/day PO to a maximum of 36 g/day
- Uraemia
  - Use general measures (see above)
  - HI and H2 receptor blockers likely to be ineffective
  - Capcaisin 0.025% or 0.075% cream applied 3-5 times daily is useful where there is localised pruritus.
    Do not apply to large body areas
- Hodgkins Lymphoma
  - Use general measures (see above)
  - HI and H2 receptor blockers likely to be ineffective

- Radiation or chemotherapy where appropriate
- Corticosteroids e.g **Dexamethasone** 4-8 mg daily
  If inefective: substitute:
- Cimetidine 400 mg bid PO or Ranitidine 150 mg bid PO

❍ Itch due to an opioid
- Use general measures (see above)
- HI and H2 receptorblockers likely to be ineffective
- May be transitory lasting a few days
- May be relieved by 'switching opioids'
- Paroxetene 5 mg/day PO to 20 mg/day can be helpful

PALLIATIVE TIPS

❍ Itching of the skin is present without obvious cause in over 50% of patients over 70 years

❍ Itching associated with cholestasis often starts on palms and soles and the severity is unrelated to the level of bile acids in skin

❍ H1 recepeptor blockers are useful in histamine based itch such as a drug reaction or urticaria

❍ **Ondansetron** is helpful when spinal opioids cause itching

❍ ***Antihistamine creams may cause a contact dermatitis***

❍ ***Lidocaine cream may cause a contact dermatitis and worsening of itching***

❍ ***Calamine cream may cause drying of the skin and worsening of the itching***

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Respiratory Secretions at the End of Life

KEYPOINTS

- Noisy upper airway secretions are heard in approximately 50% of dying patients
- Caused by air passing through airways with secretions present (as the patient is unable to swallow or clear them)
- The presence of respiratory secretions is a strong predictor of death (76% die within 48 hours from onset of this symptom)
- Repositioning the patient is often helpful and all that is necessary
- Anticholinergic medications (e.g. atropine) can be helpful in many cases to reduce the secretions and noise

ASSESSMENT

see comment on page 4

- A clinical assessment is all that is required
- Other investigations would not be appropriate at this stage as the patient's condition is very poor and death can be expected in the near future

MANAGEMENT

- Much of the management focuses on teaching and support of the family who may find this symptom difficult to watch or hear

- **Repositioning** the patient is often helpful in decreasing the noise
  - Place the patient on their side with upper body elevated
- Good mouth-care can also be helpful
- Administering anticholinergic medications can sometimes be helpful for upper airway secretions:
  - **Hyoscine hydrobromide 0.4 mg as a single dose SC.** Several doses q 30 minutes may be required
    If effective, continue using 0.3-0.6 mg q4h SC
  - **Atropine 0.6-0.8 mg SC.**
    If effective, continue, using q4h and prn.
  - **Glycopyrronium bromide 0.2 mg as a single dose SC.**
    If effective, continue using 0.2 mg q4h and prn SC
  - **Hyoscine butyl bromide 20 mg as a single dose SC.**
    If effective, continue, using **20 mg q4h SC**
- **Suctioning is usually not necessary** (or helpful) and may be distressing to the patient
  - Consider suctioning if thick mucous, blood or other fluid is in the mouth/throat and can be easily removed with a soft catheter (i.e. no deep suctioning or rigid suctioning)

PITFALLS/CONCERNS

- ***Anticholinergic drugs as mentioned above should be used cautiously in patients who are still responsive as they can cause agitation. They generally are used in patients close to death. Glycopyrronium bromide and hyoscine butyl bromide (as compared to atropine and hyoscine hydrobromide) do not cross the blood brain barrier and may therefore cause less CNS effects***

- ***Treatment with these agents is not always successful in reducing the secretions so it is important to support family***

PALLIATIVE TIPS

- Explaining to the family that the noisy respiratory secretions are unlikely to be distressing for the patient who is unconscious is an important part of helping to support the family
- The drug treatments are quite effective for upper airway secretions, but will not work for secretions deep in the lungs, pulmonary edema, pneumonia etc.
- Hydration with IV fluids may increase the severity of this symptom – use fluids cautiously in the dying

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Seizures

KEYPOINTS

- Seizures are relatively common in the palliative care population, occurring in up to 10% of patients
- Most seizures are brief, self-limited and rarely harmful themselves
- Meperidine, if used on an ongoing basis, can cause seizures due to an accumulation of normeperidine, a neurotoxic metabolite. Meperidine should therefore be avoided in palliative care patients

ASSESSMENT

see comment on page 4

Treatment is usually symptomatic and a full seizure workup is, in most cases, not necessary

- Causes of seizures include:
  - Brain tumours
  - Drug toxicity (eg. meperidine)
  - Metabolic or electrolyte abnormality
    - Hypoglycemia
    - Hyponatremia
    - Hypercalcemia
  - Hypoxia
  - Severe hepatic failure
  - Infections of the central nervous system

- Epilepsy

❍ Cancers most likely to metastasize to the brain are: lung, breast and malignant melanoma

MANAGEMENT

❍ Most seizures are brief, self-limited and rarely harmful in themselves

ACUTE TREATMENT OF SEIZURES (STATUS EPILEPTICUS)

❍ Clear airway

❍ **Diazepam 10 mg PR.**
Repeat after 15 and 30 minutes if needed
or

❍ **Lorazepam 2-4 mg SL, SC or IV.**
Repeat after 15 and 30 minutes if needed
or

❍ **Midazolam 5-10 mg SC or IV.**
Repeat after 15 minutes if needed
If no response:

❍ Consider doubling the dose of **Diazepam** or **Midazolam** or

❍ **Phenobarbital 100-200 mg SC or IV (slowly by IV over 30 minutes with 100 cc of saline). May repeat if necessary. Follow this with 100 mg tid SC**

PROPHYLACTIC MANAGEMENT OF SEIZURES

Seizure prophylaxis with anticonvulsants has only been proven useful in patients with brain metastasis due to malignant melanoma and patients with brain metastasis from other cancers who have already had a seizure

- **Anticonvulsant medication**
  - Phenytoin 300 mg PO followed by 100-200 mg PO tid
  - Carbamazepine 100 mg PO bid
  - Valproate 200 mg PO tid
  - Others options exist (lamotrigine, gabapentin, toprimate)
- **Corticosteroids**
  Are helpful in the prevention and management of seizures which are secondary to brain metastasis, by decreasing the oedema surrounding a tumour mass
- **Radiation**
  Can be helpful in preventing seizures in patients with metastatic brain disease
- **Opioid rotation**
  Opioids very rarely cause seizures. (Except Meperidine which can cause cerebral excitation and seizures). Switching to another opioid can be helpful in this situation

PITFALLS/CONCERNS

- ***There are many drug-drug interactions that occur with anticonvulsant medications***
- ***It is important to monitor the dose and duration of treatment with corticosteroids frequently especially when used for more than 4 weeks, to prevent long-term side effects such as steroid myopathy, hyperglycemia and gastrointestinal bleeding among others***
- ***Meperidine can cause cerebral excitation and seizures***

PALLIATIVE TIPS

- Prophylactic anticonvulsant therapy for all patients with cerebral metastases is unnecessary as most patients are unlikely to seize due to their metastases. If they do indeed seize, anticonvulsant therapy should then be started
- If seizures last longer than 5 minutes, or if they occur at frequent intervals and the patient does not recover fully between intervals, the patient is considered to be in status epilepticus (See acute management of seizures)

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Signs and Symptoms at the End of Life

CONFUSION/DISORIENTATION/DELIRIUM

- Confusion/delirium is very common at the end of life
- It is the result of multiple, nonreversible factors, such as: hypoxemia, metabolic and electrolyte imbalances, toxin accumulation due to liver and renal failure, adverse effects of medications, infection, and the underlying disease process
- Patients will demonstrate increased drowsiness, a need for more sleep, and decreased responsiveness
- Some patients may experience an "agitated" delirium due to central nervous system excitation. The risk of agitated delirium is increased if the patient has cerebral metastases. *Refer to the Delirium Guidelines*
- Since reversing the cause of the delirium is often not possible at the end of life, the focus should be on managing the symptoms associated with the delirium, keeping the patient safe, and reassuring the patient and family. *Refer to the Delirium Guidelines*
- Evidence suggests that unconscious patients may still be able to hear conversations, and family members can be encouraged to speak to their loved one as though they were conscious

WEAKNESS/FATIGUE

- Weakness and fatigue increase as the patient gets closer to death

- It is NOT appropriate to give stimulants (methylphenidate, steroids) to try to "wake the patient up" at this stage of the illness
- Patients may need gentle passive movement to minimize risk of pressure ulcer formation if they are too weak to turn in bed. (However, this must be done cautiously since turning and repositioning may cause pain. If death is imminent, the risk of pressure ulcer formation is not relevant)
- It is important to allow the patient to rest and to help family members understand that this weakness and fatigue is a normal part of the dying process
- Patients will have a limited amount of energy, and we can help the patient prioritize how they want to use this energy. For example, inserting a foley catheter may allow the patient to use energy talking and visiting with family that he would otherwise use moving to the toilet

DECREASED ORAL INTAKE

- Loss of oral intake (both food and fluids) is a normal part of the dying process. *Refer to the Anorexia/Cachexia Guideline*
- Actively dying patients are not hungry or thirsty, and oral intake may actually be dangerous as the risk of aspiration increases as the patient becomes weaker
- Parenteral or enteral feeding at the end-of-life has not been shown to improve symptom control or lengthen life
- Excessive parenteral fluids, especially in the setting of

hypoalbuminemia, can cause fluid overload and significantly increase patient's distress by exacerbating peripheral edema, ascites, pulmonary oedema and dyspnea
- Frequent oral care (swabbing the mouth with water, keeping lips moist with vasoline/balm) is generally more important for patient comfort than giving fluids

DECREASED BLOOD PERFUSION/RENAL FAILURE

- As cardiac output and intravascular volume decrease there will be evidence of diminished blood perfusion
- Tachycardia, hypotension, cool extremities, cyanosis and mottling of skin are common at the end of life
- Urine output is reduced as perfusion of the kidneys fails. Oliguria/anuria are expected signs
- Parenteral fluids will not reverse this circulatory failure

VITAL SIGN CHANGES

RESPIRATION

- Changes in the dying patient's breathing pattern typically indicate significant neurological compromise
- Breaths may become shallow and frequent, or shallow and slow
- Periods of apnea and increased use of accessory respiratory muscles is common
- It is important to control the symptom of dyspnea, not only for the patient's comfort, but also because family members often view this as the most distressing sign at the end of life. *Refer to Dyspnea Guideline*

TEMPERATURE

- Elevated temperature is common at the end-of-life. It can be due to infection, dehydration and/or the underlying disease (i.e."tumor fevers")
- Reversing the fever at the end of life is generally not possible
- The most effective treatment is paracetamol rectal suppositories, 650 mg given q4-6 hours either around the clock or prn
- Diaphoresis can be managed with frequent linen changes and cool sponge baths/soaks

HEART RATE/PULSE

- Heart rate may increase with an irregular rhythm
- Cyanosis can be seen as cardiac output falls, and is often first noted in the tip of the nose, nail beds and knees
- Extremities will become mottled and cooler. Progressive mottling indicates death within a few days; absence of a radial pulse may indicate death in a few hours

DECREASED OR DIMINISHED SWALLOW REFLEX

- Weakness and decreased neurologic function impair the patient's ability to swallow at the end of life
- The patient loses the ability to clear secretions from their oropharynx
- This accumulation of saliva and oropharyngeal secretions may lead to gurgling or rattling sounds with each breath, sometimes called "death rattle"

- This sound can be very distressing to family members, as it may sound as though the patient is choking. Family education is critical
- Medications such as atropine or glycopyrrolate can help reduce this symptom. Repositioning the patient in a lateral recumbent position can facilitate the clearing of secretions. Gentle oropharyngeal suction can sometimes be helpful. *Refer to the Respiratory Secretions at End of Life Guideline*

SURGES OF ENERGY

- Patients may experience a period of increased energy and mental alertness prior to their death
- This can be a time for quality interaction between family members and the patient

INCONTINENCE/URINARY RETENTION

- Fatigue and loss of sphincter control can lead to incontinence of urine and/or stool at the end of life
- Family members should be educated that this is a common occurrence
- Special attention should be paid to keeping the patient clean and dry. A foley catheter may be helpful, but may not be necessary if urine output is minimal and can be controlled with absorbent pads
- Urinary retention can occur. If a patient is restless and has a distended bladder it may indicate the bladder needs to be emptied and insertion of a foley catheter may bring relief

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Appendix 1

BREAKTHROUGH OR RESCUE DOSES OF MORPHINE

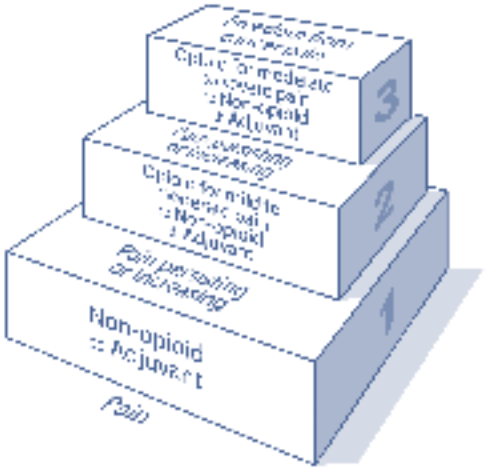
- A breakthrough or rescue dose (used interchangeably in the literature) of **Morphine** is one that is given when the patient requires **Morphine** for symptoms in addition to the regularly prescribed dose
- It is used to treat episodic or breakthrough pain which has several types:
  - Spontaneous pain (unrelated to movement or other incident)
  - Incident pain (related to an activity, action or event)
  - End-of-dose pain (occurring just prior to the next scheduled dose)
- It is made available on a prn basis **in addition** to their regular dose
- Providing a breakthrough or rescue dose of **Morphine** is an important part of managing pain, dyspnea and cough
- ***Breakthrough or rescuedoses are generally approximately 10% of the total 24 hour dose and should be ordered q1h prn (on an as needed basis)***

  EXAMPLE 1: A patient receives 10 mg q4h SC of Morphine = 60 mg in 24h SC. Therefore, appropriate breakthrough or rescue dose is 5 mg q1h prn SC

  EXAMPLE 2: A patient receives 5 mg q4h PO of Morphine = 30 mg in 24h PO. Therefore, appropriate breakthrough or rescue dose is 2.5 mg q1h prn PO

Appendix 2

WORLD HEALTH ORGANIZATION PAIN LADDER



World Health Organization. Cancer Pain Relief. 2nd Edition. Geneva: WHO; 1996

Appendix 3

ABBREVIATIONS

Abbreviation	Meaning
bid	twice daily
BTD	breakthrough dose
g	gram
h	hour
HS	bedtime
IV	intravenous
kg	kilogram
L	litre
mcg	microgram
mg	milligram
min	minute
mL	millilitre
PO	by mouth
PR	rectally
prn	as needed
qAM	every morning
q1h	every hour
q4h	every 4 hours
q6h	every 6 hours
qid	4 times a day
SC	subcutaneous
SL	sublingual
tab	tablet
tid	3 times a day

Prescribed Drugs / Medications

In this section, some basic information on number of the medications mentioned in the guidelines is given. This information is drawn from a number of sources listed on page 141 and the reader is encouraged to access these and other relevant literature for more detail. As always, sound clinical judgment should used in individual clinical cases.
In particular, it should be remembered that there can be significant variation in the pharmokinetics of a drug based on a number of factors (including the individual patient's metabolism/disease status and how the medication has been formulated).

IAHPC* List of Essential Drugs for Palliative Care

MEDICATION	FORMULATION
Amitriptyline**	50 - 150 mg tablets
Bisacodyl	10 mg tablets 10 mg rectal suppositories
Carbamazepine***	100 - 200 mg tablet
Citalopram (or any other equivalent generic SSRI except paroxetine and fluvoxamine)	20 mg tablets 10 mg/5ml oral solution 20 - 40 mg injectable
Codeine	30 mg tablets
Dexamethasone	0.5 - 4 mg tablets 4 mg/ml injectable
Diazepam	2.5 - 10 mg tablets 5 mg/ml injectable 10 mg rectal suppository
Diclofenac	25 - 50 mg tablets 50 and 75 mg/3ml injectable
Diphenhydramine	25 mg tablets 50 mg/ml injectable
Fentanyl (transdermal patch)	25 micrograms/hr 50 micrograms/hr
Gabapentin	tablets 300 mg or 400 mg
Haloperidol	0.5 - 5 mg tablets 0.5 - 5 mg drops 0.5 - 5 mg/ml injectable
Hyoscine butylbromide	20 mg/1ml oral solution 10 mg tablets 10 mg/ml injectable

MEDICATION	FORMULATION
Ibuprofen	200 mg tablets 400 mg tablets
Levomepromazine	5 - 50 mg tablets 25 mg/ml injectable
Loperamide	2 mg tablets
Lorazepam****	0.5 - 1 - 2 mg tablets 2 mg/ml liquid/drops 2 - 4 ml injectable
Megestrol Acetate	160 mg tablets 40 mg/ml solution
Methadone (immediate release)	5mg tablets 1 mg/ml oral solution
Metoclopramide	10 mg tablets 5 mg/ml injectable
Midazolam	1 - 5 mg/ml injectable
Mineral oil enema	
Mirtazapine (or any other dual action NassA or SNRI)	15 - 30 mg tablets 7.5 - 15 mg injectable
Morphine	Immediate release: 10 - 60 mg tablets Immediate release: 10 mg/5 ml oral solution Immediate release: 10 mg/ml injectable Sustained release: 10 mg tablets Sustained release: 30 mg tablets
Octreotide	100 mcg/ml injectable
Oral rehydration salts	
Oxycodone	5 mg tablet
Paracetamol (Acetaminophen)	100 - 500 mg tablets 500 mg rectal suppositories

MEDICATION	FORMULATION
Prednisolone (as an alt to Dexamethasone)	5 mg tablet
Senna	8.6 mg tablets
Tramadol	50 mg immediate release tablets/capsules 100 mg/1 ml oral solution 50 mg/ml injectable
Trazodone	25 - 75 mg tablets 50 mg injectable
Zolpidem (still patented)	5 - 10 mg tablets

* IAHPC = International Association for Hospice and Palliative Care

** Side-effects limit dose

*** Alternatives to amitriptyline and tricyclic antidepressants (should have at least one drug other than dexamethasone)

**** For short term use in insomnia

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Amitriptyline

PHARMACOLOGY

Tricyclic antidepressant that blocks the pre-synaptic uptake of serotonin and norepinephrine

- Onset of action: analgesic effect after 3-7 days; up to 30 days for depression
- Time to peak plasma concentration: 4 h PO
- Plasma 1/2 life: 9-25 h PO;

DOSING

Starting dose 10-25 mg PO hs titrating upward as required to 150 mg (higher doses rarely required in palliative care)

UNWANTED EFFECTS

Sedation, dry mouth, delirium, postural hypotension, fatigue, hyponatremia, headache, urinary retention

PITFALLS/CONCERNS

- Low doses should be used initially in the elderly
- Sedation may affect performance of some tasks
- Avoid abrupt withdrawal after discontinuation
- Should not be used with an MAOI, recent myocardial infarction, arrythmias, mania or severe hepatic impairment

Atropine

PHARMACOLOGY

Antimuscarinics/anticholinergics such as hyoscine hydrobromide, atropine, glycopyrronium, hyoscine butyl bromide are used primarily as smooth muscle antispasmodics and antisecretory agents. They are used in palliative care for intestinal colic, genitor-urinary colic, inoperable bowel obstruction with colic and respiratory secretions at end of life.

Hyoscine hydrobromide and glycopyrronium are less likely to cross the blood-brain barrier as they are less lipid-soluble thereby causing less central side-effects (eg. delirium)

Overall efficacy in reducing respiratory secretions at end of life is seen in about1/2 to 1/3 of patients

Onset of action: < 10 minutes SC/IM/IV
Plasma 1/2 life: 5-6 h

DOSING

- 0.6-0.8 mg SC. If effective, continue, using q4h and prn.

UNWANTED EFFECTS

Blurred vision, cardiovascular effects, dry mouth, constipation, heartburn, urinary retention, delirium

PITFALLS/CONCERNS

- Avoid concurrent use with prokinetics as atropine may block the action of agents such as metoclopramide
- Glaucoma may be precipitated in patients at risk

Bisacodyl

PHARMACOLOGY

Increases bowel motor activity

Onset of action:
tablets 10-12 hours; suppositories 20-60 minutes

DOSING

5-20 mg od to bid

UNWANTED EFFECTS

Intestinal colic (cramping), diarrhea

Carbamazepine

PHARMACOLOGY

Time to peak: 4-8 hours
Plasma 1/2 life: 8-24 hours

DOSING

100-200 mg od-bid, increase by 100-200 every 2 weeks, (usual maximum dose 800-1200 mg in divided doses)

UNWANTED EFFECTS

Drowsiness, headache, unsteadiness on feet, dizziness, headache, nausea and vomiting

- There are many drug-drug interactions with anti-epileptics

Carbocisteine

PHARMACOLOGY

Carbocisteine decreases the viscosity of sputum secretions

DOSING

750 mg tid

UNWANTED EFFECTS

Occasional gastro-intestinal irritation

PITFALLS/CONCERNS

- Can rarely cause gastro-intestinal bleeding

Chlorpromazine

PHARMACOLOGY

- Chlorpromazine is a phenothiazine antipsychotic which selectively antagonizes dopamine D2 receptors in the brain

Onset of action: I.M.: 15 minutes; Oral: 30-60 minutes
Plasma 1/2 life: 23-37 hours

DOSING

Intractable hiccups: Oral, I.M: 25-50 mg 3-4 times/day

UNWANTED EFFECTS

Anticholinergic effects: (constipation, dry mouth, blurred vision, urinary retention). Extrapyramidal symptoms: (pseudoparkinsonism, akathisia, dystonias, tardive dyskinesia) Sedation, orthostatic hypotension, paradoxical agitation/ excitement, restlessness, rash, photosensitivity

Clonazepam

PHARMACOLOGY

Benzodiazepines have GABA-potentiating actions in the CNS (spinal cord, hippocampus, cerebellum, cerebrum) thereby reducing neuronal activity

Onset of action: 20-60 min PO
Time to peak: 1-3 hours
Duration of action: Children 6-8 hours, adults less than 12 hours
Plasma 1/2 life: 20-60 hours

DOSING

Anxiety: 250 micrograms – 2 grams OD or BID

Neuropathic pain: 500 micrograms – 4 mg PO OD or BID

UNWANTED EFFECTS

Sedation, fatigue, decreased co-ordination, blurred vision, memory impairment, hypotension, anxiety, decreased libido, depression, headaches, insomnia, edema

PITFALLS/CONCERNS

- Benzodiazepines used alone in delirium will likely exacerbate the condition
- There are some drug-drug interactions with benzodiazepines
- Abrupt cessation of long-term benzodiazepine therapy can cause withdrawal symptoms
- May cause hypotension
- Use with caution in severe hepatic disease

Codeine

PHARMACOLOGY

Codeine is a pro-drug of **Morphine**. Its metabolites bind to the u-opioid receptor providing analgesia. It is about 1/10 as potent as **Morphine**. Codeine may not provide analgesia if the patient is a poor CYP2D6 metaboliser or if another drug such as paroxetine is acting as a CYP2D6 inhibitor.

Codeine is also an antitussive properties and will slow gastro-intestinal motility

Onset of action: 0.5 to 1 hour for analgesia;
1-2 hours for antitussive effect
Time to peak effect: 1-2 hours
Duration of action: 4-6 hours
Plasma 1/2 life: 2.5-3.5 hours

DOSING

Commonly it is given in a compounded preparation with paracetamol or another agent which may limit its use based on "ceiling dose"
Analgesia: 30-60 mg PO q 4h
Antitussive: 15-30 mg PO q 4h prn
Diarrhea: 30-60 mg PO q 4h prn

UNWANTED EFFECTS

- Common initial: nausea and vomiting, drowsiness, unsteadiness, delirium (transient)
- Common ongoing: constipation, nausea and vomiting
- Occasional: dry mouth, sweating, pruritis, hallucinations, myoclonus
- Rare: respiratory depression, dependence

PITFALLS/CONCERNS

- Causes constipation
- Some individuals (about 7% of Caucasians) are poor

metabolisers of codeine and therefore are unable to achieve a significant analgesic benefit from codeine

Desipramine

PHARMACOLOGY

Tricyclic antidepressant that blocks the pre-synaptic uptake of serotonin and norepinephrine

Onset of action: analgesic effect after 3-7 days; up to 30 days for depression
Time to peak plasma concentration: 4 h PO
Plasma 1/2 life: 9-25 h PO;

DOSING

Starting dose 10-25 mg PO hs titrating upward as required to 150 mg (higher doses rarely required in palliative care)

UNWANTED EFFECTS

Dry mouth, sedation, delirium, postural hypotension, hyponatremia, headache, urinary retention

PITFALLS/CONCERNS

- Low doses should be used initially in the elderly

- Sedation may affect performance of some tasks
- Avoid abrupt withdrawal after discontinuation
- Should not be used with an MAOI, recent myocardial infarction, arrythmias, mania or severe hepatic impairment

Dexamethasone

PHARMACOLOGY

Dexamethasone decreases inflammation by changing the permeability of capillaries and by decreasing neutrophil migration

In comparison to many other corticosteroids, dexamethasone has high glucorticoid activity but insignificant mineralocorticoid effect

Duration of action: 36-54 hours
Time to peak plasma: 1-2 hours PO, 8 hours SC

DOSING

Anorexia: 2-4 mg PO OD
Anti-emetic: 2-4-8 mg PO OD to BID
Raised intracranial pressure: 8-20 mg PO OD
Spinal cord compression: 16 mg PO daily

UNWANTED EFFECTS

Short term: hyperglycemia and diabetes mellitus, increased susceptibility to infection (eg. thrush), mental disturbances (insomnia, depression, euphoria, paranoid psychosis), peptic ulceration (especially if given with an NSAID)

Longer term: muscles wasting and weakness, osteoporosis, cushing's syndrome (moonface, striae, acne), avascular bone necrosis

PITFALLS/CONCERNS

- May exacerbate or precipitate diabetes mellitus
- Abrupt cessation of corticosteroids can precipitate an adrenal crisis
- If used with NSAIDs there is a high risk of peptic ulceration

Dextromethorpan

PHARMACOLOGY

- Controls cough by depressing the medullary cough center

Onset of action: 15-30 minutes
Duration of action: Approximately 6 hours
Plasma 1/2 life: 11 hours

DOSING

Oral: 10-20 mg every 4 hours or 30 mg every 6-8 hours

UNWANTED EFFECTS

Constipation, sedation, nausea, dizziness, respiratory depression

Diazepam

PHARMACOLOGY

Benzodiazepines have GABA-potentiating actions in the CNS (spinal cord, hippocampus, cerebellum, cerebrum) thereby reducing neuronal activity

Onset of action: 15 min PO; immediate IV
Time to peak: 30-90 min PO
Duration of action: 3-30 hours
Plasma 1/2 life: parent drug 20-50 hours; active metabolite 50-100 hours

DOSING

Anxiety: 2-10 mg PO OD
Muscle spasm/myoclonus: 5-10 mg PO OD
Anti-epileptic: 10 mg PR/IV

UNWANTED EFFECTS

Sedation, fatigue, decreased co-ordination, blurred vision, dizziness, hypotension, anxiety, decreased libido, depression, headaches, insomnia

PITFALLS/CONCERNS

- Benzodiazepines used alone in delirium will likely exacerbate the condition
- There are some drug-drug interactions with benzodiazepines
- Abrupt cessation of long-term benzodiazepine therapy can cause withdrawal symptoms
- May cause hypotension
- Use with caution in severe hepatic disease

Diclofenac

PHARMACOLOGY

NSAIDs block the synthesis of prostaglandins by inhibiting the enzyme cyclooxgenase. Through this mechanism, NSAIDs decrease inflammation and pain

Onset of action: 30-60 minutes
Time to peak: 1-2 hours
Plasma 1/2 life: 2 hours

DOSING

Analgesia: 50 mg 3 times/day, maximum dose: 150mg/day
Rheumatoid/osteoarthritis: 150-200 mg/day in 2-4 divided doses
***Have patient take with food if possible to decrease GI upset*

UNWANTED EFFECTS

Headache, dizziness, itching/rash, fluid retention, abdominal cramps/pain, constipation or diarrhea, flatulence, indigestion, nausea, peptic ulcer/GI bleed, tinnitus, acute renal failure

PITFALLS/CONCERNS

- Many of the toxic effects of NSAIDs are related to their primary mechanism of action (the inhibition of prostaglandin synthesis)

- Common adverse effects:
  - Gastrointestinal complications:
    - Dyspepsia
    - Peptic ulcer disease
    - Gastrointestinal bleeding
  - Renal toxicities:
    - Acute renal failure due to renal vasoconstriction
  - Cardiovascular:
    - Possible increased risk of myocardial infarction, stroke, and new onset or worsening of hypertension
  - Tinnitus:
    - Typically reversible after stopping NSAIDs
  - Antiplatelet effects:
    - Inhibit platelet aggregation
    - Can increase risk of significant bleeding for patients undergoing surgery, thrombocytopenic patients (platelet count < 50,000), or patients on anticoagulant therapy such as warfarin
  - Respiratory:
    - Can precipitate bronchospasm or worsen asthma in small percentage of individuals

- NSAIDs should generally be avoided in pediatric patients with fever due to risk of Reye Syndrome. Acetaminophen or paracetamol should be used instead

Bottom Line: NSAIDs are effective, inexpensive, anti-inflammatory drugs that are well tolerated in most people and can provide significant pain relief. However, patients with significant gastrointestinal problems, bleeding risks, or renal or cardiac compromise should be carefully evaluated before

beginning therapy with NSAIDs. May need to adjust dose and monitor renal function for patients with renal compromise

Dimenhydrinate

PHARMACOLOGY

- Competes with histamine for H1-receptor sites on effector cells in the gastrointestinal tract, blood vessels, and respiratory tract; blocks chemoreceptor trigger zone, diminishes vestibular stimulation, and depresses labyrinthine function through its central anticholinergic activity

Onset of action: 15-30 minutes
Plasma 1/2 life: 3.5 hours

DOSING

Adults: 50-100mg every 4-6 hours, maximum 400 mg/day

UNWANTED EFFECTS

Slight to moderate drowsiness/sedation, headache, dizziness.
Anticholinergic effects: (constipation, dry mouth, blurred vision, urinary retention)
Paradoxical CNS stimulation

Docusate

PHARMACOLOGY

An emulsifying and wetting laxative with relatively weak effect on bowel transit

Onset of action: 12-72 hours

DOSING

Starting dose 100 mg bid, increasing to 200 mg bid-tid

UNWANTED EFFECTS

Diarrhea, unpleasant aftertaste

Gabapentin

PHARMACOLOGY

Increases GABA synthesis but exact mechanism of action not fully understood

Onset of action: 1-3 hours
Time to peak: 2-3 hours PO
Plasma 1/2 life: 5-7 hours, (increases with renal failure)

Duration of action: 8-12 hours

DOSING

300 mg od increasing to 600-1200 mg tid

UNWANTED EFFECTS

Common: Drowsiness, dizziness, fatigue, ataxia, tremor, nystagmus

Other: Headache, weight gain, nervousness, dysarthria, rhinitis, diplopia, peripheral edema, constipation

Glycopyrronium

PHARMACOLOGY

Antimuscarinics/anticholinergics such as hyoscine hydrobromide, atropine, glycopyrronium, hyoscine butyl bromide are used primarily as smooth muscle antispasmodics and antisecretory agents. They are used in palliative care for intestinal colic, genitor-urinary colic, inoperable bowel obstruction with colic and respiratory secretions at end of life. Hyoscine hydrobromide and glycopyrronium are less likely to cross the blood-brain barrier as they are less lipid-soluble thereby causing less central side-effects (eg. delirium) Overall efficacy in reducing respiratory secretions at end of life

is seen in about1/2 to 1/3 of patients

Onset of action: < 30 minutes SC/IM/IV; 50 min PO
Duration of inhibition of salivation: 7 hours

DOSING

- 0.4 mg as a single dose SC.
  Then effective, continue using 0.2 mg q4h and prn SC

UNWANTED EFFECTS

Blurred vision, cardiovascular effects, dry mouth, constipation, heartburn, urinary retention, delirium

PITFALLS/CONCERNS

- Avoid concurrent use with prokinetics as antimuscarinics will block the action of agents such as metoclopramide
- Glaucoma may be precipitated in patients at risk

Haloperidol

PHARMACOLOGY

Dopamine-receptor antagonist. Inhibitory effect on the area postrema (chemoreceptor trigger zone).
In palliative care haloperidol has been used for nausea, vomiting, delirium and intractable hiccup.
Can be given PO, SC, IV

Onset of action: 10-15 min SC; >1h PO
Duration of action: Usually 24 hours
Plasma 1/2 life: 13-35 hours

DOSING

Antiemetic: 1-2 mg od at HS (usual dose 3-5 mg; maximum 10-20 mg od HS or in divided doses/day
Antipsychotic/anxiolytic: 2-5 mg PO or SC

UNWANTED EFFECTS

Extrapyramidal effects (acute dystonias, pseudoparkinsonism, and akathisia), hypotension, sedation

PITFALLS/CONCERNS

- Should not be used in Parkinson's disease
- Watch for extrapyramidal effects – if present decrease or discontinue haloperidol and treat symptoms

using anticholinergics (benztropine), beta-blockers or benzodiazepines if necessary

Hyoscine butyl bromide

PHARMACOLOGY

Antimuscarinics/anticholinergics such as hyoscine hydrobromide, atropine, glycopyrronium, hyoscine butyl bromide are used primarily as smooth muscle antispasmodics and antisecretory agents. They are used in palliative care for intestinal colic, genitor-urinary colic, inoperable bowel obstruction with colic and respiratory secretions at end of life. Hyoscine hydrobromide and glycopyrronium are less likely to cross the blood-brain barrier as they are less lipid-soluble thereby causing less central side-effects (eg. delirium)

Overall efficacy in reducing respiratory secretions at end of life is seen in about1/2 to 1/3 of patients

Onset of action: 10 minutes SC/IM/IV
Time to peak plasma concentration: 1-2 h PO
Plasma 1/2 life: 5-6 h

DOSING

- 20 mg as a single dose SC
  If effective, continue, using 20 mg q4h SC

UNWANTED EFFECTS

Blurred vision, cardiovascular effects, dry mouth, constipation, heartburn, urinary retention, delirium

PITFALLS/CONCERNS

- Avoid concurrent use with prokinetics as antimuscarinics will block the action of agents such as metoclopramide
- Glaucoma may be precipitated in patients at risk

Hyoscine hydrobromide

PHARMACOLOGY

Antimuscarinics/anticholinergics such as hyoscine hydrobromide, atropine, glycopyrronium, hyoscine butyl bromide are used primarily as smooth muscle antispasmodics and antisecretory agents. They are used in palliative care for intestinal colic, genitor-urinary colic, inoperable bowel obstruction with colic and respiratory secretions at end of life. Hyoscine hydrobromide and glycopyrronium are less likely to cross the blood-brain barrier as they are less lipid-soluble thereby causing less central side-effects (eg. delirium)

Overall efficacy in reducing respiratory secretions at end of life is seen in about1/2 to 1/3 of patients

Onset of action: < 10 minutes SC/IM/IV
Plasma 1/2 life: 5-6 h

DOSING

- 0.4 mg as a single dose SC. If effective, continue using 0.3-0.6 mg q4h SC

UNWANTED EFFECTS

Blurred vision, cardiovascular effects, dry mouth, constipation, heartburn, urinary retention, delirium

PITFALLS/CONCERNS

- Avoid concurrent use with prokinetics as antimuscarinics will block the action of agents such as metoclopramide
- Glaucoma may be precipitated in patients at risk

Ibuprofen

PHARMACOLOGY

NSAIDs block the synthesis of prostaglandins by inhibiting the enzyme cyclooxgenase. Through this mechanism, NSAIDs decrease inflammation and pain

Onset of action: Analgesic: 30-60 minutes
Anti-inflammatory <7 days
Time to peak: 1-2 hours
Plasma 1/2 life: 2-4 hours
Absorption: Oral: rapid (85%)

DOSING

Adults:
Inflammatory disease: Oral: 400-800 mg/dose 3-4 times/day (maximum: 3.2 g/day)

Analgesia/pain: Oral: 200-400 mg/dose every 4-6 hours (maximum 2.4 g/day)

***Have patient take with food if possible to decrease GI upset*

UNWANTED EFFECTS

Dizziness, headache, fluid retention, nervousness, itching/rash, dyspepsia, nausea, vomiting, heartburn, tinnitus, abdominal pain

PITFALLS/CONCERNS

- Many of the toxic effects of NSAIDs are related to their primary mechanism of action (the inhibition of prostaglandin synthesis)

- Common adverse effects:
  - Gastrointestinal complications:
    - Dyspepsia
    - Peptic ulcer disease
    - Gastrointestinal bleeding
  - Renal toxicities:
    - Acute renal failure due to renal vasoconstriction
  - Cardiovascular:
    - Possible increased risk of myocardial infarction, stroke, and new onset or worsening of hypertension
  - Tinnitus:
    - Typically reversible after stopping NSAIDs
  - Antiplatelet effects:
    - Inhibit platelet aggregation
    - Can increase risk of significant bleeding for patients undergoing surgery, thrombocytopenic patients (platelet count < 50,000), or patients on anticoagulant therapy such as warfarin
  - Respiratory:
    - Can precipitate bronchospasm or worsen asthma in small percentage of individuals

- NSAIDs should generally be avoided in pediatric patients with fever due to risk of Reye Syndrome. Acetaminophen/paracetamol should be used instead

Bottom Line: NSAIDs are effective, inexpensive, anti-inflammatory drugs that are well tolerated in most people and can provide significant pain relief. However, patients with significant gastrointestinal problems, bleeding risks, or renal or cardiac compromise should be carefully evaluated before beginning therapy with NSAIDs. May need to adjust dose and monitor renal function for patients with renal compromise

Imipramine

PHARMACOLOGY

Blocks the pre-synaptic uptake of serotonin and norepinephrine

Onset of action: analgesic effect after 3-7 days; up to 30 days for depression
Time to peak plasma concentration: 4 h PO
Plasma 1/2 life: 9-25 h PO;
active metabolite nortripyline 13-93 hours
Duration of action: 24 h

DOSING

Starting dose 10-25 mg PO hs titrating upward as required to 150 mg
(higher doses rarely required in palliative care)

UNWANTED EFFECTS

Antimuscarinic effects, sedation, delirium, postural hypotension, hyponatremia

PITFALLS/CONCERNS

- Low doses should be used initially in the elderly
- Sedation may affect performance of some tasks
- Avoid abrupt withdrawal after discontinuation
- Should not be used with an MAOI, recent myocardial infarction, arrythmias, mania or severe hepatic impairment

Lorazepam

PHARMACOLOGY

Benzodiazepines have GABA-potentiating actions in the CNS (spinal cord, hippocampus, cerebellum, cerebrum) thereby reducing neuronal activity

Onset of action: 5 min SL; 10-15 min PO
Time to peak: 1-1.5 h SL/SC, 1-6 h PO
Duration of action: 6-72 h
Plasma 1/2 life: 12-15h

DOSING

Insomnia: 0.5 to 2 mg HS
Anxiety: 1 mg SL/PO bid –
increase to 6 mg/24hrs in divided doses
Agitation: 2 mg PO every 30 minutes until patient is settled
Status epilepticus: 0.1 mg/kg (2 mg/min)

UNWANTED EFFECTS

Sedation, fatigue, decreased co-ordination, blurred vision, memory impairment, hypotension, anxiety, decreased libido, depression, headaches, insomnia

PITFALLS/CONCERNS

- Benzodiazepines used alone in delirium will likely exacerbate the condition
- There are some drug-drug interactions with benzodiazepines
- Abrupt cessation of long-term benzodiazepine therapy can cause withdrawal symptoms
- May cause hypotension
- Use with caution in severe hepatic disease

Metoclopramide

PHARMACOLOGY

Metoclopramide acts as a combined dopamine-receptor antagonist and 5HT4-receptor agonist.
It has prokinetic properties. It is used for nausea and vomiting.
It can be given PO, SC or IV

Onset of action: 10-15 min SC; 15-60 min PO
Duration of action: 1 to 2 hours (sometimes longer)
Plasma 1/2 life: 2.5-5 hours

DOSING

10 mg PO/SC tid-qid ac meals

UNWANTED EFFECTS

Extrapyramidal side effects (acute dystonias, pseudoparkinsonism, and akathisia), drowsiness, akesthesia (restlessness), depression and diarrhea

PITFALLS/CONCERNS

- Serious drug interactions exist
- Avoid concurrent use with antimuscarinics which block the action of prokinetics such as metoclopramide
- Used most commonly for nausea and vomiting due to gastric stasis due to its prokinetic properties.

Midazolam

PHARMACOLOGY

Benzodiazepines have GABA-potentiating actions in the CNS (spinal cord, hippocampus, cerebellum, cerebrum) thereby reducing neuronal activity

Onset of action: 5-10 min SC; 2-3 min IV; 15 min sublingual
Time to peak: 30 min SC; 60 min PO
Duration of action: 4 hours
Plasma 1/2 life: 2-5 hours

DOSING

2.5 – 5 mg PO/SC STAT and prn
Infusional rate 10-60 mg/24 hrs
Anti-epileptic: 10 mg SC

UNWANTED EFFECTS

Sedation, fatigue, decreased co-ordination, blurred vision, memory impairment, hypotension, anxiety, decreased libido, depression, headaches, insomnia

PITFALLS/CONCERNS

- Benzodiazepines used alone in delirium will likely exacerbate the condition

- There are some drug-drug interactions with benzodiazepines
- Abrupt cessation of long-term benzodiazepine therapy can cause withdrawal symptoms
- May cause hypotension
- Use with caution in severe hepatic disease

Morphine

PHARMACOLOGY

Opioids such as morphine act at opioid rececptors which are found both within the CNS and peripherally.
Metabolism occurs mainly in the liver but can occur in other organs including the CNS. The major metabolites of morphine are M3G and M6G. In the setting of renal failure morphine metabolites can accumulate and lead to toxicity

Morphine may be given orally, rectally, buccally, SC, IM and intraspinally. The PO: SC/IV morphine ratio is 2:1.
Morphine oral preparations come in short-acting as well as sustained release preparations

Time to peak plasma concentration: 15-60 min PO (short acting preparations); 10-20 min IM/SC
Duration of action: 3-6 h (short acting preparations); 8-12-24 h (sustained release preparations)
Plasma 1/2 life: 1.5-4.5 h PO (short acting preparations)

DOSING

A dose of morphine 2.5 mg regularly q4h PO (or 1 to 2 mg SC/IV) and a breakthrough dose every hour, as required (see Appendix 1) is suitable for an opioid-naive patient. Further titration will be required and the effective dose will vary

UNWANTED EFFECTS

Common: Constipation, dry mouth, sweating

Common (usually temporary): Sedation, nausea/vomiting

Rare: Pruritis/urticaria, urinary retention, hallucinations/ delirium, respiratory depression

PITFALLS/CONCERNS

- A laxative should be prescribed routinely when a patient is on an opioid
- An anti-emetic should be ordered at least prn for use during the first week when starting opioid therapy (this side-effect usually resolves however over time)
- Hepatic failure severe enough to increase the prothrombin time may result in an increased plasma halflife of morphine
- Warn patients about the possibility of initial drowsiness

Naproxen

PHARMACOLOGY

NSAIDs block the synthesis of prostaglandins by inhibiting the enzyme cyclooxgenase. Through this mechanism, NSAIDs decrease inflammation and pain

Onset of action: Analgesic: 1 hour, Anti-inflammatory: 2 weeks
Time to peak: 1-4 hours
Plasma 1/2 life: 12-17 hours

DOSING

Rheumatoid arthritis/osteoarthritis: 500-1000 mg/day in 2 divided doses; may increase to 1.5 g/day of naproxen for limited time period

Mild-to-moderate pain: Oral: initial 500 mg, then 250 mg every 6-8 hours; maximum 1250 mg/day

Pain/fever: 200 mg every 8-12 hours; if needed may take initial 400 mg

***Have patient take with food if possible to decrease GI upset*

UNWANTED EFFECTS

Dizziness, drowsiness, headache, itching/rash, fluid retention, diarrhea, dyspepsia, heartburn, tinnitus

PITFALLS/CONCERNS

- Many of the toxic effects of NSAIDs are related to their primary mechanism of action (the inhibition of prostaglandin synthesis)

- Common adverse effects:
  - Gastrointestinal complications:
    - Dyspepsia
    - Peptic ulcer disease
    - Gastrointestinal bleeding
  - Renal toxicities:
    - Acute renal failure due to renal vasoconstriction
  - Cardiovascular:
    - Possible increased risk of myocardial infarction, stroke, and new onset or worsening of hypertension
  - Tinnitus:
    - Typically reversible after stopping NSAIDs
  - Antiplatelet effects:
    - Inhibit platelet aggregation
    - Can increase risk of significant bleeding for patients undergoing surgery, thrombocytopenic patients (platelet count < 50,000), or patients on anticoagulant therapy such as warfarin
  - Respiratory:
    - Can precipitate bronchospasm or worsen asthma in small percentage of individuals

- NSAIDs should generally be avoided in pediatric patients with fever due to risk of Reye Syndrome. Acetaminophen should be used instead

Bottom Line: NSAIDs are effective, inexpensive, anti-inflammatory drugs that are well tolerated in most people and can provide significant pain relief.

However, patients with significant gastrointestinal problems, bleeding risks, or renal or cardiac compromise should be carefully evaluated before beginning therapy with NSAIDs. May need to adjust dose and monitor renal function for patients with renal compromise

Octreotide

PHARMACOLOGY

Synthetic analogue of somatostatin

Inhibits secretions in the gastro-enteropancreatic system. Reduces splanchnic blood flow, GI motility, gastric/pancreatic/small bowel secretions

Onset of action: 30 minutes
Time to peak: 30 minutes SC
Duration of action: 8 hours
Plasma 1/2 life: 1.5 hours SC

DOSING

50-100 micrograms daily up to 200 micrograms tid

UNWANTED EFFECTS

Sinus bradycardia, hyperglycemia, abdominal pain, constipation, nausea, flatulence, dry mouth, flushing

Olanzapine

PHARMACOLOGY

Atypical antipsychotic.
Dopamine-receptor and 5HT2A- receptor antagonist.
Compared with typical antipsychotics (eg. haloperidol) the incidence of drug-induced movement disorders is less.
It is used in palliative care for delirium and nausea.

Tablets and dispersible tablets exist

Onset of action: hours to days
Duration of action: 12 to 48 hours (sometimes longer)
Plasma 1/2 life: 34 hours

DOSING

Agitation: 2.5 mg PO HS and prn
(increase if necessary to 5-10 mg)

Anti-emetic: 1.25-2.5 mg PO HS and q2h prn
(increase to 5 mg PO HS if necessary)

UNWANTED EFFECTS

Sedation, weight gain, hypotension, dry mouth, constipation, agitation, peripheral edema, lightheadedness

PITFALLS/CONCERNS

- May cause orthostatic hypotension
- Should not be used in Parkinson's disease
- Watch for extrapyramidal effects (EPS) – if present decrease or discontinue and treat EPS symptoms using anticholinergics (benztropine), beta-blockers or benzodiazepines if necessary
- Drug interactions exist

Ondansetron

PHARMACOLOGY

$5HT_3$-receptor antagonist

Onset of action: 30 min PO, 5 min IV
Time to peak: 1-2 hours PO
Duration of action: 12 hours
Plasma 1/2 life: 3-5 hours

DOSING

8 mg every 8-12 hours

UNWANTED EFFECTS

Common: Constipation, headache

Rare: Dystonic reaction, sensation of warmth or flushing, hiccup

Phenytoin

PHARMACOLOGY

Onset of action: IV 0.5-1h
Time to peak: 4-8 hours
Plasma 1/2 life: 9-40 hours

DOSING

Loading dose 15-20 mg/kg oral in 3 divided doses every 2-4 hours; maintenance dose 300 mg/day (range 200-1200 mg/day)

UNWANTED EFFECTS

Nausea, vomiting, nystagmus, delirium, dizziness, ataxia altered speech, gingival hypertrophy and acne

- There are many drug interactions with anti-epileptics

Phenobarbital

PHARMACOLOGY

Onset of action: 60 min
Time to peak: 4-12 hours
Duration of action: 10-12 hours
Plasma 1/2 life: 72-144 hours

DOSING

Phenobarbital 30-240 SV/IV q8h & prn

Prochlorperazine

PHARMACOLOGY

- Acts as a dopamine antagonist and blocks dopamine (D1 and D2) receptors in the brain

Onset of action:
- Oral: 30-40 minutes
- Parenteral: 10-20 minutes
- Rectal: 60 minutes

Duration of action:
- Parenteral and oral-extended release: 12 hours
- Rectal and oral immediate release: 3-4 hours

Time to peak:
Plasma 1/2 half: Oral: 3-5 hours, parenteral: 7 hours

DOSING

Oral: 5-10 mg 3-4 times/day, usual maximum 40 mg/day
I.M. 5-10 mg every 3-4 hours, usual maximum 40 mg/day
I.V. 2.5-10 mg every 3-4 hours as needed,
maximum 10 mg/dose or 40 mg/day
Rectal: 25 mg as suppository every 12 hours

UNWANTED EFFECTS

Anticholinergic effects: (constipation, dry mouth, blurred vision, urinary retention)

Extrapyramidal symptoms: (pseudoparkinsonism, akathisia, dystonias, tardive dyskinesia)
Sedation, orthostatic hypotension, paradoxical agitation/ excitement, restlessness, rash, photosensitivity

Risperidone

PHARMACOLOGY

Atypical antipsychotic. Dopamine-receptor and $5HT_{2A}$- receptor antagonist

Compared with typical antipsychotics (eg. haloperidol) the incidence of drug-induced movement disorders is less

Onset of action: hours to days
Duration of action: 12 to 48 hours (sometimes longer)
Plasma 1/2 life: 24 hours

DOSING

Starting: 0.5 mg PO BID and prn
Increase by 0.5 mg PO BID every other day

UNWANTED EFFECTS

Headache, agitation, anxiety, insomnia, movement disorders, sedation, fatigue, dizziness, impaired concentration, blurred vision, dyspepsia, nausea and vomiting, constipation, urinary incontinence, rhinitis

PITFALLS/CONCERNS

- May cause orthostatic hypotension
- Should not be used in Parkinson's disease

- Watch for extrapyramidal effects (EPS) – if present decrease or discontinue and treat EPS symptoms using anticholinergics (benztropine), beta-blockers or benzodiazepines if necessary
- Drug interactions exist

Senokot

PHARMACOLOGY

Stimulant laxative
Onset of action: 8-12 h

DOSING

15 mg hs increasing up to 15 mg bid

UNWANTED EFFECTS

May discolour urine or feces, diarrhea, intestinal colic

Tranexamic Acid

PHARMACOLOGY

Inhibits the breakdown of fibrin clots.
Tranexamic acid has been used orally, topically and parentrally (rarely required)

It accumulates in renal failure

Duration of action: 24 h
Plasma 1/2 life: 2 h

DOSING

1.5 g PO stat and 1 g tid PO
Topical solution 500 mg in 5 mls soaked in gauze – apply for 10 minutes

UNWANTED EFFECTS

Nausea, vomiting, diarrhea, disturbance in colour vision, hypotension (IV), thrombo-embolism

PITFALLS/CONCERNS

- In patients with hematuria there is a risk of ureteric obstruction and retention
- There exist serious drug interactions which can increase the risk of thrombosis

SOME MEDICATION INFORMATION FROM:

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Personal Notes

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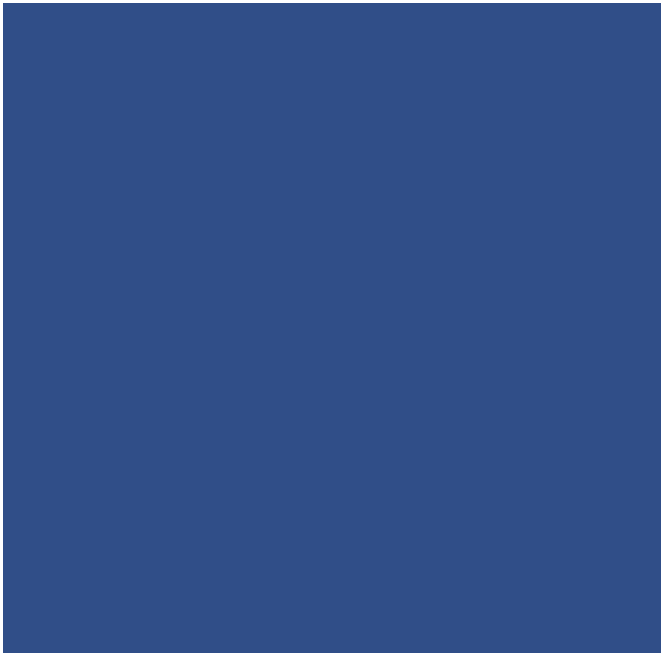

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