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THE GLOBAL HANDBOOK OF PALLIATIVE CARE

A Resource for Frontline Care Providers

Managing Editors: Dr. Megan Doherty and Dr. Lana Ferguson

global health dynamics

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

Clinical judgement should be exercised at all times.

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In memory of Ian Magrath and Melissa Adde, the founders of the International Network for Cancer Treatment and Research (INCTR), who supported palliative care for adults and children and encouraged the first edition of the handbook in 2008.

Two Worlds Cancer Collaboration

Two Worlds Cancer Collaboration (the Canadian Branch of the International Network of Cancer Treatment and Research [INCTR]) seeks to provide education and mentorship for healthcare providers and develop equitable and accessible healthcare programmes that improve disease prevention, diagnosis, treatment, and palliative and end-of-life care. Two Worlds Cancer Collaboration emphasizes international collaboration and works to improve communication among the wide range of professionals and volunteers working to control cancer throughout the world.

Global Health Dynamics

Global Health Dynamics is the publisher of the *Cancer Control* and *AMR Control* series of publications. It works at all levels with governmental organizations, international NGOs, health ministries, the private sector and many other global healthcare partners to publish on cancer control in emerging economies and the universal challenge of antimicrobial resistance. Established in 2013, Global Health Dynamics' mission is to address unmet needs and underserved populations in global healthcare. Publications are available internationally in multiple electronic and hard copy formats.

An endorsement from the UICC

Palliative care is a cornerstone of people-centred healthcare. Beyond managing symptoms, it addresses the holistic needs of patients, focusing on improving their quality of life physically, emotionally, and spiritually. By providing comfort and dignity, palliative care ensures that adults, children and their families can navigate their health challenges with resilience and a sense of peace. UICC is very pleased to endorse *The Global Handbook of Palliative Care* as an important resource that provides clear, practical, "point-of-care" guidance as part of a comprehensive approach to caring for individuals worldwide experiencing serious, life-limiting illnesses.

Cary Adams, CEO of the Union for International Cancer Control (UICC)

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Contents

Contents

Foreword

This handbook was initially created at the request of physicians, nurses, social workers and other health professionals who collaborate with the International Network for Cancer Treatment and Research (INCTR). More recently, we have revised this user-friendly guide, based on feedback and new evidence.

We hope that handbook will continue to help in the management of common palliative care problems. It is, therefore, primarily aimed at those who have completed some basic training in palliative care but are not necessarily specialists in the field.

The handbook focuses on the needs of children and adults with serious health-related suffering, those living with life-threatening and life-limiting illnesses, including cancer, but also other serious illnesses including severe respiratory, cardiovascular, renal, and neurological conditions, as well as dementia, and HIV/AIDS.

Although we have aimed at brevity there are four topics that we thought deserved special mention in this foreword. These are the philosophy of palliative care, the need for good assessment, the importance of palliative care for children and "balanced care".

The Philosophy of Palliative Care

This has been defined by the World Health Organization and other healthcare organizations in a variety of ways. In essence, it should be viewed as a holistic and interdisciplinary approach that aims to improve the quality of life of people of all ages – and their caregivers – who live with life-limiting health conditions.

In general terms, palliative care:

- Is both a philosophy and a clinical approach to care
- Responds to physical, psychosocial, and spiritual dimensions of suffering – both of the patients and of their caregivers
- Responds to people's beliefs and practices as well as their social and cultural values
- Is applicable throughout the illness continuum, including bereavement
- Can be applied in combination with other therapies or may be the sole focus of care
- Responds to the unique needs of children and their families

Assessment

Assessment is the process of gathering information to help guide patient care. Thoughtful and thorough assessments are the foundation of

good palliative care, requiring the practitioner to listen well, ask relevant questions, and understand physical evaluation. However, the physical, emotional, and spiritual dimensions of an illness that affect quality of life can also be further evaluated using appropriate tools. The patient is at the centre of this process, but it should also include the family and other caregivers.

An on-going cycle of assessment and reassessment is vital in the management of palliative care patients who often have rapidly changing symptoms from multiple causes. Investigations, particularly those which carry a physical or psychological burden, require a balanced consideration of the patient's prognosis, his or her wishes, and any likely benefit.

Palliative Care for Children and Young People

Caring for seriously ill children requires particular attention, and sensitivity to the developmental stage and cognitive abilities of the child. It is extremely important to recognize the profound distress parents and siblings may experience when a child is ill, and to provide additional family support. Children often understand more about their illness than we realize or acknowledge, and it is best to answer their questions as honestly as possible. Children may also use art, drawings, or play to express what they are feeling inside, and this can be a helpful way to explore a child's fears, worries, and hopes. The management of physical symptoms in paediatric palliative care has much in common with that of adults. However, there are some differences both in medication choice and dosage. We should ensure that children with life threatening and serious illness remain foremost in our minds and are not abandoned when cure is no longer possible. They and their parents need to be supported with compassion and understanding combined with expert symptom assessment and management.

Balanced Care

Within the context of patient's wishes and prognosis it is important to balance the benefits of investigation and treatment against the burdens and possible harm. Perhaps more than any other area of medicine a balanced approach is needed in palliative care to achieve the best quality of life for our patients. Trying to decide whether or not to carry out any particular intervention (such as an investigation or a treatment) often creates a complex clinical dilemma – and sometimes an ethical one. It may be helpful to reflect on the following questions:

Is there a reasonable chance of benefit to the patient?

Is the intervention likely to improve symptoms for the patient and enhance quality of life? Is the improvement likely to be maintained? For instance, a transfusion of blood may help a feeling of fatigue or breathlessness in a patient with anemia who has months of life ahead but for a patient close to death it is much less likely to make a positive contribution.

Will the intervention likely cause harm to the patient?

Most interventions will have drawbacks either in terms of physical suffering, wasting of valuable time, or sometimes in raising "false hope" with either the patient or the family.

For instance, carrying out a CT scan when the result will not change the treatment but may exacerbate pain as well as creates a possible expectation for disease modifying treatment (when none is planned) should be avoided.

Is the intervention a proper use of available resources (justice)?

In most situations medical resources are limited and have to be used in a fair manner. For instance, in a situation where there is a shortage of platelets for transfusion these may to have to be reserved for patients who are having curative treatment rather than those with terminal illness.

Having tried to find a balance between these elements one should ask: What are the patient's wishes?

When appropriate, the patient should be informed of the possible benefits and drawbacks of the intervention and his or her wishes identified. Their beliefs, developmental stage, cognitive abilities and life experiences (especially that of their illness) will influence their decision making and should be taken into consideration. The family or other caregivers are often a part of this process.

Caring for children creates an added complexity. Sometimes children's wishes may differ from their adult caregivers. Special effort should be made to try and understand the needs and wishes of all concerned.

List of Abbreviations and Terms

BID	twice daily
Buccal	within cheek of mouth
CHF	congestive heart failure
CSCI	continuous SUBQaneous infusion
D5W	dextrose 5% in water
g	gram
GI	gastrointestinal
hr	hour
ICU	intensive care unit
IM	intramuscular
IN	intranasal
IV	intravenous
kg	kilogram
L	litre
LLQ	left lower quadrant of abdomen
mcg	microgram
mg	milligram
min	minute
mL	millilitre
NG	nasogastric
NS	normal saline
PO	by mouth
PR	rectally
PRN	as needed
qAM	every morning
q1h	every hour
q4h	every 4 hours
q6h	every 6 hours
qHS	every day at bedtime (9pm)
QID	4 times a day
QTc	corrected QT (ecg term)
SUBQ	Subcutaneous
SL	sublingual
Stat	immediately
tab	tablet
TID	3 times a day

PHYSICAL SYMPTOM CARE

Anorexia and Cachexia

KEY POINTS

- Cancer and other diseases, including end stage heart failure, renal or liver failure, dementia, and HIV/AIDS, can often cause a lack of appetite (anorexia) and weight loss with muscle wasting (cachexia)
- Anorexia-cachexia syndrome involves a complex cascade of inflammatory and metabolic changes and is not directly due to poor nutritional intake
- The focus of management should be on honest conversations about appetite and weight loss being an expected part of advanced illness
- Encourage the individual to focus on eating for pleasure, instead of concentrating on calorific intake

- Children with solid tumours are more likely to develop cachexia than those with haematological malignancies
- Seeing a child not eating and losing weight may be very distressing for the family

ASSESSMENT

see comment on page 10

- A good patient history and clinical assessment are important to identify any reversible causes
- 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 lesions or infection
- Treatable causes of anorexia/cachexia include:
  - Pain

- Nausea and vomiting
- Depression
- Adverse effects of medications
- Dyspnoea
- Oral problems, such as
  - Dry mouth
  - Mucositis (often secondary to chemotherapy)
  - Thrush/candidiasis
  - Oral herpes
  - Dental caries
- Gastrointestinal mobility problems, such as
  - Gastroesophageal reflux
  - Gastric stasis
  - Constipation

MANAGEMENT

- Clinicians need to have honest conversations explaining that weight loss is rarely reversible in the setting of advanced illness
- Patients and family members often feel under pressure to eat, believing that they need to do so to better be able to fight the disease, or to improve their energy levels
  - Instead, clinicians should encourage patients to eat for pleasure rather than focusing on calorific intake
- Consider treatment of the underlying cause if one is identifiable

Consider if the patient is well enough to benefit

Non-Pharmacological Approaches

- Clear and honest communication with the patient and their family
- Eliminate inappropriate dietary restrictions
- Encourage the patient to eat their favourite foods when appropriate

Pharmacological Approaches

- Ensure good pain and nausea/vomiting control
- Treat constipation
- Stimulate appetite
- **Megestrol acetate 160 mg PO daily. If initial response is poor, double the dose after 2 weeks. Maximum dose: 800 mg PO daily**
- **Dexamethasone 2-4 mg qAM PO. If no improvement with 4 mg daily after 1 week then discontinue; continue for a maximum of 6 weeks**

- The focus of management should be on helping the family to understand the process of cachexia and helping them to have realistic expectations about their child's weight loss and appetite
- Megestrol acetate: Initial: 7.5-10 mg/kg/dose PO daily (may be divided into 2 to 4 doses)
- Titrate to response up to a maximum of 15 mg/kg/day or 800 mg/day (whichever is less)
- Limited evidence in children. Monitor for symptoms associated with severe adrenal suppression (e.g. hypotension, vomiting)

PITFALLS/CONCERNS

- Increasing calorie intake is unlikely to increase body weight or quality of life in advanced cancer cachexia
- Although corticosteroids may increase appetite because of their significant side effects, steroids are not recommended for the treatment of anorexia/cachexia

PALLIATIVE TIPS

- Anorexia-cachexia syndrome is NOT possible to reverse with improved nutrition, despite the similarity of the patient's appearance to that of malnutrition

- Most weight gained with pharmacotherapy is fat and fluid (not skeletal muscle mass)
- Aggressive feeding can often make symptoms such as nausea, vomiting, and pain worse
- There is no evidence that providing nutritional support either enterally or parenterally improves morbidity or mortality in terminally ill patients and is generally not indicated due to the high risk of adverse effects
- Parenteral nutrition carries an increased risk of infection, other complications, and reduced survival
- Anorexia can cause significant anxiety and distress for family members and caregivers who may not understand that loss of appetite is a common symptom in advanced illness
- Educating the family that anorexia/cachexia and wasting are a part of the disease process and not the result of the family not providing enough nutrition for the patient is important

- Smaller, more frequent meals of the child's favourite foods may help

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Ascites

KEY POINTS

- With ascities, 90% of cases come from non-malignant causes, including liver cirrhosis, CHF, and tuberculosis, and 10% are due to cancer
- Ascites is common in ovarian, breast, and GI malignancies (30% of ovarian cancer patients develop ascites)
- Malignant ascites may be caused by liver disease/metastases leading to portal hypertension, intra-abdominal metastases/peritoneal seeding, lymphatic obstruction (chylous ascites – an accumulation of lymph in the peritoneal cavity characterized by increased triglyceride concentrations), or a combination of these factors
- Non-malignant ascites may also be seen in cancer patients, i.e. due to hypoproteinemia
- Ascites often indicates a poor prognosis; generally the goal of management is to ensure comfort and reduce symptoms from the ascites
  - The exception is ovarian cancer which may still have a moderate prognosis (weeks to a few months) when ascites in present

- Paracentesis is safe in children
- Children may fear invasive procedures so it is particularly important to explain what will happen, gain the child's trust, and use procedural sedation (if available) or anxiolytics (e.g. benzodiazepines) when performing paracentesis in children

ASSESSMENT

- Clinical features include abdominal swelling, bloating, weight gain, reflux, nausea, and dyspnoea
- Examination may reveal increased abdominal girth, bulging flanks, and shifting dullness

- Investigations to consider include abdominal ultrasound, diagnostic paracentesis (cytology, albumin, bacterial culture), serum electrolytes, and albumin, but it is important to consider whether these tests will change clinical management

Consider if the patient is well enough to benefit

MANAGEMENT

- Consider treatment of the primary tumour if appropriate (particularly with ovarian cancer); however, usually the cancer is advanced, and the prognosis is poor
- Diuretics can be helpful in some patients with ascites, including those with significant liver metastases, cirrhosis, or CHF. Serum electrolytes and renal function should be monitored for risk of acute kidney injury and hepatorenal syndrome with diuretic use
- Diuretics are unlikely to be helpful in chylous ascites
- Paracentesis is best for immediate symptom relief, if the ascites does not respond to diuretics, and for chylous ascites

Paracentesis

- This is a simple procedure that can be carried out at the bedside with or without ultrasound guidance
- Ultrasound is recommended if there is diagnostic uncertainty, possible loculations, or uncertainty about catheter placement due to tumour mass
- Remove the quantity of fluid that gives optimal symptomatic relief, generally <4-6 litres
- A small number of patients (<5%) may deteriorate rapidly after paracentesis. Sepsis and catheter blockage are other possible complications
- Intravenous fluids and albumin infusions are not routinely required (unless hypotensive, dehydrated, severe renal impairment, or large volume paracentesis)
- If there is substantial ascites (tense abdomen), it is probably safe to proceed without ultrasound

Method of Paracentesis

- With the 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 a 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)
- Drain by gravity to dryness or a total of 4-6 litres
- Withdraw the needle allowing the skin to return to the original position (creates a Z-track and lowers the post-procedure leakage)

Pharmacologic Management

- Note: effective in approximately one-third of patients
- **Spironolactone 100 mg PO daily, titrate slowly up to 400 mg PO daily, adjust the dose to remove enough fluid for comfort**
- **Furosemide 40-160 mg PO daily added to spironolactone to improve effect and reduce the risk of hyperkalemia. Adjust dose every 3-5 days, maintaining the 100 mg:40 mg ratio, up to 400 mg spironolactone and 160 mg furosemide together**
- **Octreotide 200-600 mg SUBQ divided BID or TID has been effective in several cases studies for refractory ascites that is not responsive to paracentesis**

Pharmacological Management in Children: *Spironolactone*

- **Initial: 1-1.5 mg/kg/dose PO once daily to BID (Maximum: 50 mg/dose)**
- **Titrate as needed up to 4-6 mg/kg/day in divided doses q6-12h or 400 mg/day (whichever is less)**
- **Note: May cut or crush tablets for doses <25 mg**
- **Monitor for potassium and renal function**

Furosemide

- **Oral: 0.5-2 mg/kg/dose PO q6-24h**
- **Maximum: 6 mg/kg/dose or 80 mg/dose (whichever is less)**
- **IV/SUBQ: 0.5-2 mg/kg/dose IV/IM q6-24h**
- **Maximum: 2 mg/kg/dose or 80 mg/dose (whichever is less)**
- **Older children and adolescents often respond to lower doses (10-20 mg/dose)**
- **Use caution in patients with hypokalemia and hypovolemia**

Hydrochlorothiazide

- **1-2 mg/kg/dose PO BID**
- **Maximum: 100 mg/day**
- **Monitor for electrolyte abnormalities, including hyponatremia and hypokalemia**
- **Note: Potency is less compared to furosemide and can be considered an add-on therapy to loop diuretics to overcome resistance to diuresis**

PITFALLS/CONCERNS

- In patients in the final terminal phase – i.e. hours to days, it is generally inappropriate to drain the ascites (treatment should be the least invasive possible)

Consider if the patient is well enough to benefit

- In patients in the final terminal phase, provide relief through pharmacologic treatment of symptoms (e.g. provide pain relief)

PALLIATIVE TIPS

- Drain for symptomatic relief, not just because the fluid is present

- If the drainage site is leaking after the procedure, 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 tunnelled 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

Consider if the patient is well enough to benefit

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Bleeding

KEY POINTS

- Bleeding can occur in cancer and in end-stage liver or renal disease, especially as the disease progresses
- Patients and families can be very distressed by even small amounts of visible bleeding

ASSESSMENT

see comment on page 10

- It is important to make an assessment of the cause, to consider whether the cause is reversible, the severity, and the prognosis of the patient when assessing bleeding
- When appropriate, carry out relevant tests including a coagulation screen and platelet count

MANAGEMENT

- Treatment of bleeding in palliative patients depends on the patient's goals of care, disease trajectory and prognosis, and whether the treatment is likely to be effective

Consider if the patient is well enough to benefit

General Measures

- Rapid and clear communication with the patient and family is a priority as the patient may decline and die in minutes
- Reassure and explain the situation to the patient and family
- Stop medications such as NSAIDs (non-selective COX inhibitors) or anticoagulants that may be causing or exacerbating the bleeding
- Note: NSAIDs that are selective COX-2 inhibitors do not affect platelet function

Treatments to be Considered

Consider if the patient is well enough to benefit

- **Transfusion** of packed red blood cells, platelets, or other blood components
- Correction of abnormal clotting with fresh frozen plasma (if available)
- **Tranexamic acid 1000 mg PO/IV TID, administer IV doses over 5-10 minutes due to risk of hypotension**

- **Tranexamic acid IV: 10 mg/kg/dose q6-8h (Maximum: 1000 mg/dose); may administer IV doses over 5-10 minutes due to risk of hypotension**
- **Tranexamic acid PO: 25 mg/kg/dose q8h (Maximum: 1500 mg/dose)**

- Consider **vitamin K** if the patient is taking a vitamin K antagonist anticoagulant, e.g. warfarin, or is vitamin K deficient
  - Vitamin K deficiency occurs in severe malnutrition or very low-fat diets, as well as certain rare disorders with malabsorption of fat and fat-soluble vitamins such as cystic fibrosis
  - Newborns are prone to vitamin K deficiency, because limited vitamin K is transferred from the mother to the fetus during pregnancy, and they have a limited ability to synthesize vitamin K in the first few days of life
- Haemostatic radiation or embolization if available and the patient is well enough to benefit

Bleeding From a Wound/Ulcer

- Apply steady pressure
- Apply **epinephrine (1 mg/mL)**-soaked gauze topically and cover

with a dressing

- **Tranexamic acid** (crushed tablets or injectable liquid) and sucralfate (crushed tablets) can be applied topically and covered with a dressing

Bleeding From GI Tract

- Stop NSAIDS (specifically non-selective COX inhibitors) and reduce or discontinue steroids if possible
- Trial of **tranexamic acid** may be considered
- Start a **proton pump inhibitor** (e.g. omeprazole, pantoprazole) or **H2-antagonist** (e.g. cimetidine, famotidine)
- Referral for endoscopic management if possible and if patient is well enough to benefit

Bleeding From Bladder

- May benefit from continuous bladder irrigation and instillation of haemostatic agents
- If well enough, consider cystoscopy/diathermy/radiotherapy (depending on prognosis)

Bleeding From Mouth/Gums

- Gentle and cautious cleaning of the mouth with a soft cloth or sponge stick
- **Tranexamic acid: apply IV solution (500 mg diluted to 10 mL volume to make a 5% solution). Swish and swallow 10 mL QID**
  - Can also be applied topically with gauze or other topical tool

- Children: Use 2-10 mL of diluted IV solution, as described above, as a mouth rinse. Swish and spit or swallow QID

- **Sucralfate (2000 mg in 10 mL) as mouthwash/rinse BID**
- **Epinephrine (1 mg/mL)** can be applied topically if other agents are not available

- Limit epinephrine use to the short term, due to risk of rebound vasodilation and ischemic necrosis if used continuously

Bleeding From Nose

- Apply continuous pressure and packing for 15 minutes with gauze soaked in **epinephrine (1 mg/mL)**
  - Limit epinephrine use to the short term, due to risk of rebound vasodilation and ischemic necrosis if used continuously
- Apply topical **silver nitrate sticks** for small bleeds
- For posterior nose bleeds, use **xylometazoline** or **oxymetazoline** (nasal spray)
- Apply **tranexamic acid**-soaked gauze (use IV solution, undiluted)

Massive Haemorrhage in Terminal Phase

- Terminal haemorrhage is generally painless, and the patient will quickly become unconscious due to blood loss
- Stay with patient
- Use dark towels (brown, red, blue) to disguise blood
- Remain calm and reassure family that the patient is not in pain
- If the patient is distressed (e.g. bleeding in airway or esophagus causing respiratory distress or vomiting) consider sedation with **midazolam 10 mg IV/SUBQ/Buccal/Intranasal STAT, repeat in 5 minutes (IV) or 5-15 minutes (SUBQ/Buccal/Intranasal)**
- Other rapidly acting sedating medications can also be used in a similar manner

PITFALLS/CONCERNS

- Patients who have a terminal haemorrhage often have a "sentinel bleed" (smaller bleed from the same site) in the days or weeks leading up to a haemorrhage
- If a massive haemorrhage is likely or the patient has had a sentinel bleed, make preparations by discussing the risk of haemorrhage

with the family and patient and having medications (e.g. midazolam) and supplies at the bedside

- Do not use tranexamic acid when disseminated intravascular coagulation is suspected

PALLIATIVE TIPS

- Patients with advanced liver disease or renal failure may develop abnormal clotting because of their disease
- In addition, they may be taking anti-coagulants for another condition

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Constipation

KEY POINTS

- Prevention is the most important part of the treatment
- Constipation is defined as the infrequent and difficult passage of hard stools
- Constipation may be related to the underlying serious illness, the treatment, or may be unrelated
- The possibility of bowel obstruction should be considered, and treatment modified accordingly
- The prevalence of constipation in palliative care patients is 30-80%
- 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

- Normal frequency of bowel movements varies between individual children
- Painful dry, hard, or small stools are features of constipation

ASSESSMENT

see comment on page 10

- Taking a thorough patient history and performing a good clinical assessment are important in identifying the underlying cause(s) of the constipation
- Common causes of constipation in palliative care include:
  - Opioids or other medications
  - Dehydration or decreased oral intake
  - Mechanical obstruction
  - Immobility

- Emotional stress
- Electrolyte imbalances

- Investigations to consider may include an abdominal x-ray to assess the degree of constipation bowel gas pattern and rule out ileus or bowel obstruction

- Mass in LLQ may be present
- Rectal exam may show impacted faeces or fissure

MANAGEMENT

- Mild constipation (in relatively well patients these measures are generally inappropriate in last days/weeks of life)
- If possible (in relatively well patients these measures are generally inappropriate in the last days/weeks of life)
  - Increase fluids
  - Increase activity when possible

Pharmacological Recommendations

- First-line recommended medications: sennosides, lactulose, polyethylene glycol (PEG), glycerin or bisacodyl suppository
- Prophylaxic laxatives are required when opioid therapy is initiated; continue for the duration of opioid therapy
- Titrate laxatives every 1 to 2 days, to effect
- Laxative-induced diarrhoea can be resolved by holding back on medications for a few days, then restarting at a lower dose

Polyethylene glycol (PEG) 3350

- **Maintenance: 0.4-1 g/kg/dose PO once daily (Maximum: 34 g/day)**
- **Disimpaction: 1-1.5 g/kg/dose PO once daily x 3-6 days (Maximum: 100 g/day), then reduce to maintenance dose (above)**

- Onset of effect: usually 1-4 days. Consider other options if more immediate relief is desired

Bisacodyl

- Oral: 0.3 mg/kg/dose PO once daily (Maximum: 15 mg/dose), or
- 3-10 years: 5 mg PO once daily
- >10 years: 5-15 mg PO once daily
- Tablets are enterically coated: Do not chew or crush tablets. Do not give within 1 hour of antacids or milk products
- Rectal: 6-12 years: 5-10 mg once daily PR

Senna (based on 8.6 mg of senna per 1 tablet)

- 2 years: ½ tablet PO qHS-BID
- 2-5 years: ½ to 1 tablet PO qHS-BID
- 6-12 years: 1 to 1½ tablet PO qHS-BID
- ≥12 years: 2-3 tablets PO qHS-BID

Lactulose (concentration 667 mg/mL)

- 1 month-1 year: 2.5 mL PO once daily to BID
- 1-5 years: 5 mL PO once daily to BID
- 5-10 years: 10 mL PO once daily to BID
- 10-18 years: 15 mL PO once daily to BID
- Usual dose: 0.5-1.5 mL/kg/dose PO once daily to BID

PITFALLS/CONCERNS

In patients in the final terminal phase, i.e. hours to days, it may be inappropriate to treat an obstruction or constipation

Medication	Starting Dose	Maximum Dose	Onset of Action	Notes
Sennosides	**5-15 mg PO daily**	36 mg PO TID	6-12 hours	-Intestinal colic possible -Avoid in bowel obstruction (perforation risk)
Lactulose	**15 mL PO daily with food**	30 mL PO TID	1-2 days	-Requires sufficient fluid intake -May cause abdominal bloating, nausea, intestinal colic -Risk of electrolyte disorders and volume overload
Polyethylene glycol	**17 g PO daily**	17 g PO TID	1-3 days	-Requires 125-250 mL fluid intake per 17 g dose -May cause nausea, bloating, vomiting, stomach cramps -Contraindicated in intestinal obstruction, perforation, inflammatory bowel conditions
Glycerin suppositories	**1 PR daily**	-	15-30 minutes	-Use with caution in rectal irritation, neutropenia, or thrombocyctopenia (infection and bleeding risk)
Bisacodyl suppositories	**1 PR daily**	-	20 minutes up to 3 hours	-Risk of abdominal cramps, diarrhoea, local rectal irritation

- Do not use enemas or suppositories in children with neutropenia and thrombocytopenia
- Children with constipation may have developed rectal tears complicating the problem

PALLIATIVE TIPS

- Bowel regimens should be individualized and titrated to the individual patient's 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

- As with adults, encourage increased fluid intake and exercise when appropriate

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Cough

KEY POINTS

- 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, but it is often under-treated
- Using cough suppressants (e.g. dextromethorphan or morphine) can bring symptomatic relief and improve quality of life

ASSESSMENT

see comment on page 10

- Taking a thorough history and performing a good clinical assessment are important to identify the underlying cause(s) of the cough
- Common causes of cough in palliative care include:
  - Upper airway cough syndrome (formerly post-nasal drip)
  - Tumour
  - Pleural effusion
  - Asthma
  - Pulmonary edema, decompensated congested heart failure (CHF)
  - Lymphadenopathy
  - Gastroesophageal reflux
  - Angiotensin-converting enzyme (ACE) inhibitors
  - Treatment related (e.g. radiation therapy to the chest)
- Investigations to consider may include:
  - Chest x-ray/CT to assess possible cause

MANAGEMENT

- Consider treatment of the underlying cause, e.g. oncological treatment of tumour, draining of pleural effusion, treatment of infection, gastric reflux

Consider if the patient is well enough to benefit

- Simple measures such as nebulized c0.9% saline can be helpful
- Simple cough lozenges may be tried
- If productive, an expectorant such as **Guaifenesin 200-400 mg PO q4h PRN** can be tried
- **Dextromethorphan 30 mg (or higher doses) PO q4h**
- If ineffective, **morphine or another opioid** should be used
- Codeine should be avoided if at all possible because its metabolism varies significantly between individuals (see section on Pain for information about risks of codeine)

Pharmacological Recommendations

- Identify and treat cause(s) of cough
- If not possible, consider a symptomatic approach based on the type of cough:
  - Protussive treatments: mucolytic, improve effectiveness of cough
  - Antitussive treatments: peripheral or central action; reduce intensity and frequency of cough

Protussive agents:

- **Nebulized 0.9% saline solution 2.5-5 mL QID**
- **Guaifenesin 200-400 mg PO q4h; maximum: 2400 mg/day**
  - **Acetylcysteine 3-5 mL of 20% solution or 6-10 mL of 10% solution inhaled via nebulizer TID or QID**
  - Note: give nebulized salbutamol prior to treatment to reduce risk of bronchospasm

Antitussive agents:

- **Dextromethorphan 15-30 mg PO q4-8h; maximum: 120 mg/day**
- **Morphine 2.5-5 mg PO q4h; titrate to effect**

- **Gabapentin target dose of 300-600 mg PO TID; start with 100 mg PO BID for frail patients**
- **Dexamethasone 2-8 mg PO daily**
  - **Indications:** Uncontrolled asthma, stridor, tumour-related oedema, chronic interstitial lung disease, lymphangitis, radiotherapy/chemotherapy-induced pneumonitis carcinomatosis
- **Lidocaine 2% preservative-free – 2-5 mL in 1 mL of normal saline nebulized via mouthpiece q4h.** Note: keep patient NPO for at least 1 hour after use to prevent aspiration, may require salbutamol pre-treatment to prevent bronchospasm

Opioids for Cough

- The initial starting dose will depend on the patient's previous exposure to opioids
- Opioid naïve: **Morphine 2.5 mg PO q4h (or 1-2 mg SUBQ/IV) and a breakthrough or rescue dose every hour, as required**
- For patients already on opioids: increase dose by 20%

Other Pharmacological Treatments

- Inhaled corticosteroids may be helpful
- If thick secretions are difficult to clear, consider using nebulized normal saline or hypertonic saline

- **Children with persistent non-productive cough (like adults) may benefit from opioids**
- **Morphine**
  Starting doses for opioid-naïve infants less than 6 months:
  0.025 mg/kg/dose SUBQ/IV q4-6h PRN, or 0.05 mg/kg/dose PO q4-6h PRN
- **Do not use codeine in children**
  (see Pain section for details)

- **Starting dose for opioid-naïve infants/children more than 6 months: 0.05 mg/kg/dose SUBQ/IV q4-6h prn, or 0.1 mg/kg/dose PO q4-6h PRN**
- **There is limited evidence to support the efficacy of cough treatments in children. It is discouraged in children <6 years of age due to risk of adverse events from unintentional overdose**

- **Guaifenacin (for productive cough)**
  6-11 years: 100-200 mg PO q4h PRN
  (Maximum: 1200 mg/day)
  ≥12 years: 200-400 mg PO q4h PRN
  (Maximum: 2400 mg/day)

- **Dextromethorphan**
  6-11 years: 10 mg PO q4h PRN (Maximum: 60 mg/day)
  ≥12 years: 20 mg PO q4h PRN (Maximum: 120 mg/day)

- **Dexamethasone (systemic corticosteroid)**
  0.6 mg/kg/dose PO/IV (Maximum: 8 mg/dose) x 1 dose
  Reassess response to treatment before repeating doses

PITFALLS/CONCERNS

- In patients in the final terminal phase, i.e. hours to days, antibiotics will make little difference
- Suctioning should be avoided other than for tracheostomy, oesophageal obstruction, or massive secretions at end of life
- Repositioning to side-lying with head of bed raised often helps

PALLIATIVE TIPS

- A bedtime dose of morphine can help suppress the cough and allow for an undisturbed sleep

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Delirium

KEY POINTS

- Delirium (with or without hallucinations) is commonly experienced by patients with advanced illnesses
  - Up to 80% of patients with advanced cancer develop delirium in the last days of life
- Delirium presents as an acute change in the patient's attention and awareness that was not previously there, with a fluctuating course
- Possible causes are many and the cause may be multifactorial and difficult to determine
- Delirium can be caused by opioids or the accumulation of opioid neurotoxic metabolites
- Patients with a prolonged hospitalization, particularly in ICU, with associated sleep deprivation and mechanical ventilation are at high risk of delirium

- Delirium is more common in younger children (<2 years of age) and in children with chronic neurological conditions, particularly while in ICU

ASSESSMENT

see comment on page 10

- Use of validated delirium screening tools may be helpful, e.g. Confusion Assessment Method
- Consider common medical triggers which may be treatable or modifiable, including:
  - Dehydration*
  - Poorly controlled pain or other symptoms
- Hepatic and renal failure*

**Can contribute to delirium by contributing to the accumulation of opioids and their metabolites*

- Urinary retention
- Infection, e.g. urinary tract infection
- Constipation
- CNS disease, e.g. brain metastasis, neurodegenerative conditions
- Biochemical imbalances, e.g. hypercalcaemia, hyponatremia
- Medications, particularly tricyclic antidepressants, corticosteroids, benzodiazepines, opioids, anticholinergics
- Hypoxia

- Children can be screened with the Cornell Assessment of Pediatric Delirium (CAPD) to identify delirium, which includes Developmental Anchor Points for young children (<2 years)

MANAGEMENT

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

- Management includes both environmental management and pharmacological management

Environmental Management

- Ensure an appropriate level of lighting (with changes for day and night)
- Provide reorientation with a calendar, clock, and verbal and written information
- Keeping noise to a low level
- Have family members present
- Ensure patient has their glasses and hearing aids to help provide normal sensory stimulation

- Discontinue drugs that may be causing the delirium
- Consider a trial of hydration if the patient's condition would tolerate this, which may help correct electrolyte disturbances and may reduce the accumulation of toxic opioid metabolites
- Correct electrolyte imbalances: hypercalcaemia may respond to hydration and/or to bisphosphonates such as **pamidronate 60-90 mg IV single dose**

Pharmacologic Management

- Pharmacological management includes:

1) Neuroleptics

- The newer atypical antipsychotics, **risperidone**, and **olanzapine**, can also be used effectively and offer the advantage of less anti-parkinsonian/anti-cholinergic side effects
- **Haloperidol** is commonly used
- **Chlorpromazine** may be more effective in cases of severe agitation
- Note: **Quetiapine** is the preferred agent for treatment of delirium in patients with Parkinson's disease as it is the least dopaminergic antipsychotic. Haloperidol should be avoided in these patients

Neuroleptic Agent	Dose	As Needed Dose	Route
Olanzepine	**2.5 mg qHS-BID, maximum dose of 10 mg/24hrs**	**1.25-2.5 mg q12h**	PO
Risperidone	**No change**	**1-2 mg q12h**	PO/SL
Quetiapine	**6.25-50 mg BID**	**12.5 mg q4-6h**	PO
Haloperidol	**0.5-2 mg BID, maximum dose of 5 mg/24hrs**	**0.5-1 mg q4-6h**	PO/SUBQ/IV
Chlorpromazine	**15-100 mg BID, maximum of 200 mg/24hrs**	**25-50 mg q4-6h**	PO/IV

2) Benzodiazepines

- Benzodiazepines should be used with caution as they can worsen delirium, and should not be used alone for the treatment of delirium
- **Lorazepam** or **midazolam** can also be used in situations where there is considerable agitation

Benzodiazepines	Regular Dose	As Needed Dose	Route
Lorazepam	**0.5-2 mg BID to QID**	**0.25-2 mg q4-6h**	PO/IV/PR
Midazolam	**5-60 mg/24h IV/SC infusion or 5-20 mg q4h**	**0.25-5 mg q1h**	SUBQ/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
- In patients with significant renal impairment, metabolites from morphine can accumulate
- If an opioid rotation is performed, establish the equianalgesic dose from an equianalgesic table, and start the new opioid at 50% of the equianalgesic dose, if pain is well controlled; if pain is poorly controlled do not reduce the equianalgesic dose by 50% (See Appendix 3)
- The 50% dose reduction addresses incomplete cross tolerance which occurs between different opioids (see Pain chapter for more details)
- Repeated clinical assessments and consideration of patient-specific factors should always guide the approach to determining the new dose

- Try to prevent delirium by ensuring regular sleep and promote a sleep-wake cycle, by allowing natural light into the room during the day and making the room dark at night

- Promote reorientation by providing a clock, calendar, or verbal and written reorientation of the date and time for older children and teenagers
- Ensure familiar caregivers are present to reassure the child
- Provide familiar toys, stories, and activities
- **Haloperidol**
  - **>3 months of age: 0.01-0.02 mg/kg IV/PO q8h PRN (0.5-1 mg). For acute agitation: 0.025-0.05 mg/kg PO/IV; may repeat 0.025 mg/kg in 1 hour PRN**
  - **Usual onset of effect when selecting the appropriate route of administration: PO (2 hours), IV (3-20 minutes)**

- **If agitated delirium, consider the addition of:**
- **Lorazepam**
  - **0.025-0.050 mg/kg/dose (Maximum: 2 mg) AS SINGLE DOSE or q4-8h PO/SL/IV**
- **Midazolam**
  - **Oral: 0.25-0.5 mg/kg/dose (Maximum: 20 mg)**
  - **IN: 0.2-0.5 mg/kg/dose (Maximum: 10 mg, 5 mg per nostril)**
  - **SUBQ/IV bolus: 0.025-0.1 mg/kg/dose (Maximum: 10 mg)**
  - **SUBQ/IV infusion: 25-500 mcg/kg/hr**

- Benzodiazepines may worsen delirium or cause paradoxical reactions in some children

- **Clonidine (alpha-adrenergic agent)** can be helpful to promote sleep, with minimal side effects
  - **1-2 mcg/kg/dose PO q4-6h, may increase to a maximum of 4 mcg/kg/dose**
  - When initiating and titrating therapy, monitor for bradycardia and hypotension secondary to the alpha-2 agonist activity on the cardiovascular system
  - When discontinuing therapy, consider a wean over 3-7 days, as rebound hypertension, along with other withdrawal side effects (diaphoresis, headache, insomnia) may occur

PITFALLS/CONCERNS

- Antihistamines may cause paradoxical agitation and confusion
- Benzodiazepines can be useful in children in controlling agitation but at higher doses may worsen delirium for some children

PALLIATIVE TIPS

- Because of the high incidence of delirium in palliative care patients (up to 80% at end of life), regular screening is recommended using a delirium-specific screening tool (e.g. Confusion Assessment Method)
- Environmental modifications are key components of treatment
- 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
  - Generally, opioid-related delirium is due to accumulation of neurotoxins in the setting of renal or liver failure
- The newer atypical antipsychotics, such as risperidone and olanzapine, can also be used effectively and offer the advantage of less anti-Parkinsonian/anti-cholinergic side effects

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Dyspnoea

KEY POINTS

- Dyspnoea has a prevalence of 50% in people with any type of cancer (not just lung cancer)
- Dyspnoea is moderate to severe in about one-third of terminally ill cancer patients
- Opioids (e.g. morphine) are first-line medications for the symptomatic management of dyspnoea, which are started at 50% of the starting dose for analgesia
- Dyspnoea is a subjective symptom and therefore it is important to ask the patient about their feelings of dyspnoea rather than rely on clinical examination findings

- Breathlessness is common in children in the end of life phase (last days and hours)

ASSESSMENT

see comment on page 10

- A good clinical assessment is important to try and identify the underlying cause of the dyspnoea (e.g. pneumonia, CHF, pleural effusion, etc)
- Investigations to consider may include:
  - Chest x-ray to assess possible chest condition
  - Blood tests to rule out anaemia or infection
  - Oxygen saturation

- Asking a child "is your breathing troubling you?" can be very helpful in assessment. Remember that tests such as oxygen saturation do NOT correlate well with the

patient's experience of dyspnoea

- A validated assessment tool for children with dyspnoea is available (the Dalhousie Dyspnoea Scale).

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 the patient is well enough to benefit

- Reassurance and explanations about what is happening are important for children

Non-Pharmacological Treatments

- Simple measures such as repositioning (semi-sitting or leaning forward are often preferred), opening a window, providing a handheld fan, and teaching the patient simple 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 dyspnoea and is not necessary for all patients. For some patients it may make their feeling of dyspnoea worse to have their face covered by an oxygen mask or nasal prongs
- Treat the patient's symptoms, not based on physical or laboratory findings (i.e. the oxygen saturation)
- Relaxation and self-hypnosis activities, occupational and music therapy, acupuncture and acupressure, and physical therapy should be considered if available

Morphine and Other Opioids

These are the gold standard first-line treatment for dyspnoea

- The initial starting dose will depend on the patient's previous exposure to opioids
- Opioid-naïve patients: **morphine 2.5 mg regularly q4h PO** (or 1-2 mg SUBQ/IV) and a breakthrough or rescue dose as required (see Appendix 1) is suitable for an opioid-naïve patient
- If patients are already on strong opioids for pain, increase their regular dose of morphine in the same way as you would titrate for pain management – see guideline on pain (some patients may require high doses for dyspnoea)

Benzodiazepines

- Adding a benzodiazepine to decrease the anxiety or panic which often accompanies dyspnoea
- **Midazolam** 5 mg PO or 2.5 mg Buccal/SUBQ/IN q1h/PRN
- **Lorazepam** 0.5 mg PO/SL BID PRN
- **Clonazepam** 0.25-0.5 mg PO BID

Corticosteroids and **bronchodilators** may also be helpful

- Correctable causes of dyspnoea in children such as anaemia, infection, and effusion can be treated
- Consider if the patient is well enough to benefit
- As with adults, opioids such as morphine are accepted as an important and effective treatment for dyspnoea in advanced cancer and other diseases

- **Morphine**
  - **Starting doses for dyspnoea treatment with opioids are generally 50% of the starting dose for pain in opioid-naïve children**

– 0.05 mg/kg/dose SUBQ/IV q4h PRN, or 0.1 mg/kg/dose PO q4h PRN

– Higher starting and maintenance doses will be required in opioid-tolerant children; increase the child's current opioid dose by 25-50%

- **Midazolam**
  - **0.1 mg/kg/dose PO every 2-4 hours (Maximum: 10 mg/dose) or**
  - **0.05-0.1 mg/kg/dose SL/Buccal every 2-4 hours (Maximum: 5 mg/dose)**

PITFALLS/CONCERNS

For patients in the last few hours to days of life, antibiotics will make little difference to the course of events, even if infection is suspected

Intubation is not appropriate for most palliative care patients as it will not reverse their underlying condition and causes unnecessary suffering

- Fear of using opioids in children can result in unnecessary suffering at the end of life

PALLIATIVE TIPS

- Remember to ask the patient about their feelings of dyspnoea – physical examination findings and medical staff's observations of tachypnoea or perceived difficulty in breathing do not always correlate with the level of distress
- Provide the patient with a handheld fan, as air movement across the face relieves dyspnoea

- Educating the patient about relaxation techniques (including deep breathing and guided imagery) can reduce the anxiety that patients feel when short of breath
- Higher doses of benzodiazepines to provide sedation may be needed in severe cases

- Supportive treatment such as reassurance by caregivers and calm surroundings are helpful
- Older children can be taught specific relaxation techniques, such as deep breathing/belly breathing, guided imagery, and progressive muscle relaxation
- As with adults, a trial of supplemental oxygen titrated to comfort can be considered

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End of Life Care

KEY POINTS

- Care during the last hours and days of life should focus on ensuring comfort and dignity
- Physical symptoms can be difficult to control; the best way to ensure they are well managed is to develop a symptom management plan before symptoms occur
- It is often necessary to rapidly increase the doses of morphine and other medications to ensure good symptom control during this phase
- When death is approaching, most individuals look quite similar, despite their underlying medical condition

ASSESSMENT

see comment on page 10

Recognizing When Death is Imminent

- Observations that may help to identify patients who are approaching end of life:
  - Very tired and weak, spend the majority of time sleeping or lying down
  - Little or no oral intake and difficulty swallowing
  - Altered level of consciousness: confused, agitated, restless, or drowsy
  - Changes in pulse, blood pressure, and breathing, cool and mottled extremities
  - Decreased urine and stool output
- Patients with malnutrition will have a more rapid progression to end of life
- Predicting how long a patient will live is very challenging, changes in the patient's condition should guide prognostication. If changes in the symptoms (fatigue, oral intake, level of consciousness) described above are:

- Hourly, death is expected in hours to several days
- Daily, death is expected in days to several weeks
- Weeks, death is expected in weeks to months

- Discontinue vital sign assessments, pulse oximetry, non-essential medications (including IV fluids), and lab and radiological tests (discuss with the family before doing this as they may perceive this as "giving up" on the patient)

- Children are often more resilient and may survive what appears to be the imminently dying phase, because they have less age-related degeneration of vital organs

MANAGEMENT

Ensuring a Good Death

- According to recent studies, patients and family members feel that a "good death" includes:
  - Communication and clear decision-making from health-care providers
  - Adequate pain and symptom management
  - Strengthening relationships with loved ones (resolving conflicts, saying goodbye)
  - Preparation for death

Communication

- It is helpful to provide clear and prompt information about prognosis to the patient and family
  - Use phrases such as "It can be difficult to predict, but I expect that he/she will live for hours to a few days" to provide information about prognosis
- Honesty is preferred so that the family can plan appropriately, e.g. ensure that loved ones are present or have a chance to say goodbye

- Honesty does not lead to a loss of hope, but shows that you are being honest and transparent with the family

Suggested steps and phrases to use when communicating about prognosis in the end of life phase – see Communication chapter for more details

Communication Step	Suggested Phrase
Set up the conversation by introducing yourself and asking permission to proceed	"Can I talk to you about what is happening to your loved one?"
Assess understanding of the illness	"What is your understanding of where your loved one is at with his/her illness?"
Share prognosis in a clear and honest way	"I wish it were different, but I am worried that your loved one is very sick and will not be able to recover from this illness. We do not have any treatments which can cure this problem and I am worried that he/she is not going to live for very long"
Assess goals and wishes	"What is most important for your family at this time, given the information I have shared with you?"
Establish a plan	"I recommend that we focus on providing care which ensures that he/she is comfortable, and he/she can be with those he/she loves"
Close the conversation	"We will be here to treat and support him/her and your family"

Managing Common Symptoms in the Last Hours and Days:

- Guidelines and standardized order sets are helpful to ensure consistent treatment with appropriate doses of medications, and allow bedside clinicians to initiate care
  - Ensure that medications are available at the bedside to quickly treat common symptoms (such as pain, dyspnoea, and agitation/restlessness) which may arise
    - Morphine (or another opioid)
    - A short-acting benzodiazepine (e.g. midazolam)
- If symptoms are not well managed, this suffering may be the family's final memory of their loved one, which can cause further distress and a complicated bereavement
- Do not be afraid to rapidly increase the dose of medications to achieve symptom control
- For patients who experience refractory symptoms, palliative sedation can be considered; full details are beyond the scope of this chapter
- The SUBQ route is useful in this phase of illness to manage symptoms quickly, but without the trouble of needing to maintain IV access
  - Insert a butterfly needle and secure in place. This can be kept for up to 7 days (provided the SUBQ site does not have any significant redness or tenderness)
  - **Medications which can be given SUBQ (at same dose as IV) – see** Medications **and** Appendices **for complete details:**
    - Opioids: Morphine, hydromorphone, fentanyl, methadone, oxycodone, diamorphine
    - Sedative-hypnotics: Midazolam, clonazepam, phenobarbital
    - Antiemetics: Haloperidol, metoclopramide, levomepromazine (methotrimeprazine)
    - Anti-secretory agents: Hyoscine BUTYLbromide, hyoscine HYDRObromide, glycopyrrolate, octreotide
    - Antihistamines: Cyclizine, promethazine
    - Miscellaneous: Dexamethasone, methylnaltrexone, naloxone, furosemide

Pain, dyspnoea, and agitation

- These are common symptoms which often require intensive treatment near the end of life
- Rapidly escalating doses of opioids are appropriate to manage pain or dyspnoea and when used by trained providers
  - This approach will not cause respiratory depression or hasten death when used appropriately
- To facilitate rapid titration: ensure that clinicians are present and medications are available at the bedside

Delirium/confusion

- Delirium in the end of life phase is generally multifactorial and irreversible
  - Causes include the underlying disease process, metabolic and electrolyte imbalances, liver and renal failure, infection, and hypoxia
- Urinary retention is a common and potentially reversible cause, which can be managed with a Foley catheter insertion
- ***Refer to Delirium section for further details***

Weakness/fatigue

- Fatigue is expected as the patient approaches the end of life
- Do not give stimulants (methylphenidate, steroids) to try "to wake the patient up" at this stage of illness
- Gentle repositioning, if the patient tolerates, can help avoid pressure injuries

Decreased oral intake

- Reduced oral intake is a normal part of the dying process and patients do not feel hunger or thirst at this stage
  - Fluids and foods should be provided if desired by the patient, but avoid forcing a patient to eat, which can cause aspiration

Suggested Guidelines for the Management of Escalating Pain, Dyspnoea, and Agitation in children

Adapted from the *Interdisciplinary Textbook of Pediatric Palliative Care*

Escalating Pain, Dyspnoea, and Agitation

No ceiling dose exists for symptom management in the last hours or days of life (end of life phase). The correct dose is the dose which relieves the patient's symptoms and does not cause unwanted side effects. Titrate the medications rapidly (over minutes to a few hours)

Loading dose:

For patients already on opioids: Administer a loading dose of opioid equal to 10% of the total dose in the past 24 hours

For patients not already on opioids: Administer IV or SUBQ loading dose as follows:

Morphine 5 mg, children <12 years: 0.1 mg/kg

Subsequent dosing: Doses may be given q10 mins PRN for end of life symptoms

Escalate dose as follows: (Note: 5 mg is given as an example, actual dose may vary)

First dose: 5 mg, if ineffective after 10 mins, then give

Second dose: 5 mg, if ineffective after 10 mins, notify prescriber

Third dose: 7.5 mg (1.5x starting dose), if ineffective, after 10 mins then give

Fourth dose: 7.5 mg (1.5x starting dose), if ineffective, after 10 mins then give

Fifth dose: 10 mg (2x starting dose)

Once good pain relief is achieved, provide the total dose administered during the titration phase SUBQ or IV q4h regularly and as a PRN/SOS dose

Do not use ONLY as needed dosing as this will allow the symptoms to return and will lead to more distress

Pain assessment may be by pain scale or observations of verbal and nonverbal behaviour (crying, grimacing, and moaning)

Continuous infusion instructions

Recommended hourly rate – total opioid administered in the above steps divided by 4

Recommended 24-hour amount of medication – total opioid administered in the above steps multiplied by 6

- Do not provide parenteral fluids since research shows that this does not improve symptoms, quality of life, or prolong life for palliative care patients who cannot drink
  - Instead encourage families to provide oral care by swabbing the mouth with water and keeping the lips moist with petroleum jelly (Vaseline) or lip balm

Breathing pattern changes

- Breathing will change as the patient approaches end of life, breathing may be slow or rapid and shallow
- Periods of apnoea or increased work of breathing are common, but do not necessarily indicate dyspnoea and so need not be treated unless distressing to the patient

Respiratory secretions

- Patients often have impaired ability to swallow at the end of life, and oral secretions can accumulate in the back of the throat, causing gurgling or rattling sounds
- Generally, the patient is only minimally conscious or unconscious and this does not cause them distress, but family members may find it distressing
- Position the patient on his/her side with the upper body elevated to allow secretions to drain passively
- Discontinue any IV or NG artificial fluids or nutrition that increase secretions
- Avoid mechanical suctioning, as it is not usually helpful and may be distressing to the patient
- *Refer to Respiratory Secretions section for further details*
- **Medications:** (Note: These medications will not work for secretions deep in the lungs (i.e. pulmonary oedema or pneumonia), and are not always effective for upper airway secretions)
  - **Glycopyrronium: 0.2-0.4 mg SUBQ q4-6h PRN**
  - **Hyoscine BUTYLbromide: 20 mg SUBQ, then 20 mg q4-6h PRN.**

Does not cross the blood-brain barrier

- **Hyoscine HYDRObromide/Scopolamine: 0.4-0.6 mg SUBQ q4-6h PRN; OR transdermal patch; replace patch every 72 hours**

  – Note: Hyoscine HYDRObromide crosses the blood-brain barrier and is quite sedating; may increase risk of delirium in end-stage renal failure patients

- **Atropine 1% eye drops: 1-4 drops (each drop contains approximately 0.5 mg atropine) under the tongue q2-4h PRN**

  – Note: Atropine will also cross the blood-brain barrier in patients, and obtund

Incontinence and urinary retention

- Incontinence of urine and/or stool is common
- Change soiled linens promptly, aiming to keep the patient clean and dry
  - A Foley catheter may be helpful, but is not always needed since urine output is minimal and absorbent pads or cloth and plastic can be used
- Urinary retention may occur, and should be suspected in a restless patient with a distended bladder. In this case, a Foley catheter should be inserted
- Urinary retention can be a side effect of opioid medication, which is more commonly seen in infants and young children. A Foley catheter or intermittent catheterization may be needed

Seizures/convulsions

- Seizures can be caused by cancers (primary or metastatic), drug toxicity (e.g. pethidine/meperidine), metabolic or electrolyte abnormalities (hypoglycaemia, hyponatraemia, hypercalcaemia), hypoxia, severe liver failure, infections of the CNS, and epilepsy
  - Treatment is comfort-focused and a full investigative work-up is not necessary.
- For children with a history of epilepsy, if the child can no longer swallow medications, SUBQ midazolam or another benzodiazepine

should be started

Management

- **Corticosteroids** can be considered for seizures secondary to brain metastasis, to reduce peritumoural oedema
- **Acute treatment (Status Epilepticus)**
- Benzodiazepines are first-line treatment. If the seizure does not resolve within 5 minutes, consider:
  - **Lorazepam 4 mg IV over 2 minutes, OR**
  - **Midazolam 10 mg Buccal/SUBQ/IM or IV over 2 minutes**
  - **Diazepam 10 mg PR or IV**
- Can repeat ONCE after 10-20 minutes, if the seizure persists
- If ineffective, consider doubling the dose of midazolam or diazepam or give **phenobarbital**
- Continue regular **phenobarbital** after the seizure stops, to prevent further seizures
- ***Refer to Seizures section for further details***

Counselling Checklist for Family Caregivers at End of Life

Physical Care:

- Moisten mouth with ice chips or a damp cloth soaked in water or fruit juice
- Keep lips moist with balm or petroleum jelly (Vaseline)
- Keep the person clean and dry, use cloths or pads for urinary incontinence
- Give the medications to control symptoms, at the correct times
  - Do not wait until the symptoms are severe, as this will lead to symptoms which are more difficult to control
- Do not force the person to eat or drink, if he or she does not want to eat, this is okay
- Assist the person to change position or turn every few hours to prevent pressure ulcers

- Contact the home palliative care team (or whoever is providing 24-hour telephone support), if pain or other symptoms are not controlled

Emotional and Spiritual Care:

- Tell the person that they are loved and will be remembered
- Ensure that the person has opportunities to discuss any feelings of guilt, worry, or regret
- Pray or connect with spiritual or religious leaders if the person wishes this
- Sit with the person, hold his/her hand and talk to him/her

SPECIAL SITUATIONS

Unsuccessful resuscitation

- During resuscitation, the family should be permitted to be present, as this leads to less anxiety, depression, and second-guessing about the care provided and the competence of staff
- One healthcare provider should to stay with the family, to update them about what is happening, answer their questions, and provide emotional support

Discontinuing fluids and nutrition

- Discontinuing medically administered fluids and nutrition is recommended during the end of life phase
  - Medically provided fluids and nutrition can ethically be withheld or withdrawn if they are no longer in the best interests of the patient, e.g. if fluids are adding morbidity to the process of dying
  - This may be considered when a patient permanently lacks awareness and the ability to interact with the environment, such as a persistent vegetative state or a child with anencephaly
- It is important to counsel patients and families that this does not mean clinicians are "giving up" on a patient, but rather focusing intensely on comfort and support

Discontinuing ventilatory support

- It may be ethically appropriate to discontinue intensive respiratory support (e.g. non-invasive or invasive ventilation) in certain circumstances
- If the underlying cause of ventilator dependence is irreversible, then ventilatory support will not provide a meaningful quality of life and may prolong suffering
- This act of discontinuing ventilator support (or other life-sustaining treatments) is not the same thing as euthanasia or medical assistance in dying
- It is essential to involve the family in the decision to discontinue ventilatory support
  - Involving religious or cultural leaders may also be necessary
- After discontinuation of ventilation, most patients live only minutes or hours; however, there are some patients who may live for a few days or longer
- Clinicians must prepare the family for the possibility that the individual may breathe on his or her own, especially in children, where this is more common

MANAGEMENT

Before Withdrawing Ventilator

- Ensure that family are present if desired
- Turn off all monitors and alarms
- Discontinue all other life-sustaining treatments (e.g. artificial nutrition and hydration, antibiotics, dialysis)
- Remove all unnecessary medical paraphernalia (NG tubes, IV lines, etc)
- Allow any neuromuscular blocking agents to wear off
- Ensure that a rapid acting opioid (e.g. morphine), benzodiazepine (e.g. midazolam or lorazepam), and an agent managing secretions (e.g. glycopyrrolate) are available and drawn up at the patient's bedside
- Give a dose of opioids and benzodiazepine prior to withdrawing the ventilator, to ensure the patient does not feel any discomfort or dyspnoea

Process of Withdrawal

- Ensure that the patient appears comfortable
- Withdrawal by immediate extubation is recommended

After Ventilator Withdrawal

- If the patient appears distressed, symptoms should be immediately and aggressively controlled, by giving morphine and midazolam, every 10 minutes, until distress is relieved
- A clinician should be easily available to answer questions and manage symptoms
- Continuous infusions (IV or SUBQ) of medications to manage symptoms can be considered to ensure comfort

Memory Making

- This is especially relevant for parents, but is relevant for any death of a child or adult
- Many times, parents are encouraged to try to quickly forget a child that has died, but this is not recommended as it leads to a more complicated grief for parents
- Having tangible objects to remember their loved one supports family in their grief
- This is especially important in a pregnancy or infant loss, as parents have few tangible memories of their child's short life
- Common memory making activities which can be easily offered to families include:
  - Photographs or videos
  - Prints or molds of hands and feet, locks of hair
  - Linking objects, which provide a physical reminder of the connection between the child and loved one (e.g. a pair of special necklaces or bracelets, one of which is placed with the child and the other with the parent)
  - Personal items, e.g. clothing, baby blanket, small toys, hospital bracelet, birth certificate, bassinet card

- Memory boxes: items can be stored and looked at when desired
- Some parents may not want to keep any memory items, which should be respected
- All parents should be offered memory making, since in all cultures, there are some parents who will desire this

After Death Care

- Express empathy with a simple statement such as "I am sorry for your loss"
- Confirm the death by physical examination (absence of heart sounds, palpable pulse, or respirations for 60 seconds)
- Document the date and time of death in the medical record and the cause of death
- Allow the family as much time as they desire to say goodbye and to perform any religious or cultural rituals, as permitted within the limitations of the setting
- During an epidemic (e.g. Ebola), it may not be possible to release the body to the family, so assistance from a psychologist or spiritual support person is important to support the family's bereavement

Supporting Staff who Provide End of Life Care

- Witnessing frequent suffering and death can cause staff burnout, compassion fatigue, and moral distress
- Regular support meetings create a safe space for staff to reflect and express their emotions on providing end of life care
- Staff can reflect on the care that was delivered – what went well, what could be improved
- Senior staff members should attend to demonstrate the importance of seeking support
- Commemorating a patient is also important for healthcare providers, this can be done by having memorial services, attending funeral services, or having follow-up contact with families
- Letters, phone calls, or text messages from staff are deeply valued

by families, who often treasure the memories of these small acts of kindness by staff

PITFALLS/CONCERNS

- Avoid giving exact predictions for how long a patient will live, instead, give a range based on how quickly you are seeing changes in energy, alertness, and oral intake:
  - If changes are hourly, death is expected in hours to several days
  - If changes are daily or every few days, death is expected in days to several weeks
  - If changes are weekly, death is expected in weeks to months

PALLIATIVE TIPS

- Do not be afraid to rapidly increase the dose of medications to achieve symptom control during the end of life phase
- Discontinuing IV fluids and nutrition is recommended, as this will reduce symptoms, particularly with respiratory secretions and oedema, and increase suffering
- Provide families with clear and honest information about prognosis using "I wish, I worry" statements
  - "I wish it were different, but I am worried that your loved one is very sick and will not be able to recover from this illness. We do not have any treatments which can cure this problem and I am worried that he/she is not going to live for very long"
- Provide psychosocial and spiritual support which is culturally appropriate

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Hiccups

KEY POINTS

- Hiccups are repeated involuntary contractions of the diaphragm and respiratory muscles
- Gastrointestinal causes are the most common cause of hiccups
- Hiccups can be extremely distressing and can lead to fatigue and sleep disturbance
- Treatment should include both pharmacologic and non-pharmacologic strategies

ASSESSMENT

see comment on page 10

- A good clinical assessment is important to try and identify the underlying cause of the hiccups
- Finding the cause (if possible) can often help to direct treatment. However, often the cause is not known

- Common causes of hiccups in palliative care patients include:
  - Gastric or abdominal distension from obstruction, tumour, gastroparesis, ascites, or hepatomegaly
  - Irritation of the vagus nerve or diaphragm
  - Gastritis, ulcer, or oesophagitis
  - Gastro-oesophageal reflux disease
  - Local spread from tumours (gastric, oesophageal, peritoneal, from lymph nodes)
  - Infection
  - Other problems involving the thorax or abdomen: pneumonia, pericarditis, or pancreatitis:
  - Medications: corticosteriods, benzodiazepines, barbiturates, tramadol

- Metabolic problems: uraemia, hyponatraemia
- Intracranial disease: brain stem tumours, increased intracranial pressure

MANAGEMENT

- Consider treatment of the underlying cause

Consider if the patient is well enough to benefit

- Remove possible offending medications
- Correct electrolyte imbalances and treat infections
- If due to gastro-oesophageal reflux, provide treatment such as **omeprazole 20 mg PO daily or famotidine 10-20 mg BID**
- If due to gastric distension, encourage smaller, more frequent meals
  - Use a prokinetic medication such as **metoclopramide 10 mg PO QID** or **domperidone 10 mg PO QID**
    - Use with caution in patients with a history of cardiac arrhythmias or prolonged QT or those on several QT-prolonging medications
  - **Simethicone/dimethicone-containing agents 5 mL PO QID** and PRN may help to decrease gas and distension

- **Domperidone 0.4-0.8 mg/kg/dose PO TID (maximum 10 mg/dose)**

General Non-pharmacologic Measures (Many Different Measures Have Been Suggested)

- If a cause cannot be identified or corrected, then general measures should be used:
- 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

General Pharmacologic Measures

- Note that many medications have been tried, but very little evidence of efficacy exists:
  - Baclofen 5-10 mg PO TID has been shown to be effective in intractable hiccups
  - Gabapentin 300 mg PO qHS can titrate up to 3600 mg/day, increase dose every 3-5 days
  - Nifedipine 10-20 mg PO BID-TID
  - Haloperidol 1-2.5 mg every 4-12 hours PO/SUBQ/IV
  - Anticonvulsants (starting doses):
    - Phenytoin 200-300 mg PO qHS
    - Carbamazepine 100-200 mg PO BID
    - Clonazepam 0.5-1 mg PO BID
  - Lidocaine infusion 0.5-2 mg/kg/hr SUBQ or IV can be useful for intractable hiccups
- Acupuncture, vagal nerve stimulation, and phrenic nerve ablation are also sometimes considered in cases of refractory hiccups

PITFALLS/CONCERNS

- The same agents that are used to treat hiccups may also cause them
- Although sometimes used to treat hiccups, some reports suggest that benzodiazepines may cause or exacerbate hiccups
- Metoclopramide and haloperidol (and other neuroleptics) can cause extra pyramidal reactions, so consider adding diphenhydramine (or another antihistamine) to reduce the likelihood of extrapyramidal effects

PALLIATIVE TIPS

- Gastric distension and gastro-oesophageal reflux disease are the most common causes of hiccups, and a trial of treatments as outlined above should be considered
- Combinations of agents are sometimes required for intractable hiccups

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Malignant Bowel Obstruction

KEY POINTS

- Reported in 5-15% of cases of advanced cancer
- Most common in ovarian cancer (5-40% of patients) and bowel cancer (5-25% of patients)
- May resolve spontaneously or occur intermittently, especially in the early stages
- Absorption of oral administration of medications is often unreliable
- There are many possible causes of malignant bowel obstruction, so a variety of treatment options, including surgical and oncological, can be considered, depending on the patient's condition and goals of care

The goals of care must be clear: "Is this a patient that we would consider for surgery, oncological treatments or conservative/ symptomatic management only?"

- In children, non-malignant causes such as volvulus or intussusception should be kept in mind

ASSESSMENT

see comment on page 10

- Clinical features may include pain, nausea, vomiting, abdominal distension, and reduced or absent passing of stool or flatus
- Obstruction may be single, multi-level or functional (when there is no mechanical obstruction, just impaired peristaltic function)
- Investigations to consider for diagnosis include:
  - Abdominal x-ray, may show air-fluid level, dilated bowel loops
- If surgical intervention is a possibility, consider imaging (CT or contrast plain films) to help define the level of obstruction

(gastrografin is the preferable contrast as it may be useful in restoring bowel function in some cases)

MANAGEMENT

Pharmacological Treatment

Symptom Management or Possible Reversal of Bowel Obstruction

- In many cases, reversal of the bowel obstruction or reduction in symptoms may be possible by using a combination of corticosteroids, prokinetic antiemetics, and antisecretory drugs
- A trial of **dexamethasone** 8 mg SUBQ/IV daily, **metoclopramide 10-20 mg QID SUBQ/IV** (only use if partial obstruction), and **haloperidol 2-4 mg CSCI** for 3-5 days is often helpful
- Note that steroids should be stopped after 5 days if ineffective
- Steroids may be useful for antiemesis and reducing peritumoral oedema, thereby relieving the obstruction

Antiemetics

- Dopamine antagonists are first-line treatment in partial bowel obstruction
- Do not use prokinetics in complete bowel obstruction
- **Metoclopramide** 10-20 mg SUBQ/IV TID or 30-60 mg CSCI over 24 hours for prokinetic benefit
- Discontinue if pain or vomiting worsens
- **Haloperidol** 1-2 mg SUBQ/IV BID or 2-4 mg continuously over 24 hours. Maximum of 5 mg in a 24-hour period

Antisecretory Agents

- Useful for gastric outlet obstruction with high volume vomitus (particularly octreotide), but availability and cost may preclude their use in some settings
- **Hyoscine BUTYLbromide** (HBB) can be given for colicky pain. HBB will slow gastrointestinal motility, so it can be useful in complete

bowel obstruction, but it may hinder the restoration of gut function in partial bowel obstruction

- 20 mg SUBQ/IV q6h or 60-120 mg per 24 hours

- **Hyoscine HYDRObromide** 400 mcg q4h SUBQ. May cause delirium and/or sedation
- **Glycopyrronium** 200-400 mcg q4h SUBQ
- **Octreotide** – no evidence for use in standard management of malignant bowel obstruction, but useful in gastric outlet obstruction with high volume vomitus
  - 200-400 mcg SUBQ TID or via CSCI over 24 hours
- **Famotidine** – useful for reducing gastric secretions in the context of gastric outlet obstruction
  - 40 mg SUBQ BID or via CSCI over 24 hours

Pain Control

- Use of appropriate opioid analgesics such as morphine SUBQ/IV, as outlined in the Pain section is the main treatment

Non-Pharmacological Treatment

- A NG tube with low-intermittent suction or straight drainage will relieve some patients, especially those with high-level obstruction

An NG tube is usually reserved for patients with frequent or severe symptoms. Can be considered for short-term use while waiting to see if pharmacological management is effective

If necessary for the control of symptoms, conversion to a venting gastrostomy tube is beneficial if patient is expected to live for months

- Bypass surgery or 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 SUBQ may be useful in maintaining electrolyte balance and preventing adverse effects such as opioid toxicity and delirium
- Use hydration with caution as it may cause symptoms to worsen due to increased third spacing and oedema

- **Metoclopramide** – 0.1-0.2 mg/kg/dose PO/SUBQ/IV q6-8h (Maximum: 10 mg/dose, 0.5 mg/kg/day)
- Avoid in complete bowel obstruction
- **Haloperidol** – Initial: 0.01-0.02 mg/kg/dose PO/IM/IV/SUBQ q8-12h. Titrate to effect. (Maximum: 0.15 mg/kg/day)
- **Dexamethasone** – 2-4 mg PO/IV daily or BID for 3-5 days (stop after 5 days if ineffective)

PITFALLS/CONCERNS

- *In patients in the last hours to days of life, invasive treatments should be minimized*
- *Prolonged use of NG tubes can cause considerable distress as well as medical complications*
- *Hydration should be tailored to individual needs; beware of over-hydration*
- *For patients with cancer, if the bowel obstruction does reverse it is likely to recur as the disease progresses*

- Hydration should be tailored to the individual; it is unlikely to be of any benefit to the patient in the end of life phase and may cause harm

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 SUBQ infusion (hypodermolysis) up to 80 cc/hr
- In cases of partial obstruction with constipation, continue stool softeners (lactulose) but stop stimulants (senna and bisacodyl) if colic is a problem
- Try rectal measures such as suppositories
- Metoclopramide and haloperidol (and other neuroleptics) can cause extra pyramidal reactions in children, particularly adolescents, and can be used in combination with diphenhydramine to reduce the likelihood of this

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Nausea and Vomiting

KEY POINTS

- Nausea and vomiting are distressing symptoms, present in more than 50% of patients with advanced cancer
- Multiple receptors in the central nervous system, including dopaminergic, cholinergic, histaminic, and serotonergic receptors, are involved in the development of nausea. Blocking of these receptors forms the basis of antiemetic medications
- The choice of antiemetic therapy should be based on the presumed underlying cause of the nausea, which then identifies the receptor(s) involved and suggests the appropriate medication
- Concurrent medications from different classes may be required for effective control (e.g. **metoclopramide** and **cyclizine**, or **haloperidol** and **ondansetron**). Avoid combining more than one medication with the same pharmacological mechanism of action (e.g. metoclopramide and haloperidol) as this will cause increased side effects without improvement in symptom relief
- Corticosteroids such as dexamethasone are non-specific antiemetics and can be very helpful in certain situations (see MANAGEMENT below)

- In children with life-limiting diseases, common causes such as gastroenteritis, reflux, and infections should be considered
- Nausea and vomiting may also occur in children due to emotional distress

ASSESSMENT

see comment on page 10

- A history looking for the possible cause(s) or contributing factors can be very helpful, along with a targeted physical examination

- Select only the investigations that will alter your management plan
- Correct underlying causes of nausea and vomiting if possible and appropriate
- Causes of nausea/vomiting include:
  - Metabolic abnormalities (e.g. hypercalcaemia, liver and kidney abnormalities)
  - Medications including opioids (usually transient), chemotherapy, or antibiotics
  - Infection
  - Severe constipation and impaction
  - Gastric stasis
  - Gastrointestinal ulceration
  - Bowel obstruction (malignant and non-malignant)
  - Radiotherapy
  - Increased intracranial pressure (from brain metastases or primary brain tumours)

MANAGEMENT

Always balance the burdens of a possible intervention or treatment against the likely benefit for the patient

- Management should be "mechanism based" and reflect the most likely underlying cause of the nausea and vomiting
- Consider the best route for the medication as the oral route may not be helpful

General Measures

- Ensure good oral care, treat any signs of oral thrush
- Prevent and treat constipation

- Eliminate strong odours, keep air and room fresh
- Aromatherapy with a peppermint or ginger essential oil may reduce nausea
- Use of acupuncture or acupressure wrist bands may be beneficial
- If the cause is unknown or multifactorial, initial antiemetic medications include:
  - **Metoclopramide**: treats most common causes of nausea and vomiting, including gastric stasis and partial bowel obstruction. **Avoid in complete bowel obstruction**
  - **Haloperidol**
  - **Levomepromazine (methotrimeprazine)** has broad antiemetic activity, targeting most common receptors involved in nausea and vomiting

Opioid-Induced Nausea

- Consider a medication which has both prokinetic and antidopaminergic (e.g. **domperidone 10 mg PO/SUBQ/IV BID-QID**)

Gastric Stasis

- Consider a combined prokinetic and antidopaminergic (as above)

Metabolic Abnormalities or Uraemia

- Consider an antidopaminergic (e.g. **haloperidol 0.5-1 mg PO/SUBQ BID-TID**)
- **Olanzapine 2.5 mg PO daily or BID** is an atypical neuroleptic which blocks multiple receptors and can be useful if other options are ineffective, doses of up to 10 mg/day can be used, higher doses will cause more sedation

Gastric Irritation

- Consider any potentially emetogenic medications and adding an H2-antagonist (e.g. **famotidine 20 mg PO/SUBQ BID**) or a proton pump inhibitor (e.g. **omeprazole 20 mg PO daily**)

Chemotherapy or Radiation-Induced Nausea

- Consider a 5HT3 receptor antagonist, such as **ondansetron 4-8 mg q8-12h PO/IV** and/or **dexamethasone 4-8 mg qAM PO/IV/SUBQ**

Motion-Induced Nausea

- Cyclizine: start with **50 mg PO BID** and **50 mg PO PRN,** titrate to **maximum of 200 mg PO daily**. If parenteral formulation available, can give **100-150 mg/24 hours via CSCI, up to 200 mg/24 hr CSCI**

Raised Intracranial Pressure

- Consider **dexamethasone 4-20 mg qAM IV/SUBQ or cyclizine 50 mg TID PO/IV**

Hypercalcaemia

- Consider hydration and bisphosphonates, such as **pamidronate 60-90 mg IV single dose** or **zoledronate 4 mg IV single dose**, and other specific hypercalcaemia management

Anxiety/Cortical Causes (e.g. pain, previous nausea/anticipatory nausea, emotional factors)

- Treat with benzodiazepines (e.g. **lorazepam 0.5-1 mg SL q4-12h as needed**)

Constipation

See Constipation section

Bowel Obstruction

See Malignant Bowel Obstruction section

General Management Considerations:

- Medications should be dosed regularly if nausea and vomiting are constant
- If symptoms persist, add a second or third antiemetic agent that targets different receptors
- If anxiety is a contributing factor, add a benzodiazepine (e.g. **lorazepam 0.5-2 mg q4-12h PO/SUBQ**) in addition to other antiemetics
- If symptoms remain persistent despite the treatments described above, then consider corticosteroids (**dexamethasone 4-8 mg daily qAM PO/SUBQ/IV**)

- **Metoclopramide: 0.1-0.2 mg/kg/dose PO/SUBQ/IV TID-QID (Maximum: 10 mg/dose, 0.5 mg/kg/day)**
- **Haloperidol initial: 0.01-0.02 mg/kg/dose PO/SUBQ q8-12h. Titrate to effect. (Maximum: 0.15 mg/kg/day)**
- **Famotidine (if gastritis): 0.5-1 mg/kg/dose PO daily or BID (Maximum: 40 mg/dose), or 0.25-0.5 mg/kg/dose IV daily or BID (Maximum: 20 mg/dose)**
- **Omeprazole (if gastritis) 0.7-3.5 mg/kg/dose PO daily (Maximum: 40 mg/day)**
- **Lorazepam (if anticipatory nausea and vomiting): 0.04-0.08 mg/kg/dose PO/SL x 1 dose the night before and/or morning of chemotherapy/radiation (Maximum: 2 mg/dose)**
- **For treatment of anxiety or breakthrough nausea and vomiting): 0.05 mg/kg/dose PO/SL/IV q4-8h prn (Maximum: 2 mg/dose)**
- **Ondansetron: 0.2 mg/kg/dose PO/IV q8-12h (Maximum: 8 mg/dose)**
- **Dexamethasone (for highly emetogenic chemotherapy or radiation): 0.15mg/kg PO/IV q6h (Maximum: 20 mg) pre-therapy q24h (lower doses recommended for moderately emetogenic chemotherapy or radiation)**

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 avoided
  - Haloperidol is a preferred option in such cases

- Metoclopramide and haloperidol (and other antidopaminergics) can cause extra pyramidal reactions in children (as well as adults), treatment with diphenhydramine (or another antihistamine) will reduce the likelihood of this

PALLIATIVE TIPS

- For intractable nausea and vomiting, a multimodal approach combining antiemetics targeting different receptors is recommended (eg. haloperidol + dimenhydrinate (or another antihistamine) + dexamethasone)
- **Levomepromazine/methotrimeprazine** (if available) is helpful for intractable nausea since it targets most receptors involved in generating nausea and vomiting
- Ongoing nausea requires regular dosing of antiemetics rather than just "as needed" dosing
- Use non-pharmacological methods to help reduce nausea and vomiting, as well as including diet modifications (choice of foods, smaller meals) and control of odours

- Distraction, and avoiding food smells and unpleasant odours may be helpful for children

- Use caution when prescribing haloperidol, ondansetron, and metoclopramide in the setting of QTc prolongation or when patients have additional risk factors for Torsade de Pointes (e.g. hypokalaemia, hypomagnesaemia)

Nausea and Vomiting

Cerebral High CNS

Sensory:
Sights, smells, pain

Cerebral
Anticipatory N/V, memories, fear

Treatment:

Benzodiazepines
Cannabinoids
Relaxation therapies

Vestibular

Opioids
Cerebellar Tumor

Treatment:

H1 Antagonist
Dimenhydrinate
Methotrimeprazine

Anticholinergic
Scopolamine
Atropine

Increased Intracranial Pressure

Brain tumor - primary or metastatic

Treatment:

Dexamethasone

Integrative Vomiting Centre (IVC) or Emesis Centre

Treatment:

Anticholinergic
Scopolamine
Atropine

H1 Antagonist
Dimenhydrinate
Cyclizine
Methotrimeprazine

5HT2 Antagonist
Methotrimeprazine
Olanzapine

5HT3 Antagonist
Ondansetron

CB1 Antagonist
THC

NK1 Antagonist
Aprepitant

Chemoreceptor Trigger Zone (CTZ)

Drugs:
Opioids, chemotherapy

Biochemical:
Uremia, hypercalcemia

Toxic:
Septic, emetogenic peptides

Treatment:

D2 Antagonist
Phenothiazine
Haloperidol
Prochlorperazine
Methotrimeprazine
Chlorperazine

Gastrokinetic
Metoclopramide
Domperidone

5HT3 Antagonist
Ondansetron, -trons
Metoclopramide

NK1 Antagonist
Aprepitant

GI Tract - Vagal

Distension
Over-eating,stasis, extrinsic pressure

Obstruction
High,mid,low

Chemical irritants
Drugs,blood,etc.

Treatment:

D2 Antagonist
Gastrokinetic
Metoclopramide
Domperidone
Phenothiazine
Methotrimeprazine

5HT4 Antagonist
Metoclopramide

5HT3 Antagonist
Ondansetron
Metoclopramide
Octreotide
Dexamethasone

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Pain

KEY POINTS

- Pain is common in patients with advanced cancer, with at least 66% of individuals experiencing pain
- Most pain can be satisfactorily controlled using simple medications, following the World Health Organization (WHO) Guidelines
- The WHO three-step analgesic ladder provides guidance about how best to treat pain in adults and adolescents
- The WHO method includes 4 key principles: "**by mouth**", "**by the clock**", "**for the individua**l", and "**with attention to detail**"
- Acetaminophen/paracetamol and NSAIDs can be used for mild pain
- Opioids such as morphine should be used for moderate to severe pain
- Remember to prevent or treat the side effects of morphine, such as constipation and nausea/vomiting, whenever prescribing opioids

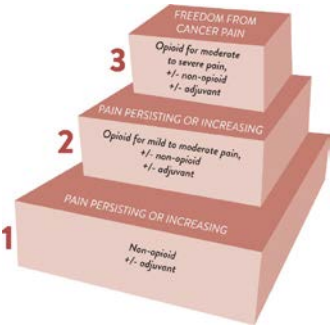

Image Reference: World Health Organization. WHO guidelines for the pharmacological and radiotherapeutic management of cancer pain in adults and adolescents.

- There is no maximum dose for strong opioids, including morphine – the correct dose is the dose that relieves the individual's pain
  - When increasing the dose of opioids, monitor for opioid-induced neurotoxicity, which can occur with rapid opioid titration, particularly in patients whose pain is only partially responsive to opioids
- Signs of opioid-induced neurotoxicity include myoclonus, hyperalgesia, delirium, allodynia (pain from a non-painful stimulus such as light touch), tremors, seizures, and hypersomnolence

- Neuropathic pain is common, as 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)
- Pain that is poorly managed initially can lead to difficult-to-treat neuropathic pain syndromes and other symptoms

- Infants and children experience pain as much as adults, and it is common in advanced cancer and in other severe life-threatening diseases
- Pain receptors are mature (and inhibitory systems are immature) at birth, therefore infants and newborns do feel pain (perhaps even more so than adults)
- Pain suffered by children with life-limiting diseases may have considerable effects on both the child, their family, and the healthcare team

ASSESSMENT

- 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" 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 Numerical Rating Scale (NRS) are important tools to use in assessing a patient's pain and the response to treatment
- Asking about the impact of pain on the person's function and sleep is important
  - Asking about the impact of pain on the person's ability to complete the activities of daily living, such as dressing, bathing, eating meals, and ambulating, can help to assess the impact of

the pain for the individual patient

- Consider whether radiological investigations will be helpful
  - X-rays can help to determine if bone metastasis are present
- Assess for the presence of neuropathic pain, which may be suggested by the following:
  - Pain may be described as stabbing, burning, or shooting
  - Allodynia or hyperalgesia may accompany the pain
    - Allodynia – a sensation that is not expected to be painful causes pain (e.g. light touch of clothing on the skin)
    - Hyperalgesia – an increased sensitivity to feeling pain and an extreme response to pain

- A quiet, sleeping child may be exhausted and withdrawn but may still be in pain
- Children may not report pain because they do not want to be thought of as "bad" or because they fear what might happen next (e.g. they will receive a painful injection)
- Children may be able to use distraction to reduce their pain, but they may still be in pain (e.g. playing or watching videos)
- Even young children (3-4 years and older) can self-report their pain
- Several pain assessment tools based on age, development, and ability to communicate have been developed and should be used to facilitate an assessment of pain severity and give children a voice in their treatment

MANAGEMENT

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

Consider if the patient is well enough to benefit

FOR MILD PAIN

- **Paracetamol/acetaminophen 325-1000 mg PO/IV q4-6**h (daily maximum 4 g/day)
- **Paracetamol/acetaminophen** can be combined with NSAIDs

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

- Consider using topical NSAIDs if these are available, e.g. **diclofenac topical cream (1.5-5%) applied to affected area QID**; do not use on open wounds
  - The peak analgesic effect occurs within 1-2 hours
  - Use with caution, particularly in patients with increased risk of GI or renal toxicities as serious side effects can include GI bleeding, renal toxicity, and congestive heart failure
- If GI bleeding occurs, NSAIDs should be discontinued
- The risk of GI toxicity can be reduced by the addition of a protective agent such as an H2-antagonist (e.g. famotidine) or a proton-pump inhibitor (e.g. omeprazole)
- There is no evidence to show that any particular NSAID is more effective than another one
- Note that selective COX-2 inhibitors (celecoxib, meloxicam) do not affect platelet function, and therefore do not increase bleeding risk

Examples of common non-selective NSAIDs include:

- **Ibuprofen 200-400 mg PO q6-8h**
- **Diclofenac 50 mg PO/SUBQ TID**
- **Naproxen 250-500 mg PO/PR BID**
- **Ketorolac 10 mg PO QID or 10-30 mg SUBQ TID**

FOR MODERATE PAIN

- **Morphine (PO, 5-10 mg q4h)** should strongly be considered as the first-line treatment for moderate pain, since recent evidence suggests that strong opioids (such as morphine) are a more effective

treatment for moderate cancer pain than weak opioids

- Weak opioids (e.g. codeine and tramadol) can be used for moderate cancer pain, when morphine is not available
  - e.g. **codeine 30 mg q4h PO or tramadol 50-100 mg PO QID**
  - Codeine is often combined with other agents such as acetaminophen/paracetamol and thus maximum doses may be limited by the amount of acetaminophen/paracetamol
  - Codeine is a prodrug which requires conversion to morphine in the liver in order to provide analgesia
    - The rate of this conversion varies widely between individuals, which leads to significant variation in the analgesic response
- Combine opioids with NSAIDs and adjuvants to achieve the best possible pain control

FOR SEVERE PAIN

- Morphine or another strong opioid should always be the first-line treatment, provided that opioids are available
- The initial starting dose will depend on the patient's previous exposure to opioids:
- **Morphine 5-10 mg PO q4h regularly (or 2-5 mg SUBQ/IV)** and a breakthrough or rescue dose every 4 hours, as required (see Appendix 1), is suitable for an opioid-naive patient or patients who have already been taking a weak opioid
- Titrate the regular dose to achieve good control (more than 3 breakthrough doses per day often means that the baseline morphine dose is too low)
- Calculate the new dose of morphine by adding the amount of breakthrough morphine being used in 24 hours and the regular total daily dose. The total is then divided by 6 to determine the new q4h dose
- If pain is poorly controlled, increasing the opioid dose by 25-50% is appropriate. Generally, this is done every 2-3 days for outpatients,

and 1-2 days for inpatients

- There is no maximum dose for morphine and other strong opioids: the correct dose is the dose that provides the individual with adequate analgesia in the absence of unwanted side effects
- Alternative routes for morphine include PO, SUBQ, buccal, IV, and via gastrostomy tube – the enteral route is generally preferred, provided that the patient is able to swallow. If the patient is unable to swallow, then SUBQ is the preferred route
- The PO: SUBQ morphine ratio is 2:1
- The PO: IV morphine ratio is 2-3:1
  - e.g. 10 mg oral morphine = 5 mg SUBQ morphine
- Be aware, educate patients/families about how to prevent and treat the common side effects of morphine:
  - Constipation: always prescribe laxatives/stool softeners when starting someone on opioids, see Constipation section
  - Nausea is generally temporary and associated with initiating opioids or dose change, ensure that antiemetics are prescribed especially when starting someone on opioids
  - Excessive sedation or drowsiness after starting opioids is generally temporary, lasting 1-2 days
    - Patients may sleep more after starting morphine if their pain was previously poorly controlled and prevented them from sleeping well, and families should be counselled about this when opioids are being initiated

NEUROPATHIC PAIN

- Patients with signs and symptoms of neuropathic pain should be managed following the three-step ladder of analgesic management as described above
- Opioids are first-line medications for treating neuropathic pain and should be used in combination with adjuvants (see below), such as a tricyclic antidepressant or anticonvulsants
- Other adjuvants such as NMDA receptor antagonists (e.g. ketamine) and

antiarrhythmic agents (e.g. lidocaine) are not routinely used as first-line medications, but are sometimes tried by clinicians with experience/skill in the use of these agents

ADJUVANTS

- Adjuvants are medications or measures that provide pain relief when administered in combination with opioids
- They are often used for pain from bone metastases and neuropathic pain
- **Bisphosphonates** can be used to prevent and treat bone pain
  - NSAIDs, corticosteroids, and radiotherapy are additional therapies which can be considered for bone pain
- For neuropathic pain, consider a trial of **tricyclic antidepressants**, starting with a low dose and increasing every 3-5 days if tolerated (e.g. **nortriptyline, amitriptyline**)
- Serotonin and norepinephrine reuptake inhibitors (SNRIs) can also be used for neuropathic pain, but evidence for their efficacy is more limited. Common examples are **duloxetine** or **venlafaxine**
- Gabapentinoids (**gabapentin** or **pregabalin**) are also useful adjuvants

- In children, a **gabapentin is often the first-line adjuvant; increase every 3-5 days, up to a maximum of 1200 mg TID or 15 mg/kg/dose**
- Morphine is the main analgesic for children with severe life-threatening or life-limiting conditions who have moderate or severe pain
- Weak opioids are not recommended due to concerns about safety, because of the wide variations in codeine and tramadol metabolism between children, and the immaturity of their liver metabolism for these medications

FOR MILD PAIN

- **Paracetamol/acetaminophen/ 10-15 mg/kg PO/IV q4-6h (Maximum: 75 mg/kg/day or 4000 mg/day)**
  OR
  Ibuprofen: <6 months: 5 mg/kg/dose PO q8h >6 MONTHS: 5-10 mg/kg/dose PO q6-8h (Maximum: 40 mg/kg/day or 2400 mg/day)
  OR
  Naproxen: 5-10 mg/kg/dose PO q12h (Maximum: 1000 mg/day)
  OR
  Ketorolac
  – PO: 1 mg/kg/dose PO q4-6h PRN (Maximum: 40 mg/day)
  – IV: 0.2-0.5 mg/kg/dose IV q6-8h PRN (Maximum: 120 mg/day)

  Usual duration of therapy is 48 to 72 hours and should not exceed 5 days of total treatment (oral and injectable) in order to minimize the risk of adverse cardiovascular and gastrointestinal side effects
  OR
- **Diclofenac**
  6 months to 12 years: 1-1.5 mg/kg/dose PO BID or 0.7-1 mg/kg/dose PO TID (Maximum: 50 mg/dose); 0.5-1 mg/kg/dose PR q8-12h PRN, (Maximum: 100 mg/day)

FOR MODERATE TO SEVERE PAIN

- **Morphine**
  Starting doses for opioid-naive patients:
  Less than 6 months of age:
  – PO/SL: 0.05-0.1 mg/kg/dose q4h
  – IV/SUBQ: 0.025 to 0.05 mg/kg/dose q2-4h

- **Greater than 6 months of age:**
  - **PO/SL: 0.2-0.3 mg/kg/dose q4h, (Maximum starting dose: 10 mg)**
  - **IV/SUBQ: 0.05-0.1 mg/kg/dose q2-4h, (Maximum starting dose: 5 mg)**

- **Continuous IV/SUBQ Infusion:**
  - **Start at 20-40 mcg/kg/hr and increase incrementally by 10 mcg/kg/hr**

- Codeine: DO NOT USE in children

- **Tramadol DO NOT USE in children, unless no other opioids are available**

  Risk due to high variation in liver metabolism and risk of serious harm

  1-2 mg/kg/dose PO/IV q4-6h (Maximum: 100 mg/dose, 400 mg/day

ADJUVANTS

- **Amitriptyline 0.1-0.5 mg/kg/dose PO nightly, (Maximum starting dose: 10 mg). May increase by 0.1-0.2 mg/kg/dose every 5-7 days to a max of 2 mg/kg/day (Maximum: 150 mg/day)**

  Monitor closely for anticholinergic side effects (e.g. constipation, dry mouth, drowsiness, blurry vision). Important to note potential drug-drug interactions with other drugs metabolized by CYP2D6

- **Gabapentin**
  Starting dose of 5 mg/kg/dose PO daily x 3 days, followed by 5 mg/kg/dose PO BID x 3 days, followed by 5 mg/kg/dose PO TID; (Maximum starting dose: 300 mg); usual dosing range of 15-60 mg/kg/day (Maximum dose: 3600 mg/day)

Management of Respiratory Depression Related to Opioids

- Inappropriate high doses of opioids may lead to respiratory depression (low respiratory rate and shallow respirations), apnoea, and respiratory arrest
- Opioids do not cause respiratory distress
- If respiratory depression occurs following a dose of opioid medication, naloxone should be administered
- Stepwise titration should be used to avoid acute and sudden physical pain and opioid withdrawal
- **Naloxone 40 mcg/dose IV/IM/SUBQ, given every 2-3 mins until respiratory depression is reversed**
- Further doses of naloxone are likely to be required every 30-60 minutes until the effect of the opioid has worn off (e.g. 4 hours for oral morphine)
- Naloxone will also cause opioid-related analgesia to be reversed and can precipitate a pain crisis

PITFALLS/CONCERNS

- Avoid using pethidine/meperidine (an opioid) in palliative care, since ongoing use leads to accumulation of its neurotoxic metabolite (normeperidine) which causes delirium and seizures
- Never ever use a slow-release opioid for breakthrough pain (use regular short-acting opioids instead)
- Serious side effects can occur with NSAIDs – they should be used with caution

- Children less than 6 months are more sensitive to opioid-induced respiratory depression and therefore need lower initial doses
- Codeine is NOT recommended for children due to the risk of rapid metabolism, which can lead to overdose and death
- Urinary retention and pruritus (as a side effect of opioids) are more commonly seen in children compared to adults

PALLIATIVE TIPS

- Treat pain promptly and aggressively
- The relief of psychological, social, and spiritual distress is also important; attempting to relieve pain without addressing the patient's non-physical concerns is likely to lead to frustration and failure
- Constant pain requires regular (around the clock) analgesia to relieve and prevent pain
- Make sure there is a breakthrough or rescue dose (BTD) in addition to the regular dose of morphine or other opioid
- Optimise pain control by increasing the dose of opioids in a gradual step-wise manner, until the pain has improved
- The PO morphine to SUBQ/IV morphine ratio is 2:1, e.g. 10 mg oral = 5 mg SUBQ/IV
- Remember to use adjuvants in the treatment of pain

- Children have less distress when they can understand what is happening and are involved in their symptom management
- Play, music, and games can be very helpful in association with the pharmacological methods as described above

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Pleural Effusion

KEY POINTS

- 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 dyspnoea, dull aching chest pain, or dry cough due to fluid accumulation
- Thoracentesis (removal of the fluid) can be helpful in relieving dyspnoea in some patients
- Pleurodesis with talc or bleomycin, done after thoracentesis and drainage, may be used to prevent re-accumulation of the fluid
- A pleural effusion may be the first presenting sign of cancer, or suggestive of recurrent or advanced disease

- Children may fear invasive procedures such as thoracocentesis. It is important to explain what will happen and gain the child's consent depending on his or her ability to understand

ASSESSMENT

see comment on page 10

- A moderate to large pleural effusion can most often be diagnosed by clinical examination 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

- Common non-malignant processes include:
  - Congestive heart failure
  - Pneumonia
  - Pulmonary embolism
  - Pancreatic disease
  - Interstitial lung disease
  - Ascites
  - Hypoalbuminaemia
- Investigations to consider may include:
  - Chest x-ray: to assess the extent of the effusion and for evidence of other diagnosis (e.g. pneumonia). Generally, if there is more than 200-300 mL of fluid this is visible on a chest x-ray
  - Chest ultrasound (including point-of-care ultrasound): smaller amounts of fluid can sometimes be detected using ultrasound
  - CT chest: can detect small amounts of fluid
  - Analysis 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 occasions can be transudative

MANAGEMENT

- The management of dyspnoea and cough are covered in the Dyspnoea and Cough sections and should be followed if these symptoms are present
- A small effusion that is not causing the patient any distress generally should NOT be drained
- Pleural effusions may spontaneously resolve with effective treatment of the underlying disease, such as congestive heart failure
- Consider drainage of the pleural fluid (thoracocentesis) if the patient is highly symptomatic

Consider only if patient is well enough to benefit

- The risks and benefits of a thoracocentesis should be explained to the patient before proceeding. These would include hemothorax, pneumothorax, post-procedure pain, and infection

Thoracocentesis procedure

(adapted from the *Oxford Handbook of Palliative Care*):

- It is recommended that all thoracocentesis should be done with ultrasound guidance
- The patient should be sitting, leaning forwards 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 anesthetic (e.g. **lidocaine**) wait for the area to be anaesthetized then advance the needle until pleural fluid is obtained
- Introduce a large bore 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 pursed 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 is complete, or the patient starts to cough, or light-headedness or chest discomfort occurs
- Remove the cannula, while having the patient take a breath, and immediately seal with an appropriate dressing
- Sometimes a chest tube is left in place while the fluid continues to drain
  - Tunnelled indwelling pleural catheters allow fluid to be drained serially and have been shown to be effective for management of dyspnoea and palliative care patients
- Pleurodesis is sometimes carried out following thoracocentesis and drainage

- It occurs by introducing inflammation of the pleura by the introduction of a sclerosing agent (such as talc or bleomycin) administered by a chest tube or indwelling catheter into the chest cavity
- 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 to proceed with pleurodesis

Generally, pleurodesis in indicated for individuals who are expected to live for at least several months. Consider if the patient is well enough to benefit

- During thoracocentesis monitor vital signs. Remove the quantity of fluid that gives optimum symptomatic relief. Not more than 10% of body fluid by volume per 24 hours

PITFALLS/CONCERNS

In patients at the end of life phase (last hours or days), it is generally inappropriate to drain a pleural effusion, instead, provide symptom relief using pharmacological and non-pharmacological techniques (see Dyspnoea section)

PALLIATIVE TIPS

- The decision whether to repeatedly perform thoracocentesis or place a tunnelled catheter ***must be carefully weighed*** against the patient's wishes, available resources, the patient's ability to tolerate the procedure, the risks involved with repeated thoracocentesis, the knowledge that the fluid will likely re-accumulate and the ability to symptomatically control dyspnoea 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 a few days

Serial thoracocentesis may result in loculated fluid and worsening of symptoms

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Pruritus

KEY POINTS

- Pruritus can be described as an unpleasant skin sensation which produces the desire to scratch
- Pruritus is relatively uncommon in advanced disease, but can be very unpleasant and difficult to treat
- A combination of systemic and topical treatments often provides the best relief
- Non-pharmacologic treatments can be very helpful
- **Mild to moderate pruritis** which occurs occasionally is normal, but **severe pruritus** is usually associated with advanced illness, most commonly uraemia (chronic renal failure), cholestasis, opioids, and haematologic disorders
- Pruritus may also occur in solid tumours via biliary obstruction (i.e. pancreatic cancer)
- Dry skin is also common is patients with severe advanced disease and further contributes to pruritis
- Opioid-induced itch is due to the release of histamines and may require switching opioids

- Opioids can cause generalized itching and is more common in children than adults

ASSESSMENT

see comment on page 10

- History should include the times at which the itching occurs (whether continuous and whether at night or day), its quality (burning, itching, etc), location, and relevant medication history
- Inquire about whether other members of the household are also itching, which may suggest scabies

- Schistosomiasis may cause intermittent itchy wheals or urticaria
- Examination should include a review of the dryness of the skin, possible presence of scabies (itchy bumps on the genitals, finger webs, and other areas), and possible presence of jaundice
- Review medications which may induce photosensitivity and exacerbate itching, including NSAIDs, diuretics, antineoplastics, and ciprofloxacin

MANAGEMENT

GENERAL MEASURES

- Pruritus is often caused by dry skin, so a good first measure is a simple moisturizer cream
- Keep the patient cool and avoid extra blankets or warm clothing, encourage the patient to wear loose cotton clothing
- Showers or baths should be cool and avoid using strong soap, follow with gentle drying and application of moisturizing cream
- Adding baking soda (sodium bicarbonate) to bathwater can help form a protective layer and maintain skin hydration
- Keep fingernails short to avoid skin trauma from scratching, wear cotton gloves if scratching occurs while sleeping
- Avoid alcohol and spicy foods which cause the skin to become warmer and dried out, leading to more itching
- Apply cool packs or wet water dressings (e.g. clothing soaked in water), which provide temporary relief and speed up healing

TOPICAL AGENTS

- Petroleum jelly (Vaseline) is considered the most effective lubricant for dry skin
- **Menthol (0.5-2%) and/or camphor (0.5-3%)** compounded into a bland emollient base such as Vaseline, can be used several times a day as needed. These agents produce a mild anaesthetic action in the skin, but use with caution as cutaneous reaction can occur
- **Creams containing pramoxine and calamine** are also effective

against itching

- **Mild to moderate potency topical corticosteroids** can reduce inflammation
- **Ketamine (0.5-5%) with amitriptyline (1-2%) in a compounded cream**
- **Lidocaine cream (2.5%)** will anaesthetize sensory nerve endings; however, potential toxicity from systemic absorption can occur if used over large areas
- Ultraviolet B light therapy, 3 times per week can be useful for cholestasis, uraemia, and malignant skin infiltrations

SYSTEMIC AGENTS

- Can be used if other treatments tailored to the specific cause are ineffective
  - **Mirtazepine 7.5-15 mg PO nightly, increase by 15 mg after 1 week, up to a maximum of 30 mg/day**
  - May cause drowsiness, but this can be beneficial for patients with itching
  - May cause QTc prolongation. Consider risk versus benefits of this option
  - Do not discontinue abruptly as discontinuation symptoms can occur
  - May cause QTc prolongation. Consider risk vs. benefits of this option
- **Gabapentin 100 mg PO TID, titrate every 3-7 days, maximum dose of 3600 mg/day**
  - Works by blocking central nociceptive signals to brain

CAUSE SPECIFIC THERAPY

Cholestasis

- Use general measures above
- Antihistamines (H1 and H2 receptor antagonists) are generally ineffective. They can be reserved for use in post-operative pruritis (e.g. if spinal anaesthesia was used)

- Consider surgical referral for placement of biliary stent (if available and depending on patient's general condition)

The burden of investigation and treatment should always be weighed against the prognosis, the likely benefit of treatment, and the patient's wishes

- **Cholestyramine 4 g PO 1-6 times/day to a maximum of 36 g/day**
  - Note that cholestyramine will be ineffective in complete biliary obstruction because it works by binding bile salts to promote their excretion
- Additional medications to consider:
  - **Naltrexone 6-12.5 mg SUBQ daily, increase by 12-25 mg BID, maximum of 300 mg/day**
  - **Sertraline 25 PO once daily, adjust by 25 mg every 4-5 days, maximum of 100 mg/day**
  - **Rifampicin 75 mg once daily, titrate by doubling the dose every week, maximum 300 mg,** has many drug interactions and can contribute to hepatic dysfunction

Uraemia

- Use general measures as above
- Antihistamines (H1 and H2 receptor antagonists) are generally ineffective
- **Capcaisin 0.025% or 0.075% cream applied 3-5 times daily** is useful where there is localized pruritus. Do not apply to large areas of the body
- Correct hyperphosphataemia
- **Sertraline 25 mg PO once daily, increase by 25 mg every 4-5 days, maximum of 100 mg/day or paroxetine starting dose of 20 mg OD, increase by 10 mg weekly to max of 50 mg.** Doses of 20 mg have been reported to be effective for this indication
- **Paroxitine 7.5-15 mg PO qHS**
- **Gabapentin 100 mg PO once daily**, increase dose with caution due

to impairment in renal function

Hodgkin's Lymphoma

- Use general measures as above
- Antihistamines (H1 and H2 receptor antagonists) are generally ineffective
- Palliative chemotherapy to reduce symptoms

Consider if the patient is well enough to benefit

- Corticosteroids, e.g. **dexamethasone 4-8 mg PO daily or prednisolone 10-20 mg PO TID**
- If ineffective, substitute: **cimetidine 400 mg PO BID or famotidine 20 mg PO BID**

Opioid-Induced

- Use general measures as above
- Commonly transitory, lasting only a few days
- Opioid rotation (if possible) or addition of an opioid antagonist at a low dose (e.g. **naloxone**).

- **Naloxone 0.25-2 mcg/kg/hr IV as continuous infusion** is particularly effective in children with sickle cell disease who are often very itchy due to the high doses of opioids required for severe pain
- Doses up to 3 mcg/kg/hr can be used, but the risk of loss of pain control increases with doses greater than 3 mcg/kg/hr and may require increased opioid doses
- Ondansetron can also be considered
- **Ondansetron 0.1-0.15 mg/kg/dose PO/IV q8-12h PRN (Maximum: 8 mg/dose, maximum 3 doses in 24-hour period)**

- Potential side effects of antihistamines may be agitation or confusion

PITFALLS/CONCERNS

- Itching associated with cholestasis often starts on palms and soles and the severity is unrelated to the level of bile acids in the skin
- H1 receptor blockers are ONLY useful in histamine-based itch, such as a drug reaction or urticaria, and rarely help in itching associated with advanced disease in palliative care
- Ondansetron is helpful ONLY when opioids cause 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

KEY POINTS

- During the last few hours and days of life, many individuals will not be able to swallow or clear upper airway secretions, these secretions often accumulate and lead to gurgling or rattling sounds. This is often referred to as "congestion"
- Generally, this occurs when the individual is only minimally conscious or unconscious and does not cause them any distress
- The presence of respiratory secretions is a strong predictor of death (75% of individuals die within 48 hours from the onset of this symptom)
- Repositioning the patient (into side-lying) is often helpful and all that is necessary
- Anticholinergic medications (e.g. atropine eye drops 1% solution applied topically in the mouth) can be helpful in many cases to reduce the secretions and noise

- Children (and adults) are generally unaware of this symptom, but it can be very distressing for family members
- Ongoing support and education of the family around this symptom is very important to minimize the distress of the family witnessing this in their dying child

ASSESSMENT

see comment on page 10

- A clinical assessment is generally 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 soon (meaning hours to several days)

MANAGEMENT

- Positioning the patient on their side with their upper body elevated will allow secretions to passively drain out of the mouth
- Avoid mechanical suctioning of secretions since this is not generally helpful and may be distressing to the patient
  - Consider suctioning only if thick mucus or blood is present in the mouth and can easily be removed with a soft catheter
- Much of the management focuses on teaching and supporting the family who may find this symptom difficult to observe
- Ensure good mouth care
- Reduce or stop IV fluids, which generally worsen secretions
- Administering anticholinergic medications can sometimes be helpful for upper airway secretions (if available):
  - **Glycopyrronium – 0.2-0.4 mg SUBQ q4-6h PRN**
  - **Hyoscine BUTYLbromide – 20 mg SUBQ, then 20 mg q4-6h PRN**
  - **Hyoscine HYDRObromide/Scopolamine – 0.4-0.6 mg SUBQ q4-6h PRN; or transdermal patch, replace patch every 72 hours**
    - Note: Hyoscine HYDRObromide is quite sedating; may increase risk of delirium in end-stage renal failure patients
  - **Atropine 1% eye drops – 1-4 drops (each drop contains approximately 0.5 mg atropine) under the tongue q2-4h PRN**

- **Glycopyrronium 40-100 mcg/kg/dose PO q6-8h (Maximum: 3000 mcg/dose)**
  - **IV/SUBQ: 4-10 mcg/kg/dose q 3-4h (Maximum: 200 mcg/dose)**

- **Hyoscine BUTYLbromide**
  - **<5 yrs: 0.3 mg/kg/dose IV q6-8h**
  - **5-<12 yrs: 5-10 mg IV q6-8h**
  - **12 years and above: 10-20 mg IV q6-8h**

- **Hyoscine HYDRObromide (Scopolamine)**
- **IV/IM/SUBQ/PO: 5-6 mcg/kg/dose q6-8h (Maximum: 300 mcg/dose). Parenteral formulation of hyoscine HYDRObromide can be given orally**
- **Transdermal patch (1.5 mg/patch): 12-17 kg: ½ patch q72h; >17 kg: 1 patch q72h. Ref: care beyond cure**
  - Note: do not cut the patch, but instead only remove only the portion of the backing required for the dose OR apply occlusive dressing (i.e. Tegaderm) to a portion of the patch
- **Atropine 1% eye drops – dosed in the same way as for adults**

PITFALLS/CONCERNS

- Anticholinergic medications should be used cautiously in patients who are still responsive as they can cause agitation. They are generally used in patients close to death
- Glycopyrronium and hyoscine BUTYLbromide do not cross the blood-brain barrier and may therefore cause less sedation than hyoscine HYDRObromide and atropine
- Treatment with these agents is not always successful in reducing the secretions so it is important to counsel the family about what to expect

- Parenteral glycopyrrolate can be given PO (at same dose) and is usually well tolerated by children

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
- Medications may be effective in upper airway secretions, but the

same medications generally do not have any effect on secretions deeper in the lungs, such as when a patient has pulmonary oedema or pneumonia

- Hydration with IV fluids or artificial feeding (e.g. NG or gastrostomy tube) will increase the severity of this symptom
- It is recommended to reduce or stop artificial hydration in the last few days of life or when the patient develops respiratory secretions, since this improves comfort and reduces symptoms

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Seizures

KEY POINTS

- Seizures occur in up to 10% of patients receiving palliative care
- Most seizures are brief, self-limited and rarely harmful, but they can be extremely frightening to family members
- Pethidine/meperidine will cause seizures if used on an ongoing basis due to an accumulation of neurotoxic metabolites. Pethidine/meperidine should therefore NOT be used in palliative care patients

- Seizures are relatively common at the end of life in children, as children are more likely to have life-limiting neurological conditions

- Opioid-induced myoclonus is often misinterpreted as seizure activity by caregivers and clinicians, myoclonus tends to respond to conservative treatment, including correction of dehydration and reduction and/or rotation of opioid

ASSESSMENT

see comment on page 10

Treatment is usually symptomatic and a full seizure work up is, in most cases, not necessary in the context of a serious illness, which is known to cause seizures

Causes of seizures include:

- Brain tumour or metastasis
- Head trauma
- Strokes – ischemic or haemorrhagic
- Drug toxicity (e.g. pethidine/meperidine)
- Metabolic or electrolyte abnormalities

- Hypoglycaemia
- Hyponatraemia
- Hypercalcaemia

- Infections of the central nervous system
- Cancers most likely to metastasize to the brain are lung, breast, and malignant melanoma

Common causes in children:

- Epilepsy
- Degenerative neurological conditions
  - Metabolic and genetic disorders
- Hypoxic ischemic encephalopathy
- In children with a longer prognosis, a review by a neurologist to optimize antiepileptic treatment may be appropriate
- For children who have a history of epilepsy, if the child can no longer swallow medications in the terminal phase of their illness, they should be given antiepileptics by an alternative route, such as SUBQ midazolam

MANAGEMENT

- Clear airway and ***provide supplemental oxygen (if available and the patient is not actively dying***)
- Benzodiazepines are the first-line treatment. If the seizure does not resolve within 5 minutes, consider:
  - **Lorazepam 4 mg IV over 2 minutes, OR**
  - **Midazolam 10 mg buccal/SUBQ/IM or IV over 2 minutes**
  - **Diazepam 10 mg PR or IV**
- Can repeat ONCE after 10-20 minutes, if the seizure persists
- If benzodiazepine dose is ineffective, give phenobarbital: 10-15 mg/kg (up to 1000 mg) STAT
  - IV (dilute with normal saline to administer 100 mg/min)

- IM (undiluted), with larger doses (>1.5mL volume of fluid) split between multiple injection sites)

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
- **Levetiracetam 250 mg PO BID; titrate to achieve seizure control, maximum of 3000 mg/day. Note: can also be administered SUBQ, 1 mg PO = 1 mg SUBQ**
- **Carbamazepine 50-100 mg PO BID; if necessary, increase by 50-100 mg increments every 1-2 weeks. Usual maintenance dose = 800-1200 mg/day (divided BID)**
  - **Note: important to titrate slowly, to avoid Stevens-Johnson Syndrome risk, use modified-release tablets for doses larger than 100 mg**
- **Valproate 150-200 mg PO BID (use modified-release formulation); titrate by 150-200 mg BID every 3 days to 2500 mg/day**
  - **Note: most patients require no more than 1500 mg/day total dose**
- Other common antiepileptics include levetiracetam, lamotrigine, and topiramate
- Corticosteroids are helpful in the prevention and management of seizures which are secondary to brain metastasis, by decreasing the oedema surrounding a tumour mass
- Radiotherapy can be helpful in preventing seizures in patients with metastatic brain disease (if available and appropriate for the patient's general condition)
- Opioids very rarely cause seizures, except pethidine/meperidine, switching to another opioid is recommended if using pethidine/meperidine

- As in adults, benzodiazepines remain first-line treatment in status epilepticus. Consider lorazepam or midazolam first. Evidence suggests diazepam is less effective
  - If IV access is not immediately available, consider non-IV routes of administration, e.g. buccal, intranasal, rectal
  - If still seizing ≥5 minutes after a single dose, may repeat once
  - If seizures persist after ≥2 first-line treatments, consider available second-line treatments, e.g.phenytoin, phenobarbital, levetiracetam, or valproic acid

Acute Treatment

- **Lorazepam**
  - **0.1 mg/kg/dose IV, IO, buccal, SUBQ, or PR (Maximum: 4 mg/dose)**
  - **Note: Sublingual tablet(s) are given buccally between the gum and cheek. Massage the outside of the cheek gently to help dissolve the tablet**
- **Midazolam**
  - **0.1 mg/kg/dose IV, IO, or SUBQ (Maximum: 5 mg/dose) OR**
  - **0.5 mg/kg/dose buccal (Maximum: 10 mg/dose) OR**
  - **0.2 mg/kg intranasally (Maximum: 5 mg/nostril)**
  - **Note: Midazolam injectable solution can be given buccally between the gum and the cheek. Use a syringe to draw up the appropriate dose from the vial/ampoule**
- **Diazepam**
  - **0.3 mg/kg/dose IV, IO, or SUBQ (Maximum: 5 mg/dose in <5 years old; 10 mg/dose in ≥5 years old) OR**
  - **0.5 mg/kg/dose PR (Maximum: 20 mg/dose) OR**

- **Phenobarbital**
  - **20 mg/kg/dose IV or IO (Maximum: 1000 mg/dose)**
  - **Mixed in NS or D5W, infused over 20 minutes**
  - **If seizures persist after 10 minutes, may give additional 5-10 mg/kg/dose**

- **Phenytoin**
  - **20 mg/kg/dose IV or IO (Maximum: 1500 mg/dose)**
  - **Mixed in NS only. Insoluble precipitates form if mixed in D5W**
  - **Infused over 20 minutes**
  - **If seizures persist after 10 minutes, may give additional 5-10 mg/kg/dose**

Prophylactic/Maintenance Treatment

- **Phenobarbital**
  - **Initial: <12 years old: 2.5 mg/kg/dose PO BID or 5 mg/kg/dose PO daily**
  - **>12 years old: 1.5 mg/kg/dose PO q12h or 3 mg/kg/dose PO daily**
  - **Usual range: 3-8 mg/kg/day according to serum drug monitoring and clinical response**

- **Levetiracetam**
  - **Initial: 5-10 mg/kg/dose PO BID**
  - **Usual range: 15-30 mg/kg/dose PO BID**
  - **Maximum: 50 mg/kg/dose BID or 1500 mg/dose PO BID (whichever is less)**

- **Valproate**
  - **INITIAL: 2.5-5 mg/kg/dose PO BID**
  - **Increase by 2.5-5 mg/kg/dose PO BID at weekly intervals**
  - **MAINTENANCE: 20-30 mg/kg/dose PO BID or 1500 mg/dose BID (whichever is less)**
  - **Parents should be trained in the use of SL lorazepam or rectal diazepam as abortive medication if a child is likely to have a seizure at home**

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, hyperglycaemia, and gastrointestinal bleeding among others

- Parents should be trained in the use of IN midazolam (or another benzodiazepine) if there is a likelihood of the child having prolonged seizures at home

PALLIATIVE TIPS

- Avoid prophylactic anticonvulsant therapy for patients with brain tumours (primary or metastases) if the patient has never had any seizures, due to lack of benefit and risk of medication burden
- 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 in status epilepticus (see Acute Management of Seizures)

➔ **Rectal administration of medications to treat status epilepticus can be done using a syringe with a small feeding tube cut at 5 cm to deliver medication up to 4 to 5 cms beyond the anal margin for an older child and less for an infant**

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Spinal Cord Compression (SCC)

KEY POINTS

- Acute SCC is a palliative care emergency
- Pain is the presenting symptom for more than 90% of patients; the pain is either localized (at the site of compression) or radicular (from spinal root compression)
- SCC is common in lung, prostate, kidney, thyroid, breast cancer and multiple myeloma
- Generally, if the patient has lost the ability to walk before treatment, they will not regain ambulatory function (<10% chance, even with prompt treatment)
- Many patients can live a relatively long time after experiencing SCC, with the added burden of paralysis

ASSESSMENT

see comment on page 10

- A high level of suspicion is required
- Increasing back pain is often the earliest sign, and pain is often worse at night, i.e. the patient wakes with back pain
- Sensory, motor, and autonomic symptoms may also occur
- Autonomic symptoms include loss of bowel and bladder function, sexual dysfunction

- Pain may be difficult to evaluate in paediatric patients who cannot verbalize their pain, so other markers can be used, including regression in motor milestones or refusal to ambulate

- It is important to ask about bowel and bladder function, as patients may not volunteer this information, and urinary retention and constipation may also be early signs

- Loss of bowel function does not always present as incontinence; constipation may also be present

MANAGEMENT

- Acute SCC should be considered an emergency and treated without delay
- The extent of the diagnostic work up should be determined by the overall condition of the patient and the duration of symptoms prior to diagnosis
- Imaging: MRI spine is the recommended imaging modality, however, in many cases the diagnosis is made clinically
  - An MRI is recommended when radiation is available, and the patient is expected to be well enough to benefit
  - If radiation is unavailable, MRI is not a priority investigation
  - Avoid MRI if the patient has not been able to walk for more than 48 hours, since the only treatment in such a case will be dexamethasone
- If SCC is suspected, immediately administer high-dose **dexamethasone (16 mg PO)**, **then continue with 16 mg PO once daily** (there is no evidence of benefit in splitting the dose) **until surgery is completed or radiotherapy has started** (if appropriate and available)
  - Continue **dexamethasone 8 mg PO daily until radiation is completed**; then taper over 1-2 weeks
- Dexamethasone may assist initially in decreasing spinal cord oedema to improve neurological features while definitive therapeutic options, such as surgery, radiation and/or chemotherapy, are being considered
- Consider confirmatory imaging and emergency referral for radiation therapy or sometimes for surgical decompression if available

Consider if the patient is well enough to benefit from investigation or treatment

- Some patients may require a maintenance dose of dexamethasone to preserve neurological function

- **Paediatric dosing: Dexamethasone**
- **Loading dose: 1-2 mg/kg PO/IV x 1 dose , followed by 0.25 mg/kg/dose q6h or 0.5mg q12h**
- **It is important to note that dexamethasone can induce tumour lysis, so precautions should be taken/considered in patients at risk of developing tumour lysis syndrome, especially those with leukaemia and lymphoma**

- GI tract ulcer prophylaxis with a **proton pump inhibitor (e.g. omeprazole or pantoprazole)** is recommended when prescribing high-dose dexamethasone
- Consider the use of prophylactic anticoagulation in cases of immobility
- Treat severe pain with opioids to achieve analgesia

PITFALLS/CONCERNS

- A delay in diagnosis or treatment may result in preventable paralysis and/or bowel and bladder dysfunction
- The degree of neurologic function at diagnosis and at the start of treatment is the most significant factor in determining the recovery of function
- Rapid onset (less than 48 hours) and progression of symptoms are poor prognostic factors for recovery of spinal cord function (e.g. mobility)
- If the patient has been paralyzed for more than 48 hours, the chance of neurological recovery is very poor

PALLIATIVE TIPS

- Back pain exacerbated by the Valsalva manoeuvre should increase suspicion of developing cord compression

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Superior Vena Cava Syndrome

KEY POINTS

- A syndrome of dyspnoea, headache, swelling of the face, neck, and upper limbs should be an alert to this possible diagnosis
- Due to compression or obstruction of the superior vena cava
- Can sometimes be life-threatening, but usually occurs with a gradual increase in signs and symptoms
- Common symptoms include dyspnoea, facial oedema, headache, cough, chest pain, and visual disturbances
- Symptoms are often affected by position (e.g. symptoms are slightly better when sitting up)

ASSESSMENT

see comment on page 10

- Physical examination for facial plethora or cyanosis, proximal vein dilation, oedema of the face, neck, upper chest, and arms
- Definitive diagnosis requires a CT scan
- Chest x-ray and point-of-care ultrasound may assist in clinical decision-making when CT is not available
- Diagnosis can be made clinically if imaging is not available or appropriate for the patient's general condition

MANAGEMENT

- Elevate the head of the bed
- A single dose of steroids typically stabilizes the patient prior to any diagnostic procedure
- **Dexamethasone** should be used in the short term (24-48 hours) and can be sufficient therapy for some patients **(16 mg PO/IV daily)**

- Paediatric dosing:
  Dexamethasone 0.6 mg/kg/dose IV/PO daily

- Diuretics can help reduce preload (e.g. **furosemide 12-80 mg PO/IV/SUBQ daily-BID)**

- Paediatric dosing: **Furosemide 0.5-2 mg/kg/dose PO/IV/SUBQ q6-24h, dose may be increased by 1-2 mg/kg/dose to achieve desired response (Maximum: 6 mg/kg/dose, 80 mg/dose)**

  - Monitor for electrolyte abnormalities, including hyponatraemia and hypokalaemia, as well as metabolic alkalosis
  - Administer at a maximum of 0.5 mg/kg/min to reduce the risk of ototoxicity
- Radiotherapy, chemotherapy, and SVC stenting are frequently effective at reducing tumour bulk and external compression of the SVC

Consider if the patient is well enough to benefit

PALLIATIVE TIPS

- May also be caused by thrombus around a subclavian arterial catheter

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Wound Care

KEY POINTS

- Malignant ulcers or wounds can be caused by direct invasion of the skin by a primary tumour or by metastasis to the skin
- Malignant wounds occur in 5-10% of patients with advanced disease, most commonly in breast cancer
- 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 are relatively rare in children; they occur primarily with solid tumours, particularly when treatment with chemotherapy and/or radiation has been limited

ASSESSMENT

see comment on page 10

- 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. Wound location, size, and condition of the surrounding skin should also be assessed
- Wound cultures can sometimes be helpful in determining 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 PO or IV antibiotics may be considered
- The potential for serious complications, such as haemorrhage, should be evaluated and a plan developed for management

MANAGEMENT

Cleaning the Wound

- Gentle irrigation of the wound with saline or cooled boiled water is helpful and can be done as often as needed, generally daily or every 2 days
- DO NOT USE antiseptic or antibacterial washes on open wounds, as these harm newly developing skin cells which are important for wound healing
- Local debridement can be done by very gently rubbing the necrotic areas with gauze saturated with saline. This must be done carefully and gently to avoid bleeding or pain
- Proper cleaning reduces odour by removing necrotic tissue and decreasing bacterial counts

Managing Exudate or Discharge

- Inflammation and oedema from malignant wounds can cause significant exudate (drainage)
- Using absorbent dressings to absorb exudate while keeping the wound covered will reduce odour and prevent infestation with maggots
- Change dressings 1-2 times per day, based on the amount of exudate and odour
- For heavy exudate, menstrual pads or diapers can be used to absorb exudate
- For small wounds producing a large volume of exudate, a stoma appliance can be placed over the wound

Odour Control

- Wound odour is caused by bacterial overgrowth and necrotic tissue
- Managing odour is extremely important for the wellbeing of the patient and family
- Wound cleaning, debridement, and absorption of discharge (as described above) are important to reduce odour
- Metronidazole (topically or systemically) can be very helpful for reducing odour
  - **Metronidazole** crushed tablets or injectable solution applied topically to the wound; generally only 1-2 applications are required to significantly reduce odour
  - **Metronidazole 500 mg PO BID for 7 days** can also be considered

  - **Paediatric dosing 10 mg/kg/dose PO/IV q8h or 7.5 mg/kg/dose PO/IV q6h (Maximum: 500 mg/dose)**

- Activated charcoal dressing or charcoal in a basket placed under the bed or table can help absorb and reduce odour
- Essential oils, particularly peppermint, or incense may be helpful to mask strong odour, but can sometimes cause breathing difficulties for patients or may induce nausea

Pain

- Provide pain medication, including morphine and analgesic medications (see Pain section), prior to dressing changes to ensure good pain control
- Limit the frequency of dressing changes if particularly painful
- Give a breakthrough or rescue dose of **morphine** 15 minutes prior to the dressing change
- Malignant wounds can also cause neuropathic pain, which can be treated using the guidelines from the section on Pain
- **Topical morphine** can be helpful for some patients. **Injectable**

morphine (e.g. 1mL of 10 mg/ml injectable solution) can be mixed in a water-soluble gel that may be applied to the wound using a gloved finger or applied to a non-absorbent dressing placed over the wound up to TID

Control of Bleeding

- Tissue in a malignant wound is often friable and bleeds with minimal manipulation
- Care must be taken when removing dressings to avoid bleeding
  - Use warmed normal saline or water for irrigation to moisten the dressing and prevent trauma during dressing changes
- Use non-adherent dressings and Vaseline to reduce adherence of the dressing to the wound
- Apply direct pressure if bleeding occurs (10-15 minutes). Local ice packs can also assist in controlling bleeding
- Crushed tablets of **tranexamic acid** or **sucralfate** can be applied topically to stop bleeding
- Topical application of epinephrine can also help reduce bleeding through vasoconstriction
- Haemostatic or pressure dressings may be required severe bleeding occurs, although cost may be restrictive
- Consider radiotherapy depending on the patient and if the tumour is thought to be radiosensitive
- If the patient is at the end of life and having significant bleeding from a large wound, use dark towels to mask the blood and decrease anxiety for the patient and family. Pain control and sedation with a benzodiazepine can also be considered in this situation (see section on Bleeding)
- In cases where the risk of severe bleeding is high, consideration should be given to gently warning the family of this possibility and advising that dark towels be available nearby

Maggots (Myiasis)

- Infestation of open wounds by fly larvae (maggots) is frequent in

tropical and subtropical locations

- Mechanical removal of all larvae is required to eradicate the infestation, generally this is done with forceps
- A variety of substances can be used to cause deeper larvae to migrate to the surface of the wound so they can be removed with forceps
  - Substances including animal fat, petrolatum (Vaseline), beeswax, and paraffin are effective
  - Turpentine vapours will also draw maggots to the surface (avoid touching turpentine to the wound itself)
  - The choice of agent can be guided by local availability since there is no evidence to suggest that one agent is more effective than another
- After removal of all the larvae, ensure the wound is completely covered, with particular attention to the edges of the wound and dressing
  - Frequent dressing changes and proper wound care are essential to avoid recurrence

PITFALLS/CONCERNS

- Ensure that the dressing used does not cause excessive drying of the wound, which will cause more pain and bleeding when changing the dressing

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 to reduce the social isolation that often occurs with strong odour by using medications to reduce odour, such as topical metronidazole

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PSYCHOSOCIAL CARE

"People come to palliative care not as a disease… but as complex human beings, with hopes and fears, needs, history, and expectations based on the context and experiences of their lives, their families, and their culture"

Psychosocial care is an essential component of palliative care. There are a complex range of experiences and issues (psychological, spiritual, cultural, emotional, physical, socioeconomic, informational, and practical) that may impact patients and family/caregivers,* and healthcare teams.

This section provides information and tools to assist healthcare professionals in providing psychosocial support to patients and family/caregivers from the point of contact and throughout the care continuum, including bereavement.

Psychosocial care is an expanding field within palliative care and the literature supports a range of theories, models, and practice approaches. Cultural and social diversity reminds us there are no universal methods for providing psychosocial care; therefore, it is important that the information provided in this section is used and adapted to suit the individual and the collective needs of people within each community and healthcare setting.

** The concept of family can have many meanings. The term "family/caregivers" refers to the people that the patient identifies as their source of support.*

Psychosocial Assessment

KEY POINTS

- A holistic approach to assessment includes attending to the range of biological, psychological, social, cultural, and spiritual aspects of a person
- Assessment involves collecting information as well as identifying strengths, resources, and needs
- Assessment is an ongoing process as the needs of patients will change over the course of an illness

INITIAL ASSESSMENT

- Gather information about the context of the patient and the family, and the impact the illness is having on various areas of their lives
  - Explore how the patient defines quality of life, their strengths, goals, and barriers to achieving these goals
- Generally, it takes several sessions to gather all the relevant information
- The assessment is not diagnostic, its purpose is to join the patient and family in an empowering and ongoing collaborative process to achieve their goals

Areas to Consider in the Assessment:

- **Ecological factors** – marital status, status of children, family, social support systems (e.g. family, co-workers, friends, and neighbours), pattern and style of communication, family structure, roles, dynamics, abuse and/or violence, and sexuality
- **Psychological factors** – self-concept, self-esteem, coping abilities, affect, attitude, mental status, substance abuse, developmental stage, defence mechanisms, cognitive abilities, response to previous losses, and social skills
- **Cultural factors** – beliefs, identity, practices, rituals, and values

- **Social factors** – education, employment, housing, financial and/or legal status, leisure activities, physical environment, and healthcare experiences
- **Spiritual factors** – meaning applied to what gives purpose and hope
- **Biomedical factors** – diagnosis, previous or concurrent health issues, traditional and integrative health practices

STRATEGIES FOR ASSESSMENT

The following are examples of questions that may help to facilitate discussion during the initial and on-going assessment:

General Questions

- What is your understanding of the illness?
  - What do you think caused the illness?
  - What do you want to know about your illness?
  - Are there others in your family who want to know other things?
- What kind of impact has the illness had on you and your family?
  - How have roles and responsibilities changed within your family?
- Can you share information with me about your family and community of origin?
- What is most important to you?
- What are you most worried about?
- Who do you turn to for help?
- Who should be involved in decision making?
- What would be most helpful to you at this time?

Strengths-Focused Questions

- What is giving you strength to cope with your illness?
  - What has helped you in the past to cope with difficult situations?
- What helps you connect with your spirituality or faith?

- How is your family supporting you? What is challenging in your family?
- What is giving you hope right now? What are you hoping for in the future?

Practical Needs Questions

- What are your practical needs right now? In the future?
  - Finances, housing, transportation, food, childcare, care planning, burial, funeral, etc.
- Which other psychosocial professionals have you connected with? (e.g. social worker, counsellor, etc.)
- Do you need assistance accessing other supports?

Cultural Safety

- Culture is the common characteristics (values, norms, family styles, social roles, and behaviours) which are present in a group of people
- Culture is an important factor which influences many aspects of serious illness, including:
  - Experiences and expression of pain and other physical symptoms
  - Maintenance of hope in the face of a poor prognosis
  - End of life care decisions
  - Responses to illness, treatment, grief, and loss
- Culture extends beyond ethnicity and includes age, gender, faith, religion, sexuality and gender, lifestyle, language, and socioeconomic status
- In healthcare, we may care for people with very different explanatory models of illness, with different expectations about medical care and views on death
- When thinking about providing palliative care consider that in some cultures:
  - Pain and suffering are expressed differently
  - A serious diagnosis may not always be disclosed to the dying

person

- Dying may not be discussed openly
- The family, not the patient, may make the final healthcare decisions

- Cultural safety means that healthcare providers are able to provide patients with care that is respectful and inclusive of their culture and beliefs

Basic Psychosocial Support

KEY POINTS

- Basic psychosocial support is provided by ALL members of the healthcare team
  - This support enhances the overall well-being of patients and their families by strengthening their abilities and helping them to have the resources to achieve their goals
- These strategies can be easily taught to patients and family members
- It is important to ask permission of the person prior to engaging with any of these approaches
- Some people may already have techniques that are part of their spiritual or cultural practice: asking about these and encouraging the person to use these is important

GENERAL STRATEGIES

Exploring Resources: Internal and External

- Internal resources include personal resiliency and ability to cope, honesty, and awareness of one's limitations
- External resources include the patient's supportive networks of family, friends, community, and work colleagues

Providing Information (Breaking Bad News)

- This is discussed in more detail in the next chapter
- Helping patients gain an understanding of their diagnosis, prognosis, and other information about the illness

Normalizing

- Involves providing information to patients and families to show that what they are experiencing is common in their situation

- E.g. “Many people in your situation have similar fears and worries to those you have just shared with me”

- This serves to reassure people that their responses and feelings are “normal” for their situation

SUPPORTIVE COUNSELLING

- Using active listening and reflection to explore the internal and external resources of the patient and family
- In supportive counselling, the goal is not to “solve the patient’s problems” but to listen and respond to the experiences they are having

GROUNDING

Example Script:

- “Take a moment to bring awareness of how your body is making a connection to the ground/chair/bed”
- “Now, notice your feet and how they feel as they connect with the ground”
- “If you are standing, notice other parts of your body – your legs, arms, and head – and how in this moment they are all interconnected and connecting with the ground”
- “If you are sitting or lying down, notice the other parts of your body – your legs, arms, head, and how they feel as they make connection with the chair or bed”
- “As you bring awareness to these connections notice the sensations that may be present for you – heat, coolness, tingling, tightness, or numbness”
- “You can pause now and make adjustments to make yourself comfortable as you ground yourself in the present moment”

Example Script:

- Place one hand on your abdomen and one hand on your chest
- Inhale slowly and deeply through your nose, breathing all the way down to your belly (this allows more airflow into the lungs)
- Notice how your abdomen rises and your chest follows
- Exhale slowly out of your nose or mouth, whichever is most comfortable
- Take a moment to pause between each inhalation and exhalation
- Count to three as you breathe in, pause, and count to three as you breathe out
- Notice the nice, slow rhythm of your breath
- Notice any changes that may be happening in your body
- This exercise may last for only a few minutes or longer

Quick Tools

These exercises may be helpful in distressing situations where there is little time to prepare

Quick Tool #1

1. Breathe in deeply and clench your fists
2. Breathe out slowly and let yourself go as limp and loose as possible
3. Start yawning
4. Repeat these steps when needed

Quick Tool #2

1. Breathe in slowly through your nose to the count of four
2. Breathe out slowly through your mouth to the count of six
3. As you are exhaling, imagine that you are blowing bubbles, and hold your mouth in a circular shape

RELAXATION

Focus Word

- Pick a focus word: this can be a word, a short phrase, or a prayer that is firmly rooted in your belief system
- Sit or lie quietly in a comfortable position and close your eyes
- Relax your muscles, starting at your head and neck, your shoulders, moving to your chest, abdomen, and down your legs to your thighs, down to your calves, to your feet and all the way through to your toes. (This may take several minutes, or as long as the individual needs)
- Breathe slowly and naturally, and as you do, say your focus word, silently to yourself as you exhale
- If other thoughts come to your mind, don't worry. Gently return to your focus word
- Slowly open your eyes. Continue to stay where you are without moving for a minute or two before starting to moving around

Quick Tool #1

This quick, yet effective tool naturally calms the mind and helps induce the relaxation response

1. Sitting down, gently place one hand on the forehead and the other hand on the back of the neck
2. Breathe in and out slowly, noticing your breath

Quick Tool #2

1. While you are sitting, standing, or lying down, take a moment to notice your breathing and where you feel the breath is going in your body
2. As you breathe in, imagine that your breath is filling you wherever your attention to your body goes
3. As you breath out, notice any changes that may be happening in your body

IMAGERY AND VISUALIZATION

- Imagery and visualization are ways of daydreaming or creating an inner picture that you find peaceful at that moment using all your senses
- These approaches for reducing stress combine deep breathing and meditation
  - Close your eyes and imagine a peaceful scene, place, or experience you have had
  - "What do you see, what do you feel in this place?"
  - "What do you hear and smell?"
  - "Spend time breathing in and out deeply and slowly"
  - "In this place of calm relaxation, you may imagine pain, tension, or discomfort washing away, and your body becoming relaxed"

Depression

KEY POINTS

- The prevalence of depression in palliative care may be as high as 38% in patients with advanced illness
- Depression leads to greater physical, social, and existential distress, and reduced quality of life in palliative care patients
- Depression can be more difficult to diagnose given the changes of the disease process, which may mimic signs and symptoms of depression (loss of appetite, energy, etc.) and common emotional responses to advanced illness
  - Depression screening tools exist, but they are not specific to the palliative care population
- A combination of non-pharmacological and pharmacological approaches can be used, based on the individual, the severity of symptoms, and their response to treatment
  - Choosing an approach may vary depending on the time and resources available, the patient's prognosis, and the patient's desire for support

ASSESSMENT

- Interdisciplinary assessment is helpful to identify the range of physical, psychological, social, spiritual, and existential factors

Common Features:

- Excessive feelings of worthlessness, guilt, shame, hopelessness, helplessness
- Recurrent thoughts of death and suicide
- Loss of interest/pleasure in almost all activities
- Physiological symptoms such as fatigue, anorexia, or insomnia are not as reliable because these are common in advanced illness

RISK FACTORS FOR DEPRESSION

- Uncontrolled pain or other symptoms
- Unrelieved emotional and spiritual distress
- Overwhelming financial or family distress
- Isolation and abandonment from family, community, and spiritual connections
- Pre-existing mental health issues in patient and/or family caregivers

MANAGEMENT

Non-Pharmacological

- Counselling support by a social worker, psychologist, psychiatrist, or spiritual care provider can be helpful
- Cognitive behavioural therapy, of which dignity therapy is a form designed for end of life, is a common approach to counselling
- Dignity therapy is a brief focused form of therapy which is designed to address psychosocial and existential distress in patients with advanced illness
- The focus is on maintaining hope, preserving the patient's cherished roles, reducing worry about being a burden to others, and leaving a legacy

Pharmacologicals

- Most categories of antidepressants can be used in palliative care, although the time needed for efficacy (e.g. SSRIs) may limit their use in patients nearing the end of life
  - For patients with a prognosis of weeks, consider psychostimulants, which start to act immediately (e.g. **methylphenidate 5 mg in the morning and at noon**)
- Consider **duloxetine** or **venlafaxine** when neuropathic pain is present
- When polypharmacy is present, consider **citalopram, escitalopram,** or **mirtazapine**

- **Mirtazapine** is helpful if the patient has insomnia, nausea, or anorexia
- Closely monitor patients initiated on an antidepressant for adverse effects and dose titration

Class	Action	Advantageous Effects or Side Effects	Harmful Side Effects	Use in Palliative Care	Daily Dose Ranges
Tricyclics	Inhibits 5-HT and NA uptake, antimuscarinic, antihistaminic, anti-alpha 1	Co-analgesic, sedative	Constipation Dry mouth Urinary retention Hypotension Syncope Confusion	Pain Insomnia Depression	Amitriptyline 25–150 mg
Selective serotonin reuptake inhibitors (SSRI)	Inhibition of 5-HT reuptake		Sexual dysfunction Nausea and vomiting Diarrhoea QTc prolongation at higher doses Serotonin Syndrome	Depression Anxiety Obsessive- compulsive PTSD	Citalopram 10–60 mg Fluoxetine 10–80 mg Paroxetine 10–60 mg Sertraline 25–200 mg Escitalopram 5–20 mg
Selective serotonin and noradrenaline reuptake inhibition (SSNRI)	Inhibition of 5-HT and NA reuptake	Co-analgesic	Hypertension in higher doses Nausea GI tract	Severe depression Anxiety	Venlafaxine 37.5–450 mg Duloxetine 15–60 mg
Selective dopamine and noradrenaline reuptake inhibitors	Inhibition of dopamine and noradrenaline reuptake	Improves attention and concentration Reduces fatigue	Anxiety Seizures Agitation	Depression Fatigue	Bupropion 150–450 mg
Noradrenergic and specific serotonergic antidepressants	Increases 5-HT and NA activity, antihistaminic	Stimulates appetite Helps sleep Co-analgesic	Dry mouth Drowsiness Neutropenia rare	Depression, anxiety Appetite and weight gain Insomnia	Mirtazapine 7.5–60 mg
Serotonin antagonists and reuptake inhibitors	Increases 5-HT activity, anticholinergic	Helps sleep	Dry mouth, Constipation Urinary retention Drowsiness	Sleep Depression	Trazodone 50–300 mg
Psychostimulant	Increase dopamine activity	Improves alertness Rapid effect	Agitation Insomnia Anorexia Seizures Hallucinations Psychosis Arrhythmia Nightmares	Depression Opioid induced sedation	Methylphenidate 5–60 mg Modafinil 100–400 mg Dextroamphetamine 5–60 mg

Anxiety

KEY POINTS

- Anxiety is a common experience for both patients and family/caregivers
- Up to 25% of individuals with cancer and 50% of those with congestive heart disease or COPD experience significant anxiety
- Anxiety is influenced by type, stage, and site of disease, coping mechanisms, and access to social and emotional support
- Management of physical symptoms is very important, since unrelieved symptoms such as pain or dyspnoea may create or worsen anxiety
- Psychological, social, and spiritual distress are all important contributing factors to anxiety
- Anxiety is best addressed by combining both pharmacological and non-pharmacological interventions

ASSESSMENT

- Interdisciplinary assessment to identify stressors
  - Stressors are stimuli that disturb a person's normal psychological balance
  - Stressors may be physical, psychological, social, spiritual, or existential
  - In advanced illness, the knowledge that death is imminent, inability to work, perception of becoming a burden, and loss of physical abilities are often stressors
- Assess the characteristics, severity, and duration of the anxiety
- Explore the individual's previous experiences of anxiety
- Observe and explore the reactions of family members to the anxiety and their concerns
- Continue ongoing assessments of the individual's response to anxiety treatment

- Consider whether any medications are causing increased anxiety (e.g. corticosteroids, psychostimulants, anti-dopaminerics, and some antidepressants)
- Discontinuation of alcohol, opioids, benzodiazepines, nicotine, clonidine, antidepressants, and corticosteroids can also worsen anxiety

MANAGEMENT

- Anxiety can vary in duration and intensity
- Both pharmacological and non-pharmacological interventions may be helpful
- Adverse drug effects: corticosteroids, psychostimulants, and some other medications

Non-Pharmacological

- Counselling support
- Therapeutic interventions: See Therapeutic Interventions section for more details
  - Relaxation techniques
  - Guided imagery
  - Breathing exercises
  - Meditation
  - Coping skills
  - Cognitive behavioural approaches
  - Music
  - Cultural activities and rituals

Pharmacological

- A short course of low dose benzodiazepines (e.g. **lorazepam, clonazepam, diazepam)** may be helpful
- Treatment with antidepressants (SSRIs or SNRIs) are helpful in treating anxiety in some individuals, particularly for patients who are expected to live for longer (i.e. not at end of life)

- **SSRIs: sertraline, citalopram, and escitalopram**
- **SNRIs: venlafaxine, duloxetine**
- **Mirtazepine**

Self-Care

KEY POINTS

- Caring for someone at the end of life can be a tremendous challenge for healthcare providers and family members, which can lead to burnout, compassion fatigue, and trauma
  - In many settings, family members often have a primary caregiving role and may need self-care support from the healthcare providers
- People may experience a range of physical, emotional, social, and spiritual experiences from stress and burnout
- Self-care involves paying attention to how we are impacted by providing care, developing strategies to manage stress and prevent burnout, and accessing additional supports as needed
- There are a wide range of physical, emotional, social, and spiritual strategies which can support self-care

FACTORS WHICH CAN AFFECT RESILIENCE

A variety of factors may impact a person's capacity to provide care, including:

- Coping mechanisms and previous traumatic experiences
- Type of disease and other characteristics of the ill individual
- Previous experiences, comfort, and skill in providing care to a sick person
  - Access to skilled healthcare providers who can provide support and advice
- Personal medical conditions, particularly mental health conditions
- Isolation from usual self-care supports – home, community, and spiritual/religious
- Access to psychological and spiritual supports – from professionals and/or informal supports

Additional Factors for Healthcare Providers

- Work environment – supportive environment, access to debriefing support
- Adequate training to effectively provide palliative care and relieve suffering

Additional Factors for Family Caregivers

- Presence of family conflict
- Cultural and social expectations of caregiving
- Staying in a health facility far from the home community
- Financial needs – availability and cost of medications and supplies

SIGNS OF STRESS AND BURNOUT

These reactions may occur in both family caregivers and healthcare providers

Physical:

- Fatigue
- Headaches, muscle aches, and generalized or localized body pains
- Changes in sleep
- Numbness
- Poor concentration
- GI symptoms – changes in appetite, nausea
- Difficulty breathing
- Palpatations

Emotional, Social, and Spiritual:

- Feelings of powerlessness or helplessness
- Loss of hope
- Withdrawal from family and social support system
- Survivor guilt

- Fears about the future
- Resentment for the demands and responsibilities of caregiving
- Guilt around care provided
- Unresolved or complicated grief
- Spiritual or religious or existential concerns
- Distress, depression, and anxiety
- Harmful illicit drug and alcohol use

SELF-CARE STRATEGIES

Assessment

The following questions may be helpful in assessing the experiences of others and ourselves:

- How are you doing with providing care for ….?
  - What do you feel you are doing well, what is challenging?
- How do you feel physically?
  - Have you been experiencing any problems with sleep, pain, poor concentration, etc.?
- How are you feeling emotionally?
  - How have you been coping with the range of feelings and emotions?
- How are you caring for yourself?
  - What is giving you strength at this difficult time?
- What does your personal support system look like?
  - What supports do you find most helpful?

Management

Different people will find different strategies more effective for them personally. The following list includes some common strategies which many people find helpful:

- Basic needs – nutritious food, exercise, adequate sleep
  - Attend to your own health needs

- Balance – between personal life and work life
  - Set aside regular times to do things you enjoy
- Relaxation and self-reflection – taking time to assess your personal feelings, through meditation, prayer, or journaling
  - Acknowledge what you are doing well in your care-giving
- Informal support – connect with family and friends
- Formal support – peers, supervisor, debriefing, might include access to counselling and support groups
- Ritual – memorial services or other forms of remembering and providing closure
- Education and training – aimed at understanding issues regarding dying and grief, effects of providing care, communication techniques

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COMMUNICATION

Communication

KEY POINTS

- Communication is a cornerstone of palliative care affecting both quality of care and quality of life
- Communication is about sharing ideas and feelings, with the aim of reaching an understanding
  - If we have not understood the individual's concerns or the individual has not understood our message, then we have not achieved our goal of communication
  - A large portion of communication occurs non-verbally, through our facial expressions, body posture, and gestures
- Good communication in healthcare:
  - Builds trust and creates relationships, allowing for shared decision making
    - Shared decision making is a collaborative process which includes the patient, their family, and the healthcare team
  - Gathers and provides information
  - Improves understanding, reducing myths and misconceptions about illnesses
  - Reduces uncertainty, fear, and worry
  - Maintains hope
  - Enables expression of feelings
  - Improves patients' satisfaction with care and their adherence to treatment recommendations
  - Addresses advance care plans
- Consequences of poor communication in healthcare:
  - Reduced confidence and trust in the healthcare team and system
  - The individual may not reveal important information which would

help inform their care

- Increased distress, pain, and other symptoms for the patient and family
- The patient and family may choose or insist on ineffective care
- Leads to increased stress and burnout among healthcare workers and lowers job satisfaction

- Communication skills can be learned and improved with practice
  - We can all learn and improve our communication skills which will facilitate supportive conversations with patients and their families

CORE COMMUNICATION TECHNIQUES IN PALLIATIVE CARE

- Active Listening with Open-Ended Questioning
- Use of Silence
- Responding with Empathy

Active Listening with Open-Ended Questioning

- Active listening is a powerful therapeutic intervention
- It involves ways of listening, giving full attention, expressing empathy, and responding to another person that improves mutual understanding
  - We should concentrate on receiving the complete message communicated through the person's body language, facial expressions, and tone of voice
- People's ways of thinking, seeing, hearing, and interpreting the world is influenced by their beliefs, values, fears, and social and cultural backgrounds
- Active listening is best done without interpretation or evaluation

Key actions which are part of active listening:

- Sit facing the person, with a relaxed facial expression – to show that you are listening
- Have an open body posture – avoid crossed arms or legs

- Give your full attention to the person – avoid multitasking; it is okay to take a few notes with pen and paper if needed
- Plan enough time to have the conversation so that all the people involved do not feel rushed
- Turn your phone on silent and do not take any calls during the meeting (unless absolutely necessary)
- Avoid interrupting the patient and family (unless absolutely necessary)
- Make some eye contact (if culturally appropriate)
- Voice encouraging responses, such as nodding head and small responses such as "yes", "I see", and "Okay"
- Use open-ended questions to encourage the person to share more

Facilitating conversation with open-ended questions – examples include:

- "How are you feeling today?"
- "What has been worrying you most?"
- "How have you been coping with these experiences?"
- "I understand that you have some questions and concerns about your care. Can you tell me more about that?"
- "How do you see things going from here?"

Using open-ended questions to clarify responses – examples include:

- "Can you give me an example of what you are talking about?"
- "Tell me more about…"

Paraphrasing and summarizing:

- Paraphrasing and summarizing let's people know that you are listening by repeating a summary of what they have just shared
- Examples: "What I hear you saying is that you have been experiencing …which has been making you feel … Have I understood that correctly?"

- "What would be most helpful? Is there anything else you need?"

Use of Silence

- People often pause before they say something important or painful
  - Silence allows a space for the person to process feelings and thoughts and gain clarity on what they want to say
  - Silence allows a space for feelings or emotions to be felt or expressed

What to do

- Avoid prompting the person to speak, instead remain quiet for a moment and use active listening skills
- Keep your attention fully with the other person, while maintaining a non-threatening, relaxed posture, and facial expression
- Silence can feel uncomfortable when you first try using it within a conversation; it may feel more natural to start talking and fill in the gap
- After a short period of silence, if the person has not spoken, continue to speak
  - It may feel appropriate to ask what the person is thinking or feeling
  - You can silently and slowly count to 10 to help you give a long enough period of silence
- Avoid prolonged silence, which may be interpreted by the person as a lack of interest
- Silence can be used when a person suddenly becomes quiet in a conversation
  - It may also be used when a person is sharing their feelings or something that seems important to them
  - If the person pauses, avoid trying to fill the silence, instead, give them time and space, so that they feel comfortable to continue talking and do not feel rushed

Responding with Empathy

- Recognizing and responding to a person's emotions with empathy tells the person that you are listening and that you care and gives the person permission to discuss sensitive topics
- When a person feels understood, they feel less isolated, and trust develops within the relationship
- Naming an expressed emotion can help a person to feel understood
- It can also help the person to better understand a situation, express their needs, decrease emotional distress, and make choices
- People take a risk when they share their emotions, so thanking them and offering support really helps. "I wish" statements allow you to align with the person and their emotions while acknowledging the reality of the situation

What to do

- First use active listening and deliberate silence to allow the person space to express their emotions
- Be aware of your own emotions. Your feelings of sadness, anger, anxiety, or happiness are often the first clue that a person is communicating an important emotional message
- Avoid trying to stop or change a person's feelings. Avoid trying to use problem solving
- The acronym "NURSE + 'I wish"' is a tool to guide verbal expressions of empathy

Skill		Example Phrases
Naming	State your observation of the person's emotion	"I can hear you are feeling angry" "I can see that you are worried"
Understanding	Legitimize the person's emotion	"I can imagine this news must be a shock for you" "I can see how important this is to you" "I can't understand how difficult this must be"
Respecting	Give praise to the person	"I am impressed with your courage" "You are such a strong/ dedicated/caring person"
Supporting	Let the person know they are not alone	"Our team is here to help you through this" "Thank you for sharing how you are feeling"
Exploring	Ask the person to share more about their feelings	"Could you say more about what you mean when you say.....?" "Can you say more about that?"
"I wish"	Express a wish that the situation was different	"I wish the situation were different" "I wish I had better news"

Non-Verbal Communication

- How people communicate is rooted in cultural and social traditions, values, and beliefs
- Observing people's body language, posture, gestures, and facial expressions can provide clues to people's feelings, emotions, and capacities for coping
- Consider your own non-verbal communication and how this may impact our attempts to convey respect, compassion, and understanding
- Physical touch may be appropriate, depending on the culture (e.g. a hand placed on the shoulder)

Considerations when Communicating with Patients and Families

- What information about the patient and their family/caregivers would be helpful?
  - How do patients and family/caregivers want to be involved in information sharing and decision making?
- How does the patient understand their situation? What information is known and what do they want to know or not know?
- How does the family/caregiver understand the situation? What information is known and what is being shared or not shared between patient and family/caregivers?
- What opportunities and challenges exist within the patient and family relationship?
- What tools or resources may be helpful when sharing information? E.g. visual aids, written information, interpreters, presence of a loved one

Common Communication Pitfalls (Things Which are Not Effective and Should be Avoided)

- Using medical terms or jargon, which families are unlikely to understand
  - Instead, speak clearly using a basic vocabulary

- Giving false reassurance
  - E.g. if a seriously ill patient asks “Will I get better?”, do NOT simply respond “Don’t worry, I’m sure you will”
  - Telling people not to worry is NOT an effective or therapeutic communication strategy, since you have not addressed the reason for the person’s worries or concerns
- Moralizing, philosophizing
  - E.g. if a patient asks “Will I die?”, do NOT respond with statement such as “We will all die”

Breaking Bad News

KEY POINTS

- Bad news can include any information that may seriously affect a person's perception and experience of their future
- How information is delivered has tremendous impact on how patients and family/caregivers hear the news, how they cope, and how they make decisions
- Everyone is unique in how they would like to be given information, what information they want to know, and whom they want to know it
- Providing clear and accurate information with compassion and empathy shows patients and family/caregivers that you care

When giving bad news, the aim is to:

- Provide clear and accurate information
- Maintain trust between patient, family, and healthcare workers
- Support adjustment to the reality of the situation
- Encourage informed choice about care options
- Reduce or acknowledge uncertainty about the future
- Enable patients and families to regain a feeling of some control over their situation

When giving bad news, remember that:

- The bigger the gap between the person's expectations and reality, the bigger the impact the news will be for the person
- Delivering bad news is a complex communication task. It requires the verbal component of giving the bad news, AND responding with empathy to a person's emotional reactions, managing the person's expectations, and involving the person in decision making

- The way bad news is delivered to patients and families can have a significant impact on their satisfaction with the discussion, understanding of the information, satisfaction with healthcare, level of hopefulness, psychological adjustment to serious illness, and future ability to trust healthcare workers

Truth-telling

- In many cultures, ill-health is not openly discussed since healthcare providers may want to protect the family from bad news
- However, studies from a wide variety of different settings around the world have shown that patients and their families generally want to know the truth about their illness
- Most individuals cope better and maintain their trust in the healthcare team if they are given this information

BARRIERS TO BREAKING BAD NEWS

- Fear of their own emotions
- Fear of patient and family showing strong emotions, reactions, and uncertainty about how to support these responses
- Communicating complex information in non-technical language is challenging
- We prefer to avoid discussion of distressing information (e.g. death)
- Giving false hope – telling patients and family/caregivers what we think they want to hear
- Lack of time

Barriers from Patients and Families

- Collusion among family members, which prevents the patient from knowing the extent of their disease
- Expectations of medical miracles
- A culture which avoids discussion about death or serious illness
- The feeling that healthcare providers are not being truthful or honest

- The feeling that their decisions and hopes are not being respected
- Societal and family pressures – different family members may have different opinions and beliefs related to serious illness and death

Dealing with Collusion

- Collusion describes a situation when information about diagnosis, prognosis, or treatment is selectively disclosed or not disclosed at all to the patient and/or certain family members
- Collusion occurs in different forms and intensities, and is rarely absolute
  - Some illness-related problems may be discussed openly in the family, while others are not
  - Collusion generally comes from a place of love, as family members seek to protect their loved one from bad news about their illness
- Collusion occurs in all societies, and commonly includes information about illness recurrence, deterioration, and palliative care
- It is particularly important to break down collusion in a timely manner, because patients are more likely to become anxious or depressed if collusion is not addressed
  - Collusion isolates the patient and they are often upset and hurt by deception from their family members
  - Patients may also have more pain or physical distress if collusion is not addressed
  - Relatives need time to address their emotional issues related to the illness and their grief
- Prevention – addressing possible collusion early in the disease and ensuring clear communication with the patient

Steps to Address Collusion

Interview the relatives to gain their trust

- Acknowledge the presence of collusion
- Acknowledge the difficulty of the situation for the relatives and that

they know the patient well

- Assess the relative's understanding of the disease and its impact on the family
- Review the reasons for not telling the patient; acknowledge some of these are good and come from the best of motives
- Describe the consequences and potential harm of not telling the truth
- Focus on the personal cost to the relative of maintaining a deception
- Ask what the relative thinks is the patient's level of understanding
- Suggest that research evidence indicates that most patients would like to know the truth and that they are already aware that something serious is happening

Seek permission to speak to the patient alone

- Inform the relatives that you have no intention of revealing the truth to the patient but only to assess how much they know and how much they want to know
  - This allows healthcare providers to start an open dialogue about the illness
- State that you will not break the collusion unless the patient asks a direct question when it will be inappropriate to lie to them

Establish the patient's level of awareness

- Explore with the patient what they understand about their illness by asking direct questions
- During this discussion, most patients will reveal that they are already very aware of their health condition, in contrast to what their relatives believe
- Seek permission to convey this awareness to the relatives
- Occasionally the relative is right and the patient gives clear signal he does not want to know, in this case do not force unwanted information upon them

Have an open discussion with the patient and family

- Meet with the patient and their family together to share information, to offer support and follow up, and to start setting realistic goals for the future

SPIKES – A PRACTICAL TOOL FOR DELIVERING BAD NEWS

The goal of a conversation using SPIKES has four main objectives:

- To gather information from the individual about what they understand about their condition
- To give medical information about the individual's medical condition and prognosis – this is generally the "bad news"
- To provide emotional support to the family
- To develop a strategy for next steps in care

There are six steps in SPIKES which should be followed in order. The steps are described below:

S = Setting

- Arrange for some privacy
- Limit interruptions
- Confirm which family members will join
- Gather and read all the relevant medical information (review the medical file and notes before the meeting)
- Sit down

P = Perception of condition/seriousness

- Ask what the individual knows or suspects about their medical condition
- Listen carefully to what the person says

I = Invitation to give information

- Ask the individual if they would like to have more information
- Accept a person's right not to know if they state they do not wish to know

K = Knowledge: giving medical facts

- Give a warning that bad news is coming by saying – "I have bad news" or "It is not good news"
- Use simple language
- Give information in small chunks
- Check whether the person has understood what you said
- Respond to the patient's reactions and emotions

E = Emotions and Empathy

- Respond with empathy as described above
- Allow family to express emotion
- State "I wish the situation were different"

S = Strategy and Summary

- Repeat the key points that were discussed
- Ask if the family has any questions
- Say what will happen next, for example "I will come to see you tomorrow"

The following table provides sample language which can be used to conduct a conversation which shares "bad news"

Step	Suggested Words to Use
1. Setting: plan ahead to establish the environment	– "I'd like to meet with you to talk to you about what is happening with your illness and what might be ahead, would that be okay"
2. Perception: explore what the patient knows already	– "Tell me what you understand about your illness?" – "What have the other doctors told you about your illness?"
3. Invitation: information-sharing preferences	– "Would it be okay for me to discuss what we have learned from the medical tests with you now?" – "How do you prefer to discuss medical information in your family?" – "Some people prefer a big picture of what is happening and others like all the details; what do you prefer?"
4. Knowledge: give the information	– Give a warning: "I have something very serious we need to discuss" or "I'm sorry to say that I have some bad news" – Say it simply and stop (e.g. "The tumour has grown—the cancer is getting worse despite our best treatments")
5. Empathy: respond to emotion	– Use silence – "I know this is not what you expected to hear today" – "This is very difficult news"
6. Strategy and Summary: discuss next steps and follow-up plan	– "We've talked about a lot of things today, please tell me what you understand as the main messages from our meeting" –· "I will see you tomorrow morning"

DEBRIEFING

- It is important that healthcare professionals reflect after the meeting and consider their own feelings and responses, and the concerns they may experience (e.g. sadness, frustration, anger, guilt, relief, uncertainty, helplessness, or disagreement)
- Discussing the meeting with team members is helpful:
  - Perceptions and concerns can be discussed
  - The team can identify supports and suggestions for how care can be improved
  - Team members can reflect on new skills they may want to work on

Supporting Hope

KEY POINTS

- Patients and families are adapting and adjusting to the changes that occur with progressive illness, as they shift from a goal of cure or life prolongation to comfort
- Patients and families require time to adjust and cope with each change
- Hope is about possibility and is a common effective coping mechanism
  - Hope builds strength, and is critical to the psychosocial well-being of patients and family
- Feelings of hope and hopelessness may occur at the same time
- Healthcare professionals can influence hope, helping to support specific hopes
  - Supporting hope involves providing patients and families with adequate information about the disease so that they can develop personal goals and participate in decision making about their medical care
  - Providing honest information about prognosis does not take away hope, instead it allows patients and families to adjust their hopes to their current situation
  - Evidence shows that honest communication reduces patients' feelings of hope (see References below)
- Hope will evolve and change over time and circumstance
- Hopes expressed by patients and family/caregivers may be very different from that of the healthcare team
  - It is important to find a balance between being honest and providing hope

Examples of hopes in seriously ill individuals and their families:

- For a cure

- For comfort, through control and management of pain and symptoms associated with the disease
- For quality of life and relief of suffering
- For dignity
- For continued connections and for maintaining social relationships
- For reconciliation of interpersonal conflicts or issues
- That they are not a burden on their family
- That family will be okay after they die
- For spiritual connection or peace or an afterlife (depending on the patient's beliefs)

STRATEGIES FOR HEALTHCARE WORKERS TO SUPPORT HOPE

- Be honest and authentic
  - Effective communication through active listening and showing empathy will support hope
  - After breaking bad news (using SPIKES), in a follow-up conversation you can ask patients: "Given what you know about your diseases, what do you hope for at this time?"
- Facilitate care relationships
  - Be physically present in times of crisis, so that the patient does not feel abandoned
- Encourage determination and courage
- Engage in remembering, reflecting back on life with the patient and family, journaling
- Listen attentively
- Help patients and families to establish short-term, attainable goals
- Support spirituality and connections to family and others who are important to the patient
- Manage pain and other symptoms

Coping with Serious Illness

Tools for Coping with Serious Illness:

- The following ideas are helpful for people facing a serious illness (either as a patient or a family member)
- Everyone of us is unique, so if some of the ideas don't now work for you, ignore them; take only what fits
- Use these ideas to stimulate more of your own

Enlist the support of others	Studies show that a support network can be helpful in coping with this situation. Because your friends and family may not be able to support you as often, or in the way you would like, or may be struggling to cope as well, it may be helpful to utilize additional resources such as religious or community supports, healthcare staff, etc.
Eat healthy	This is tough when you don't feel like eating. When you are stressed, your appetite is affected. Follow any guidelines given to you by your doctor or healthcare professional, but eating small amounts more often is usually better than trying to face a big meal
Take a deep breath	When under stress we tend to breathe very shallowly, which doesn't allow enough oxygen to the brain. Breathing deeply every so often helps to maintain that balance and give you an edge
Use your sense of humour	Humour will go a long way to carry you through this stressful time. Laughter creates a release of tension and releases endorphins into the system to give you a sense of well being. This will help to cope with the stress of dealing with serious illness
Write down your thoughts	A journal is one way of sorting through your experiences. Sometimes ideas and thoughts run around in your mind and it is hard to get a handle on what really is happening for you. Writing is one way to help with this. You cannot write as fast as you think and, as a result, your mind is forced to slow down
Personal coping kit	Based on what gives you energy; put together a kit. This kit may contain pictures, mementos, videos, letters, crossword puzzles, a good book, magazines, etc. – whatever you think would help you through the difficult times.

Common Reactions When Coping with Serious Illness

Inability to focus or concentrate	Things which may have been routine in your daily life are now difficult, such as reading, etc.
Poor memory	Even such things as a familiar phone number may be a challenge to recall
Physical reactions	Reactions such as tight muscles, headaches and exhaustion may also be a part of this experience. If you are experiencing these symptoms, it is a good idea to check with your family doctor
Increased irritability	Your tolerance level may not be as high as it used to be. This may be particularly true within your own family, or with those you care about
Confusion/ disorientation	You may find yourself losing track of place/time.
Less self-confidence than usual	This incident has turned your world upside down and has shaken up your beliefs, including what you believed about yourself
Difficulty in making decisions	Sometimes what once seemed the simplest of decisions becomes a challenge
Difficulty sleeping	When you try to sleep or rest, your thoughts may run all over the place
Sense of unreality	"This can't really be happening to me!"
Feelings of helplessness	The feeling that there must be something you could do to make a difference to the situation
Feelings of being "on alert" at all times	You may find that you are easily startled and that it is hard to settle yourself down, particularly at night
Being on an "emotional roller coaster"	You may feel that you are never quite sure what is going to happen day by day as you deal with the situation

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APPENDICES AND SUGGESTED FURTHER READING

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)
- Breakthrough doses of morphine should be available on a PRN or SOS basis **in addition** to the patient's regularly scheduled doses
- Providing a breakthrough dose of **morphine** is an important part of managing pain, dyspnoea, and cough

- Breakthrough doses are generally approximately 10% of the total 24-hour dose and should be ordered every 1-4 hours as needed (PRN or SOS)

Example 1: A patient receives 10 mg q4h SUBQ of **morphine**

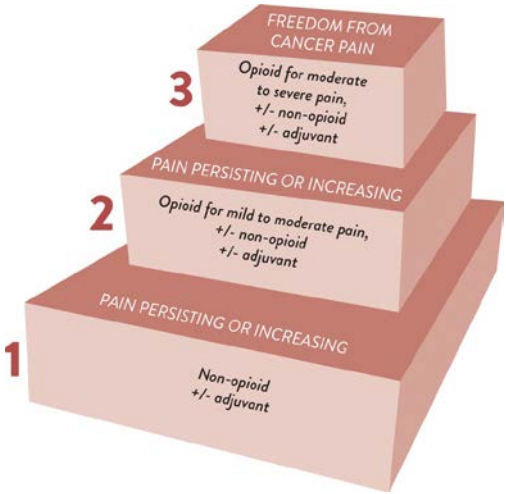
= 60 mg in 24h SUBQ. Therefore, the appropriate breakthrough or rescue dose is 5 mg q1h PRN SUBQ

Example 2: A patient receives 5 mg q4h PO of **morphine**

= 30 mg in 24h PO. Therefore, the appropriate breakthrough or rescue dose is 2.5 mg q4h PRN (Note that 2.5 mg was selected for ease of dosing as most morphine tablets are commonly 5 mg or 10 mg)

Appendix 2

WORLD HEALTH ORGANIZATION PAIN LADDER FOR USE IN ADULTS AND ADOLESCENTS



This figure shows the three-step ladder of analgesic management for cancer pain as recommended by the World Health Organization (2018)

NOTE: Pain control should be based on the level indicated by the patient. For example, it may be clinically indicated to start at "Level 3" on the analgesic ladder for patients who present with severe, difficult pain

Appendix 3

OPIOID CONVERSION TABLES

Conversion from oral morphine to fentanyl patch

Oral 24-hour Morphine Equivalent Daily Dose (mg)	Fentanyl Patch Dose Equivalent (mcg/hour)
60-134	25
135-224	50
225-314	75
315-404	100
405-494	125
495-584	150
585-674	175
675-764	200
785-854	225
855-944	250
945-1034	275

NOTE: This table is unidirectional and should NOT be used to convert fentanyl to morphine equivalent

EQUIANALGESIC TABLE FOR CHRONIC OPIOID DOSING

Drug	Oral (PO)	Parenteral (SUBQ, IV)
Morphine	**10 mg**	**5 mg***
Codeine	**100 mg**	**65 mg**
Hydromorphone	**2 mg**	**1 mg***
Oxycodone	**5.0-7.5 mg**	**-**
Methadone	**1 mg** *Requires advanced training and specialist knowledge***	*Not readily available*
Fentanyl patch	*See table above*	

** Common ratio PO:SC is 2:1, but 3:1 may also be used*

*** Rotation is complex, with delayed accumulation. Ratio varies from MOR:METH 5:1 at low doses to 10:1 or up to 20:1. Must be individualized*

NOTE: Due to incomplete cross-tolerance, if the symptom is well controlled, then reduce the equivalent dose of the new medication by 25-50% and then titrate to effect

Appendix 4

THE USE OF NALOXONE IN RESPIRATORY DEPRESSION DUE TO OPIOID OVERDOSE

- The fear of respiratory depression is sometimes a reason why physicians are reluctant to use opioids
- The risk of respiratory depression in a patient who has already been on a regular opioid dose (for even a few days) is very low
- Even if there is a slowing in the respiratory rate (e.g. 6-8/min) this is usually not a cause for alarm as the patient can often simply be monitored. Sometimes it is appropriate for the next dose of opioid to be omitted or reduced
- Take care to distinguish this from respiratory changes at the very end of life which are to be expected and need no intervention
- It is very rare therefore that an opioid antagonist such as **naloxone** needs to be used
- However, if a significant respiratory depression does occur (perhaps if the patient mistakenly receives an overdose) and if it is deemed absolutely necessary to give an opioid antagonist, the following approach should be used:
  - Dilute a 1 mL ampule **naloxone** (0.4 mg/mL) with 9 mL of saline
  - Give 40 mcg (1mL) IV/SUBQ/IN/IM every minute until the respiratory rate increases
  - Aim for partial opioid reversal, but not loss of analgesia
  - Give additional doses every 30-60 minutes to maintain an adequate respiratory rate, generally for the usual duration of action of the medication (e.g. 4 hours for oral morphine)

NOTE: Giving the complete ampule instead will result in an acute withdrawal from the opioid and cause immediate extreme pain or dyspnoea

Appendix 5

MEDICATIONS WHICH CAN BE GIVEN SUBQ (GENERALLY THE DOSES OF SUBQ AND IV ARE THE SAME)

Medications which can be given SUBQ (same dose as IV):

- Opioids: Morphine, hydromorphone, fentanyl, methadone, oxycodone, diamorphine
- Sedative-hypnotics: Midazolam, clonazepam, phenobarbital
- Anti-emetics: Haloperidol, metoclopramide, levomepromazine (methotrimeprazine)
- Anti-secretory agents: Hyoscine BUTYLbromide, hyoscine HYDRObromide, glycopyrrolate, octreotide
- Anti-histamines: Cyclizine, promethazine
- Miscellaneous: Dexamethasone, methylnaltrexone, naloxone, furosemide

Appendix 6

USE OF BLOOD PRODUCTS IN PALLIATIVE CARE

Transfusion of blood products in patients with advanced and life-threatening disease can be a lead to difficult ethical and clinical situations.

There are two common scenarios encountered:

- A new situation arises in which giving a transfusion may alleviate symptoms (for instance, bleeding from a tumour which has caused a patient to become anaemic and have symptoms of fatigue and breathlessness)
- An ongoing disease process in which the transfusion of blood products has been part of normal supportive care. As the disease progresses the question arises whether these should be continued (for instance, with a child with relapsed leukemia for whom there is no further curative therapy)

In both situations within the context of patient's wishes and prognosis there should be a balance between the benefits of transfusion and the burden and possible harm (see comments regarding Balanced Care on page 10).

At all times the patient and family/caregivers should be part of the process of deciding whether a transfusion should take place or regular transfusions should be ceased.

Red Blood Cells

- If the patient is found to be anaemic transfusion may help symptoms of weakness, fatigue, breathlessness and headache
- If the life expectancy of the patient allows, a trial of the transfusion of red cells may be warranted. If the patient continues to be

anaemic further transfusions may be warranted

- If the patient deteriorates then continued transfusion may become futile or increasingly burdensome
- Adverse effects such as fluid overload and transfusion reactions should be monitored in the usual manner

Platelet Transfusion

- Transfused platelets last only two days inside the patient
- May be considered, in the setting of distressing spontaneous bleeding for patients whose prognosis makes the transfusion worthwhile
- Should generally NOT be considered to prevent possible bleeding unless there is a specific reason to prevent spontaneous bleeding (i.e. during travel)

Fresh Frozen Plasma

May be considered in special circumstances in palliative care when coagulation is affected by:

- warfarin overdose
- liver disease
- Disseminated intravascular coagulation (DIC)

Appendix 7

PALLIATIVE PERFORMANCE SCALE (PPS)

PPS Level	Ambulation	Activity & Evidence of Disease	Self-care	Intake	Conscious Level
100%	Full	Normal activity and work No evidence of disease	Full	Normal	Full
90%	Full	Normal activity and work Some evidence of disease	Full	Normal	Full
80%	Full	Normal activity with effort Some evidence of disease	Full	Normal or reduced	Full
70%	Reduced	Unable to do normal job/work Significant disease	Full	Normal or reduced	Full
60%	Reduced	Unable to do hobby/ house work Significant disease	Occasional assistance necessary	Normal or reduced	Full or confusion
50%	Mainly sit/lie	Unable to do any work Extensive disease	Considerable assistance required	Normal or reduced	Full or confusion
40%	Mainly in bed	Unable to do most activity Extensive disease	Mainly assistance	Normal or reduced	Full or drowsy +/- confusion
30%	Totally bed bound	Unable to do any activity Extensive disease	Total care	Normal or reduced	Full or drowsy +/- confusion
20%	Totally bed bound	Unable to do any activity Extensive disease	Total care	Minimal to sips	Full or drowsy +/- confusion
10%	Totally bed bound	Unable to do any activity Extensive disease	Total care	Mouth care only	Drowsy or coma +/- confusion
0%	Death bound	–	–	–	–

INSTRUCTIONS FOR USE OF PALLIATIVE PERFORMANCE SCALE

- PPS scores are determined by reading horizontally at each level to find a "best fit" for the patient which is then assigned the PPS% score.
- Begin at the left column and read downwards until the appropriate ambulation level is reached, then read across to the next column and downwards again until the activity/evidence of disease is located.

These steps are repeated until all five columns are covered before assigning the actual PPS for that patient. In this way, "leftward" columns (columns to the left of any specific column) are "stronger'" determinants and generally take precedence over others.

Example 1: A patient who spends the majority of the day sitting or lying down due to fatigue from advanced disease and requires considerable assistance to walk even for short distances but who is otherwise at a fully conscious level with good intake would be scored at PPS 50%.

Example 2: A patient who has become paralyzed and quadriplegic requiring total care would be PPS 30%. Although this patient may be placed in a wheelchair (and perhaps may seem initially to be at 50%), the score is 30% because he or she would be otherwise totally bed bound due to the disease or complication if it were not for caregivers providing total care including lift/transfer. The patient may have normal intake and full conscious level.

Example 3: However, if the patient in example 2 was paraplegic and bed bound but still able to do some self-care such as feed themselves, then the PPS would be higher at 40% or 50% since he or she is not in "total care."

- PPS scores are in 10% increments only. Sometimes, there are several columns easily placed at one level, but one or two which seem better at a higher or lower level. The clinician should make a "best fit" decision. Choosing a "half-fit" value of PPS 45%, for example, is not correct. The combination of clinical judgment and "leftward precedence" is used to determine whether 40% or 50% is the more accurate score for that patient.
- PPS may be used for several purposes. First, it is an excellent communication tool for quickly describing a patient's current functional level. Second, it may have value in criteria for workload assessment or other measurements and comparisons. PPS has also been shown to have prognostic value in both cancer and non-cancer conditions.

DEFINITION OF TERMS FOR PPS

As noted below, some of the terms have similar meanings with the differences being more readily apparent as one reads horizontally across each row to find an overall "best fit" using all five columns.

1. Ambulation

The items "mainly sit/lie," "mainly in bed," and "totally bed bound" are clearly similar. The subtle differences are related to items in the self-care column. For example, "totally bed bound" at PPS 30% is due to either profound weakness or paralysis such that the patient not only can't get out of bed but is also unable to do any self-care.

The difference between "sit/lie" and "bed" is proportionate to the amount of time the patient is able to sit up versus the need to lie down.

"Reduced ambulation" is located at the PPS 70% and PPS 60% level. By using the adjacent column, the reduction of ambulation is tied to inability to carry out their normal job, work occupation or some hobbies or housework activities. The person is still able to walk and transfer on their own but at PPS 60% needs occasional assistance.

2. Activity and extent of disease

"Some," "significant," and "extensive" disease refer to physical and investigative evidence which shows degrees of progression. The extent of disease also considers the person's ability to continue work and hobbies/activities.

For example

Some: breast cancer, a local recurrence

Significant: breast cancer with 1-2 metastatic sites

Extensive: breast cancer with multiple metastases in lung, bone, liver, brain, hypercalcemia, or other major complications.

3. Self-Care considers how much assistance the person requires to get out of bed, walk, bathe, toilet, and eat meals

"Occasional assistance" means that most of the time the person can transfer out of bed, walk, wash, toilet, and eat by their own means, but that on occasion they require minor assistance.

"Considerable assistance" means the patient needs help everyday. For example, the person needs help to get to the bathroom, but is then able to brush their teeth or wash their hands and face.

"Mainly assistance" means that the person needs help getting up, but also needs assistance washing his face, and can usually eat with minimal or no help. This may fluctuate according to fatigue during the day.

"Total care" means that the patient is completely unable to eat without help, toilet or do any self-care. Depending on the clinical situation, the patient may or may not be able to chew and swallow food once prepared and fed to him or her.

4. Intake

"Normal intake" refers to the person's usual eating habits while healthy.

"Reduced" means any reduction from that and is highly variable according to the unique individual circumstances.

"Minimal" refers to very small amounts, usually pureed or liquid, which are well below the levels required for sustenance.

5. Consciousness level

"Full consciousness" implies full alertness and orientation with good cognitive abilities in various domains of thinking, memory, etc.

"Confusion" is used to denote the presence of either delirium or dementia and is a reduced level of consciousness.

"Drowsiness" implies either fatigue, drug side effects, delirium, or closeness to death.

"Coma" in this context is the absence of response to verbal or physical stimuli; some reflexes may or may not remain. The depth of coma may fluctuate throughout a 24-hour period.

Does the scale consider psychological factors which may impact the items?

PPS only considers what a person is capable of doing, not what they choose to do. For example, anxiety, sadness, or demoralization may result in the patient sitting a lot, but unless they actually require some assistance to get up (PPS 50% or 60%), the PPS would be higher.

We often see people at diagnosis who are fully ambulatory, normal activity and work, but have extensive disease where do they fit in?

This necessitates a clinical judgment decision. In this case, the aspect of full ambulatory and normal activity indicates quite a high PPS and the "extensive disease" is clinically less relevant, at least for the moment. A PPS 80% would be appropriate designation.

People who are unable to work because chemotherapy is demanding, but only have some evidence of disease, how do I score them?

The PPS should be determined by the actual ability to do something, not by desire, or lack of. In this case, it is not clear what "demanding" means. If the patient is so physically sick or fatigued that they cannot work, then the PPS is rated accordingly – PPS 70% would be appropriate if can do some work at home, but could be reduced to PPS 50% if they were so sick that they required actual assistance at home.

Can PPS be used in people with dementia?

In general, the answer is yes, as PPS is a functional performance scale which primarily focuses on ambulation, activity, and self care. Particularly in the advanced stages of Alzheimer's disease, the patient fits quite well into such levels as PPS 50% through PPS 10%.

What level of staff are using this tool – nurses, physiotherapists, volunteers?

PPS can be used by many types of healthcare workers, including nurses, physicians, respiratory therapists, physiotherapists,

occupational therapists, dieticians, spiritual care providers (chaplains), and volunteers.

How often do you recommend the use of this tool in a home care palliative care setting where there are various levels of caregivers in the home? Daily visits?

In generally, PPS should be assessed during each visit ,which of course may vary from daily to weekly or less. In our Palliative Care Unit, it is done each day or at any time the patients' condition changes.

When a patient's mobility is limited due to a fracture in a weight bearing bone, will it translate into the same score as if the inactivity was due to extreme weakness and fatigue?

Yes, as the person will be less able to ambulate. If in full traction, PPS would likely be PPS 40% since he or she is bed-bound but can do some self care. If in a cast and using a walker or crutches, PPS might be 50%. It would also be expected that, all things being equal, the PPS will increase shortly as mobilization improves.

How is the "Intake" domain scored for patients whose primary or total intake is via a feeding tube?

This is a situation where the intake is difficult to interpret.

Use the other four domains to determine the PPS level, regardless of intake.

Try to incorporate observations that the tolerability and the volume of fluid given via parenteral tubes usually decreases with overall decline and closeness to death.

Can PPS be used in the paediatric population?

There is no evidence to support its use in children. Generally, the Lanksy Play-Performance Scale is used in children. This scale uses a parent's description of the child's activity to assess ability and response to treatment.

Karnofsky Scale (recipient age ≥ 16 years)		Lansky Scale (recipient age <16 years)	
Able to carry on normal activity; no special care is needed		**Able to carry on normal activity; no special care is needed**	
100	Normal, no complaints, no evidence of disease	100	Fully active
90	Able to carry on normal activity	90	Minor restriction in physically strenuous play
80	Normal activity with effort	80	Restricted in strenuous play, tires more easily, otherwise active
Unable to work, able to live at home cares for most personal needs, a varying amount of assistance is needed		**Mild to moderate restriction**	
70	Cares for self, unable to carry on normal activity or to do active work	70	Both greater restrictions of, and less time spent in active play
60	Requires occasional assistance but is able to care for most needs	60	Ambulatory up to 50% of time, limited active play with assistance/supervision
50	Requires considerable assistance and frequent medical care	50	Considerable assistance required for any active play, fully able to engage in quiet play
Unable to care for self, requires equivalent of institutional or hospital care, disease may be progressing rapidly		**Moderate to severe restriction**	
40	Disabled, requires special care and assistance	40	Able to initiate quite activities
30	Severely disabled, hospitalization indicated, although death not imminent	30	Needs considerable assistance for quiet activity
20	Very sick, hospitalization necessary	20	Limited to very passive activity initiated by others (e.g., TV)
10	Moribund, fatal process progressing rapidly	10	Completely disabled, not even passive play

References specific to PPS

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- Paediatric Formulary Committee. *BNF for Children* 2021-2022. Pharmaceutical Press; 2021. 1248 p.
- British Columbia Children's Hospital. BC Children's and Women's Hospital (C&W) Online Formulary. 2023 [cited 2023 Aug 8]. Available from: http://www.pedmed.org/DrugApp/index.html

Suggested Further Reading

Resources which can be freely downloaded

Amery J. A REALLY PRACTICAL HANDBOOK OF CHILDREN'S PALLIATIVE CARE for Doctors and Nurses Anywhere in the World. 2016: Lulu Publishing Services; 466 p.

https://www.lulu.com/shop/justin-amery/a-really-practical-handbook-of-childrens-palliative-care/ebook/product-22659977.html?page=1&pageSize=4

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MEDICATIONS

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Amitriptyline	Serotonin and noradrenalin (norepinephrine) reuptake inhibitor. Also blocks sodium channels, muscarinic, 5HT2A, 2C, H1, and alpha1 receptors	**PO:** 0.1-0.5 mg/kg/dose qHS **Max initial dose:** 10 mg May increase by 0.1-0.2 mg/kg/dose q5-7days **Max:** 2 mg/kg/day or 150 mg/day	Neuropathic Pain: **PO:** start with 10 mg qHS. Increase to 25 mg after 3-7 days. Can increase (if needed) by 25 mg q7 days. **Max:** 150 mg qHS	Anticholinergic, antihistaminergic and antimuscarinic. Sedation, delirium, postural hypotension, hyponatremia, urinary retention, dry mouth, blurred vision, mydriasis, tachycardia, arrhythmias, extrasystoles. Caution use with other drugs metabolized by CYP2D6
Atropine	Tertiary Amine. Blocks acetylcholine in parasympathetic smooth muscle, secretory glands, and CNS. Muscarinic antagonist Uses: managing oropharyngeal secretions	**Buccal:** 1% eye drops - 1-4 drops (each drop contains approximately 0.5mg atropine) under the tongue q2-4h PRN	**SUBQ:** 0.4-0.6mg q4-6h PRN	Antimuscarinic effects (drowsiness, cognitive impairment, delirium, agitation, mydriasis, blurred vision, tachycardia, palpitations, arrhythmias, dry mouth, heartburn, constipation, urinary retention, reduced sweating) At toxic doses: central vagal excitation, respiratory stimulation, agitation, delirium

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Baclofen	Binds to GABA receptors, resulting in hyperpolarization of neurons to relieve muscle spasticity	**PO:** 02.5-5 mg PO TID. Titrate by 5 mg q3-7days **Max:** 40-80 mg/day	**PO:** PO: Start with 5 mg TID. May increase by 5 mg per dose every 3 days based on response/ tolerability. **Max:** 80 mg/day	Drowsiness, dizziness, fatigue, nausea, vomiting
Bisacodyl	Directly irritates smooth muscles of intestine (colonic intramural plexus) to stimulate peristalsis; promotes water and electrolytes secretions into bowel	**PO:** 0.3 mg/kg/ dose PO once daily >10 years: 5-10 mg PR once daily **Max:** 15 mg/dose **Rectal:** >5 years: 5-10mg once daily	**PO:** 5 to 15 mg PO once daily **Rectal:** 10 mg once daily	Abdominal pain, diarrhoea, ischemic colitis, headaches Tablets may be enterically coated: Do not chew or crush these tablets and do not give within 1 hour of antacids or milk products

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Carba-mazepine	Inhibits voltage-gated sodium channels	**PO:** <6y: Initial dose of 1.7-3.3 mg/kg/dose TID Increase by 2mg/kg/day over several weeks Usual: 5-6.7 mg/kg/dose **Max:** 35 mg/kg/day ≥6y: Initial: 100-200 mg BID Usual: 200-600 mg/dose **Max:** 1000 mg/day in 6-12y; 1600 mg/day >12y	**Neuropathic pain:** **PO:** start with 200-400 mg/day in 2-4 divided doses. Increase in increments of 200 mg/day as needed over several weeks. Usual maintenance dose: 600-800 mg/day in 2-4 divided doses **Max:** 1200 mg/day **Seizure Control:** **PO:** 50-100mg BID; if necessary, increase by 50-100 mg increments every 1-2 weeks Usual maintenance dose: 800-1200mg/day (divided BID) Note: Titrate slowly, to avoid Stevens-Johnson Syndrome risk, use modified-release tablets for doses larger than 100 mg	Drowsiness, dizziness, fatigue, blurred vision, constipation, nausea, vomiting, photosensitivity, increased liver function tests, osteopenia Rash (benign or severe including Stevens-Johnson syndrome and toxic epidermal necrolysis), hypersensitivity syndrome Teratogenicity (especially in 1st trimester)
Cetirizine	Second generation antihistamine. Inhibits histamine (H1)	**PO:** 6 mo-2y: 2.5 mg once daily 2-5y: 2.5-5 mg once daily >5y: 5-10 mg once daily	**PO:** 5-10 mg once daily **Max:** 10 mg/day	Drowsiness, fatigue, headache

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Chlor-promazine	Low potency first-generation antipsychotic. Inhibits dopamine receptors, but also alpha-adrenergic, histamine, muscarinic, and serotonin receptors	**IV/PO:** 0.5-1 mg/kg/dose q6-8h **Max:** 50 mg/dose	**PO:** 15-50 mg once daily. Titrate up to 3-4 times daily **Max:** 200 mg/day	Drowsiness, dizziness, hypotension, tachycardia, blurry vision, dry mouth, constipation, urinary retention extrapyramidal symptoms, hyperprolactinemia (with regular use) Avoid in seizure disorders and delirium. Caution in prolonged QTc Avoid long term use due to risk of tardive dyskinesia Poorly tolerated in elderly
Clonazepam	Benzodiazepine binds to GABA-A receptors which enhances the inhibitory effect on the cortical and limbic systems		**PO:** Start with 0.5-1.5 mg/day in 1-3 divided doses. May increase in increments of 0.5-1 mg q3-7days based on response/tolerability to usual maintenance dose of 2-8 mg/day in 1-2 divided doses **Max:** 20 mg/day	Drowsiness, dizziness, ataxia, respiratory depression, hypotension

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Clonidine	Non-selective stimulation of alpha-2 adrenergic receptors in the brainstem, resulting in decreased sympathetic outflow and peripheral resistance	**PO:** 1-2 mcg/kg/dose q4-6h. Titrate to effect **Max:** 4 mcg/kg/dose or 200 mcg/dose or 10 mcg/kg/day or 800 mcg/day	**PO:** Start with 100 mcg BID. Increase in increments of 100 mcg/day at weekly intervals. Usual dose: 200-600 mcg/day in 2 divided doses **Max:** 2400 mcg/day (manufacturer); but generally >800 mcg/day (clinical practice)	Dizziness, hypotension, bradycardia, drowsiness, headache, rebound hypertension (with abrupt discontinuation of consistent use)
Codeine	Full opioid agonist: binds to opioid receptors in CNS, causing inhibition of ascending pain pathways, altering the perception of and response to pain; causes cough suppression by direct central action in the medulla; produces generalized CNS depression	Should not be used in children < 12 years of age. Only consider if lack of other options available or other medications are contraindicated. Additionally, avoid in patients with increased risk of respiratory depression Children > 12 yrs: **PO/SUBQ:** 0.5-1 mg/kg/dose q3-6h PRN **Max:** 60 mg/dose, 240 mg/day	**Pain:** **PO:** Start with 15-60 mg every 4 hours PRN **Max:** 360 mg/day; patient with prior opioid exposure may require higher initial doses **Cough:** **PO:** 30-60 mg QID	Drowsiness, dizziness, constipation, respiratory depression

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Desipramine	Serotonin and noradrenalin (norepinephrine) reuptake inhibitor. Also blocks sodium channels, muscarinic, 5HT2A, 2C, H1, and alpha1 receptors		**PO:** Start with 12.5-25 mg once or twice daily. Increase dose q2-7days based on response/ tolerability up to 150 mg/day	Anticholinergic, antihistaminergic and antimuscarinic Sedation, delirium, postural hypotension, hyponatremia, urinary retention, dry mouth, blurred vision, mydriasis, tachycardia, arrhythmias, extrasystoles Caution use with other drugs metabolized by CYP2D6
Dex-amethasone	Long-acting corticosteroid with minimal mineralocorticoid effect. Reduces downstream effects of inflammatory mediators. Antiemetic mechanism not completely known	**IV/PO:** 0.25-0.6 mg/kg/dose q6-24h **Max:** 16 mg/day See separate sections for specific dosing in cough, nausea/ vomiting, malignant spinal cord compression, and superior vena cava syndrome	**PO/SUBQ** High dose: 8 mg Low dose: 2-6 mg BID or once daily	Abdominal pain, heartburn, nausea, vomiting, hyperglycemia, hypertension, bradycardia, insomnia, acute psychiatric reactions (psychosis), increased liver function tests Long-term risks include adrenal suppression, osteonecrosis, osteoporosis, immunosuppression

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Dextrome-thorphan	Activates sigma opioid receptors on the medullary cough centre, resulting in suppression of the cough reflex	**PO:** 6-11y: 10 mg q4h PRN **Max:** 60 mg/day ≥12y:20 mg q4hr PRN **Max:** 120 mg/day	**PO:** 15-30 mg q4-8h **Max:** 120 mg/day	Drowsiness, nausea Weak evidence to support routine use in children. Not recommended in <6 years old.
Diazepam	Long-acting benzodiazepine. Binds to GABA-A receptors which enhances the inhibitory effect on the cortical and limbic systems	**IV/IO/SUBQ:** 0.3 mg/kg/dose **Max:** 5 mg in <5y; 10 mg in ≥5y	**IV/SUBQ/PR:** 5-10 mg q3-4h PRN **Max:** 30 mg/dose	Drowsiness, dizziness, hypotension, respiratory depression, paradoxical excitation (especially in children) Caution use in patients with hepatic dysfunction and high risk of respiratory depression
Diclofenac	Reversibly inhibits COX-1 and -2 enzymes resulting in decreased formation of prostaglandin precursors to exert antipyretic, analgesic, and anti-inflammatory effect	**PO:** 0.7-1 mg/kg/dose TID PRN OR 1-1.5 mg/kg/dose BID PRN **Max:** 50 mg/dose PR: 0.5-1 mg/kg/dose BID-TID PRN **Max:** 50 mg/dose, 100 mg/day	**PO/SUBQ:** 50 mg q8-12h (Immediate release formulation) OR 75 mg q12h (Sustained release formulation) **PR:** 50-100 mg q8h	Abdominal pain, heartburn, nausea, vomiting, edema, hypertension, thrombotic events (e.g. stroke), prolonged bleeding, renal dysfunction Use with caution in patients with cardiac, hepatic, or renal impairment, and asthma

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Dimen-hydrinate	Inhibits histamine (H1) receptor	**PO/IV/SUBQ/PR:** 0.5-1.25 mg/kg/dose q6h PRN **Max:** 50 mg/dose, 300 mg/day	**PO/IV/SUBQ/PR:** 50 mg q4-8h CSCI : 150 mg per 24 hours	Drowsiness, dry mouth, blurred vision, constipation, paradoxical excitation and insomnia (especially in children)
Diphen-hydramine	First generation antihistamine. Inhibits histamine (H1) receptors	**PO/IV/SUBQ:** 0.5-1 mg/kg/dose q6-8h PRN **Max:** 50 mg/dose	**PO/IV/SUBQ:** 25-50 mg q4-8h PRN	Drowsiness, dry mouth, blurred vision, constipation, paradoxical excitation and insomnia (especially in children)
Domperidone	Increases gastric motility and emptying by inhibiting peripheral dopamine receptors	**PO:** 0.4-0.8 mg/kg/dose TID or 0.3-0.6 mg/kg/dose QID **Max:** 10 mg/dose	**PO:** 10 mg TID-QID	Headache, dry mouth, abdominal cramping, hyperprolactinemia, QTc prolongation, cardiovascular events Avoid in co-existing cardiac disease, moderate or severe liver dysfunction, significant electrolyte abnormalities, or on QTc prolonging drugs QTC prolongation risk >30 mg/day

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Epinephrine	Stimulates alpha, beta-adrenergic receptors resulting in relaxation of smooth muscle of bronchial tree		**Anaphylaxis:** **IM:** 0.3-0.5 mg q5 minutes PRN up to 3 doses Asthma/reversible bronchospasm: **SUBQ** 0.3-0.5 mg q20minutes PRN (max 3 doses) or **Nebulized:** 5 mg over 10-15 minutes; may repeat q3h PRN **Topical:** (for bleeding malignant wounds): Apply epinephrine (1 mg/mL) soaked gauze topically and cover with dressing	Hypertension, pulmonary edema
Famotidine	Competitively inhibits histamine (H2) receptors of the gastric parietal cells to inhibit gastric acid secretion	**PO:** 0.5-1 mg/kg/dose q12-24h **Max:** 40 mg/dose **IV:** 0.25-0.5 mg/kg/dose q12-24h **Max:** 20 mg/dose	**PO/IV:** 10-20 mg BID PRN **Max:** 40 mg/day **Onset:** within 1 hour **Duration:** 10-12 hours (PO,IV)	Headache, constipation, diarrhoea
Fentanyl (transdermal patch)	Full opioid agonist binding to mu opioid receptors within CNS, increasing pain threshold, altering pain reception and inhibiting ascending pain pathways		To determine dose, calculate patient's 24-hour OME requirement. With OME, use dose conversion table to convert to appropriate fentanyl transdermal dose (45 mg/day OME = 12 mcg/h fentanyl)	Constipation, nausea/vomiting, sedation, drowsiness, delirium, urinary retention, syncope, myoclonus, respiratory depression

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Furosemide	Inhibits reabsorption of sodium and chloride in the proximal and distal tubules and ascending loop of Henle, leading to increased excretion of sodium and water	**PO/IV/SUBQ:** 0.5-2 mg/kg/dose q6-24h. Titrate by 1-2mg/kg/dose to achieve desired response. **Max:** 6 mg/kg/dose or 80 mg/dose	**PO/IV/SUBQ:** Start with 20-80 mg daily-BID. Then titrate PRN to effective dose **Max:** effective single dose: 80-200 mg depending on renal function **Max total daily dose:** 600 mg/day	Hypotension, hypokalemia, hypomagnesemia, hypocalcemia, hyperuricemia, alkalosis, acute kidney injury, reversible tinnitus
Gabapentin	Structurally similar to GABA. Inhibits voltage-gated calcium channels to modulate the release of excitatory neurotransmitters involved in nociception and elipetogenesis	**PO:** 5 mg/kg/dose daily x 3 days, then increase to BID, then TID, titrate up every 3-5 days **Max initial dose:** 300 mg Usual dosing range 15-60 mg/kg/day **Max:** 3600 mg/day	**PO:** Start with 100-300 mg TID. Increase dose based on response/tolerability to target dose of 300-1200 mg PO TID. **Max:** 3600 mg/day	Drowsiness,, dizziness, ataxia, fatigue, nausea, constipation Separate from antacids by at least 2 hours
Glycerin	Osmotic laxative. Draws fluid into colon by increasing osmotic pressure to stimulate evacuation	**PR:** <2y: Tip of paediatric suppository (~0.25-3 g) 2-6y: 1 paediatric suppository (1-2 g) >6y: 1 adult suppository (>2 g) >6y: 1 adult suppository (>2 g)	**PR:** 1 suppository. Suppository should be retained for 15 minutes.	Abdominal cramping, tenesmus, mild rectal irritation Avoid suppositories in patients with severely reduced WBC or platelet counts due to risk of bleeding or infection

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Glyco-pyrronium/ glycopyrrolate	Competitively inhibits muscarinic receptors in smooth muscle, secretory glands, and the central nervous system.	**PO:** 40-100 mcg/kg/dose q6-8h **Max:** 3000 mcg/dose **IV/SUBQ:** 4-10 mcg/kg/dose q3-4h **Max:** 200 mcg/dose	**IV/SUBQ:** 0.2-0.4 mg q4-6h **CSCI:** 0.6-1.2 mg per 24 hours	Does not cross blood brain barrier; CNS adverse effects may be minimized
Guaifenesin	Expectorant. Reduces the viscosity of respiratory mucus to facilitate removal by natural processes	**PO:** 6-11y: 100-200 mg q4h PRN **Max:** 1200 mg/day ≥12y: 200-400 mg q4h PRN **Max:** 2400 mg/day	**PO:** 200-400 mg q4h PRN **Max:** 2.4 g/day	Nausea, vomiting Weak evidence to support routine use in children. Not recommended in <6 years old
Haloperidol	Inhibits postsynaptic dopamine (D2) receptors	**PO/IV/SUBQ/ IM:** 0.01-0.05 mg/kg/dose q6-24h **Max:** 0.5 mg/kg/day or 30 mg/day See chapters for specific dosing in nausea/vomiting and delirium	**PO/IV/SUBQ/ IM:** 0.5-5 mg q8h **CSCI:** 1.5-5 mg 24 hours	Sedation, hypotension, extrapyramidal symptoms (e.g. dystonia), prolonged QTc interval, delirium, hyperprolactinemia (with regular use) Caution use in patients with epilepsy and receiving QTc prolonging drugs, metoclopramide (increased risk of EPS) PO haloperidol is 60-70% bioavailable, consider reducing SUBQ, IV, IM dose by 30%.

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Hydro-chlorothiazide	Inhibits sodium reabsorption in the distal tubules, leading to increased excretion of sodium and water (as well as potassium and hydrogen)	**PO:** 1-2 mg/kg/dose BID **Max:** 100 mg/day	**PO:** Start with 25-50 mg daily or BID Increase dose as needed based on response and tolerability **Max:** 200 mg/day.	Hyponatremia, hypokalemia, hypomagnesemia, photosensitivity, gout
Hydroxyzine	First generation antihistamine. Inhibits histamine (H1) receptors.	**PO:** 0.5-0.7 mg/kg/dose TID-QID **Max:** 2 mg/kg/day or 100 mg/day	**PO:** 10-25 mg TID-QID. May increase dose in 10-25 mg increments at weekly intervals based on response/tolerability **Max:** 200 mg/day	Drowsiness, dizziness, dry mouth, blurred vision, constipation
Hyoscine BUTYL-bromide (Buscopan®)	Same as atropine	**IV/SUBQ:** <5y: 0.3 mg/kg/dose q6-8h 5-12y: 5-10 mg q6-8h ≥12y: 10-20 mg q6-8h	**IV/SUBQ:** 20 mg STAT then repeat 20 mg q4-6h **CSCI:** 60-120mg/24h	*Does not cross blood-brain-barrier (BBB) (Use TALLman lettering to avoid confusion with hydrobromide)
Hyoscine HYDRO-bromide	Same as atropine	**PO/IV/SUBQ:** 5-6 mcg/kg/dose q6-8h **Max:** 300 mcg/dose **Transdermal:** ½ patch (12-17 kg) or 1 patch (≥17 kg) topically q48-72hrs	**IV/SUBQ:** 400-600mcg q4-6h **Transdermal:** 1 patch topically q48-72hrs	Can be sedating Avoid in end-stage renal failure (increased risk of delirium)

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Ibuprofen	Reversibly inhibits COX-1 and -2 enzymes resulting in decreased formation of prostaglandin precursors to exert antipyretic, analgesic, and anti-inflammatory effect	**PO:** 5-10 mg/kg/dose q6-8h PRN **Max:** 40 mg/kg/day or 2400 mg/day	**PO:** 200-800 mg q8h **Max:** 2400 mg/day	Abdominal pain, heartburn, nausea, vomiting, edema, hypertension, thrombotic events (e.g. stroke), prolonged bleeding, renal dysfunction Use with caution in patients with cardiac, hepatic, or renal impairment, and asthma
Ketamine* (WHO)	Non-competitive NMDA receptor antagonist. Provides general/procedural anesthesia, analgesia Of note, spontaneous respiration and airway tone maintained	**PO:** 5-10 mg/kg/dose **IV:** 0.5-2 mg/kg/dose May administer 0.5 - 1 mg/kg/dose IV q5-15 mins as required **IN:** 3-6 mg/kg/dose **CSCI:** 100-1200 mcg/kg/hr **Onset:** 30-60 sec (IV), 5-10 min (IN), 15-30 min (PO) **Duration:** 5-10 min (IV), up to 60 min for analgesia (IN), 60 min or greater (PO)	**Analgesic adjuvant:** **PO:** start with 10-25 mg q8h. Titrate in steps of 10-25 mg **Max:** 200 mg PO q6h. **CSCI:** 100mg over 24 hours. Increase after 24 hours to 300 mg CSCI over 24 hours and further increase to 500 mg CSCI over 24 hours if ineffective	Oropharyngeal secretions, laryngospasm, increased blood pressure, emergence reaction (including agitation, confusion, and delirium)

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Ketorolac	NSAID. Reversibly inhibits COX-1 and -2 enzymes resulting in decreased formation of prostaglandin precursors to exert antipyretic, analgesic, and anti-inflammatory effects	**PO:** 1 mg/kg/dose q4-6h PRN **Max:** 10 mg/dose **IV:** 0.2-0.5 mg/kg/dose q6-8h PRN **Max:** 30 mg/dose Usual duration of therapy is 48-72h, max of 5 days to minimize risk of adverse effects	**PO:** 20 mg once, followed by 10-30 mg q4-6h PRN **Max:** 120 mg/day, max duration: 5 days total **IV:** 15 mg once or 15 mg q6h PRN **Max:** 60 mg/day; max duration: 5 days total	Abdominal pain, heartburn, nausea, vomiting, GI ulceration and bleeding, edema, hypertension, thrombotic events (e.g. stroke), prolonged bleeding, renal dysfunction Use with caution in patients with cardiac, hepatic, or renal impairment, and asthma
Lamotrigine (WHO)	Anticonvulsant inhibits release of excitatory glutamate and inhibits voltage-sensitive sodium channels, which stabilizes neuronal membranes		**PO:** Start with 25 mg daily x 2 weeks, then 50 mg/day in 1-2 divided doses x 2 weeks, then increase daily dose by 50 mg q1-2 weeks to max 400 mg/day in 1-2 divided doses	Caution with concurrent medications which inhibit lamotrigine metabolism, warranting more gradual, lower and slower dose titration (50% of typical titration dosing regimen) Rash (if develops, discontinue lamotrigine)

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Levomepromazine (Methotrimeprazine)	A phenothiazine that antagonizes dopamine, serotonin, histamine and muscarinic receptors, giving rise to antipsychotic, antiemetic, anxiolytic, analgesic and sedative	**PO:** 0.125-0.5 mg/kg/day divided BID to TID **IV:** 0.0625-0.125 mg/kg/day divided BID to QID **Max:** 0.5 mg/kg/dose, 50 mg/dose	**PO:** 6-25 mg/day divided TID May increase based on response/tolerability **SUBQ:** 6.25 mg/day daily or BID **CSCI:** 6-250 mg/day	Sedation, anticholinergic effects (dry mouth, urinary retention), orthostatic hypotension, extrapyramidal
Lidocaine	Class Ib antiarrhythmic. Blocks sodium channels thereby blocking the initiation and conduction of nerve impulses resulting in local anaesthesia	**SUBQ infiltration:** Up to 4.5 mg/kg/dose (0.9 mL/kg of lidocaine 0.5%, or 0.45 mL/kg of lidocaine 1% or 0.225 mL/kg lidocaine 2%) **Max:** 300 mg Not to be administered in intervals of less than 2 hours	**IV/SUBQ:** 5-12.5 mg/kg over 120 minutes q2 weeks OR **IV/SUBQ:** continuous infusion 0.5-2 mg/kg/hr	Pain, redness and burning at the injection site, edema, respiratory depression Increased risk of methemoglobinemia in patients with G6PD deficiency Use with caution in patients with cardiac failure Dose adjustment required in hepatic or renal impairment

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Loperamide	Binds to the mu opioid receptors in the intestinal muscles thereby inhibiting peristalsis and increasing gut transit time in order to reduce fecal volume, increase viscosity and decrease fluid and electrolyte depletion	**PO:** 2-5 yrs: 1 mg after first loose stool, 1 mg/dose after each subsequent loose stool **Max:** 3 mg/day 6-8 yrs: 2 mg after first loose stool, 1 mg/dose after each subsequent loose stool **Max:** 4 mg/day 8-11 yrs: 2 mg after first loose stool, 1 mg/dose after each subsequent loose stool **Max:** 6 mg/day ≥12yrs: 4 mg after first loose stool, 2 mg/dose after each subsequent loose stool **Max:** 16 mg/day	**PO:** 4 mg, followed by 2 mg after each loose stool **Max:** 16 mg/day For diarrhoea persisting >24 hours, administer 2 mg q2h Continue until 12 hours have passed without a loose bowel movement	Abdominal cramping and discomfort, constipation, nausea, vomiting, sedation Should be avoided in children with acute gastroenteritis in order to not delay the passage of infectious agents
Lorazepam	Benzodiazepine. Binds to benzodiazepine receptors of postsynaptic GAGA chloride channel neurons resulting in the enhanced inhibitory effect of GABA	**PO/SL/IV/SUBQ:** 0.025 - 0.05 mg/kg/dose q4-8h PRN **Max:** 2 mg/dose Note: for seizures, 0.1 mg/kg/dose **Max:** 4 mg/dose	For status epilepticus: **IV/SUBQ/SL:** usual dose of 4mg (range of 2-8 mg) STAT then repeat dose q10-20 minutes until controlled	Drowsiness, respiratory depression (especially in combination with opioids), psychomotor impairment, hypotension, habit-forming potential Risk of propylene glycol toxicity with repeated dosing in renal impairment

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Megestrol Acetate	Synthetic derivative of progesterone. Mechanism for appetite stimulation unknown	**PO:** 7.5-10 mg/kg/day daily to BID **Max:** 15 mg/kg/day, 800 mg/day	**PO:** 160-800 mg PO once daily If initial response poor, can double dose after 2 weeks	Skin rash, impotence, hypertension, nausea/vomiting, flatulence
Methadone* ***requires additional expert training and supervision**	Synthetic opioid agonist that binds to the mu receptor thereby inhibiting ascending pain pathways, altering the perception of and response to pain. Also has NMDA receptor antagonism	Opioid naive: <6 mo: **PO:** 0.05 mg/kg/dose q4-8h PRN >6 mo: **PO:** 0.1-0.2 mg/kg/dose q4-8h PRN **Usual Max:** 5-10 mg/dose Titrate to effect to max 30 mg/dose **Onset:** 10-20 min (IV), 30-60 min (PO) **Duration:** 4-8h (PO) but can increase with repeat exposure	Opioid naïve: **PO:** start with methadone 2.5-5 mg q8-12h. May increase dose by 2.5 mg per dose no more often than q5-7 days (gradual titration) or by 2.5-5 mg per dose q3 days (faster titration, monitored). Once stable dose is reached, the dosing interval may be extended to q8-12h or longer Some guidelines note dose increases should not be >10 mg/day Q5-7 days Opioid-tolerant: There are several proposed ratios for converting OME to PO methadone (refer to conversion tables). Total PO methadone dose should be divided to	QT prolongation, cardiac dysrhythmias, CNS depression, respiratory depression, hypotension, sweating, constipation Associated with significant variability in absorption, metabolism and analgesic potency. Accumulation occurs with repeated dosing secondary to long half life, which can contribute to significant sedation and respiratory depression Potential for many drug-drug interactions

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
			reflect intended schedule. Patients who have not taken opioid for 1-2 weeks should be considered opioid naïve The higher the daily OME, the more potent methadone is. Starting dose should not exceed 30-40 mg/day, even in patients on high doses of other opioids	
Metoclo-pramide	Antagonist of dopamine and serotonin receptors in the chemoreceptor trigger zone of the CNS. It also increases GI motility and accelerated gastric emptying by promoting increased acetylcholine release	**PO/IV/SUBQ:** 0.1-0.2 mg/kg/dose q6-8h **Max:** 10 mg/dose, 0.5 mg/kg/day	**PO/IV/SUBQ:** 5-10 mg TID-QID given before meals **CSCI:** 30-60 mg/24hrs	Extrapyramidal symptoms (dystonia, akathisia, parkinsonism, tardive dyskinesia), drowsiness, restlessness, diarrhoea Avoid using in combination with other drugs that can cause EPS Avoid in complete bowel obstruction

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Midazolam	Benzodiazepine. Binds to benzodiazepine receptors of postsynaptic GAGA chloride channel neurons resulting in the enhanced inhibitory effect of GABA	**IV:** 0.025-0.1 mg/kg/dose **Max:** 10 mg **IN:** 0.2-0.5 mg/kg/dose **Max:** 10 mg, 5 mg per nostril **PO:** 0.25-0.5 mg/kg/dose **Max:** 20 mg **CSCI:** 25-500 mcg/kg/hr	Palliative sedation: specialist level intervention **IV/SUBQ :** 2.5-5 mg q5-15minutes PRN Usual dose: 0.25-5 mg. If infusion, start with 0.25-1 mg/h, titrate for symptom management **CSCI:** usual dose range: 0.5-5 mg/h up to 20 mg/h for some patients Status epilepticus: **IV/SUBQ/IM:** 10 mg x 1 over 2 mins or 0.2 mg/kg x 1, repeat after 10-20minutes if seizure persists **Max:** 10 mg per dose If refractory, follow with continuous **IV/SUBQ infusion** at 0.05-2 mg/kg/h	Drowsiness, respiratory depression (especially in combination with opioids), psychomotor impairment, hypotension, habit-forming potential Intranasal administration can cause burning sensation Rapid tolerance (48-72h) with continuous infusion resulting in higher dosage requirements

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Morphine	Binds to opioid receptors thereby inhibiting ascending pain pathways, altering the perception of and response to pain	Opioid-naive patients: <6 mo of age: **PO/SL:** 0.05-0.1 mg/kg/dose q3-4h PRN **IV/SUBQ:** 0.025-0.05 mg/kg/dose q2-4h PRN >6 mo of age: **PO/SL:** 0.2-0.3 mg/kg/dose q4-6h PRN, usual max starting dose of 10-15 mg **IV/SUBQ:** 0.05-0.1 mg/kg/dose q2-4 h PRN, usual max starting dose of 2-5 mg **Continuous IV or SUBQ Infusion:** Start at 20-40 mcg/kg/hr and increase incrementally by 10 mcg/kg/hr, usual maximum infusion of 100 mcg/kg/hr Dyspnoea: **IV/SUBQ:** 0.05mg/kg q4h PRN OR PO 0.1 mg/kg q4h PRN	Pain: Opioid-naïve: **PO:** start with morphine 5-10 mg q4h PRN **IV:** 2-5 mg q1-4h PRN. Adjust dose based on response/ tolerability Dyspnoea: **PO:** 2.5 mg q4h OR **IV/SUBQ:** 1-1.5 mg q4h. If severe dyspnoea, consider morphine **IV/SUBQ:** 5 mg q5-10 minutes PRN	Drowsiness, constipation, pruritus, respiratory depression, psychomotor impairment, hypotension, habit-forming potential Have the potential to cause withdrawal syndrome if abruptly discontinued in patients maintained on therapy for a week or more. Gradual taper required when morphine discontinued Adjust dose in renal impairment due to reduced clearance of and accumulation of neurotoxic metabolite Doses for dyspnoea are generally 50% less than those for pain, in opioid naïve patients

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Naproxen	NSAID. Reversibly inhibits COX-1 and -2 enzymes resulting in decreased formation of prostaglandin precursors to exert antipyretic, analgesic, and anti-inflammatory effects	**PO/PR:** 5-10 mg/kg/dose q12h **Max:** 1000 mg/day	**PO/PR:** 250-500 mg q12h PRN or 250 mg q6-8h PRN **Max:** 1 g/day	Abdominal pain, heartburn, nausea, vomiting, edema, hypertension, thrombotic events (e.g. stroke), prolonged bleeding, renal dysfunction Administer with food to decrease GI adverse effects Use with caution in patients with cardiac, hepatic, or renal impairment, and asthma Avoid concomitant administration with other NSAIDs
Octreotide		Diarrhoea: **IV/SUBQ:** 1-10 mcg/kg/dose q8-12h **Continuous IV or SUBQ infusion:** 24-48 mcg/kg/hr	Chemotherapy associated diarrhoea: **IV/SUBQ:** Low grade/uncomplicated: 100-150 mcg TID Severe/complicated: 100-150 mcg TID, may increase to 500-2000 mcg Variceal haemorrhage: **IV:** 50 mcg bolus, followed by 50 mcg/h by continuous IV infusion	Abdominal pain, diarrhoea, nausea, vomiting, hyperglycemia, hypertension, diaphoresis, injection site pain

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
			Malignant bowel obstruction: **IV/SUBQ:** 200-900 mcg/day in 2-3 divided doses or by CSCI	
Olanzapine	Atypical antipsychotic. Although the actual mechanism is unclear, it likely exerts an antagonistic effect by binding to serotonin and dopamine receptors	**PO:** 2.5-5 mg daily Titrate by 2.5-5 mg/week **Max:** 15-20 mg/day Acute agitation: **IM:** <10 yrs: 1.5-5 mg >10 yrs: 5-10 mg Repeated doses: 5-10 mg 2 hours after first dose and third dose 4 hours after second dose	Nausea/vomiting: **PO:** 2.5-10 mg daily or BID x 3 days Hyperactive delirium/ agitation: **PO:** 1.25-5 mg once daily PRN. Titrate daily based on response in 2.5-5 mg increments up to 20 mg/day **IM:** 2.5-5 mg once daily or PRN **Max:** 20 mg/day	Somnolence, dizziness, orthostatic hypotension, anticholinergic effects, weight gain, hyperglycemia Avoid administering IM olanzapine within one hour of a parenteral benzodiazepine due to potential for respiratory depression and death Cigarette smoke can increase clearance of drug by up to 40%
Omeprazole	Proton pump inhibitor. Inhibits the H+/K+ ATP pump of parietal cells resulting in the suppression of gastric acid secretion	**PO:** 0.7-3.5 mg/kg/dose daily or 0.35-1.25 mg/kg/dose BID **Max:** 3.5 mg/kg/dose or 40 mg/day	**PO:** 20-40 mg once to twice daily	Diarrhoea, nausea, headache

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Ondansetron (on WHO)	5-HT3 receptor antagonist that blocks binding of serotonin on vagal nerve terminals of the GI tract and in chemoreceptor trigger zones in the brain	**PO/IV:** 0.15-0.2 mg/kg/dose q8-12h **Max:** 8 mg/dose Single-dose regimen for chemotherapy- or radiation-induced nausea/vomiting: **PO:** 8-14 kg: 2 mg 15-30 kg: 4 mg >30 kg: 8 mg	**PO/IV/SUBQ:** 4-8 mg q8-12h **CSCI:** 16-24 mg per 24 hours **Max:** 24 mg/day	Headache, constipation, dizziness Potential for QT prolongation - avoid in patients with congenital long QT syndrome, caution when administering in conjunction with other QT prolonging medications
Oxycodone	Binds to opioid receptors thereby inhibiting ascending pain pathways, altering the perception of and response to pain	**PO:** 0.1-0.2 mg/kg/dose q4-6h PRN **Max:** 10-20 mg/dose **Onset:** 10-15 min **Duration:** 3-6h	**PO:** Opioid naïve: start with 2-10 mg q4-6h PRN. Adjust dose based on response. Usual dose: 5-15 mg PO q4-6h PRN	CNS depression, constipation, hypotension, respiratory depression, nausea, vomiting Conversion from oxycodone may require some precaution due to potential of variable polymorphism and different active metabolites produced

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Pantoprazole	Proton pump inhibitor. Inhibits the H^+/K^+ ATP pump of parietal cells resulting in the suppression of gastric acid secretion	**PO/IV:** 1-1.5 mg/kg/dose q24h **Max:** 40 mg/day GI bleed: **IV:** 5-15 kg: 2 mg/kg/dose x 1 then 0.2 mg/kg/hr infusion >15-40 kg: 1.8 mg/kg/dose x 1 and then 0.18 mg/kg/hr infusion >40 kg: 80 mg/dose x 1 then 8 mg/hr infusion **Max:** 80 mg/dose Max rate: 8 mg/hr Max infusion duration: 72 hours	**PO/IV:** 40 mg once daily. In patients with refractory or recurrent disease, may increase the dose to 40 mg BID Upper GI bleed: **IV:** 80 mg bolus, followed by 8 mg/hr infusion x 72 hours prior to endoscopy. If no endoscopy performed within 12 hours, 80 mg bolus, followed by 40 mg q12h Where IV PPIs are unavailable, high-dose oral PPI therapy may be a reasonable alternative – consider using pantoprazole 40 mg PO BID if IV not available	Diarrhoea, nausea, headache, hypomagnesemia, vitamin B12 deficiency, enteric infections (gastroenteritis, C. difficile associated diarrhoea)

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Phenytoin	Anticonvulsant. Promotes the efflux of sodium ions from motor cortex neurons thereby stabilizing the neuronal membranes and inhibiting the spread of seizure activity	**IV/IO:** Loading dose: 20 mg/kg (max: 1500 mg/dose) Repeat dosing (for seizures lasting >10 mins): 5-10 mg/kg/dose Dilute in 0.9% NaCl only. Insoluble precipitates form in D5W Administer at 1-3 mg/kg/min to a maximum of 50 mg/min Maintenance Dose: **PO:** 4-10 mg/kg/day divided q8-12h; adjust dose based on response/serum concentrations **Max:** 300 mg/day	**IV/IO:** Loading dose: 20 mg/kg. Repeat dosing of 5-10 mg/kg 10 mins after loading dose; max total loading dose: 30 mg/kg. OR **PO:** Loading dose: 1 g divided into 3 doses (400 mg, 300 mg, 300 mg) administered at 2-hour intervals; begin maintenance dose 24 hours after first loading dose Maintenance dose: **PO:** 100 mg PO TID-QID; adjust dose based on response/serum concentrations To ensure optimal absorption, individual oral doses should not exceed 400 mg Therapeutic total phenytoin trough concentration: 40-80 umol/L Therapeutic free phenytoin trough concentration: 4-8 umol/L	Drowsiness, hypotension, bradycardia, cardiac arrhythmias, thrombocytopenia, pancytopenia Phenytoin toxicity: Dose related: drowsiness, confusion, nystagmus, ataxia, slurred speech, nausea, unusual behaviour, mental changes, coma (>200 umol/L) Non-dose related: hirsutism, acne, gingival hyperplasia, folate deficiency, osteomalacia, hypersensitivity reactions (including Steven's Johnson syndrome), SLE

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Paracetamol (Acetomin-ophen)	Activates descending serotonergic inhibitory pain pathways, has effects in opioid and cannabinoid systems Antipyrexial mechanism: inhibits heat-regulating centre in hypothalamus	**PO:** 10-15 mg/kg/dose q4-6h PRN **Max:** 75 mg/kg/day or 4000 mg/day **PR:** 10-20 mg/kg/dose q4-6h PRN **Max:** 80 mg/kg/dose or 4000 mg/day Oral drops (but not suspension) may be administered PR	**PO:** 325-1000 mg q4-6h **Max:** 4000 mg/day (those at risk of hepatotoxicity, existing hepatic impairment, or advanced age – do not exceed 2000-3000 mg/day)	**PO:** skin rashes Most likely with IV formulation: dyspepsia, nausea, vomiting
Phenobarbital	Barbiturate. Prolongs the opening of chloride ion channels in postsynaptic neuronal membranes thereby causing hyperpolarization and inhibitions of nerve impulse propagation	Seizures: **IV/IO:** Loading dose: 20 mg/kg/dose Mixed in NS or D5W, infused over 20 minutes **Max:** 1000 mg/dose Repeat dosing (for seizures lasting >10 mins): 5-10 mg/kg/dose Maintenance: **PO/IV:** 3-6 mg/kg/day divided daily to BID (max 200 mg/day) Administer over a minimum of 20 minutes and do not exceed 1 mg/kg/min to a max of 30 mg/min	Seizures: **IV/IO** 10-20 mg/kg IV (infused at 50-100 mg/min); if necessary, may repeat once after 10 minutes with an additional 5-10 mg/kg Maintenance dose: **PO/IV:** 2 mg/kg/day PO/IV in divided doses Sedation: **IV/PO/IM:** 30-120 mg/day in 2-3 divided doses. **Max:** 400 mg/day	Sedation, ataxia, respiratory depression, hypotension, bradycardia, hyperactivity in children (paradoxical reaction), nystagmus

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Phyto-menadione (Vitamin K)	Synthetic lipid-soluble form of vitamin K1. Promotes liver synthesis of clotting factors II, VII, IX and X	Deficiency: **IV/SUBQ:** 1-2 mg once Significant bleed: **IV/SUBQ:** 5mg once Acute fulminant hepatic failure: **IV/SUBQ**: Infant (<1yrs): 1-2 mg Child: 5-10 mg	Vitamin K deficiency coagulopathy: **PO/IV:** 10 mg once; may repeat after 48-72 hours if coagulopathy persists Warfarin reversal, severe bleeding: **PO/IV:** 2.5-10 mg based on INR. Measure INR after 12-48 hours (PO) or 6-12 hours (IV) Note: high doses of vitamin K (e.g. >10-15 mg) may cause warfarin resistance for ≥1 week	Local injection site reaction (pain, swelling), hypotension, flushing Potential for hypersensitivity reactions with IV and IM administration – administer at a max rate of 1 mg/min
Risperidone	Atypical antipsychotic that exert an antagonistic effect on serotonin and	**PO:** 0.25-0.5 mg daily or BID Titrate by 0.5-1 mg every 3-5 days **Max:** 3 mg/day	**PO:** Start with 1-2 mg/day in 1-2 divided doses; may increase by 1-2 mg/day at intervals ≥24 hours to usual dose range 2-6 mg/day. In general, assess full effect for ≥1 week before dose titration **Max:** 6-8 mg/day	Somnolence, orthostatic hypotension, anticholinergic effects, weight gain, extrapyramidal symptoms, hyperprolactinemia, neuroleptic malignant syndrome

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Sennosides	Stimulant laxative that stimulates peristaltic activity in the intestine by irritating the luminal sensory nerve endings thereby stimulating colonic motility	**PO:** Note: based on 8.6 mg tablet <2 years: ½ tablet qHS-BID 2-5 years: ½ to 1 tablet qHS-BID 6-12 years: 1 to 1½ tablet qHS-BID ≥12 years: 2-3 tablets qHS-BID	**PO:** Start with 12-24 mg qHS; may titrate dose based on response/tolerability. **Max:** 36 mg TID	Abdominal cramping, diarrhoea, nausea/vomiting Avoid in bowel obstruction (perforation risk)
Tramadol	Synthetic opioid agonist that weakly binds to opioid receptors thereby inhibiting ascending pain pathways, altering the perception of and response to pain. Also inhibits norepinephrine and serotonin, which are involved in inhibitory pain pathways	**DO NOT USE in children, unless no other opioids available** **Risk due to high variation in liver metabolism and risk of serious harm** **PO:** 1 - 2 mg/kg/dose q4 - 6h PRN **Max:** 100 mg/dose, 8 mg/kg/day or 400 mg/day	**PO:** Start with 50 mg q4-6h PRN. Increase dose as needed and tolerated to 50-100 mg PO q4-6h **Max:** 400 mg/day	Drowsiness, constipation, nausea, respiratory depression, habit-forming potential, lowers seizure threshold, serotonin syndrome (with concomitant CYP 2D6/3A4 inhibitors and other serotonergic agents) Has the potential to cause withdrawal syndrome if abruptly discontinued in patients maintained on therapy for a week or more. Gradual taper required when morphine discontinued

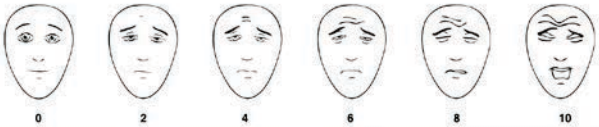
Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Tranexamic Acid	Antifibrinolytic agent. Binds to lysine binding sites on plasminogen, inhibiting plasmin formation and inhibition of fibrinolysis	**PO:** 25 mg/kg/dose q8h **Max:** 1500 mg/dose **IV:** 10 mg/kg/dose q6-8h **Max:** 1000 mg/dose IV Loading: 15 mg/kg/dose IV Infusion: 1.5-2 mg/kg/h **Max:** 125 mg/hr, total of 1000 mg over 8 hours Administer IV doses over 5-10 mins (max 100 mg/min) to reduce risk of hypotension	**IV:** 1 g (or 10-15 mg/kg) IV once. Administer at a rate not to exceed 100 mg/min (generally over 10-20 minutes). Followed by 1 g over next 8 hours as continuous infusion Hemoptysis: **Nebulized:** 500 mg (use injectable solution) TID for up to 5 days **Topical:** soak cotton in 5 mL of 100 mg/mL injectable solution and apply to wound OR apply 500-1000 mg to the wound and apply with pressure for 10-20 minutes	Nausea, vomiting, abdominal pain, vision changes, thromboembolic events (DVT, PE), seizures

Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Trazodone	Antidepressant. Serotonin reuptake inhibitor that also blocks alpha-1 adrenergic and histamine receptors. Often used off-label as a sleep aid	Insomnia: **PO:** 1-2 mg/kg/dose **Max:** 25-50 mg qHS May increase by 25 mg every 2 weeks to maximum of 100 mg/dose	Insomnia: **PO:** start with 12.5-50 mg qHS. May consider increasing dose based on response/ tolerability up to 200 mg PO qHS Insomnia in patients with depression: **PO:** 50-300 mg PO qHS. May titrate doses up to 600 mg/ day which have been evaluated, but evidence of greater benefit is uncertain and side effects may be greater	Drowsiness, fatigue, dizziness, syncope, nausea, vomiting, dry mouth, blurred vision Avoid abrupt discontinuation to minimize rebound insomnia and withdrawal symptoms – wean over several weeks

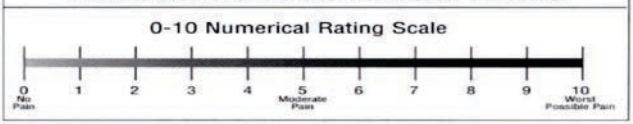
Drug Name	Mechanism of Action	Paediatric Dosing (Titration)	Adult Dosing (Titration)	Adverse Reactions
Valproic Acid	Anticonvulsant. Although the actual mechanism is unclear, it likely increases the availability of GABA in the brain thereby exerting an inhibitory effect. It also blocks sodium channels thereby suppressing neuronal firing	Seizures: Loading dose: **IV/IO:** 30 mg/kg (max: 3000 mg/dose) Repeat dosing (for seizures lasting >10 minutes): 10 mg/kg/dose Administer over 5 minutes for status epilepticus Maintenance Therapy: **PO:** 15 mg/kg/day q8-24h. Titrate by 5-10 mg/kg/day weekly to a maximum of 30-60 mg/kg/day divided BID to QID	Seizures: **IV/IO:** loading dose: 20-40 mg/kg administered at a rate up to 10 mg/kg/min (max dose: 3 g) Maintenance: **PO:** 150-200mg BID, increase by 150-200mg at 3-7 day intervals until optimal clinical response and/or therapeutic levels are achieved **Max:** 2500mg/day or 60 mg/kg/day Within 3-4 days of initiation or dose adjustment, trough concentrations should be drawn just before next dose. Therapeutic trough level: 350-700 umol/L	Dizziness, drowsiness, nausea, vomiting, diarrhoea, thrombocytopenia, tremors, alopecia, hepatotoxicity, hyperammonemia, encephalopathy

FACES SCALE: REVISED

"These faces show how much something can hurt. This face *[point to left-most face]* shows no pain. The faces show more and more pain *[point to each from left to right]* up to this one *[point to right most face]* – it shows very much pain. Point to the face that shows how much you hurt *[right now]*."



PAIN SCORE 0-10 NUMERICAL RATING



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