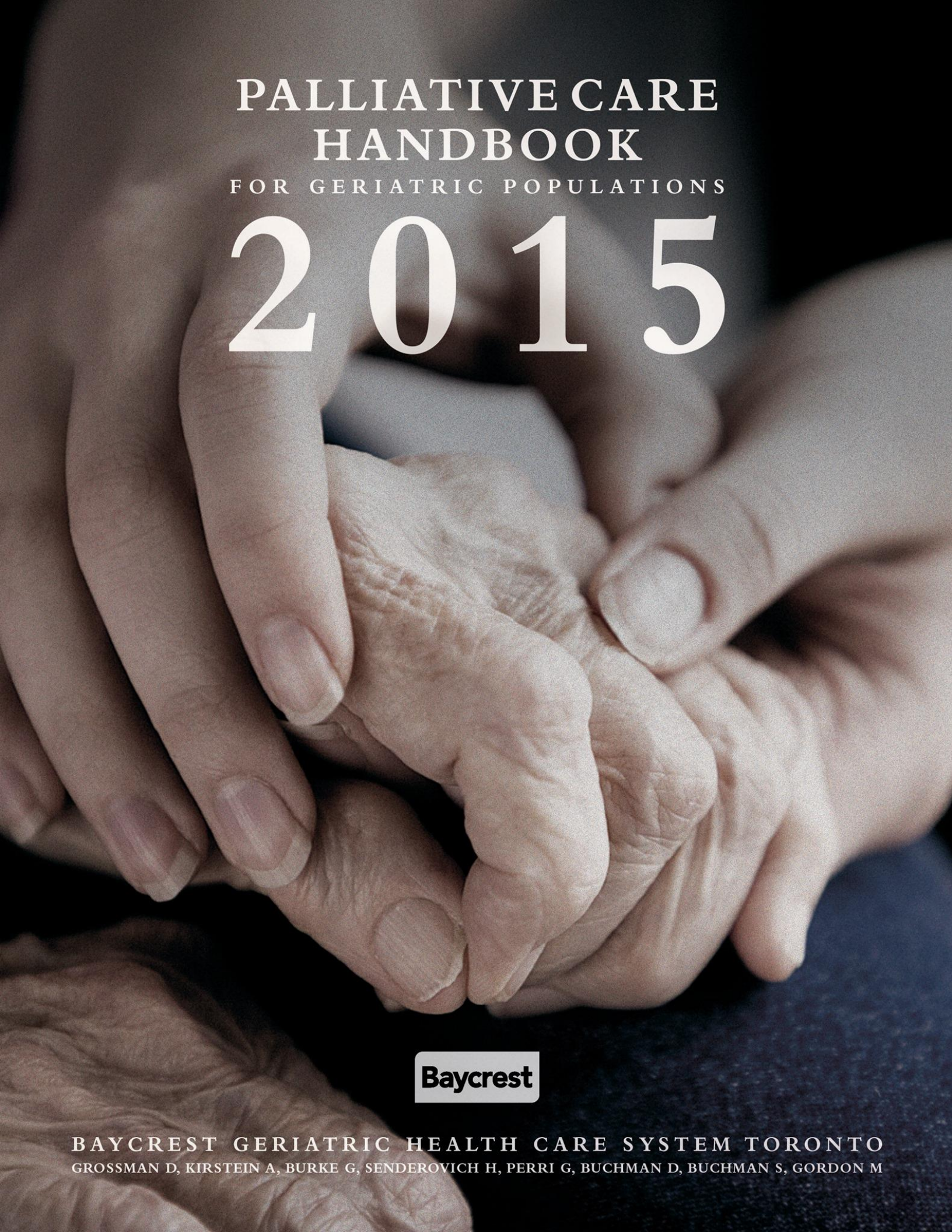


PALLIATIVE CARE HANDBOOK

FOR GERIATRIC POPULATIONS

2015

Baycrest

BAYCREST GERIATRIC HEALTH CARE SYSTEM TORONTO

GROSSMAN D, KIRSTEIN A, BURKE G, SENDEROVICH H, PERRI G, BUCHMAN D, BUCHMAN S, GORDON M

Palliative Care Handbook
For Geriatric Populations
2015

Baycrest Geriatric Health Care System
Toronto

Grossman D, Kirstein A, Burke G, Senderovich H, Perri G,
Buchman D, Buchman S, Gordon M

NOTE FROM AUTHORS:

This handbook is intended to be used as a guide to help clinicians who care for the frail elderly. This handbook is based, with many modifications and with more current information, on the Baycrest Geriatric Health Care System *Palliative Care Handbook*, 2011, Toronto, by Grossman D, Kirstein A, Buchman D, Buchman S, Gordon M, which drew on information from Librach, L.S & Squires, B.P. (1997). *The Pain Manual: Principles and Issues in Cancer Pain Management*, by Pegasus Healthcare International, Toronto as well as many current publications. Some of the dosages of medications may be significantly less than those found in the literature. The authors have based these dosages on their experience with using these medications in the frail elderly admitted to the Baycrest Palliative Care Unit. This handbook is not intended for publication.

USEFUL SCALES AND ASSESMENT TOOLS

Functionality Scale

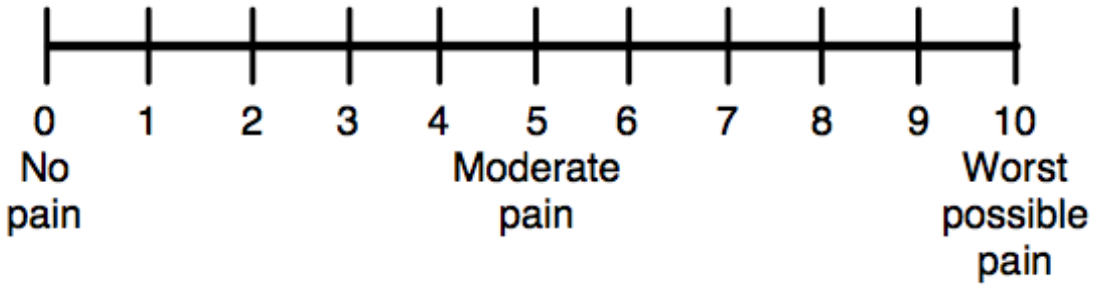
Palliative Performance Scale (PPS)[1]

PPS Level	Ambulation	Activity & Evidence of Disease	Self-Care	Intake	Conscious Level
100%	Full	Normal activity & work No evidence of disease	Full	Normal	Full
90%	Full	Normal activity & 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 Normal Job/Work Significant disease	Full	Normal or reduced	Full
60%	Reduced	Unable 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	-	-	-	-

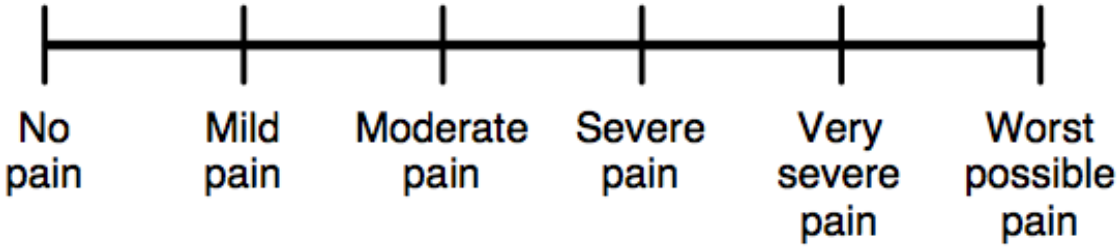
Pain and Symptom Assessment Scales

There are many pain assessment scales in use. The ones demonstrated below are examples of those commonly used in the palliative care community and might be useful in some individuals who suffer from cognitive impairment or dementia.

0-10 Numeric Pain Rating Scale[2]



Verbal Pain Intensity Scale[3]



Faces Pain Scale[4]

Pain Assessment in Advanced Dementia Scale (PAINAD)[5]

Behavior	0	1	2	Score
Breathing Independent of vocalization	• Normal	• Occasional labored breathing • Short period of hyperventilation	• Noisy labored breathing • Long period of hyperventilation • Cheyne-Stokes respirations	
Negative vocalization	• None	• Occasional moan or groan • Low-level speech with a negative or disapproving quality	• Repeated troubled calling out • Loud moaning or groaning • Crying	
Facial expression	• Smiling or inexpressive	• Sad • Frightened • Frown	• Facial grimacing	
Body language	• Relaxed	• Tense • Distressed pacing • Fidgeting	• Rigid • Fists clenched • Knees pulled up • Pulling or pushing away • Striking out	
Consolability	• No need to console	• Distracted or reassured by voice or touch	• Unable to console, distract, or reassure	
			TOTAL SCORE	

Scoring:

The total score ranges from 0-10 points. A possible interpretation of the scores is: 1-3=mild pain; 4-6=moderate pain; 7-10=severe pain. These ranges are based on a standard 0-10 scale of pain, but have not been substantiated in the literature for this tool.

Edmonton Symptom Assessment System (ESAS)[6]

Please circle the number that best describes how you feel NOW:

No Pain	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Pain
No Tiredness *(Tiredness = lack of energy)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Tiredness
No Drowsiness *(Drowsiness = feeling sleepy)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Drowsiness
No Nausea	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Nausea
No Lack of Appetite	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Lack of Appetite
No Shortness of Breath	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Shortness of Breath
No Depression *(Depression = feeling sad)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Depression
No Anxiety *(Anxiety = feeling nervous)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Anxiety
Best Wellbeing *(Wellbeing = how you feel overall)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible Wellbeing
No _____ Other Problem *(for example constipation)*	0	1	2	3	4	5	6	7	8	9	10	Worst Possible _____

[1]Victoria Hospice Society, 2006
[2]McCaffery M, Pasero C. Pain: Clinical Manual, St. Louis, 1999, P. 16. Copyrighted by Mosby, Inc.
[3]Pain Management: Theory and Practice, edited by RK Portenoy & RM Tanner, copyright 1996 by Oxford University Press, Inc.
[4]Faces Pain Scale – Revised, ©2001, International Association for the Study of Pain
[5]Warden V, Hurley AC, Volicer L. Development and psychometric evaluation of the Pain Assessment in Advanced Dementia (PAINAD) scale. J Am Med Dir Assoc. 2003;4(1):9-15.
[6]Cancer Care Ontario, 2010

Sedation Scale

0 = none; alert patient 1 = mild; occasionally drowsy patient, but easy to arouse 2 = moderate; increased drowsiness, but still easy to arouse 3 = severe; somnolent patient, difficult to arouse S = sleep; patient is asleep and is easily aroused with stimulation

Approach to the introduction of pain management depending on level of pain and response to intervention (some of the points in this section have been made in the previous section but this duplication was intended to avoid the necessity of going back and forth between sections of the guide)

Analgesics: Non-Opioids: NSAIDs, Acetaminophen
Weak Opioids: Codeine, Tramadol (Non Opioid Analgesic)
Strong Opioids: Morphine, Oxycodone, Hydromorphone and Fentanyl
(**never use Fentanyl patch in opioid naïve patients**)

Pharmacologic Adjuvant (used to promote the effectiveness of another drug when used in combination with it): Antidepressants, anticonvulsants, corticosteroids, bisphosphonates, local anesthetics, antispasmodics, palliative chemotherapy, NSAIDs

Non-pharmacologic Adjuvant: radiation therapy, acupuncture, TENS, ultrasound, therapeutic touch, massage, splints, surgery, counseling, cognitive behavior therapy, music and art therapy, relaxation techniques.

Symptom Management

This section is based, with many modifications with more current information, on the Baycrest Geriatric Health Care System *Palliative Care Handbook*, 2011, Toronto, by Grossman D, Kirstein A, Buchman D, Buchman S, Gordon M, which drew on information from Librach, L.S & Squires, B.P. (1997). *The Pain Manual: Principles and Issues in Cancer Pain Management*, by Pegasus Healthcare International, Toronto.

Opioid Dosing Table

Drug	Dosage Forms	Strengths Available	Suggested Dosing Interval	Onset of Action (minutes)
Codeine	Codeine Tablets	15mg, 30mg	q4h	15-30
	Codeine Syrup	5mg/ml	q4h	15-30
	Codeine Contin® Long acting)	50mg, 100mg	q8-12h	Peaks in 1.2 hours
	Codeine Injection	30mg/ml	q4h	10-30
Tramadol	Ultram and Ultram ER®	Ultram 50 mg and Ultram ER: 100,200, 300 mg	Ultram 50-100 mg q4-6h Ultram ER 100-300 mg/day	30-60
Morphine	Morphine tabs	5, 10, 25, 50 mg	q4h	10-30
	Morphine syrup	1mg/ml	q4h	10-30
	M-Eslon® (long-acting Morphine)	10, 15, 30, 60, 100 (mg)	q8-12h	Peaks between 3-4 hours.
	Morphine Injection	2mg/ml, 10mg/ml, 15mg/ml, 50mg/ml, 250mg/5ml, 500mg/10ml	q4h or infusion	15-60
Hydromorphone	Hydromorphone Tabs *(Dilaudid®)*	1, 2, 4, 8 (mg)	q4h	15-30
	Hydromorphone Contin® (long acting)	3, 4.5, 6,12,18 24, 30 (mg)	q8-12h	Peaks at mean of 4-8 hours
	Hydromorphone Injection *(Dilaudid®)*	2mg/ml, 10mg/ml, 50mg/5ml, 100mg/50ml, 500mg/50ml, 2500mg/50ml	q4h or infusion	10-15

Oxycodone	Oxycodone IR	5, 10 mg	q4h	10-15
	Oxycocet®	Acetaminophen 325 mg/ Oxycodone 5mg	q4h	10-15
	Oxycodone Controlled Release CR (eg. OxyNeo)	10, 15, 20, 40 mg	Q8-12h	Peaks in 2.8 hours
Fentanyl	Fentanyl® Patch	12, 25, 50, 75, 100 (µg)	Q3days **DO NOT USE fentanyl patch in opioid naïve patients**	Time to peak: 20-72 hours. Steady state is reached in approximately 6 days. The dosage should not be titrated more frequently than every 3 days after the initial dose or every 6 days thereafter. Note: Upon discontinuation approximately 17 hours are required for a 50% decrease in serum levels
Buprenorphine	Butrans Patch	5 mcg/h patch = 10 mg morphine PO/24h	Q7days	Titrate dose once weekly

Equi-analgesic Chart

When an opioid is administered by the IV route, it is 3x more potent than the PO route. Therefore the IV dose is 1/3 the PO dose. When an opioid is administered by the SC route, it is 2x more potent than the PO route. Therefore the SC dose is 1/2 the PO dose. In summary the equi-analgesic dose can be represented as follows: **P.O : S.C : IV = 3 : 2 : 1**

Drug	P.O. mg	S.C. mg	I.V. mg	Schedule
Morphine	20	10	6	q4h
Hydromorphone	4	2	1-2	q4h
Oxycodone	10	N/A	N/A	q4h
Codeine	200	100	50-100	q4h
Fentanyl Patch	*25 μg/hr fentanyl ≈ 60 mg oral morphine/24 hours			q3days

- *Health Canada says that the equivalent is 120 mg. Morphine but many palliative care physicians do not agree and prefer the lower dose equivalent as noted in chart above.
- 10-20% of population cannot convert codeine to morphine and therefore codeine is not effective at all.

Rules of Thumb

- When converting from one opioid to another decrease the equivalency dose by 30-50% because of incomplete cross tolerance

Example: Codeine 80 mg PO q4h.
Codeine to Morphine = 10:1
Therefore: Codeine 80 mg PO q4h = Morphine 8 mg PO q4h

To account for incomplete cross-tolerance, reduce this dose by 30%. Therefore, the starting dose would be Morphine 5mg PO q4h.

Longer Acting Opioids

- Sustained release (SR) preparations should not be used for uncontrolled pain or in patients whose opioid needs have not yet been determined. Always titrate with short acting and convert to long acting when the appropriate dose is reached.

- Slow release preparations of **morphine (MS Contin®, M-Eslon®, MOS-SR®, Oramorph SR®), hydromorphone (Hydropmorph Contin®), codeine (Codeine Contin®) and oxycodone (OxyNEO®, Oxycontin®)**: calculate total 24-hour dose (oral equivalent), divide by 2 and administer q12h regularly. If pain repeatedly recurs before 12 hours, increase dose or shorten interval to q8h

- **Transdermal Fentanyl** *(Duragesic®)* – continuous release for 72 hours. Calculate oral morphine (mg/day) equivalency and apply appropriate dose of patch (μg/hr)

Example: *If the patient is controlled on Morphine 5mg PO q4h then the total 24 hour dose of Morphine = 30mg. The patient can be converted to M-Eslon 15mg PO bid*

Breakthrough Pain Medication

It is extremely important when titrating the dosage of an opioid analgesic to supply the patient with sufficient "breakthrough" pain medication. This is referred to as "rescue" medication. The dosage of rescue medication is generally 10 – 20% of the total daily dose of opioid at an interval of q1h PRN.

- The breakthrough dose is approximately 10% of the total 24-hour dose. Regular use of 2 or more PRN (breakthrough) doses in 24 hours indicates inadequate pain control. The background opioid dose may need to be adjusted accordingly.

Example: *If the patient is taking Morphine 5mg PO q4h (30 mg per day) then the breakthrough dose would be 2.5 mg PO q1h PRN. If the patient is converted to M-Eslon 15mg PO bid, the hourly breakthrough dose would still be 2.5mg PO q1h PRN.*

If patient no longer able to take oral medication → Indication for SC/IV use

PO: SC dose = 2: 1
Therefore Morphine 5 mg PO q4h = Morphine 2.5 mg SC q4h
Breakthrough: Morphine 2.5 mg PO q1h PRN = Morphine 1 mg SC q1h PRN

Pain

Bone Pain

- Often due to metastatic malignant disease with tumours in the bones
- Aching, localized

Medications:

- Opioids
- ± NSAID or COX-2 (Not recommended in the elderly other than for short courses)
- Steroids (if unable to tolerate NSAID or in conjunction with radiation therapy)
  - Dexamethasone *(Decadron®)* 4 mg PO/SC od-qid,
  - In the frail elderly consider starting Decadron 1 mg od unless acute cord compression (see specific section)
- Bisphosphonates:
  - Clodronate *(Bonefos®)* – 800 mg PO bid or 1500mg SC in 250-500 ml NS and infuse over 4-6 hours
  - Pamidronate *(Aredia®)* – 90 mg IV infused over 3-4 hours once/month
  - Zoledronic Acid (Zometa) – 4 mg IV in 100 ml NS over 15-30 min, renal adjustment required

Non-Pharmacological:

- Radiotherapy
- Splinting
- Surgical fixation

Adjuvant Pain Medication

Antidepressants

Drugs	Dosage	Adverse Effects	Comments
Amitriptyline	10-25 mg PO qhs Increase dose q3-5 days by 10-25 mg as tolerated (max 100 mg od)	Anticholinergic	Max of 50 mg/day in the elderly
Nortriptyline	10-25 mg PO qhs Increase dose q3-5 days by 10-25 mg as tolerated (max 75-150 mg od)	Reduces blood pressure Fewer anticholinergic side effects than Amitriptyline	Max of 50 mg/day in the elderly
Duloxetine	30-60 mg/day	Generally well tolerated	SNRI Must be renally dosed
Venlafaxine	37.5-150 mg/day	Generally well tolerated	SNRI
Mirtazapine (Remeron®)	7.5-30 mg qhs	Less sedating at doses over 15 mg/day	NaSSA

Anticonvulsants for Neuropathic Pain

Drugs	Dosage	Adverse Effects	Comments
Gabapentin *(Neurontin®)*	100-300 mg PO on Day 1: (once/day) Day 2: (bid) Day 3: (tid)	Sedation	Max = 3600 mg/day Often use less in those suffering from late stage dementia Renal adjustment required

Pregabalin (*Lyrica*®)	25-50 mg up to tid	Sedation	Max = 300 mg/day Often use less in those suffering from late stage dementia Renal adjustment required
Valproic acid *(Depaken®e, Epival®)*	250-500 mg h.s increasing to 1000 to 1500 mg h.s; can be given p.r.	Sedation, thrombocytopenia	May monitor blood levels to avoid toxicity
Carbamazepine *(Tegretol®)*	100-200 mg b.i.d increasing slowly to a maximum of 400 mg t.i.d.	Drowsiness, nausea, interaction with anti-depressants may increase effects of both	May monitor blood levels to avoid toxicity
Clonazepam *(Rivotril®)*	0.25 mg h.s increasing to 2 to 3 mg max daily	Drowsiness common and limiting	Less often used

In elderly patients especially those with dementia the starting doses are adjusted to lower levels

Other

Drug	Dosage	Adverse Effects	Comments
Sativex®	1 spray q12h Titrate to effect Max 12 sprays/day	Can sting mouth	May be given sublingual or buccal
Nabilone	0.25 mg qhs Can increase to a maximum of 1 mg q12h	Sedation, confusion	

Methadone	0.5 PO q12h and titrate to effect	Multiple drug interactions Sedation Constipation	Requires license In elderly used most commonly as an adjuvant Metabolites excreted through bowel PRN dosing: no more frequent than q3h
Ketamine			Refractory neuropathic pain Requires referral to pain/palliative care specialist

Procedural Approaches to Pain Control

- Nerve block
- Epidural
- Trans-cutaneous Electronic Nerve Stimulation (TENS)

Controlling Opioid Side Effects

Anticipate Opioid side effects:

- Drowsiness may be transient and usually resolves after 2-3 days
- PO/SC/IV is 1:2:3 (IV is 3x more potent than PO and SC is 2x more potent than PO).
- When rotating opioids, decrease the equivalency dose by 30-50% because of incomplete cross tolerance
- Avoid morphine in renal failure. Hydromorphone may be better tolerated.
- **Never use IM route** because of increased local pain and cachexia. SC is the preferred parenteral route.
- Nausea and vomiting occur in 50 to 70% of patients starting opioids. Order an anti-emetic PRN along with the opioid. If the nausea is persistent, consider around the clock anti-emetics.

Anti-emetics

Drug	Dosage	Adverse Effects	Comments
First-Line Agent			
Metoclopramide (Maxeran®)	5-10mg PO/SC tid 1/2 hr ac and qhs 5-10mg PO/SC q1h PRN up to 80mg/d	Extra-pyramidal symptoms possible Do not give in combination with neuroleptics	Prokinetic agent Contra-indicated in complete bowel obstruction
Haloperidol *(Haldol®)*	0.5-2mg PO / SC up to q1h PRN. Not to exceed 16mg/d May use scheduled dosing up to q4h for persistent nausea	Extra-pyramidal symptoms (rare at low doses)	Antidopaminergic Avoid in Parkinson's Disease
Secondary Drug			
Prochlorperazine *(Stemetil®)*	5-10 mg PR/ PO/SC q4h PRN	More sedating than haloperidol	Antidopaminergic with anticholinergic activity
Other Drugs			
Chlorpromazine *(Largactil®)*	12.5-50 mg PO/SC q4h PRN	More sedating than haloperidol Anticholinergic side effects	Antidopaminergic with anticholinergic activity SC administration may cause skin irritation
Methotrimeprazine (Nozinan®)	2.5-25mg q1-4h PRN PO/SC	More sedating than haloperidol Anticholinergic side effects	Antidopaminergic with anticholinergic activity SC administration may cause skin irritation
Olanzapine (Zyprexa®)	2.5 mg PO bid – titrate to effect	May cause anticholinergic side effects	Antidopaminergic

Ondansetron (Zofran®)	4-8mg 1-3 times per day (max 32mg/day) PO/SL/SC/IV	May cause/worsen constipation	Selective 5-HT3 receptor antagonist Expensive- reserve for refractory cases
Granisitron (Kytril®)	1-2mg/day in 1 or 2 divided doses PO/SC/IV	May cause/worsen constipation	Selective 5-HT3 receptor antagonist Expensive- reserve for refractory cases
Dimenhydrinate *(Gravol®)*	25-50 mg PR/ PO/SC q4-6h PRN	Sedation/anticholinergic Side effects may occur, especially in the elderly	Antihistamine Especially useful if vertigo present
Motility Agents			
Metoclopramide *(Maxeran®)*	5-10mg PO/SC tid 1/2 hr ac and qhs 5-10mg PO/SC q1h PRN up to 80mg/d	Extra-pyramidal symptoms possible Do not give in combination with neuroleptics	Prokinetic agent. Contra-indicated in complete bowel obstruction
Domperidone (Motilium®)	10-30 mg PO/ day in divided doses (ac meals)	Second line prokinetic due to small increased risk of serious cardiac events in high risk patients	Give before meals. Not available SC. Does not cross BBB therefore less of antiemetic effect

Constipation

- Always anticipate when using opioids
- Optimize diet, fluids, exercise, privacy
- **REASSESS DAILY** and adjust laxatives as necessary

Medications:

Drug	Dosage	Adverse Effects	Comments
Senna *(Senokot®)* (stimulant)	2-4 tabs PO od-bid. Max 8 tablets/day	Cramping may occur	May cause colic with incomplete bowel obstruction Do not use with complete bowel obstruction

Bisacodyl *(Dulcolax®)* (stimulant)	5 mg PO, 10 mg Supp once/daily (ineffective if crushed)	Cramping may occur	May cause colic with incomplete bowel obstruction Do not use with complete bowel obstruction
Lactulose *(Chronulac®, Cephlac®*) (osmotic)	15-45ml PO 1-4 times daily	Bloating, gas, cramping	Very sweet taste may be limiting First choice in hepatic encephalopathy
Polyethalene Glycol (*Restorolax®)* *(osmotic)*	17 mg powder mixed in fluid PO once or twice daily		
Docusate *(Colace®)* (stool softener)	100-200 PO bid		Limited evidence in terms of effectiveness. Do not use as single agent in patients on opioids
Glycerine Suppository	PR PRN		
Enemas *(Fleet Enema®)*	PR PRN		
Magnesiun Hydroxide (Milk of Magnesia) (osmotic)	15-30ml PO once or twice daily		Do not use in renal impairment

Methylnaltrexone (Relistor®) (peripheral opioid receptor antagonist)	SC <38 kg: 0.15 mg/kg (round dose up to nearest 0.1 mL of volume) 38 to <62 kg: 8 mg 62-114 kg: 12 mg >114 kg: 0.15 mg/kg (round dose up to nearest 0.1 mL of volume)	May cause abdominal pain, nausea, dizziness	Where laxatives have failed in opioid induced constipation, the patient is not taking anything by mouth, and where rectal administration of enemas and suppositories is not possible Caution in renal impairment. CrCl <30 mL/minute: Administer 50% of normal dose Contraindicated in bowel obstruction but may be considered in partial obstruction as per physician judgment and discretion Expensive

Diarrhea

Octreotide – 100-300mcg SC bid-tid
Cholestyramine – 1 packet PO od-tid
Loperamide- 4 mg PO followed by 2 mg every 4 hours or after each unformed stool; Maximum: 16 mg/day (Benson, 2004) Not to be used in diarrhea associated with c difficile colitis.

Myoclonic Jerks

- Consider reversible causes where possible e.g.dehydration, electrolyte imbalances (Na, K, Ca, Mg), infection, medications e.g. opioids (especially when dose increased rapidly), new medications altering the metabolism of opioids, progression of disease.
- If opioid related
  -Consider dose reduction if appropriate
  -Rehydrate patient if possible
  -Attempt to rotate opioid

Medical Management of Myoclonic Jerks

Drug	Dosage	Adverse Effects	Comments
Lorazepam *(Ativan®)*	0.5-1 mg SC/PO/SL q1h PRN and ATC if needed	Paradoxical agitation may occur in the elderly	Titrate dose to effect Anxiolytic
Diazepam *(Valium®)*	2.5-5 mg PO q8-12h	Paradoxical agitation may occur in the elderly	Titrate dose to effect
Clonazepam *(Rivotril®)*	0.25-0.5 mg PO bid-tid	Drowsiness Paradoxical agitation may occur in the elderly	Titrate dose to effect
Midazolam *(Versed ®)*	0.5-1 mg/hr SC infusion and 0.5 mg q30min PRN If patient requires 2 x 0.5 mg in 1 hour, increase drip by 0.5 mg/hour There is no ceiling dose	Paradoxical agitation may occur in the elderly	Titrate dose to effect For severe myoclonic jerks Associated with tachyphylaxis therefore infusion may not be appropriate for long-term use

Respiratory Depression

Protocol for the Administration of SC Naloxone (Narcan®) for the Management of Opioid-Induced Respiratory Depression in Patients Receiving Opioids

Goal: To reverse respiratory depression without reversal of analgesia.
To avoid *pain-crisis* and *withdrawal-reaction*:
If respiratory rate is > 10 per minute and/or sedation score = 3 then hold opioid
If respiratory rate < 10 per minute and/or sedation score ≥ 3 then see Naloxone protocol
0 = none; alert patient
1 = mild; occasionally drowsy patient, but easy to arouse
2 = moderate; increased drowsiness, but still easy to arouse
3 = severe; somnolent patient, difficult to arouse
S = sleep; patient is asleep and is easily aroused with stimulation

Purpose: Emergency reversal of opioid-induced respiratory depression.

Patient Population: Patients who are receiving opioids.

Indication:

Reversal of respiratory depression characterized by both of the following:

Respiratory rate < 10 per minute
And/or
Sedation scale of 3 (decreased level of consciousness, difficult to rouse)

Contraindications:

- Patients who are awake
- Patients who are sedated but easy to rouse, regardless of the respiratory rate.
- Patients who are actively dying

Management Protocol:

1. Stop opioid.
2. Notify physician.
3. Administer O_2 5L/min via nasal prongs.
4. Nurse to monitor the following:
   Respiratory rate
   Blood pressure
   Heart rate
   Level of consciousness (sedation scale)
5. Have equipment ready to start hydration if indicated

During chronic opioid therapy (e.g. cancer pain) small doses of Naloxone are recommended to avoid withdrawal reactions and re-emergence of pain.

6. Administer Naloxone: select ampoule containing Naloxone 0.4 mg per 1 ml; dilute to 10 ml with normal saline to give 0.04 mg/ml (9ml of NS + 0.4 mg/ml Naloxone); give 0.04 mg (1 mL) SC or IV over 5 seconds.

7. Wait 5 minutes. Repeat vital signs. If respiratory rate < 10/min and/or sedation scale ≥ 3, give a second dose of Naloxone 0.08 mg (2ml) SC or IV over 5 seconds.

8. Wait 5 minutes. Repeat vital signs. If respiratory rate < 10/min and/or sedation scale ≥ 3, give another dose of Naloxone 0.08 mg (2ml) SC or IV over 5 seconds.

9. Continue giving 0.08 mg q5min until patient awake and resp rate > 10/min

10. Continue vital signs every 5 minutes until patient condition stable or otherwise specified by physician.

Naloxone has a short half-life. If patient responds to 0.1 mg they may need either a Naloxone infusion or a Naloxone 0.1 mg SC or IV q1h PRN until respiratory rate or sedation score stabilizes.

Note: If patient does not respond to 10mg of Naloxone then other causes for respiratory depression should be explored.

To Initiate Infusion

The dose per hour should be 2/3 of the total dose given to awake the patient (ideally an IV infusion but if not possible then SC). Give ½ the total dose to awaken the patient as a bolus when infusion starts

For IV infusion (first choice):

- Naloxone 5mg in 500ml NS which equals 0.01mg/ml

For SC infusion:

- Naloxone 5mg in 50ml NS which equals 0.1mg/ml

Skin Care

Pruritis

Topically:

- Consider non-allergenic sheets
- Mild soaps
- Moisturizer
- Menthol/camphor
- Topical steroids
- Doxepin topical cream

Oral Medications:

Drug	Dosage	Adverse Effects	Comments
Doxepin *(Sinequan)*	Start at 10 mg PO qhs and titrate to max of 150 mg/day	Anticholinergic eg. Drowsiness, Dry mouth	
Cholestyramine *(Questran)*	4 mg PO tid to max 16 g/day	Constipation Nausea Unpleasant taste	Biliary stasis induced pruritis
Oral antihistamines	Diphenhydramine (Benadryl) 25-50 mg PO/SC q6h PRN Hydroxyzine (Atarax) 10-25 mg PO q8h PRN	Anticholinergic sedating	
Mirtazapine (Remeron®)	7.5-30 mg PO qhs	Sedating or activating	Less sedating at doses over 15 mg/day
Dexamethasone (Decadron®)	1 mg PO daily titrate to effect	Steroid induced side effects	Use minimum effective dose
Paroxetine	10-20 mg PO/day	Nausea Vomiting Sedation	Multiple drug interactions
Gabapentin (Neurontin®)	100 to 300 mg PO on Day 1: (once/day) Day 2: (bid) Day 3: (tid)	Sedation	Max = 3600 mg/day Often use less in those suffering from late stage dementia Renal adjustment required
Olanzapine	2.5 mg PO bid – titrate to effect	May cause anticholinergic side effects	Antidopaminergic

Skin Breakdown

- **Prevention:** turn q2h, pressure relief mattress (Therarest, Advance 2000®)
- Protect normal skin with barrier cream or moisturizer

Stage	Skin Breakdown	Rx
1	Non-blanchable erythema – intact skin The skin will show apparent redness over pressure point(s) which does not fade 30-45 minutes after relief of pressure. This is reversible with intervention.	1. Cleanse with normal saline; apply Tegaderm or Opsite to protect from shearing forces. 2. Apply transparent film dressing or thin hydrocolloid dressing. May use liquid skin sealant to promote better adhesion of dressing.
2	Superficial break in epidermis and dermis. There is no necrotic tissue. Observe for skin loss, edema, colour, location, depth and size. May have linear split, viable flap or dead skin flap. Fluid filled intact blister.	1. Clean with Normal Saline and pat dry with dry sterile gauze. *2.* *Abrasions*. Apply hydrocolloid dressing (Duoderm). Change every 2-3 days if dead skin tissue is present or every 4-6 days if wound is clean. 3. *Skin Tears and Blisters*: Apply non-adherent dressing. Change every 3-4 days.
3	Full thickness skin loss involving damage or necrosis of subcutaneous tissue that may extend down to fascia Look for thick black eschar (possibly brown or grey). The wound may be partially or completely covered with eschar, or with "string like" slough or with loose necrotic tissue, which may be brown or grey in colour. Assess for blood supply to ensure healing ability of the wound. (Debridement is contraindicated if there is poor blood supply.)	Cleanse area with Normal Saline. Protect surrounding skin from maceration with plasticized film coating (e.g. Skin Prep®). Use one of these methods to remove the dead tissue: ♦ *Surgical Debridement*: Involves use of scalpel, scissors or other sharp instrument to remove dead tissue. This is the most effective and fastest means of removing dead tissue. -Done only by a physician or an Advanced Practice Nurse with additional education either at the bedside as in cases of small ulcers or at the clinic. -Generally indicated when there is an urgent need for debridement (e.g. in cases of advancing cellulitis or sepsis.)

		♦ *Autolytic debridement*: Apply hydrogel (e.g. Intrasite Gel ®) to necrotic area ensuring that the entire wound is completely covered. If the eschar is thick, cross hatch the eschar to facilitate penetration of gel into the eschar. Cover with semi occlusive dressing (e.g. hydrocolloid or foam dressing fastened by dressing retention sheets (e.g. Mefix®, Hypafix®, Opsite®. -For smaller necrotic areas, or wounds with relatively thin eschar, a small amount of Intrasite Gel® covered with Opsite® may be effective. -Change dressing every 24-72 hours to remove liquefied necrotic material. Do not leave the dressing longer than 3 days. ♦ *Enzymatic debridement.* Accomplished by application of topical debriding agents to necrotic tissues on the wound surface. Collagenase (Santyl®) is an example of this agent.
	Granulating (Red) Wound Look for bright red tissue with slightly "bumpy" appearance. There may be small to large amount of sero-sanguinous drainage	Attending physician and assess for antibiotics. Granulating (Red) Wound 1. Clean with Normal Saline. Ensure that the skin around the wound is clean and dry. 2. In cases where there is large amount of drainage, cover with absorbent dressing (e.g Mepilex Foam Adhesive® or Mepilex® border dressing. Change dressing every 1-3 days or PRN.
	Exudating (Yellow) Wound Look for moderate or heavy drainage at the wound site	3. Apply/swab surrounding skin with plasticized coating (e.g. Skin Prep®) to protect from maceration and irritation from the drainage. Exudating (Yellow) Wound 1. Clean with Normal Saline. Ensure that the

		skin around the wound is clean and dry. 2. If wound is draining small amount, cover with hydrocolloid dressing (e.g. Mepilex®/ Tegasorb®). 3. If wound is draining moderate to large amount, cover with absorbent foam dressing (e.g. Mepilex® adhesive/ or Mepilex® border). Change dressing as needed according to saturation of exudate on the dressing.
4	Full thickness skin loss with extensive destruction of tissue, necrosis or damage to muscle, bone or supporting structures. Wound presents as a deep crater or cavity. May either be dry or exudating. May include undermining or sinus formation.	1. Irrigate and clean ulcer bed with Normal Saline. Use 30cc. syringe with 18 g. needle to flush ulcer bed with normal saline. A urethral catheter may be attached to the syringe to flush/irrigate the sinus tract. 2. If cavity is sloughy, line the cavity with hydrogel (Intrasite Gel®) and then fill loosely with Normal Saline and Intrasite® saturated gauze or packing strips and cover with Mepilex® adhesive or sheets or dry sterile dressing fastened by dressing retention sheets (e.g. Mefix®, Flexifix®). 3. If draining heavily, cover with **absorbent dressings** (e.g. Exu-Dry® gauze, Mepilex® dressing) and change dressing every 1-2 days and PRN. 4. Protect surrounding skin with liquid sealant (e.g Skin Prep®). 5. Implement preventive measures.

Medications:

- Topical Metronidazole gel, cream or tabs (crushed and mixed in water to make paste) directly on wounds
- Dressing soaked in Metronidazole injectable solution
- Metronidazole 500 mg PO q12h

Delirium and Restlessness

Rule out underlying causes and treat if appropriate e.g. electrolyte imbalance, dehydration, constipation, cerebral metastases, infection, hypoxia, urinary retention, medications (opioids, anticholinergic medications, sedatives). If opioid induced, consider a reduction in dose or rotation to another opioid

Medications:

Drug	Dosage	Adverse Effects	Comments
Haloperidol (*Haldol*)	0.5-2mg PO / SC up to q1h PRN. Not to exceed 16mg/d	Extra-pyramidal symptoms (rare at low doses)	Potent antidopaminergic Avoid in Parkinson's Disease
Methotremeprazine *(Nozinan)*	2.5-25mg PO/SC q1h PRN followed by ATC dose (more sedating than haloperidol)	Nausea with colic pain Sedating	
Chlorpromazine *(Largactil)*	12.5-50 mg PO/PR/IV q4h PRN followed by ATC dose	Sedation	SC administration may cause skin irritation
Risperidone *(Risperdal)*	0.5 mg PO bid – titrate to effect	Extra-pyramidal	Potent antidopaminergic
Olanzapine/Olanzapine Zydis *(Zyprexa)*	2.5 mg PO bid – titrate to effect	May cause anticholinergic side effects	Antidopaminergic
Quetiapine *(Seroquel)*	25 mg PO qhs – titrate to effect	Sedating	Antidopaminergic
Lorazepam *(Ativan)*	0.5-1 mg PO/SL/SC q1h PRN	Paradoxical agitation may occur in the elderly	Anxiolytic
Midazolam *(Versed)*	0.5-1 mg/hr SC infusion, with increments as required. Start infusion at 0.5 mg/hr. Give 0.5 mg q30' PRN until sedated. If patient requires 2 x 0.5 mg in 1 hour, increase drip by 0.5 mg/hour. There is no ceiling dose.	Paradoxical agitation may occur in the elderly	Associated with tachyphylaxis therefore infusion may not be appropriate for long-term use

For persistent symptoms use around the clock dosing.

****If using benzodiazepines, these should be used in combination with antipsychotic medications to avoid paradoxical agitation secondary to benzodiazepines.***

Seizures

In palliative care situations it is not always feasible to achieve IV access. Therefore the management of seizures may have to be achieved through the SC route.
Perform stat blood sugar and treat with 50 ml of 50% glucose IV

If suspect brain metastases give Dexamethasone 10 mg PO/SC/IV stat followed by 4 mg qid urgent referral to radiation therapy if appropriate

Seizures at the End of Life *causes can be multifactorial
Brain tumors (primary or metastatic) Metabolic causes (hypoglycemia, hyperglycemia, hyponatremia, hypernatremia, renal or hepatic failure, hypercalcemia) Drug toxicity (i.e. opioid induced neurotoxicity) Drug withdrawal (i.e. alcohol, barbituates, benzodiazepines, opioids) Hypoxia Infection Pre-existing epilepsy or seizure disorder Intracerebral hemorrhage Stroke or TIA Trauma Radiation-induced edema/necrosis

Drug	Dosage	Adverse Effects	Comments
Lorazepam	1 mg SL/SC q5min x4. Maintenance 1 mg PO/SC/SL q4-6h	Paradoxical agitation may occur in the elderly	If no response use another medication
Diazepam	10 mg PR x 1 dose. Maintenance 5 mg PO/PR q6h	Paradoxical agitation may occur in the elderly	

Midazolam	0.5-1 mg/hr SC infusion, with increments as required. Start infusion at 0.5 mg/hr. Give 0.5 mg q30' PRN until seizure stops. If patient requires 2 x 0.5 mg in 1 hour, increase drip by 0.5 mg/hour. There is no ceiling dose.	Paradoxical agitation may occur in the elderly	Associated with tachyphylaxis therefore infusion may not be appropriate for long-term use
Phenobarbital	1-3mg/kg stat SC q10min to maximum of 20 mg/kg. Maintenance dose of 1-5mg/kg/day in two to three divided doses or as SC infusion	Sedating	

* Post-acute seizure, for maintenance consider PO anti-convulsants

Acute Cord Compression

	Clinical level		
Sign	*Cord*	*Conus medullaris*	*Cauda equina*
Motor	Paraparesis usually flaccid Pyramidal signs can be present	Same as cord	Never pyramidal signs Often asymmetrical Weakness
Reflex	Absent or hyperactive	Patellar hyperactive Ankle hypoactive	Hypoactive Asymmetrical
Babinski	Usually present	Usually present	Never present
Sensory	Dermatome level sensory loss (Locates compression within two dermatomes above the sensory level)	Same as cord (level usually at L1)	Asymmetrical findings in the lower extremities and perineum
Sphincter Control	Can be initially preserved	Early involved Sometimes selectively	Can be preserved

Treatment

- **Dexamethasone** 10 mg PO/SC/IV stat then 4 mg PO/SC/IV qid
- Consider urgent radiation referral to radiation oncology if appropriate and if life expectancy sufficient and symptoms sufficient to merit such intervention

Mouth Care

Avoid commercial mouthwashes, lemon, glycerin swabs or artificial saliva.

Dry Mouth

Consider:

- Biotene® Gel (1st line)
- Sour candies
- Ice chips, Popsicles
- Moisten with water or normal saline (spray bottle, syringe, red rubber catheter)
- K-Y Jelly to inside of mouth
- Petroleum Jelly for lips
- Humidifier or humidified air/oxygen
- Moisture Spray

Oral Candidiasis

- Due to antibiotics, steroids, etc

Medications:

Drug	Dosage	Adverse Effects	Comments
Mycostatin *(Nystatin®)*	500,000 units swish &swallow qid x 7 days	Well tolerated	If patient cannot swallow, may paint mouth and palate
If Nystatin Fails…			
Ketoconazole *(Nizoral®)*	100-200 mg PO od x 7-14 days		Multiple drug interactions
Fluconazole (*Diflucan*®)	100-200 mg PO od x 7-14 days		Multiple drug interactions

Ulceration and Stomatitis

Drug	Dosage	Adverse Effects	Comments
Normal saline rinses or Sodium bicarbonate solution (sodium bicarbonate 5 ml in 500 ml saline or water)	Rinse as needed		
Benzydamine HCl *(Tantum®)*	Rinse or gargle 15 ml qid or q3h PRN	Stinging	Spit solution from mouth after use If stinging occurs mix with equal volume of lukewarm water
Chlorhexidine 0.1% (Peridex)	Rinse or gargle 15 ml qid		
Mycostatin *(Nystatin®)* *If thrush present*	500,000 units swish & swallow qid	Well tolerated	If patient cannot swallow may paint mouth and palate
Lidocaine viscous 2% OR Lidocaine:Nystatin 1:1 solution (if thrush present)	5 ml swish and swallow or swish and spit **If swallowing do not eat 1 hour after dose**		Can add low dose morphine/ hydromorphone liquid and/or dexamethasone to solution for severe mouth pain <u>Example:</u> Dexamethasone 10 mg (2.5 ml from 20 mg/ 5 ml injection) Hydromorphone 20 mg (20 ml of 1 mg/ml oral solution) qs with Lidocaine viscous 2% to 100 ml total volume Sig: 5 ml swish & spit/swallow qid

Sucrulfate Suspension	1 g swish & swallow/spit qid		Acts as protective agent May mix 1:1 with Lidocaine or Nystatin Can also add low dose morphine/ hydromorphone liquid and/or dexamethasone to solution for severe mouth pain
Lidocaine 2% jelly	Apply to mouth sores		May add 1 mg hydromorphone/ morphine oral solution to each 5 ml lidocaine jelly
Tranexamic acid (Cyklokapron) for mouth bleeding	50 mg/ml solution Gargle and **spit** 10 ml qid		10 x 500 mg tablets in 100 ml sterile water (crush tablets well and add water gradually) Stability: 10 days in fridge OR 500 mg/ 5 ml ampoules: Open 5 amps (2500 mg/ 25 ml) and add 25 ml sterile water
Systemic therapy Eg. Antibiotics, antifungals, opioids			May be required for severe infections or severe mouth pain

Hiccups

1 tsp white granulated sugar─swallowed dry

Medications:

Drug	Dosage	Adverse Effects	Comments
Baclofen *(Lioresal ®)*	5-10 mg PO q6h PRN	Anticholinergic	
Chlorpromazine *(Largactil®)*	10-25 mg PO/PR q6h PRN	Sedation	SC administration may cause skin irritation
Metoclopramide *(Maxeran®)*	5-10 mg PO/SC qid 5-10 mg PO/SC q1h PRN up to 80mg/d	Extra-pyramidal symptoms possible Do not give in combination with neuroleptics	Prokinetic agent Contra-indicated in complete bowel obstruction.
Haloperidol	0.5-2 mg PO/SC up to q1h PRN. Not to exceed 16 mg/d	Extra-pyramidal symptoms (rare at low doses)	Antidopaminergic Avoid in Parkinson's Disease
Gabapentin *(Neurontin®)*	100-300 mg PO on Day 1: (once/day) Day 2: (bid) Day 3: (tid)	Sedation	Max = 3600 mg/day Often use less in those suffering from late stage dementia Renal adjustment required
Nortriptyline	10-25 mg PO qhs. Increase dose q3-5 days by 10-25 mg as tolerated (max 75-150 mg od)	Reduces blood pressure Fewer anticholinergic side effects than Amitriptyline	Max of 50 mg/day in the elderly

Dyspnea (Shortness of Breath)

- Treat underlying cause if able to do so
- May have dyspnea with normal oxygen saturation
- Cool air, increase air circulation (open window, bedside fan)

Medications/Treatments:

Drug	Dosage	Adverse Effects	Comments
Oxygen			Caution in COPD Patients
Morphine	Oral or SC low dose. If currently on opioid increase dose by 25-50%		Hydromorphone or Oxycodone in renal insufficiencies
Lorazepam	0.5-1 mg SL/SC q1h PRN or regularly	Paradoxical agitation may occur in the elderly	Anxiolytic
Midalzolam	0.5-1 mg/hr infusion, with increments as required. Start infusion at 0.5 mg/hr. Give 0.5 mg q30' PRN until symptoms well controlled. If patient requires 2 x 0.5 mg in 1 hour, increase drip by 0.5 mg/hour. There is no ceiling.	Paradoxical agitation may occur in the elderly	Associated with tachyphylaxis therefore infusion may not be appropriate for long-term use
Dexamethasone	4 mg PO/SC/IV od-qid	Steroid induced side effects	
Lasix	Dose may be given PO, IV, or SC		Lasix SC or IV twice as potent as PO 20 mg may be given per SC site

Consider:

- Radiotherapy
- Thoracentesis/pleuradesis (if collections of fluid in thoracic cavity-pleural effusion)
- In cardiac disease if dyspnea is associated with poor ejection fraction or tachycardia, consider digoxin

Terminal Airway Secretions/Congestion

The cause of terminal airway secretions is thought to be due to a pooling of respiratory secretions that occurs as a person becomes weaker, loses consciousness and the ability to cough or swallow normally.

Non-pharmacological Approaches:

- Good mouth care
- Repositioning
- Minimizing parenteral fluids
- Gentle oral suctioning should only be used if effective and tolerated – avoid pharyngeal suctioning as this is generally poorly tolerated.

Pharmacological:

Anti-cholinergics are effective in reducing both saliva and mucus production. They should be used at the first sign of congestion as anti-cholinergics do not dry up secretions that are already present.

Medication	Dosage	Adverse Effects	Comments
Glycopyrolate	0.2-0.4 mg SC q4h PRN or ATC		Does not cross the blood brain barrier and has the least amount of anticholinergic and cardiac side effects.
Scopolamine (hyoscine hydrobromide)	0.4-0.6mg SC q4h PRN or ATC or Scopolamine transdermal patch (Transderm V) – 1 patch q72h behind ear		Both scopolamine (hyoscine hydrobromide) and Atropine cross the blood brain barrier and should be used cautiously in patients who are still responsive as they can cause agitation. They are generally used in patients close to death. Atropine is the most potent with most amount of anticholinergic (sedation and delirium) and cardiac side effects.
Atropine	0.3-0.6 mg SC q4h PRN or ATC or Atropine 1% ophthalmic solution (0.5mg/drop) administered SL q2-4h PRN		
Treatment with these agents is not always successful in reducing the secretions so it is important to support the patient (if alert) and family.			

Malignant Bowel Obstruction

Medication	Dosage	Adverse Effects	Comments
Anti-nausea			
Haloperidol *(Haldol®)*	0.5-2mg PO/SC up to q1h PRN. Not to exceed 16mg/d Consider using scheduled dosing bid-q4h	Extra-pyramidal symptoms (rare at low doses)	Antidopaminergic Avoid in Parkinson's Disease

Metoclopramide *(Maxeran®)*	5-10mg PO/SC q1h PRN up to 80mg/d Consider using scheduled dosing bid-q4h	For partial obstruction may cause colic Extra-pyramidal symptoms possible Do not give in combination with neuroleptics	Prokinetic agent Contra-indicated in complete bowel obstruction
Methotremeprazine *(Nozinan®)*	SC or PO 2.5-25mg Q1h PRN Consider using scheduled dosing bid-q4h	More sedating than haloperidol Anticholinergic side effects	Antidopaminergic with anticholinergic activity SC administration may cause skin irritation
Anti-secretory			
Octreotide (Sandostatin®)	SC 100-500 mg q8-12h or continuous infusion Long acting preparation given q monthly	May cause bradycardia (caution with preexisting bradycardia), nausea, vomiting, abdominal cramps	Dries up secretions in bowels
Anti-colic			
Scopolamine (*TransdermV* ®)	Transdermal patch behind ear Q3 days	May cause delirium due to anticholinergic activity	Can use one patch behind each ear
Glycopyrrolate	0.2-0.4 q4h PRN may require scheduled dosing		Does not cross blood-brain barrier therefore less likely to cause central adverse effects
Hyoscine Butylbromide (*Buscopan* ®)	5-10 mg SC q4h PRN Max of 120 mg per day	Anticholinergic side effects	
Anti-inflammatory			
Dexamethasone (Decadron®)	SC/PO/IV 0.5-16 mg per day (1-4 times daily)	Steroid induced side effects	Decreases edema around the tumour

Ranitidine	50mg SC q8h or 150 mg PO bid	Can cause confusion in elderly	Decreases gastric secretions Renal dosing required
Omeprazole	20mg PO od		Decreases gastric secretions (PPI)
Pantoprazole	40mg PO od		Decreases gastric secretions (PPI)
Lansoprazole	30mg PO/SL od		Decreases gastric secretions (PPI)

Subcutaneous Injections

- Use a 25 gauge short butterfly needle when repeated subcutaneous injections anticipated
- Butterfly must be flushed between injections
- Cover site with **Opsite®** or **Tegaderm®**
- Range of injection: 0.1- 2 ml.
- Change site if red, bleeding, swollen, leaking or sore

Steroid Equivalency Chart

Drug	Dosage (mg)	Route of Administration
Dexamethasone *(Decadron®)*	1	SC/IV/PO
Prednisone	7	PO

Commonly Used Abbreviations

Acronym	Term
SC	Sub-cutaneous
PO	Per os (oral)
SL	Sub lingual
PR	Per rectum
IV	Intra-venous
IM	Intra-muscular
SR	Sustained Release
XR	Extended Release
CR	Controlled Release
IR	Immediate Release
CSCI	Continuous-Sub-Cutaneous-Infusion
od	Once daily
bid	Two times per day
tid	Three times per day
qid	Four times per day
PRN	As needed
ATC	Around the Clock
qxh	q = every; x = number; h = hours, i.e. q4h = every four hours
PCA	Patient Controlled Analgesia
(q)hs	At bedtime
ac	Before meals
R_x	Prescription
P_x	Prognosis
T_x	Treatment