

**SYMPTOM: ASTHENIA**

Definition: *Asthenos* (Greek) means absence or loss of strength. Asthenia includes three different major symptoms: fatigue or lassitude defined as easy tiring and decreased capacity to maintain performance; generalized weakness defined as the anticipatory sensation or difficulty in initiating a certain activity; and mental fatigue defined as the presence of impaired mental concentration, loss of memory, and emotional lability.

Incidence: 90%

Causes:	<u>Caused by cancer (7):</u>	<u>Caused by treatment (5):</u>	<u>Related to cancer and/or debility (6):</u>
	<input type="checkbox"/> Progression of disease	<input type="checkbox"/> Surgery	<input type="checkbox"/> Insomnia
	<input type="checkbox"/> Anemia	<input type="checkbox"/> Chemotherapy	<input type="checkbox"/> Exhaustion
	<input type="checkbox"/> Hypercalcemia	<input type="checkbox"/> Radiation	<input type="checkbox"/> Prolonged bed rest
	<input type="checkbox"/> Hypo-adrenalism	<input type="checkbox"/> Drugs	<input type="checkbox"/> Infection
	<input type="checkbox"/> Neuropathy	<input type="checkbox"/> Hypokalemia	<input type="checkbox"/> Dehydration
	<input type="checkbox"/> Myopathy		<input type="checkbox"/> Malnutrition
	<input type="checkbox"/> Depression		

Evaluation 2: Evaluation should focus on the severity of asthenia and its effects on the patient’s level of independence and psychological well-being. Specific effects should also be noted; for example, weakness of respiratory muscles may cause dyspnea and difficulty in clearing secretions. Patients with progressive generalized weakness are usually aware that death is approaching. This may cause anxiety, sadness and/or depression.

Bruera E. MacDonald NR. Asthenia in patients with advanced cancer. *Journal of Pain and Symptom Management*. 1988;3(1):9-14.

**PHARMACOLOGICAL MANAGEMENT:**

Comments:

	Drug (generic):	Dose (PO unless indicated):	Peak(PO):	t 1/2	Routes of Administration						
					PO	SL	PR	SC	IV	IM	LQ
Improvement after 2 weeks; improvement diminishes after 4 weeks.	dexamethasone	0.75 mg-4 mg qam	1-2 h	36-54 h	✓	✓	✓	✓	✓	✓	✓
Less myopathy than with dexamethasone.	prednisone	10-30 mg qam	1-2 h	18-36 h	✓		✓		✓	✓	✓
Improvement in appetite, caloric intake, nutrition status and energy.	megestrol acetate	400 mg qd	1-5 h	1 h	✓						✓
Significant improvement in the level of activity.	methylphenidate	5-20 mg qam	1-3 h	3-4 h	✓						
Stimulant; compromised GI function; chewable tablets.	pemoline	18.75-75 mg qd	2-4 h	12 h	✓						

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**SYMPTOM: CACHEXIA-ANOREXIA**

Definition: Cachexia: marked weight loss and muscle wasting  
 Anorexia: loss of appetite

Incidence: >50%

Clinical Features:  marked weight loss  anorexia  weakness  lassitude

Causes of Cachexia: Paraneoplastic (4): Concurrent (8):

- |  |   |
|--|---|
| <input type="checkbox"/> Increased metabolic rate (increased energy expenditure)   | <input type="checkbox"/> Anorexia (deficient food intake)   |
| <input type="checkbox"/> Abnormal host metabolism of:<br>protein<br>carbohydrate<br>fat<br>hormones  | <input type="checkbox"/> Vomiting   |
| <input type="checkbox"/> Nitrogen trapped by tumor   | <input type="checkbox"/> Diarrhea   |
| <input type="checkbox"/> Cytokine production by:<br>host cells<br>tumor, e.g. tumor necrosis factor<br>interleukin 1 and interleukin 8<br>gamma interferon | <input type="checkbox"/> Mal-absorption   |
|  | <input type="checkbox"/> Intestinal obstruction   |
|  | <input type="checkbox"/> Debilitating effect of treatment:<br>surgery<br>radiotherapy<br>chemotherapy |
|  | <input type="checkbox"/> Ulceration   |
|  | <input type="checkbox"/> excessive loss of body protein   |
|  | <input type="checkbox"/> Hemorrhage   |

Causes of Anorexia:

- |  |   |  |  |
|--|---|--|--|
| <u>Situational (4):</u>                          | <u>Illness-related (10):</u>                      | <u>Treatment-related (3):</u>              | <u>Other (2):</u>                        |
| <input type="checkbox"/> Poorly-fitting dentures | <input type="checkbox"/> Delayed gastric emptying | <input type="checkbox"/> Nausea            | <input type="checkbox"/> Delayed gastric |
| <input type="checkbox"/> Too much food           | <input type="checkbox"/> Organ failure:           | <input type="checkbox"/> Pain              | <input type="checkbox"/> Radiotherapy    |
| <input type="checkbox"/> Unpalatable food        | renal failure                                     | <input type="checkbox"/> Fatigue           | <input type="checkbox"/> Chemotherapy    |
| <input type="checkbox"/> Malodor of food cooking | liver failure                                     | <input type="checkbox"/> Sepsis            |  |
|  | <u>Biochemical:</u>                               | <input type="checkbox"/> Dehydration       |  |
|  | Hypercalcemia                                     | <input type="checkbox"/> Constipation      |  |
|  | Hyponatremia                                      | <input type="checkbox"/> Sore mouth/throat |  |

**Pharmacological Management:**

Comments:

	Drug (generic):	Dose (PO unless indicated):	Peak(PO):	t 1/2	Routes of Administration							
					PO	SL	PR	SC	IV	IM	LQ	
Improve appetite in 80%; consult dietitian/nutritionist	megestrol acetate	180 mg qd ↑ maximum 800 mg/24 h	1-5 h	1 h	✓							✓
Improve appetite in 50% (short-term use only <4 wks)	dexamethasone	2-4 mg qam	1-2 h	36-54 h	✓	✓	✓	✓	✓	✓	✓	✓
Less myopathy than with dexamethasone	prednisone	15-30 mg qam	1-2 h	18-36 h	✓		✓		✓	✓	✓	
Improve appetite and mood, with anti-emetic benefit	dronabinol	2.5 mg bid, 1 h ac ↑ 20 mg bid	30-60 min	25-36 h	✓							
Anorexia due to cancer-associated dyspepsia syndrome	metoclopramide	10-20 mg qid or 40-60 mg/24 h CSCI	30-60 min	4-6 h	✓			✓	✓	✓	✓	✓

**SYMPTOM: CONSTIPATION**

**Definition:** Constipation is the evacuation of hard stools less frequently than is normal for an individual. Healthy people do not all defecate daily. Constipation can cause several serious secondary symptoms, e.g. overflow diarrhea, urinary retention, bowel obstruction, pain.

**Incidence:** 65%

**Causes:** Related to cancer and/or debility (7): Caused by drugs (6):

<input type="checkbox"/> Hypercalcemia		<input type="checkbox"/> Opioids
<input type="checkbox"/> Inactivity		<input type="checkbox"/> NSAIDs
<input type="checkbox"/> Poor Nutrition:		<input type="checkbox"/> Anticholinergics:
decreased intake		antihistaminic anti-emetics
low residue diet		phenothiazines
<input type="checkbox"/> Poor fluid intake		tricyclics
<input type="checkbox"/> Dehydration		<input type="checkbox"/> 5HT <sub>3</sub> antagonists
vomiting		<input type="checkbox"/> Vincristine
polyuria		<input type="checkbox"/> Diuretics:
fever		dehydration
<input type="checkbox"/> Weakness		hypokalemia
<input type="checkbox"/> Inability to reach toilet when urge to defecate		

**Five-Step Treatment Plan:**

The following recommendations apply to patients with uncomplicated constipation. Intestinal obstruction and fecal impaction must first be excluded.

- Step #1: A stimulant laxative should be given first i.e. bisacodyl 5 mg once or twice daily.
- Step #2: If this is ineffective, the dose should be increased i.e. bisacodyl tablets up to a maximum of 20 mg twice daily.
- Step #3: If this is still ineffective, an osmotic laxative may be added (i.e. lactulose 15-30 ml by mouth once or twice daily).
- Step #4: If there is still no effect, or if there are unacceptable side effects, the osmotic laxative should be replaced with an emulsion of magnesium hydroxide in mineral oil (10-30 ml qd or bid).
- Step #5: Finally, if the above treatment fails, a bisacodyl suppository (10-20 mg) should be added, followed by a saline (phosphate or citrate) enema 2 hours later if there is no response.

World Health Organization. *Symptom Relief in Terminal Illness*. World Health Organization. Geneva. 1998. 32.

**Pharmacological Management:**

Comments:

	Drug (generic):	Dose (PO unless indicated):	Peak(PO):	Routes of Administration						
				PO	SL	PR	SC	IV	IM	LQ
Contact cathartic; tablets easier to swallow than senna	bisacodyl	5-20 mg qd or bid (PO); 10-20 mg qd (PR)	6-8 h	✓		✓				✓
Contact cathartic; for opioid-induced constipation	senna	187-600 mg q 24/ h ↑ 1600 mg/24 h	6-8 h	✓						✓
Osmotic cathartic; may take 24-48 hours to work	lactulose	15 ml bid (adjust accordingly)	24-48 h	✓						✓
Stool softener; for patients who strain during defecation	docusate sodium	100 mg bid ↑ 200 mg bid or tid	24-72 h	✓						✓
Prokinetic agent; enhance intestinal function	metoclopramide	10-20 mg qid or 40-60 mg/ 24 h CSCI	30-60 min	✓			✓	✓	✓	✓



**SYMPTOM: DEPRESSION**

**Definition:** The diagnosis of a major depressive syndrome in a terminally ill patient often relies more on the psychological or cognitive symptoms of major depression (worthlessness; hopelessness; excessive guilt; and suicidal ideation) rather than the neurovegetative or somatic signs and symptoms of major depression. The presence of neurovegetative signs and symptoms of depression such as fatigue, loss of energy and other somatic symptoms is often not helpful in establishing a diagnosis of depression in the terminally ill. Terminal illness itself can produce many of these physical symptoms so characteristic of major depression in the physically healthy.

**Incidence:** <25%

- Diagnostic Criteria:**
- \_\_ Low mood which the patient recognizes as being qualitatively and quantitatively different from normal variations in mood and from previous periods of unhappiness.
  - \_\_ Depression of mood which persists for at least two weeks and occupies over 50% of each day.
  - \_\_ Patient not able to banish the depression or be distracted out of it.
  - \_\_ Other symptoms of depression which cannot be attributed to the physical disease:
 

sleep disturbance	loss of interest
loss of weight/appetite	feelings of guilt
impaired concentration	fatigue or loss of energy
psychomotor retardation	suicidal ideation or thoughts of death

A helpful mnemonic on identifying the symptom of depression is **SIG: E CAPS**

**S - Sleep (either increased or decreased)**  
**I - Interest (decrease in interest)**  
**G - Guilt**  
**E - Energy (fatigue or loss of energy)**  
**C - Concentration (inability to focus)**  
**A - Appetite (either increased or decreased)**  
**P - Psychomotor agitation/regardation**  
**S - Suicidal thoughts**

Breibart W. Passik SD. *Psychiatric aspects of palliative care*. In: Doyle D. Hanks GWC. MacDonald N. eds. *Oxford Textbook of Palliative Medicine*. Oxford University Press: 1997. 609-626.

**Pharmacological Management:**

Comments:

	Drug (generic):	Dose (PO unless indicated):	Peak(PO):	t 1/2	Routes of Administration						
					PO	SL	PR	SC	IV	IM	LQ
With pain; sedation a benefit; titrate slowly to effect	amitriptyline	10-75 mg qhs ↑ 150 mg/24 h	2-4 h	10-50 h	✓						✓
With pain; fewer side effects than amitriptyline	desipramine	25-75 mg qhs ↑ 150 mg/24 h	2-4 h	14-62 h	✓						
With pain; oral solution available	nortriptyline	25 mg qhs ↑ 75 mg over 3-5 days	7-8.5 h	28-31 h	✓						✓
SSRI; may benefit diabetic neuropathic pain	paroxetine	10 mg qam ↑ 50 mg/24 h	5.2 h	21 h	✓						
SSRI; no known analgesic benefit; least sedating SSRI	sertraline	50 mg qam ↑ 200 mg/24 h	4.5-8.4 h	26-65 h	✓						
Psycho-stimulant (lethargic); do not discontinue abruptly	methylphenidate	2.5 ↑ 60 mg qam	1-3 h	3-4 h	✓						
Psycho-stimulant (mild); chewable tablets available	pemoline	18.75-75 mg qd	2-4 h	12 h							



**SYMPTOM: NAUSEA AND VOMITING**

**Definition:** Nausea is an unpleasant feeling of the need to vomit, often accompanied by autonomic symptoms (i.e. pallor, cold sweat, salivation, tachycardia and diarrhea). Retching is rhythmic, labored, spasmodic movements of the diaphragm and abdominal muscles, generally occurring in the presence of nausea and often culminating in vomiting. Vomiting is the forceful expulsion of gastric contents through the mouth.

**Incidence:** < 75%

- |   |                                       |   |   |
|---|---------------------------------------|---|---|
| <b>Causes:</b>                              |                                       | <b>Related to cancer and/or debility (2):</b> |   |
| <u>Caused by cancer (14):</u>               | <u>Caused by treatment (3):</u>       |   | <u>Concurrent causes (4):</u>                 |
| <input type="checkbox"/> Gastroparesis      | <input type="checkbox"/> Radiotherapy | <input type="checkbox"/> Cough                | <input type="checkbox"/> Renal failure        |
| <input type="checkbox"/> Blood in stomach   | <input type="checkbox"/> Chemotherapy | <input type="checkbox"/> Infection            | <input type="checkbox"/> Functional dyspepsia |
| <input type="checkbox"/> Bowel obstruction: |                                       |   | <input type="checkbox"/> Peptic ulcer         |
| partial                                     | <input type="checkbox"/> Drugs (4):   |   | <input type="checkbox"/> Alcohol gastritis    |
| complete                                    |                                       |   |   |

**Causes of drug-induced nausea and vomiting:**

<input type="checkbox"/> Constipation	<b><u>Mechanism:</u></b>	<b><u>Drug:</u></b>	<b><u>Mechanism:</u></b>	<b><u>Drug:</u></b>
<input type="checkbox"/> Hepatomegaly	<b><u>Gastric Irritation:</u></b>	antibiotics	<b><u>Area postrema stimulation:</u></b>	antibiotics
<input type="checkbox"/> Gross ascites		iron supplements		cytotoxics
<input type="checkbox"/> Raised intracranial pressure		NSAIDs		digoxin
<input type="checkbox"/> Cough		tranexamic acid		imidazoles
<input type="checkbox"/> Pain				opioids
<input type="checkbox"/> Anxiety	<b><u>Gastric stasis:</u></b>	antimuscarinics	<b><u>5HT<sub>3</sub>-receptor stimulation:</u></b>	antibiotics
<input type="checkbox"/> Cancer toxicity		opioids		cytotoxics
<input type="checkbox"/> Hypercalcemia		phenothiazines		SSRIs
<input type="checkbox"/> Hyponatremia		tricyclics		
<input type="checkbox"/> Renal failure				

**Pharmacological Management:**

Comments:

	Drug (generic):	Dose (PO unless indicated):	Peak(PO):	t 1/2	Routes of Administration							
					PO	SL	PR	SC	IV	IM	LQ	
Bowel obstruction (with colic); Raised intracranial pressure	diphenhydramine	25-50 mg q 4 h	2-4 h	2-8 h	✓			✓	✓	✓	✓	
Bowel obstruction (with colic); second-line agent	meclizine	12.5-50 mg tid	2-3 h	3.5 h	✓							
Bowel obstruction (with colic); third-line agent	glycopyrrolate	0.2-0.4 mg SC q 4-6 h (0.6-1.2 mg/24 h CSCI)	30 m (SC)	1.7 h	✓			✓	✓	✓	✓	
Bowel obstruction (without colic); broad spectrum	metoclopramide	10-20 mg tid or qid	30-60 min	4-6 h	✓			✓	✓	✓	✓	
Gastric stasis; first -line agent; for gastric emptying	metoclopramide	10-20 mg tid or qid	30-60 min	4-6 h	✓			✓	✓	✓	✓	
Gastric stasis; second-line agent; strong prokinetic	cisapride	10-20 mg bid or qid	1-1.5 h	6-12 h	✓							✓
Motion sickness; pharyngeal stimulation; vertigo	diphenhydramine	25-50 mg q 4 h	2-4 h	2-8 h	✓			✓	✓	✓	✓	
Motion sickness; raised intracranial pressure	meclizine	50-100 mg tid or bid	1 h	6 h	✓							
Raised intracranial pressure or perineural tumor	dexamethasone	8-16 mg PO or SC qam	1-2 h	36-54 h	✓	✓		✓	✓	✓	✓	✓
Opioid induction; radio -therapy; most chemotherapy	haloperidol	1.5-5 mg qhs or bid	3-6 h	17 h	✓	✓		✓	✓	✓	✓	✓
Moderate chemical emetogenic stimuli; secondary agent	prochlorperazine	5-10 mg tid	30-40 min	10-12 h	✓		✓		✓	✓	✓	
Hypercalcemia; renal failure	haloperidol	1.5-5 mg qhs or bid	3-6 h	17 h	✓	✓		✓	✓	✓	✓	✓
Broad spectrum	chlorpromazine	10-25 mg qid	30-60 min	10-12 h				✓	✓	✓		
Intractable chemotherapy induced nausea/vomiting	dronabinol	2.5 mg bid, 1 h ac ↑ 20 mg qd	30-60 min	25-36 h	✓							
Non-specified and indeterminate	haloperidol	1.5-5 mg tid	3-6 h	17 h	✓	✓		✓	✓	✓	✓	✓

**SYMPTOM: PAIN**

Definition: Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.

Incidence: 90%

**TYPES OF PAIN AND IMPLICATIONS FOR TREATMENT**

<u>TYPE OF PAIN</u>	<u>MECHANISM</u>	<u>EXAMPLE</u>
<u>1.Nociceptive</u>	Stimulation of nerve endings	
Visceral		Hepatic capsule pain; epigastric pain
Somatic		Bone pain Muscle pain (cramp; myoclonus)
	<u>RESPONSE TO OPIOIDS</u>	<u>TREATMENT</u>
	+	Analgesic
	+/-	Analgesic
	-	Benzodiazepine

-Don't use combination products for intermediate to high doses! (acetaminophen toxicity!)

**Lipophilic:** Fentanyl, Methadone, cross BBB fast  
**Hydrophilic:** Morphine, Hydromorphone, Oxycodone  
(Morphine- T1/2= 4 hr, Tmax= 1 hr)

**Fentanyl to MS Conversion**

Don't have to worry about cross-tolerance

Fentanyl 100mcg/hr = MSO4 200mg po qd

Duragesic 100 mcg/hr = MS Contin 100 mg po q12

75	75	
50	50	
25	25	
Atiq (oralets) suck	peak	gone
0-15 min	15-20 min	30-60 min
200(weak)/400/600/800/1000/1200/1600 pops		

**Methadone to MS Conversion**

20:1 if taking >1000mg MSO4 po qd

10:1 if taking 500-1000mg MSO4 po qd

5:1 if taking <500mg MSO4 po qd

Only drug to hit both Nociceptive and Neuropathic Pain

Preps	<u>Liquids</u>	<u>Tablets</u>
	5mg/5cc	10mg
	10mg/5cc	40mg
	10mg/1cc	

**Morphine Sulfate**

Preps	<u>Liquids</u>	<u>Tablets</u>
	10mg/5cc	IR- 15, 30 mg, soluble tabs 10, 15, 30mg
	20mg/5cc	SR- Ms Contin 15, 30, 60, 100, 200mg
(Roxanol) 20mg/1cc		Oramorph 15, 30, 60, 100mg
		Oxycontin 10, 20, 40, 80mg
		Kadian 20, 50, 100mg

\*Kadian may need to be given q 12 rather than Qd

\*MS Contin may be PR but must be put in capsule with NS

**TYPE OF PAIN****MECHANISM****EXAMPLE****2. Neuropathic**

Nerve compression injury	Stimulation of nervi nervorum (?) neuropathy	carpal tunnel
Nerve injury	Ischemic damage Peripheral nerve injury	Neuroma or nerve infiltration
	CNS injury	Spinal cord compression
Sympathetically maintained	Abnormal sympathetic activity	Causalgia

  

<b><u>RESPONSE TO OPIOIDS</u></b>	<b><u>TREATMENT</u></b>
+/-	Analgesics; corticosteroids
(+)/-	Trial of opioid; NSAID; trial of corticosteroid; tricyclic antidepressant; anticonvulsant; local anesthetic congener; spinal analgesic; TENS
-	Sympathetic nerve block

**Salicylates**

Trilisate

750-1500mg po bid, liquid available

Does not affect platelet adherence

Low GI profile

Disalcid

**TCAs**

Amitriptyline- only 30% efficacious, very anticholinergic

Desipramine (Norpramine)

Nortriptyline (Pamelor)

Venlafaxine (Effexor) 37.5mg po qhs, increase to 75mg after 1 wk.

**Anticonvulsants**

Gabapentin (Neurontin) often need &gt;3600mg/d, start 300mg po tid (slow dosing)

Carbamazepine (Tegretol)- too many drug interactions

Depakote- 85% (per Twycross), start 250mg po qhs, up to 1000mg

Draw level, therapeutic &lt;100

**Antiarrhythmics**

Lidocaine 1-2 mg/kg iv/sq load in 15 minutes, then 1-2mg/kg/hr, draw level qd to q week, therapeutic 1-5 ug/ml

**MSO4 IV:PO**

1:3 opiate tolerant patient

1:6 opiate naïve patient

**Hydromorphone to MSO4 Conversion**

5:1 IV

3:1 PO

**Oxycodone to MSO4 Conversion**

<i>Prep</i>	<i>Liquids</i>	<i>Tablets</i>
	5mg/5cc	IR 5mg
(oxyfast)	20mg/cc	SR 10, 20, 40, 80mg

**OPIOIDS**

- Morphine (nr), Example of brand name: Roxanol-T, receptors-  $\mu+\kappa-\delta-$ , Peak: 30-60m, t1/2: 2.5-3h, Duration: 3-6h, Potency to morphine ratio: -, EQUIANALGESIC DOSE: oral 30mg, Parenteral 10mg, Available Routes of Administration: PO, SL, PR, SC, IV, IM, LQ
- morphine (sr), Example of brand name: Oramorph SR, receptors:  $\mu+\kappa-\delta-$ , Peak: 1-4 h, t1/2: 2.5-3h, Duration: 8-12h, Potency to morphine ratio: -, EQUIANALGESIC DOSE: oral 90-120mg, Parenteral:30-04 over 24 hours, Available Routes of Administration: PO, SL, PR, LQ
- Hydromorphone, Example of brand name: Dilaudid, receptors:  $\mu+\kappa-\delta-$ , Peak: 45m, t1/2: 4-5h, Duration: 2-4h Potency to morphine ratio: 7.5, EQUIANALGESIC DOSE: oral 7.5mg, Parenteral: 1.5, Available Routes of Administration: PO, SL, PR, SC, IV, IM, LQ
- Methadone, Example of brand name: Dolophine, receptors:  $\mu+\kappa-\delta+$ , Peak: 30-60m, t1/2: 13-100h, Duration: 4-24h, EQUIANALGESIC DOSE: oral 4-5mg, Parenteral: 3mg, Available Routes of Administration: PO, SL, PR, SC, IV, IM, LQ
- Oxycodone (nr), Example of brand name: Roxicodone, receptors:  $\mu+\kappa-\delta-$  Peak: 30-60m, t1/2: 3-4, Duration: 3-4h, Potency to morphine ratio: 1- 1.5, USUAL DOSE 5-30 mg, Available Routes of Administration: PO, SL, PR, LQ
- Tramadol, Example of brand name: Ultram, receptors:  $\mu-\kappa-\delta-$ , Peak:2-3h, t1/2: 6-7, Duration: 4-6h, Potency to morphine ratio: 1/5, USUAL DOSE: oral 50-100mg, Parenteral: -, Available Routes of Administration: PO
- Transdermal fentanyl, Example of brand name: Duragesic, receptors:  $\mu+\kappa+\delta-$ , Peak: 16-24h, t1/2: 17h, Duration: 48-72h, Potency to morphine ratio: 150,