

Symptoms Control in Palliative Care

: Principle & Management

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Prognosis on average in cancer patient

- **Likelihood of cure:**
 - High (> 60%): patients willing to undergo toxic treatments
 - Intermediate (30-60%): some patients will decline toxic treatment
 - Low ((5-30%): heterogeneous; acute and late toxicity
 - Remote (0-5%): heterogeneous
- **Decision-influencing factors:**
 - Response to treatment
 - Clinical benefit
 - Adverse events
 - Physician bias
 - Cultural and religious influence
 - Family influence
 - Economic consideration

Supportive and palliative care in cancer

Definitions: supportive care

- Optimize comfort, function and social support to patients and family in **all stages of the disease**
- Characterized by:
 - Optimal, stage appropriate anti-cancer care
 - Prevention and management of side effects
 - Optimal symptom control**
 - Optimal social and family support
 - Optimization of function

Supportive and palliative care in cancer

Definitions: palliative care

- Optimize comfort, function and social support to patients and family in **all stages of the disease in patients for whom cure is not possible**
- Palliative care is **active total care** aiming to improve the quality of life of patients and families who face life-threatening illness, by providing pain and symptom relief, spiritual and psychosocial support from diagnosis to the end of life and bereavement (WHO definition 2002)

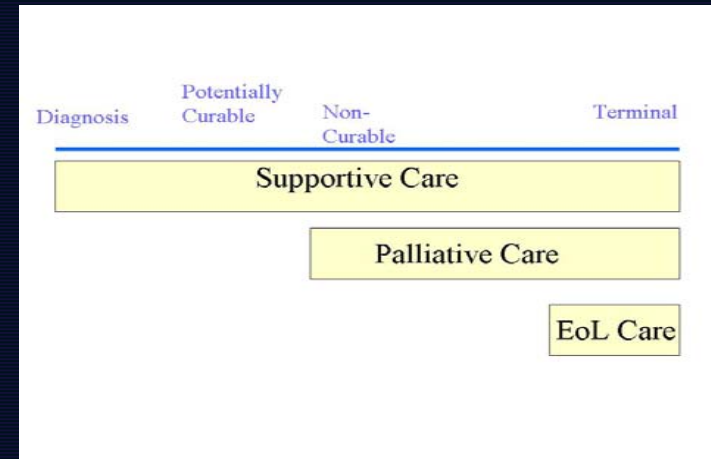
Supportive and palliative care in cancer

Definitions: end-of-life care

- Palliative care when death is imminent
- Emphasizes optimal symptom control:
 - Physical
 - Psychological
 - Social
 - Spiritual
- Family support

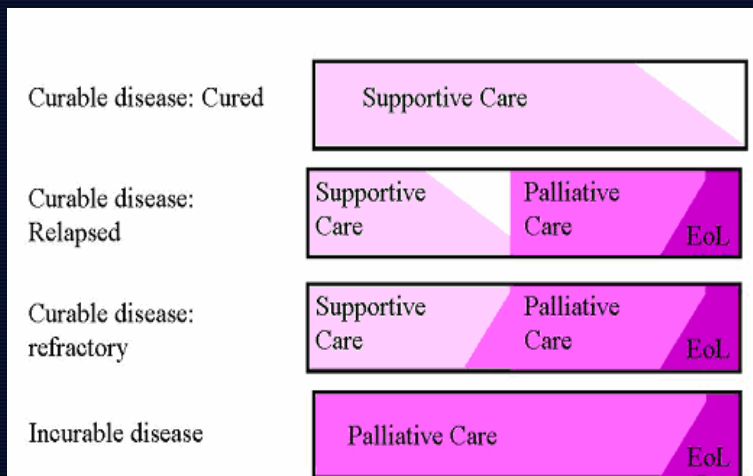
Supportive and palliative care in cancer

Care stages



Supportive and palliative care in cancer

Care in relation to disease



Supportive and palliative care in cancer

Problems of cancer patients

■ Problems related to disease:

□ Physical impact of cancer:

- Pain, ulceration, dysphagia, dyspnea

□ Psychosocial impact:

- Anxiety, depression
- Social isolation, loss of work, loss of role in family

□ Spiritual impact:

- Meaning of life, disease, existential issues

■ Problems related to treatment:

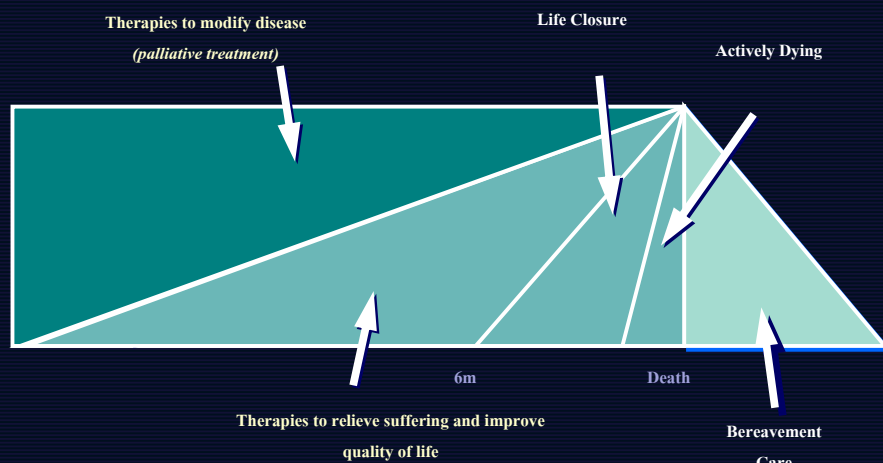
□ Short-term

□ Long-term

Palliative care

Supportive and palliative care in cancer

Continuum of palliative care



Supportive and palliative care in cancer

Principles of palliative care

- Affirms life and regards dying as a normal process
- Neither hastens nor postpones death
- Provides relief from pain and other distressing symptoms
- Integrates the psychological and spiritual aspects of care
- Offers a support system to help patients live as actively as possible until death
- Offers a support system to help patients' families cope during the patient's illness and in their own bereavement

Supportive and palliative care in cancer

Components of palliative care

- Symptom control
- Effective communication
- Rehabilitation
- Continuity of care
- Terminal care
- Support in bereavement
- Education
- Research

Supportive and palliative care in cancer

Attention for the informal caregivers

- Most patients want to be at home during their final illness
- Informal caregivers:
 - Are vital to the support of patients at home
 - Have often unmet needs
 - Anxiety and depression are common among them
- Many informal caregivers feel isolated, particularly after the patient's death

Supportive and palliative care in cancer

Needs of the informal caregivers

- Information and education about
 - The patient's diagnosis
 - Causes, importance, and management of symptoms
 - How to care for the patient
 - Likely prognosis and how the patient may die
 - Sudden changes in patient's condition, particularly those which may signal that death is approaching
 - What services are available and how to access them (including in emergencies)
- Support during the patient's illness
 - Practical and domestic
 - Psychosocial
 - Financial
 - Spiritual

Supportive and palliative care in cancer

Attention for the professional caregivers

- Risk factors for psychiatric morbidity among palliative care professionals
 - For senior professionals, young age or fewer years in post
 - High job stress
 - Low job satisfaction
 - Inadequate training in communication and management skills
 - Stress from other aspects of life
 - Previous psychological difficulties or family history of psychiatric problems

Supportive and palliative care in cancer

Attention for the professional caregivers

- **Strategies for improving mental health of professionals providing palliative care**
 - Maintaining culture of palliative care despite the shift within health care from service to business, including
 - Autonomy
 - Good management
 - Adequate resources, particularly with regard to workforce, so that high levels of patient care can be maintained
 - Providing more effective training in
 - Communication skills including role playing of difficult interpersonal situations with patients, relatives, and professionals
 - Management skills
 - Providing effective clinical supervision which addresses the physical, psychological, social, spiritual, and communication dimensions of patient care
 - Providing a confidential mental health service that is independent of management and covers both personal and work-related problems

Supportive and palliative care in cancer

Conclusion

- Supportive and palliative care are integral parts of cancer care
- Care should be given by an interdisciplinary team
- Patient and family should receive optimal support
- Professional caregivers should also receive support

Symptoms Control in Palliative Care

Indications for Palliative Radiation

Pain Control

- Bone Metastases
- Pressure of tumour on nerves

Relief of Superior Vena Obstruction

Spinal Cord Compression

Bleeding

- Most commonly hemoptysis
- May also be from other sites
 - Gyne
 - Rectal
 - Bladder
 - Prostate

Brain Metastases

- Whole brain radiation
- Stereotactic (Gamma Knife)

Relief of Obstruction

- Airway/Bronchus
- Esophageal

Subcutaneous Metastases

- Lung primary
- Lymphoma
- Leukemia

GI Issues Causing Nausea/Vomiting

- Medications
- Radiation
- Constipation
- Bowel obstruction
- Diarrhea
- Ascites
- Hemorrhage
- Viscus perforation
- Esophageal/gastric/ biliary duct obstruction
- Liver failure
- Pancreatic failure
- Absorption syndromes
- Infections
- Electrolytes

Approach To Symptom Control

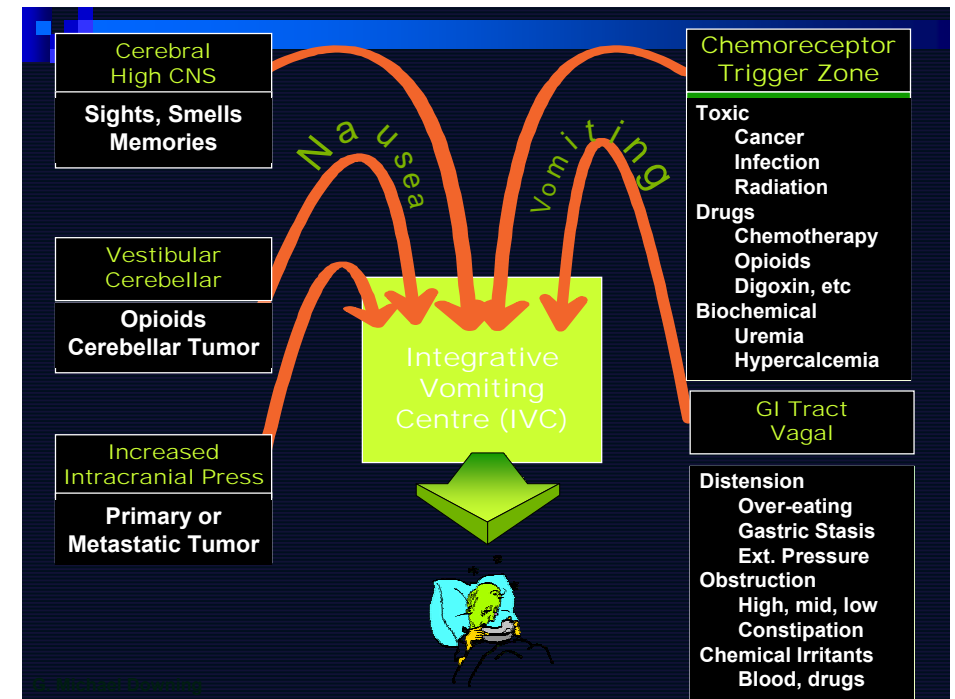
- **Thorough assessment**
 - history; physical examination
- **Discussion**
 - goals of care, hopes, expectations, anticipated course of illness (impact on investigations & interventions)
- **Investigations**
 - blood tests, X-Ray, CT, MRI, etc
- **Treatments**
 - pharmacological and non-pharmacological; interventions
- **Ongoing reassessment/review**
 - Options, goals, expectations, etc.

Prevalence

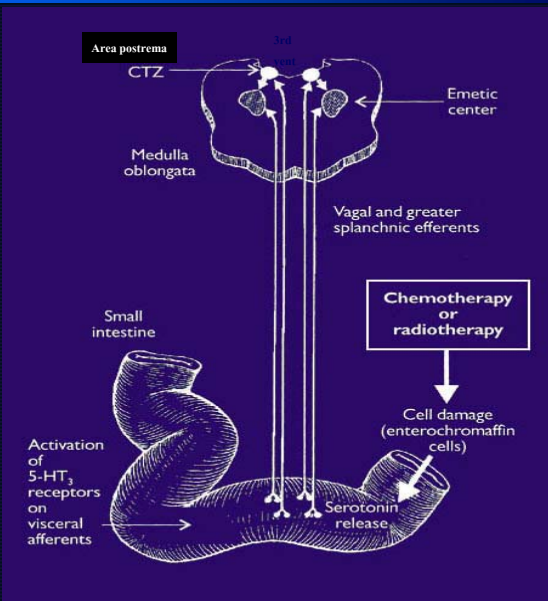
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|---------------------------------|-----------------------|
| ■ Pain | ■ 80 - 90+% |
| ■ Fatigue/Asthenia Constipation | ■ 75 - 90% |
| ■ Dyspnea | ■ 70% |
| ■ Nausea | ■ 60+% |
| ■ Vomiting | ■ 50 - 60% |
| ■ Delirium | ■ 30% |
| ■ Depression/suffering | ■ 30 - 90% / 40 - 60% |

Mechanisms of Nausea & Vomiting

- **vomiting centre:** medulla
- **activated by stimuli from:**
 - **Chemoreceptor Trigger Zone (CTZ)**
 - area postrema, floor of 4th ventricle
 - outside BBB (fenestrated venules)
 - **Upper GI tract & pharynx**
 - **Vestibular apparatus/Cerebellum**
 - **Higher cortical centres**



Pathogenesis of chemo- & RT-induced emesis (CIE, RIE)



N/V Related Problems

- **Medical**
 - dehydration / electrolyte abnormalities
 - esophageal tears / GI bleed
 - aspiration pneumonia
- **Decreased QoL**
 - weight loss / anorexia
 - weakness / lethargy
- **Psychological distress**
- **Refusal of beneficial therapy**

Principles of Therapy

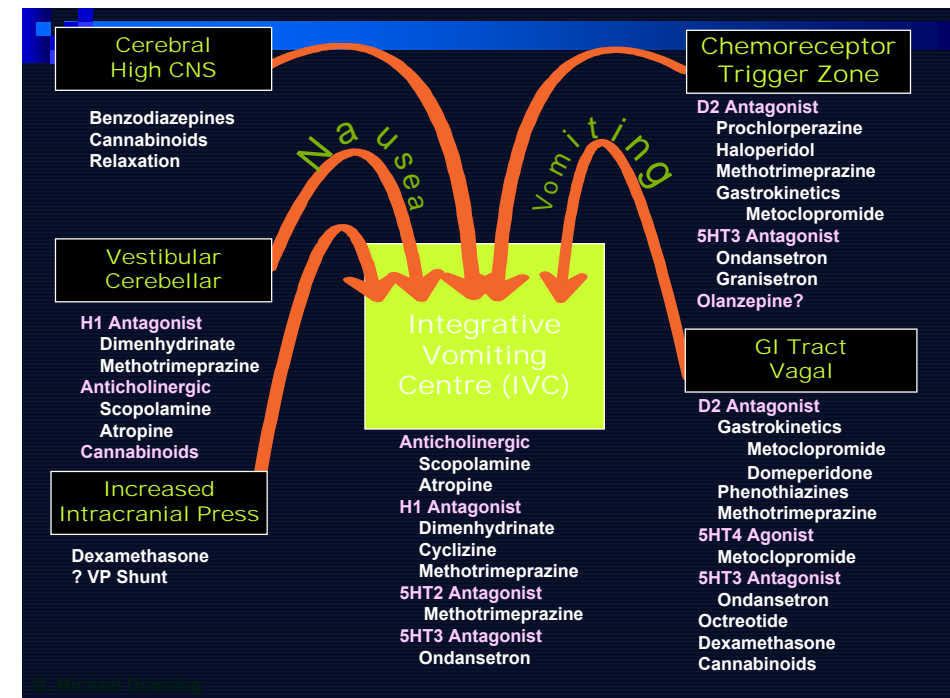
- Treat the underlying cause
- Environmental measures
- Antiemetic use:
 - anticipate need
 - use adequate, regular doses
 - aim at receptor involved
 - combinations if necessary
 - anticipate need for alternate routes

Environmental Measures

- Limit exposure to food smells
 - open food trays prior to presentation
- Bland foods (BRAT)
- Small, frequent snacks/meals
- Good oral hygiene
- Fresh air, calming environment
- Sitting upright post meal
- Avoid alcohol

Anti-Emetic Agents

- Transdermal scopolamine
- Benzodiazepines
- Antihistamines
- Cannabinoids
- Metoclopramide, Domperidone
- Neuroleptics / Anti-psychotics
- Corticosteroids
- 5-HT₃ Antagonists
- NK1 Antagonists (aprepitant)



Antiemetics and Dosing

DOPAMINE ANTAGONISTS	Haloperidol 0.5 - 1 mg po/sq/iv q4-12h
	MTMZ 5 - 10 mg po/sl/sq q4-8h
	Prochlorperazine 5 - 20 mg po/pr/iv
	CPZ 25 - 50 mg po/pr/iv
ANTIMUSCARINIC	Scopolamine patch (Transderm-V)
PROKINETIC	Metoclopramide 10 - 20 mg po/sq/pr q4-8h
	Domperidone 10 mg po q4-8h

Antiemetics and Dosing

H1 ANTAGONISTS	Dimenhydrinate 25 - 100 mg po/pr q4-8h
	Promethazine 25 mg po/iv q4-6h (<i>Not sq</i>)
	Meclizine 25 mg po q6-12h
SEROTONIN ANTAGONISTS	Ondansetron 8 -16 mg q 12 h po/sq/iv
MISCELLANEOUS	Dexamethasone 4-16 mg po/sq/iv daily
	Lorazepam 0.5 - 1 mg po/sl q4-12h
	Olanzapine 2.5-10 mg OD

Olanzapine

- Atypical antipsychotic agent
- Used in schizophrenia, delirium
- Blocks multiple receptors
 - D_{1-4} , $5-HT_{2/3/6}$, α_1 adrenergic, H_1 , M_{1-4}
- High affinity for serotonin vs dopaminergic
- Well tolerated
- Few drug interactions

Special Situations for GI problems

- Constipation
- Obstruction

Symptom Prevalence

■ Pain	■ 80 – 90+%
■ Fatigue/Asthenia	■ 75 - 90%
■ Constipation	■ 70%
■ Dyspnea	■ 60+%
■ Nausea	■ 50 - 60%
■ Vomiting	■ 30%
■ Delirium	■ 30 - 90%
■ Depression/suffering	■ 40 - 60%

Cancer

■ Direct effects

obstruction by tumor in wall
external compression by tumor
neural damage
L/S spinal cord
cauda equina/pelvic plexus
hypercalcemia

Cancer

■ Secondary effects

poor po intake
dehydration
weakness/inactivity
confusion
depression
unfamiliar toilet arrangements

Medications

■ Opioids

- ↑ Ileocecal & anal sphincter tone
- ↓ Peristaltic activity (SI & C)
- Impaired defecation reflex
 - ↓ sensitivity to distension
 - ↑ internal anal sphincter tone
- ↑ Water, electrolyte absorption (SI & C)

Concurrent Disease

- Diabetes
- Hypothyroidism
- Hypokalemia
- Hernia
- Anal fissure/stenosis
- Hemorrhoids
- Autonomic neuropathy
- diabetes
- spinal cord disease
- chemotherapy
- Parkinson's disease
- ALS/MS
- Dementia

Treatment

- Prophylaxis
 - good symptom control
 - activity
 - adequate hydration
 - recognize drug effect
 - create a favorable environment

Treatment : Laxatives

- >80% pts on opioids need laxatives
- Little research to guide choice
- Softener and stimulant best first choice
- May require oral/rectal routes
- Enemas useful in impaction
- Bulk forming agents worsen situation

Treatment: Laxatives

- Surfactants: docusate
- Contact cathartics: senna, bisacodyl
- Osmotic laxatives: lactulose
- Saline osmotics: MgOH, Phosphasoda
- Enemas: oil, saline, soap suds, Fleet

Other Approaches

- Prokinetic agents:
 - domperidone, metoclopramide
- Antibiotics: erythromycin
- Herbal preparations: mulberry, rhubarb, licorice, prune juice

New Agents

- Selective opioid antagonists
- Active in periphery, esp. gut
- Methylnaltrexone, Alvimopan
- Studies used IV and oral application
- S/E
 - abd cramping, flatulence, nausea, dizziness

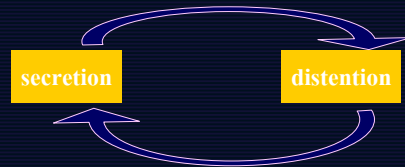


Bowel Obstruction

- Common problem
- Associated with advanced cancers
 - GI, ovarian, lymphoma
- Relapse / local spread of intrabdominal tumour
- Diffuse peritoneal carcinomatosis, encasement by tumour
- Multiple partial bowel occlusions
 - (delaying or preventing propulsion of intestinal contents)
- Symptoms of nausea/vomiting
 - abdominal pain, distention

Bowel Obstruction : Etiology

- Mechanical obstruction causes:
 - ↑ secretions, gas proximal to the obstruction
 - distention from gas, ingested fluids, digestive secretions in turn causes ↑ secretions



Mercadante et al. JPSM 1997

Bowel Obstruction

Standard Therapy

- NG tube/IV fluids (“drip & suck”)
- Bowel rest
- Pain control (opioids)
- Radiological assessment
- Surgical intervention

Bowel Obstruction

Palliative Therapy

- Opioid analgesics, dexamethasone
- Promotility agents
 - metoclopramide/domperidone
- Octreotide (Sandostatin[®])
- Hyoscine butylbromide (Buscopan[®])

Somatostatin Analogues

- Octreotide, vapreotide, lanreotide
- Receptor activity
 - brain, pituitary, pancreas, GI tract, immune cells
- Used in many conditions
- Prolongs GI transit time
 - ↓ fluid secretion in jejunum
 - ↑ water/electrolyte absorption
- decreases peristalsis
- reduces GI blood flow
- Inhibits exocrine pancreatic secretion

Bowel Obstruction in Ovarian Cancer

- 13 pts, advanced ovarian cancer, inoperable GI obstruction
- Octreotide dose of 300 - 600 µg/day
- Octreotide controlled vomiting in all cases
- Vomiting stopped in 2-3 days of starting tx

Mangili et al., Gynecologic Oncology 1996

Bowel Obstruction in Ovarian Cancer

- NG drainage ↓ from 2000 to <100 ml/day
- Complete relief of symptoms within 3 days (range 1-6 days)
- 8/13 pts D/C from hospital, continued treatment at home

Mangili et al., Gynecologic Oncology 1996

Delivery Routes for Medications

- | | |
|--------------------------|-------------------------|
| ■ Standard | ■ Alternative |
| ■ Oral | ■ Sublingual |
| ■ Intravenous | ■ transmucosal |
| ■ Inhalation (nebulized) | ■ mouthwashes |
| ■ Subcutaneous | ■ Intranasal |
| | ■ Transdermal (topical) |
| | ■ Rectal |
| | ■ Vaginal |
| | ■ Intraosseus |

Alternative Routes of Drug Administration

- Alternative delivery routes
 - transmucosal
 - transdermal (topical)
 - rectal
- Review of the science

Oral Mucosal Delivery

■ Advantages:

High vascular permeability

Avoids “first pass” hepatic elimination

High potency of drug (small volumes)

Less intimidating/ “low-tech” administration

easier in home, PCH, LTC

Alternate administration route

pt NPO, difficulty swallowing, SBO, etc.

Oral Mucosal Delivery

■ Barriers:

■ Lipophilic Rx: needs intact mucosal cell membrane

■ Hydrophilic Rx: poor absorption

■ Volume of dose

□ Ideally ≤ 0.5 ml; $> 1-2$ ml \rightarrow swallowed

■ Excessive salivation \rightarrow swallowing of dose

■ Acceptable delivery vehicle/taste

Topical Route

■ Oral route not desirable

□ Mucositis

□ Inability to swallow

□ Nausea/vomiting

□ Obstruction

□ Poor taste of product

□ Dry mouth

■ More localized action

Topical Route: Advantages

■ Avoids the GI tract and hepatic first-pass metabolism

■ Delivers to a specific site

■ Controls absorption rate

■ Provides constant dosing \rightarrow depot effect with anhydrous gels

■ Reduces systemic side effects

Topical Route: Advantages

- Improves compliance
- Allows ↑ concentration of Rx at site of application
- Plasma concentrations of <10% compared to oral route

Heir, Gary DMD, et al. IJPC 2004; 8:337-343

Topical Route: Drawbacks

- Variations in the stratum corneum barrier
- Delivery dosing may require adjustment
- Rate of absorption may vary
- Rash most common SE

Topical Route

- Mouthwash/rinses
 - Misoprostol, Diphenhydramine, Lidocaine, Triamcinolone,
 - Sucralfate, Dry Mouth Formulations
- Transdermal Route
 - Fentanyl, Oxybutinin, Estrogen, Nitrate patches
 - Transdermal gels
- Buccal spray
 - Morphine, Fentanyl, Triamcinolone, Lidocaine
- Medicated lollipops
 - Fentanyl, Nicotine, Tetracaine, Dextromethorphan, Diphenhydramine, Nystatin



Subcutaneous Antiemetics

Haloperidol 0.5 - 1 mg po/sq/iv q4-12h

MTMZ 5 - 10 mg po/sl/sq q4-8h

Metoclopramide 10 - 20 mg po/sq/pr q4-8h

Ondansetron 8 -16 mg q 12 h po/sq/iv

Granisetron 1- 2 mg q 12 h po/sq

Dexamethasone 4-16 mg po/sq/iv daily

Dimenhydrinate 25 - 100 mg po/pr/sq q4-8h

Scopolamine 0.3-0.6 mg sq

Promethazine (*Not sq*)

Rectal Route

- Drug absorption
- Limiting factors
- Conditions/methods of administration

Care Beyond Cure: A Pharmacotherapeutic Guide to Palliative Care; Andree Neron
Editor, 2000

Rectal Drug Absorption

- First 6-8cm of rectum drain directly into systemic circulation
- Drugs admin by this route: no hepatic first-pass effect
- Rx high hepatic extraction may ↑ in bioavailability; variable due to:
 - Patient
 - Absorption site
 - Drug formulation, penetration of mucosa

Care Beyond Cure, 2000

Rectal Drug Absorption

- Rectum vs upper GI tract:
 - Absorption area
 - rectal mucosa: 200-400 cm² (no villi in rectum)
 - small intestine: 2,000,000 cm²
 - pH
 - Fluid content
- Absorption mechanisms same (passive diffusion)
- Formulation of drug is critical factor
 - May have to increase dosage interval i.e. Q8H vs Q12H

Rectal Limiting Factors

- Drug insertion level
 - 6-8cm (lower rectum) → systemic circulation
 - 15-20cm (upper rectum) → portal vein → hepatic first-pass effect
- Solutions:
 - Aqueous & alcohol solutions are the best and most rapidly absorbed
- Fecal matter in rectum
- Defecation reflex, involuntary expulsion

Rectal Administration

- Use liquid formulations whenever possible
 - Use volumes <10-25 ml
 - >80 ml ↑ risk of spontaneous expulsion
- Administer liquids with a small lubricated syringe
 - Rectal canula or catheter tip syringes beneficial
 - Cut a NG tube (#14) to 5 cm; attach to prefilled syringe
 - reduces chance of portal vein absorption

Rectal Administration

- Administer capsules and tablets directly into the rectum
- Compounding pharmacy: “designer” rectal suppositories
 - Administration a lot easier
 - Hepatic absorption usually not a problem with the use of suppositories

Rectal Administration

- Lorazepam
 - Use parenteral preps or tablets
 - Bioavailability of injection > 80%
 - Serum concentrations < ½ of IV route
- Metoclopramide
 - Tablets or suspensions
- Phenobarbital
 - Excellent bioavailability → 90-100%
 - Peaks at ~ 4 hours

Rectal Administration

- For refractory cases, use combinations that act at different receptor sites
 - Cerebral cortex
 - CTZ
 - GI tract
- Severe or refractory nausea may benefit from corticosteroid

Triple Suppository

- Metoclopramide 10 - 20mg
- Dimenhydrinate 25 - 75mg
- Prochlorperazine 10 - 25mg
- Use a formulation with a single medication or combinations of up to 3 medications

Other Antinauseant Suppositories

- **Dimenhydrinate 75mg/Metoclopramide 15mg/Prochlorperazine 10mg**
- Dimenhydrinate 25mg/Metoclopramide 10mg/ Prochlorperazine 15mg
- Metoclopramide 10mg/Haloperidol 1mg
- Dimenhydrinate 25mg/ Metoclopramide 20mg/ Prochlorperazine 10mg/ Dexamethasone 2mg

Dyspnea in palliative

Dyspnea

An uncomfortable awareness of
breathing

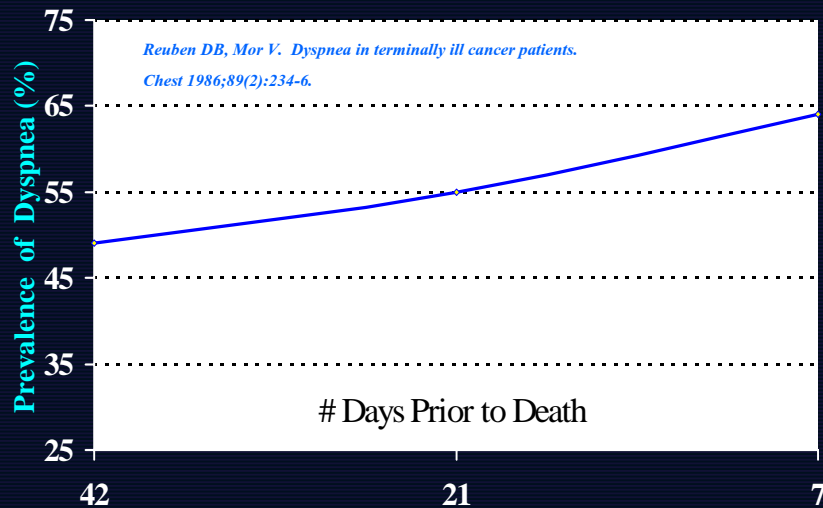
Dyspnea

“...the most common severe symptom in the
last days of life”

Davis C.L. *The therapeutics of dyspnoea*. Cancer Surveys, 1994, Vol.21 p.85 - 98.

National Hospice Study

Dyspnea Prevalence



CAUSES OF DYSPNEA IN PALLIATIVE CARE

1. Direct tumor effects
2. Indirect tumor effects
3. Treatment-related
4. Unrelated to cancer

DIRECT TUMOR CAUSES

- Parenchymal
- Lymphangitic carcinomatosis
- Obstruction
- Pleural effusion / tumor
- Pericardial effusion
- Superior vena cava obstruction
- Ascites, hepatomegaly
- Tumor microemboli

INDIRECT CANCER CAUSES

- Cachexia
- Mineral & electrolyte imbalances
- Infections
- Anemia
- Pulmonary embolism
- Neurologic paraneoplastic syndromes
- Aspiration

TREATMENT-RELATED CAUSES OF DYSPNEA

- Surgery
- Radiation pneumonitis / fibrosis
- Chemotherapy-induced pulm. fibrosis (bleomycin)
- Chemotherapy-induced cardiomyopathy
(adriamycin, cyclophosphamide)
- Neutropenic infection

APPROACH TO THE DYSPNEIC PALLIATIVE PATIENT

Two basic intervention types:

1. Non-specific, symptom-oriented
2. Disease-specific

SIMPLE MEASURES IN MANAGING DYSPNEA

- calm reassurance
- sitting up / semi-reclined
- open window
- fan

NON-SPECIFIC PHARMACOLOGIC INTERVENTIONS IN DYSPNEA

- Oxygen - hypoxic and ? non-hypoxic
- Opioids - complex variety of central effects
- Chlorpromazine - start with 10 mg po q6h
- Benzodiazepines - literature inconsistent but clinical experience extensive

TREAT THE CAUSE OF DYSPNEA - IF POSSIBLE AND APPROPRIATE

- Anti-tumor: chemo/radTx, hormone, laser
- Infection
- CHF
- SVCO
- Pleural effusion
- Pulmonary embolism
- Airway obstruction

DISEASE-SPECIFIC MEDICATIONS FOR DYSPNEA

- Corticosteroids
 - obstruction: SVCO, airway
 - lymphangitic carcinomatosis
 - radiation pneumonitis
- Furosemide
 - CHF
 - lymphangitic carcinomatosis
- Antibiotics
- Anticoagulation – pulm. embolus
- Bronchodilators

DYSPNEA CRISIS

- Sudden onset / rapid worsening of dyspnea
- Often imminently terminal situation (minutes or hours)
- Examples:
 - » pulmonary embolism
 - » fulminant pneumonia
 - » upper airway obstruction
 - » hemoptysis

APPROACH TO DYSPNEA CRISIS

- Aggressively pursue comfort
- Remain on site until comfortable
- Ideally use intravenous route
- Generally employ non-specific measures:
 - » calm reassurance
 - » oxygen
 - » opioids
 - » possibly sedatives:
 - methoprineprazine, CPZ, benzodiazepines (lorazepam, midazolam)

Opioids in Dyspnea

- Uncertain mechanism
- Comfort achieved before resp compromise; rate often unchanged
- Often patient already on opioids for analgesia; if dyspnea develops it will usually be the symptom that leads the need for titration
- Dosage should be titrated empirically; may easily reach doses commonly seen in adults
- May need rapid dose escalation in order to keep up with rapidly progressing distress

OPIOIDS IN DYSPNEA CRISIS

q10 min. IV push with escalating doses

Example using morphine IV push:

5 - 10 mg



If no better in 10 min.

10 - 15 mg



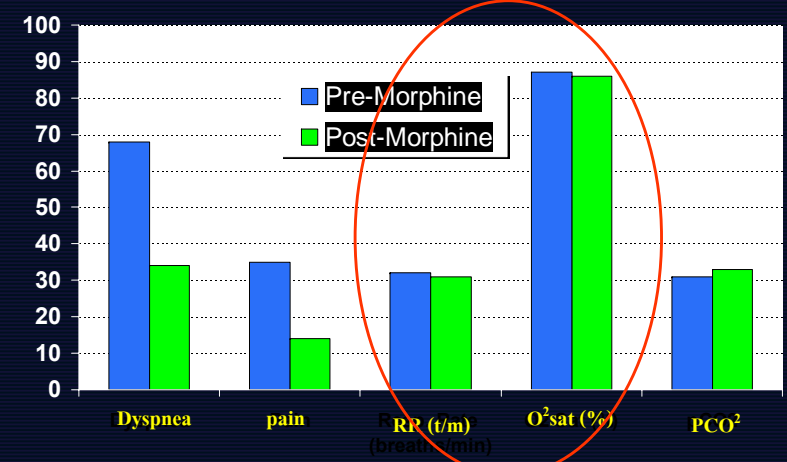
If no better in 10 min.

15 - 20 mg

A COMMON CONCERN ABOUT AGGRESSIVE USE OF OPIOIDS IN THE FINAL HOURS

How do you know that the aggressive use of opioids for pain or dyspnea doesn't actually bring about or speed up the patient's death?

SUBCUTANEOUS MORPHINE IN TERMINAL CANCER



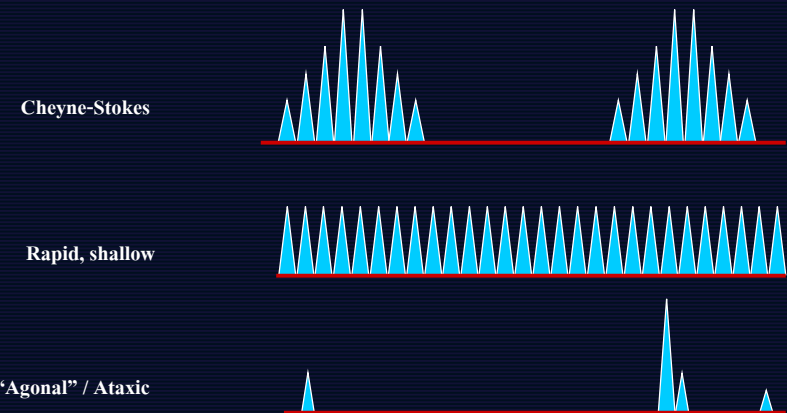
Bruera et al. J Pain Symptom Manage. 1990; 5:341-344

Typically, with excessive opioid dosing one would see:

- pinpoint pupils
- gradual slowing of the respiratory rate
- breathing is deep (though may be shallow) and *regular*

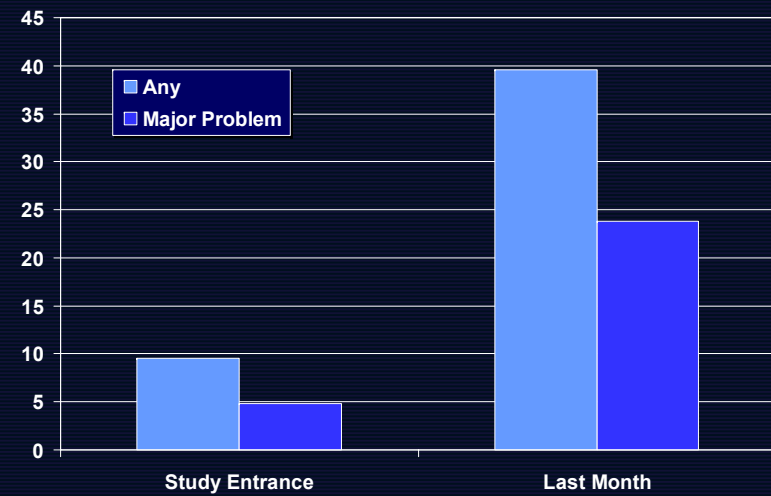


COMMON BREATHING PATTERNS IN THE FINAL HOURS



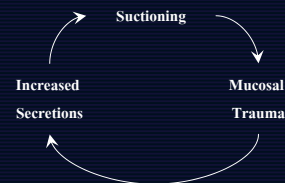
Palliative Management of Secretions

Secretions - Prevalence At Study Entry And In Last Month Of Life



Managing Secretions in Palliative Patients

- Factors influencing approach management:
 - ❖ Oral secretions vs.. lower respiratory
 - ❖ Level of alertness and expectations thereof
 - ❖ Proximity of expected death
- “Death Rattle” – up to 50% in final hours of life
- At times the issue is more one of creating an environment less upsetting to visiting family/friends
- Suctioning: “If you can see it, you can suction it”



CONGESTION IN THE FINAL HOURS

“Death Rattle”

- Positioning
- *ANTISECRETORY* : Scopolamine, glycopyrrolate
- Consider suctioning if secretions are:
 - distressing, proximal, accessible
 - not responding to antisecretory agents

Atropine Eye Drops

For Palliative Management Of Secretions

- Atropine 1% ophthalmic preparation
- Local oral effect for excessive salivation/drooling
- Dose is usually 1 – 2 drops SL or buccal q6h prn
- There may be systemic absorption... watch for tachycardia, flushing

CONGESTION IN THE FINAL HOURS

“Death Rattle”

- Positioning
- **ANTISECRETORY**
 - Scopolamine 0.3 - 0.6 mg SQ q1h prn
 - Atropine 0.4 - 0.8 mg SQ q1h prn
 - Glycopyrrolate 0.2 - 0.4 mg SQ q2h prn
 - » less likely to cause delirium, sedation
 - » ? less effective
- Consider suctioning if secretions are:
 - distressing, proximal, accessible
 - not responding to antisecretory agents

Fatigue in the Advanced Cancer Patient

Fatigue & Cancer

- Definitions
- Causes
- Pathophysiology
- Assessment
- Treatment issues

Fatigue & Asthenia

- Greek (Asthenos)
“absence or loss of strength”
- Combination of physical & mental fatigue
- May precede diagnosis
- Often ass'd with cachexia
- Worsened by chemo/RT/surg
- Rarely assessed or treated

Symptom Prevalence

- | | |
|---------------------------|-------------------|
| ■ Pain | ■ 80 - 90% |
| ■ Fatigue/Asthenia | ■ 75 - 90% |
| ■ Constipation | ■ 70% |
| ■ Dyspnea | ■ 60% |
| ■ Nausea | ■ 50 - 60% |
| ■ Delirium | ■ 30 - 90% |
| ■ Depression/suffering | ■ 40 - 60% |

Asthenia

- 3 elements
- **Fatigue**
easily tired; ↓ ability to maintain adequate performance
- **Weakness**
subjective sensation; difficulty initiating activity (not neuro/muscular disease)
- **Mental fatigue**
impaired concentration, memory loss & emotional lability

Etiology

- | | |
|-------------------------|-------------------------|
| ■ Cachexia/malnutrition | ■ Endocrine disorders |
| ■ Dehydration | ■ Insomnia |
| ■ Infection | ■ Chronic overexertion |
| ■ Hematologic causes | ■ Pharmacologic |
| ■ Metabolic disorders | ■ Cardio/pulm disorders |
| ■ Chronic hypoxia | ■ Liver failure |
| ■ Neurologic dysfn | ■ Renal failure |
| ■ Psychogenic causes | ■ Chemo/RT |

Causes

- **Electrolyte disorders**

↑ Ca^{++} , ↓ K^{+} , ↓ Mg^{++} , ↓ Na^{+}

- **Endocrine disorders**

↑ thyroid, ↓ cortisol, diabetes

- **Hematologic**

↓ Hgb, ↓ WBC

Causes

- **Infections**

TB, viral (e.g. hepatitis), fungal

- **Neurologic disorders**

auto dysf'n, myasthenia, parkinsonism

- **Pharmacologic**

chemotx, sedatives, EtOH, narcotics

Mechanisms

- **3 factors**

Direct: produced by tumor

Induced: secondary to tumor effect

Accompanying: associated with malignancy, contribute to asthenia

CNS Mechanisms

- Hypothetical, little actual research

- RAS active in fatigue experience

cortical stimulation & sensory activity

- Chronic stimulation (pain) may yield fatigue

- Physical fatigue may protect RAS

- Asthenia d/t breakdown of RAS by stimuli from

environment & cortex; humoral factors

Mechanisms in Muscle

- Cachexia = loss of muscle and fat
- Pts with N caloric intake may show:
 - ↓ lactate production
 - atrophy of type II fibres
 - ↑ cathepsin-D
 - impaired mm function
- Caused by 'asthenins'/cytokines

Assessment

- Why?
- Subjective sensation; self-assess best
- Characterize, monitor, research purposes
- Many tools developed
- Gold standard (nonexistent):
 - simple, easily understood
 - valid, reliable, multidimensional

Assessment Tools

- **Unidimensional**
 - Performance status (Karnofsky, ECOG)
 - Rhoten Fatigue Scale
- **Multidimensional**
 - F[']nal Assessment of Cancer Tx (FACT)
 - Edm F[']nal Assessment Tool (EFAT)
 - Multid[']nal Fatigue Inventory (MFI-20)

Management

- **Pharmacologic measures**
 - Corticosteroids (Decadron)
 - ↑ appetite, energy, short-term
 - Amphetamines (Ritalin)
 - ↓ sedation, ↑ activity, opioid ass'n
 - Megesterol acetate (Megace)
 - ↑ appetite, ? asthenia, expensive

Management

■ Promising Rx treatments

Thalidomide

↓ AIDS wasting, anti-TNF

Melatonin

Cannabinoids

Clenbuterol

Ω-3 fatty acids

Management

■ Non-pharmacologic measures

■ Moderate exercise

■ Adapting ADL

■ Rest, energy conservation

■ Psychotherapy

■ Self-help; activity diary

■ Family/caregiver involvement

Conclusions

- Common condition
- Multiple causes
- Mechanisms unclear
- Assessment important
- Multidimensional treatment
- More research needed

Delirium in the Cancer Patient

Delirium

- Definition
- Recognition
- Screening/diagnostic tools
- Etiologic factors
- Treatment of underlying cause
- Prevention

Definition

- Etiologically **non-specific global cerebral dysfunction** associated with **changes in LOC, attention, thinking, perception, memory, psychomotor behavior, emotion and the sleep/wake cycle**

DSM-IV Criteria

- **A)** Change in **consciousness** with reduced ability to focus, sustain or shift attention
- **B)** Change in **cognition** (e.g., memory, disorientation, change in language, perceptual disturbance) that is not dementia
- **C)** **Abrupt onset** (hours to days) with fluctuation
- **D)** Evidence of medical condition judged to be etiologically related to disturbance

Characteristics

- **Abrupt onset**
- **Disorientation, fluctuation of symptoms**
- **Hypoactive vs hyperactive vs mixed**
- **Early signs often mistaken as**
 - **anger, anxiety, depression, psychosis**

Delirium Types

- **Hypoactive**
 - confusion, somnolence, ↓ alertness
- **Hyperactive**
 - agitation, hallucinations, aggression
- **Mixed (>60%)**
 - features of both

Prevalence of Delirium

- **Common in terminally ill**
 - **Steifel et al:** 20% of medical in-pts
 - **Massie et al:** >75% terminally ill
 - **Pereira et al:** 44% on admission
 - 62% at death
 - 30% reversible

Incidence

- **Gagnon et al, (J Pall Care 1998)**
 - 89 consecutive pts, CRS used
 - 20% delirious on admission
 - 30-40% during stay
 - 44% reversed, >50% died in delirium
 - Associated with high opioid dose

Delirium vs Dementia

- | ■ Delirium | ■ Dementia |
|----------------------|------------------------------|
| ■ Impaired memory | ■ Impaired memory |
| ■ Impaired judgement | ■ Impaired judgement |
| ■ Impaired thinking | ■ Impaired abstract thinking |
| | ■ Impaired cortical function |
| ■ Disorientation | ■ Disorientation |

Delirium vs Dementia

- | | |
|-----------------------------|--------------------------|
| ■ Delirium | ■ Dementia |
| ■ Abrupt onset | ■ Insidious, progressive |
| ■ Decreased LOC | ■ Alert, LOC intact |
| ■ Sleep/wake cycle Δ | ■ Minimal Δ |
| ■ Reversible | ■ Irreversible |

Screening Tools

- | | |
|--------------------------------|-------------------------|
| ■ Delirium Rating Scale | ■ MMSE |
| ■ temporal onset | ■ orientation |
| ■ perceptual Δ | ■ registration |
| ■ hallucinations | ■ attention/calculation |
| ■ psychomotor behavior | ■ recall |
| ■ cognitive status | ■ language |
| ■ mood lability | |
| ■ variability of symptoms | |

Causes

- CNS effects:**
- tumour
 - seizures
 - RT

- Indirect:**
- Ca^{++}
 - Na^+ , - Na^+
 - K^+
 - Mg^{++}
 - O_2 , - CO_2

Causes

- **Infection:**
 - pneumonia, sepsis
- **Hematologic:**
 - \downarrow Hgb, \uparrow WBC, \uparrow protein
- **Metabolic encephalopathy:**
 - organ failure, paraneoplastic syndromes

Causes

- **Endocrine:**
 - hyper/hypothyroidism, Cushing syndrome
- **Drug withdrawal:**
 - alcohol, narcotics, hallucinogens
- **Immunologic:**
 - SLE, vasculitis
- **Nutritional deficiencies**

Drug Causes

- **Chemotherapy:**
 - MTX, 5FU, VCR/VBL, Bleo, Plat, IL-2
- **Steroids**
- **Opioids**
- **BZD, phenothiazines**

Opioid-Induced Neurotoxicity (OIN)

- **Neuropsychiatric syndrome**
 - Cognitive dysfunction
 - Delirium
 - Hallucinations
 - Myoclonus/seizures
 - Hyperalgesia/allodynia

OIN: Risk Factors

- **High opioid doses**
- **Prolonged opioid treatment**
- **Borderline cognition/delirium**
- **Dehydration**
- **Renal failure**
- **Psychoactive drugs**
- **Advanced age**

Treatment

- Stop any offending Rx
- Hydration (oral, IV, SC)
- Correct metabolic abnormalities
- Structured setting
 - quiet room, low lights, calendar, clock
- Family support

Treatment

- Opioid rotation
- Adjunct medications
 - haloperidol (Haldol): 0.5-5 mg q2-4 h PO/SC/IV/IM
 - midazolam : 1-20 mg q2 h SC/IV or 30-100 mg/24 h CSCI or CIVI

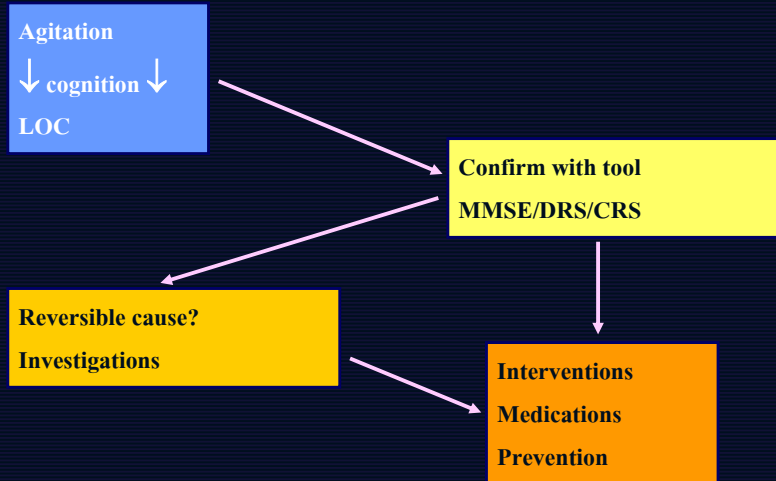
Sedation in Terminal Delirium

- Mild:** haloperidol 1-2 mg PO/SC q8h plus q1h prn
- Moderate:** haloperidol 2.5 - 5 mg
+
midazolam 2.5 - 5 mg
SC q4h plus q1h prn
- Severe:** haloperidol 5 mg
+
midazolam 5 - 20 mg
SC q4h plus q1h prn
- OR CSCI or CIVI:*
haloperidol 1.25 mg/hr + midazolam 1.25 - 5 mg/hr

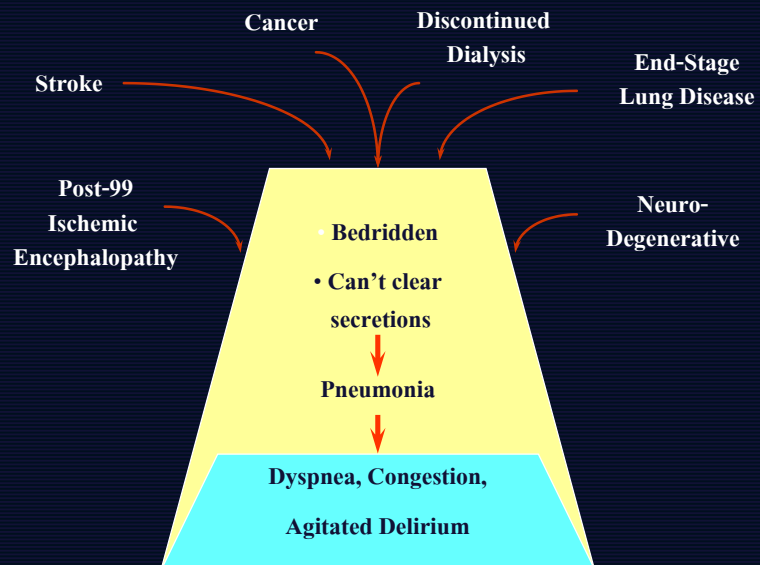
Prevention

- Staff and family awareness
- Structured settings
- Minimize use of medications
- Opioid rotation
- Hydration

Algorithm



The Final Days



Main Features of Approach to Care

- Perceptive and vigilant regarding changes
- “Proactive” communication with patient and family
 - » anticipate questions and concerns
 - » available
 - » don't present “non-choices” as choices
- Aggressive pursuit of comfort

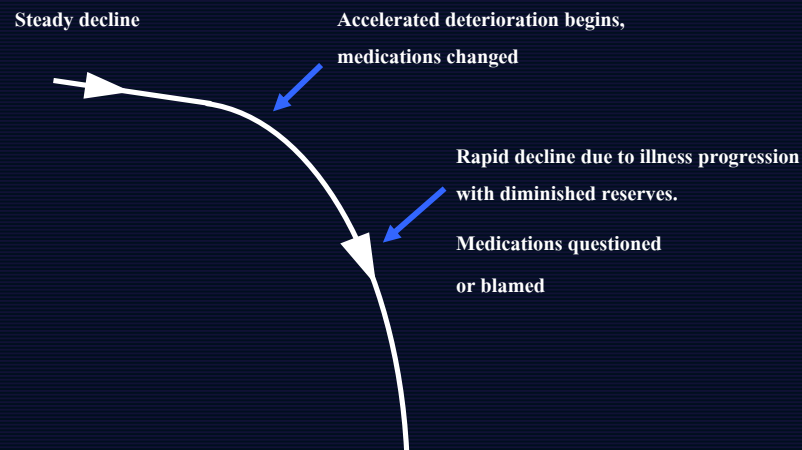
Predictable Challenges in the Final Days

- Functional decline- transfers, toileting
- Can't swallow meds- route of administration
- Terminal pneumonia
 - dyspnea
 - congestion
 - delirium:> 80% At times ++ agitation
- Concerns of family and friends

Concerns of Patients, Family, and Friends

- How could this be happening so fast?
- What about food & fluids?
- Things were fine until that medicine was started!
- Isn't the medicine speeding this up?
- Too drowsy! Too restless!
- Confusion... he's not himself, lost him already
- What will it be like? How will we know?
- We've missed the chance to say goodbye

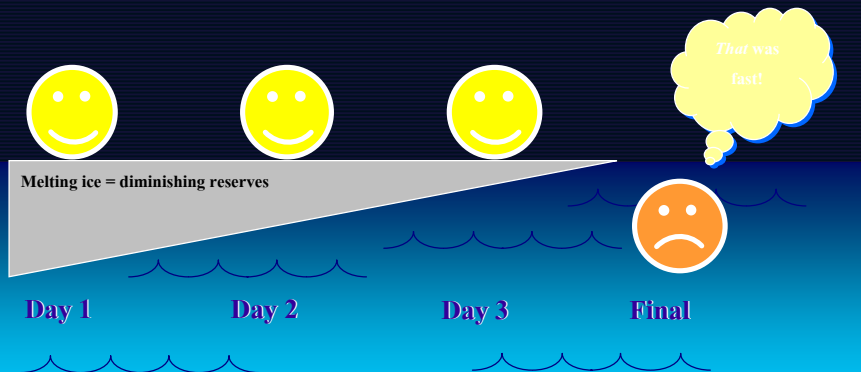
Which Came First.... The Med Changes or the Decline?



The Perception of the "Sudden Change"

When reserves are depleted, the change seems sudden and unforeseen.

However, the changes *had* been happening.



Family / Friends Wanting to Intervene With Food and / or Fluids

- discuss goals
- distinguish between **prolonging living vs. prolonging dying**
- parenteral fluids generally not needed for comfort
- pushing calories in terminal phase does not improve function or outcome

Time that death would have occurred
without intervention

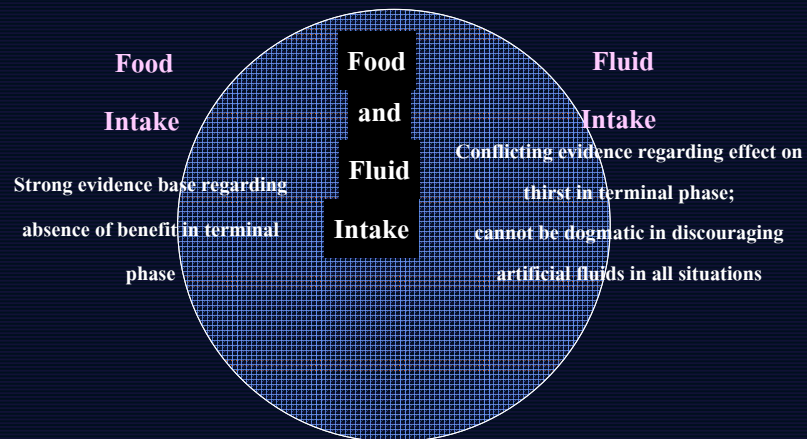
Patient's Lifetime

Extending the final days in terminal illness:

Prolonging life or prolonging the dying phase?

Consider carefully the rationale of trying to prolong life by adding time to the period of dying

Consider Concerns About Food And Fluids Separately



OBTAINING SUBSTITUTED JUDGMENT

You are seeking their thoughts on what the patient would want,

not what they feel is “the right thing to do”.

PHRASING REQUEST: SUBSTITUTED JUDGMENT

“If he could come to the bedside as healthy as he was a year ago, and look at the situation for himself now, what would he tell us to do?”

Or

“If you had in your pocket a note from him telling you what to do under these circumstances, what would it say?”

TALKING ABOUT DYING

“Many people think about what they might experience as things change, and they become closer to dying.

Have you thought about this regarding yourself?

Do you want me to talk about what changes are likely to happen?”

First, let's talk about what you should *not* expect.

You should *not* expect:

- ❖ pain that can't be controlled.
- ❖ breathing troubles that can't be controlled.
- ❖ “going crazy” or “losing your mind”

If any of those problems come up, I will make sure that you're comfortable and calm, even if it means that with the medications that we use you'll be sleeping most of the time, or possibly all of the time.

Do you understand that?

Is that approach OK with you?

You'll find that your energy will be less, as you've likely noticed in the last while.

You'll want to spend more of the day resting, and there will be a point where you'll be resting (sleeping) most or all of the day.

Gradually your body systems will shut down, and at the end your heart will stop while you are sleeping.

No dramatic crisis of pain, breathing, agitation, or confusion will occur -
we won't let that happen.

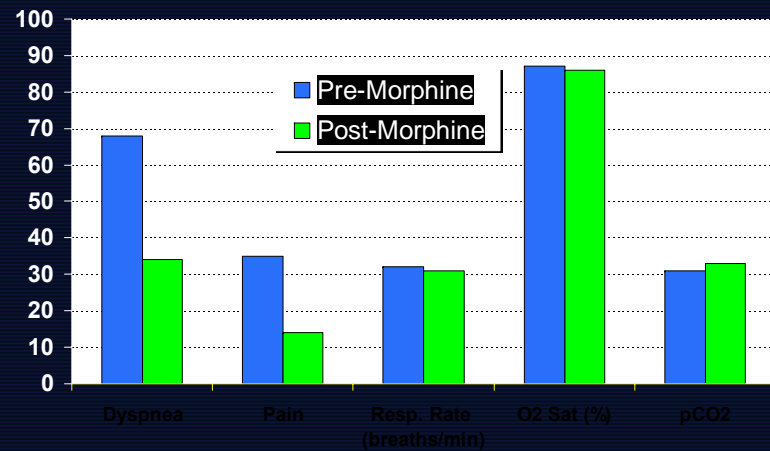
Basic Medications in The Final Day(s)

SYMPTOM	MEDICATION
Pain	Opioid
Dyspnea	Opioid
Secretions	Scopolamine
Restlessness	Neuroleptic (haloperidol or methotrimeprazine) +/- benzodiazepine

A COMMON CONCERN ABOUT AGGRESSIVE USE OF OPIOIDS IN THE FINAL HOURS

How do you know that the aggressive use of opioids doesn't actually bring about or speed up the patient's death?

SUBCUTANEOUS MORPHINE IN TERMINAL CANCER



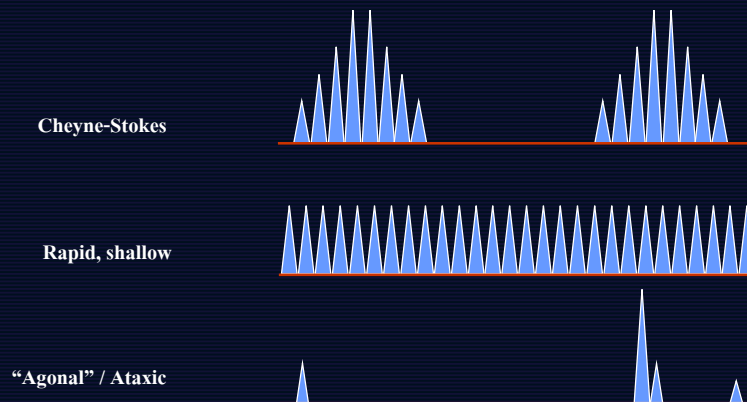
Bruera et al. J Pain Symptom Manage. 1990; 5:341-344

Typically, With Excessive Opioid Dosing
One Would See:

- pinpoint pupils
- gradual slowing of the respiratory rate
- breathing is deep (though may be shallow) and *regular*



COMMON BREATHING PATTERNS IN THE FINAL HOURS



- The difference in aggressive opioid use in end-of-life circumstances is that the "bad effect" = Death
- The doctrine of double effect exists to support those health care providers who may otherwise withhold opioids in the dying out of fear that the opioid may hasten the dying process
- A problem with the emphasis on double effect is that there is an implication that this is a common scenario.... in day-to-day palliative care it is extremely rare to need to even consider its implications

DON'T FORGET...For death at home

- **Health Care Directive: no CPR**
- **Letters (regarding anticipated home death) to:**
 - **Funeral Home**
 - **Office of the Chief Medical Examiner**
 - **Copy in the home**
- **physician not required to pronounce death in the home, but be available to sign death certificate**