Palliative Care

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Geneva Foundation
for Medical Education and Research
Palliative care: a global perspective

- Tens of millions of people worldwide are affected by lifethreatening illnesses such as HIV/AIDS and cancer.

- Majority of cases occur in the developing world, where access to prompt and effective treatment is often still difficult.

  
  **Cancer deaths:**
  
  *Out of 9 Mo new cases worldwide in 1985, 55% were in the developing world.*
  
  *In 2005, they will represent 15 Mo and 66% of cases.*

  Ref: Information and communication Unit. WHO regional office for Africa.

- Source of major suffering for patients and families as well as economical hardships.
Palliative care: a global perspective

- There are major differences in access to palliative care services between regions and countries,

- as well as serious impediments to opioid availability in many countries
Palliative care: WHO’s definition (1)

- Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual
Palliative care: WHO’s definition (2)

- Provides relief from pain and other distressing symptoms
- Affirms life and regards dying as a normal process
- Intends neither to hasten or postpone death
- Integrates the psychosocial and spiritual aspects of patient care
- Offers a support system to help patients live as actively as possible until death
- Offers a support system to help the family cope during the patient’s illness and in their own bereavement
- Uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated
- Will enhance quality of life, and may also positively influence the course of illness
Old vision of palliative care

Curative approach

Palliative care

"We can't do anything any more..."
Complementarity between curative approach and palliative care

- Curative approach and rehabilitation
- Needs of patients / families

Palliative care

Illness
- acute
- chronic
- terminal

Death of the patient
Bereavement

Mazzocato C
Soins palliatifs
CHUV
Curative treatments and palliative care

Curative approach – rehabilitation

Palliative care

Curative phase
Palliative phase
Terminal phase

Usual trajectory
Minimal trajectory
Potential reversibilities
## Symptom prevalence in cancer patients

- 275 consecutive advanced cancer patients

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Prevalence</th>
<th>95% confidence interval</th>
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</thead>
<tbody>
<tr>
<td>Asthenia</td>
<td>90</td>
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<td>Anorexia</td>
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<td>Pain</td>
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<td>Sedation-confusion</td>
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<td>40-75</td>
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<tr>
<td>Dyspnea</td>
<td>12</td>
<td>8-16</td>
</tr>
</tbody>
</table>

Prevalence of symptoms in advanced cancer


There are statistically significant differences in symptom prevalence depending on lary site of cancer and the hospice:

* Moderate to severe pain: 51%
  (43% in stomach cancer - 80% in gynecological cancer)

* Nausea: most prevalent in gynecological (42%) and stomach (36%) cancers

* Dyspnea most prevalent in lung cancer (46%)
Definition of pain

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

Pain is always subjective.

IASP (International Association for the Study of Pain)
Patient suffering from pain: what should we do?

1. Assess his/her/pain(s):

- History
  (ask patients, relatives and professional caregivers)

- Validated assessment tools

- Physical examination, including neurological

- Complementary tests, if/when appropriate, in order to answer specific questions
Patient suffering from pain: what should we do?

2. Diagnose the pain(s):

😊 Origin(s):
   primary disease, treatments, other

😊 Type of pain:
   nociceptive, neuropathic

😊 Mecanism of pain

😊 Different dimensions of the pain experience and other symptoms
Origin of pain in cancer patients

- Underlying disease (78%)
- Treatments (19%)
  - Chemotherapy: eg, mucositis, post-chemotherapy neuropathies
  - Radiotherapy: eg, post-radiation plexopathies
  - Surgery: eg, post-thoracotomy pain
- No direct relationship with one or the other (3%)
  - Ex: postherpetic neuralgias, inflammatory or degenerative arthropathies, diabetic neuropathies,…
Types of pain

Nociceptive pain
Activation of nociceptors in the different tissues/organs by tissue damage

Somatic pain
Well localised

Visceral pain
Poorly localised, deep, dull, cramping, referred

Modified from Mazzocato, Sylvana 02
Types of pain

Neuropathic pain

Peripheral or central alteration of nerve conduction

Dysesthesias: burning sensation, numbness, tingling, as well as sharp and shooting, paroxystic exacerbations

Associated with a sensory deficit, hyperesthesia, allodynia; in the region innervated by the affected nerve structure (dermatoma, radicular distribution, etc.)

Modified from Mazzocato, Sylvana 02
History of pain

- How/when did the pain begin?
- Localisation(s)
- Intensity
- Temporal characteristics
  Does it have a periodicity? How long?
- How is the pain described:
  words used by the patient (gives clue to the underlying etiology/sensation and emotional component)
- What improves the pain?
  Types of therapies tried and what benefit they had
- What makes the pain worse?
- How does the pain impact the patient’s life? (home, friends, work)
- Patient’s understanding of pain
- Important elements in past medical and psychological history
Assessment of pain intensity

- Visual analog scale:

  No pain ________________________________ Worst possible pain

- Numerical scale:

  No pain 0 1 2 3 4 5 6 7 8 9 10 Worst possible pain

- Categorical scale:

  No pain Week pain Moderate pain Severe pain Very severe pain Extreme pain
Benefits of a systematic pain assessment

- Identification of patients in pain, even if they don’t complain
- Active role for the patient, and an attentive ear
- Prescription of effective treatments
- Monitoring of treatment effects and pain evolution
- Facilitation of communication between doctors, nurses and other healthcare professionals
Pain management

- Systematic multidimensional assessment, regular reassessments

- **Treat the cause:**
  - when possible and reasonable (benefits > disadvantages)

- **Treat symptoms:**
  - systemic analgesics (WHO guidelines)
  - local measures: eg; cold, heat, position, local application of anaesthetics or opioids in painful ulcerations
  - invasive treatments: injection of trigger zones, blocks (eg coeliac plexus in painful pancreatic cancer), spinal analgesia, if specialist available and simple analgesics fail

- **Treat the patient as a whole human being** (body, mind, spirit)
  Interdisciplinary communication, patient and family education

- **Consider the patient and his family as the unit of care**
Symptomatic pain medications

By the mouth

By the ladder

By the clock
WHO analgesic ladder

**Step 1**
Non-opioid:
Paracetamol, AINS
 +/- adjuvants

**Step 2**
Codeine, tramadol
 +/- non-opioids
 +/- adjuvants

**Step 3**
Reference: oral morphine
Hydromorphone, methadone, fentanyl,
 +/- non-opioids
 +/- adjuvants

*WHO, in collaboration with IASP 1999*
Step 2: Codein

- Biotransformation into morphine by Cyt. P450.

Iso-enzyme absent in 7-10% caucasians. In those cases, codein will probably be poorly effective.

Dose: 30-60 mg/4h
Step 2: tramadol

- Opioid (week affinity for the μ receptor) + noradrenergic effect (noradrenaline and serotonin)

- Peak plasma concentration: approx. 70 min, prolonged in the elderly
  - T1/2 env 6 h, prolonged in liver failure

- Kidney elimination of tramadol and its metabolites

- Doses:
  - initially: 50 mg/6-8h and 15-20 mg breakthrough
  - (analgesic effect: 3-7h with chronic administration)
  - maximal studied dose: 400 mg/d.
  - In the elderly > 75 yrs: 300 mg
Step 2: tramadol

- Side effects:
  - frequent nausea/vomiting
  - dizziness
  - sweating
  - dry mouth
  - constipation
  - convulsions
Step 2: tramadol

- Potentially dangerous drug interactions, particularly with antidepressants: SSRI s, tricyclics, IMAO:

  serotoninergic syndrome

Schaad, Med et Hyg 2001;2346
## Serotoninergic Syndrome

<table>
<thead>
<tr>
<th>Category</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastro-intestinal</td>
<td>Cramps, Diarrhea</td>
</tr>
<tr>
<td>Neurological</td>
<td>Headaches, Dysarthria, Incoordination, Myoclonia</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Tachycardia, Hypo/hypertension, Cardiovascular collapsus</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>Confusion, Dysorientation</td>
</tr>
<tr>
<td>Other</td>
<td>Sweats, Hyperthermia, Hyperreflexia</td>
</tr>
</tbody>
</table>
Step 3: initiation of treatment

- Morphine is the narcotic of first choice, since it is the most cost-effective

Give explanations to the patient, patient and family education

- Start with a short acting substance; oral morphine
  
  A. Opioid naive patient:
  5 mg/4h
  Breakthrough, if pain in between regular dosis: 4-hourly dose, to be repeated if needed up to every hour. Monitor treatment response (analgesic as well as possible adverse effects)

  B. Patient previously treated with another opioid (ex.: step 2):
  Start at least by the equianalgesic dose!
Step 3: dose titration

A/ Increases by approx. 30%

Regular doses + breakthroughs taken in 24h

B/ _____________________________________________________________________ = new 4 hourly dose

6

😊 Adjust breakthrough doses (4 hourly dose)

😊 Reassess if need for more than 3 breakthroughs/day
Step 3: when stable and well controlled pain

- Switch to a slow-release form if necessary: for eg MST
  24h dose in slow-release form = 24h dose in short acting form
  Slow release morphine tablets: q 12h

- Prescribe breakthrough doses (in short acting form):
  Equivalent to the 4 hourly dose, q 1h

- Reassess at regular intervals
  Adapt doses by approx. 30%
Transdermal fentanyl

- Not a first choice!

- **Indications:**
  
  * Stable pain
  * Effective dose previously determined by a short acting opioid
  * Swallowing difficulties, alteration of drug absorption or other intolerances to the oral route
Transdermal fentanyl

**Contraindications:**

* Economical considerations: expensive +++++
* Acute pain
* Unstable pain
* Skin problems
* Generalised edema
Morphine and other opioids: feared effects

- **Addiction**
  Almost *never* in a well managed pain treatment

- **Physical dependance**
  Means withdrawal when medication abruptly stopped
  of in the case of administration of an antagonist

- **Tolerance**
  Need to increase doses in order to maintain the same effect
  *Very rarely* a problem in clinical practice
Morphine: side effects

- **Classical:**
  - nausea, vomiting (prevent)
  - constipation (systematically prescribe laxatives)
  - drowsiness

Sometimes also:
- Sweating, itching, urinary retention
Morphine: side effects

- **Nausea/vomiting: prevent**
  - for eg metoclopramide
    - 10 mg po if occasional episodes (breakthrough only)
    - if necessary, 10 mg/4h + 10 mg breakthrough

  alternative: haloperidol
  - 1 mg po if occasional episodes
  - if necessary, 1 mg/12h + 1 mg breakthrough

  NB: both metoclopramide and haloperidol can be given sc
Morphine: side effects

- **Constipation: to be systematically prevented:**

  **stimulant laxative:**
  eg: Na picosulfate 10 drops morning + evening, to be adjusted
  alternatives: bisacodyl, senne derivatives

  +

  **osmotic:**
  eg. lactilol: 10 mg tds

  reassess min. twice a week and adjust
Morphine: adverse effects

- **Neurotoxicities:**
  - myoclonias,
  - delirium,
  - hyperalgesie/allodynia,
  - hallucinations

  mainly in the case of renal failure (accumulation of active metabolites)
Opioid toxicities

- **Hydrate**
  If oral route not possible/sufficient, prefer sc route: NaCl 0.9% or min 1/3 NaCl, eg 80-100cc/h

- **If possible, change opioid**
  eg: switch from morphine to hydromorphone

- **Rule out other aggravating factors**
  eg: renal failure, hypercalcemia, etc.

- **Treat symptoms**
  haloperidol for hallucinations/agitation
Buprenorphine

- Not a first choice

- Partial mu receptor agonist, weak intrinsic activity and efficacy, ceiling effect

- Maximal effective dose unknown in humans
  30-70 times more potent than morphine
  Duration of action: 6-9h

- Metabolised by the liver. No modification of pharmacokinetics in renal

- Possible indications: severe renal failure, need for relatively low doses of opioids

- Do not associate it with a pure agonist!
meperidine / pethidine

- Contraindicated for chronic administration:
  - neurotoxicities (normeperidine) with risks of myoclonus /seizures
  - short duration action
Co-analgesics

- **NSAI DS:**

  Particularly in bone metastasis

  Beware of adverse effects, and of the increased risks of opioid toxicity through renal failure
Co-analgesics

Corticosteroids:

Examples of indications:
- Intracranial hypertension
- Tumor compressions, eg epidural spinal cord compression
- Nerve infiltrations
- Distension of the liver capsule

Eg: dexamethasone 12-16 mg/d
Decrease gradually to determine minimal effective dose

Beware of side effects!
Co-analgesics

- **Antidepressants**: (tricyclics or SSRIs)

  Neuropathic pain

  Beware of side effects as well as drug interactions
Co-analgesics

**Anticonvulsants:**

- gabapentine (Neurontin®)
  Initial doses: 100 mg/8h
  Increase progressively and monitor clinical effects

- clonazepam (Rivotril ®)
  Initial doses: 0.5 mg nocte
  Increase carefully. Risks of drowsiness, confusion, falls
Co-analgesics

NMDA antagonists, eg:

* methadone
  Very useful and cheap opioid, could be more effective than others in neuropathic pain.
  Needs to be used by experienced professionals, because of its particular pharmacological characteristics (long half-life, 1 to over 60 hrs, important interindividual variability)

* dextrometorphan

* ketamine (not a 1st choice, indicated in neuropathic pain if other treatments fail, and in resistant pain. To be used by experienced professionals)
Co-analgesics

- **Bisphosphonates:**

  Decreased « bone events » due to bone mets.

  Demonstrated particularly for breast carcinomas, myelomas, prostate cancer.
  Also indicated in bone metastases from other origins.

  Injection every 4 weeks

  Eg: zoledronate: 4 mg iv 15 min every 3-4 weeks
  pamidronate: 60-90 mg iv
  (if 0 iv line, clodronate can be given sc; less effective)
Crescendo pain: look for...

- Complications of the underlying disease
  (e.g., pathological fracture, epidural spinal cord compression, intestinal obstruction)

- Accumulation of opioid toxic metabolites

- Delirium (impaired capacity to express pain)

- Urinary retention/fecal impaction in a patient with cognitive failure or impaired capacity to communicate

- Somatisation; expression of a global suffering as pain

- Opioid tolerance (usually develops slowly)
Epidural spinal cord compression

- **Emergency**: functional prognosis depends on neurological deficits at the time of initiation of treatment

- High suspicion if:
  * Vertebral pain that:
    - changes, increases, worsens in recumbent position,
    - Lhermitte’s sign
  * Radiculopathy
  * Muscle weakness +/- sensory deficits, incontinence

- Dexamethasone 12-16 mg/d, emergency MRI if possible (CT Scan as 2nd choice)

- Radiotherapy +/- vertebroplasty +/- laminectomy
Edmonton Symptom Assessment System

No pain

No fatigue

No nausea

No depression

No anxiety

No drowsiness

Excellent appetite

No shortness of breath

Best sensation of well-being

Worst possible pain

Worst possible fatigue

Worst possible nausea

Worst possible depression

Worst possible anxiety

Worst possible drowsiness

No appetite

Worst possible shortness of breath

Worst possible sensation of well-being

Best sensation of well-being

Excellent appetite

No shortness of breath

No drowsiness

No anxiety

No depression

No nausea

No fatigue

No pain
**Incidence of bowel obstruction**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Primary cancer</th>
<th>% patients with intestinal obstruction</th>
</tr>
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<tbody>
<tr>
<td>Castaldo et al, 1981</td>
<td>Ovary</td>
<td>5.5</td>
</tr>
<tr>
<td>Lund et al, 1989</td>
<td>Ovary</td>
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<td>Solomon, 1983</td>
<td>Ovary</td>
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<td>Tunca et al, 1988</td>
<td>Ovary</td>
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<td>Beattie et al, 1989</td>
<td>Ovary</td>
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<td>Soo et al, 1988</td>
<td>Gynecological Ca</td>
<td>5</td>
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<tr>
<td>Kyllonen, 1987</td>
<td>Rectum</td>
<td>4.4</td>
</tr>
<tr>
<td>Baines et al, 1985</td>
<td>Colorectal</td>
<td>10</td>
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<td>Philipps et al, 1985</td>
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<td>Kyllonen, 1987</td>
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<tr>
<td>Steiner, 1991</td>
<td>Miscellaneous</td>
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</tbody>
</table>
Pathophysiology

**Mechanical obstruction**
- Extrapleural tumor (78%)
- Intraluminal tumor

**Functional obstruction**
- Tumor extension in the retroperitoneum, with coeliac plexus infiltration
- Dysfunction of autonomous nervous system
- Tumor extension in the serous membranes or digestive wall muscle layers
- Lung infection, M infarction, pancreatitis, electrolyte abnormalities
- Drugs
Pathophysiology

Partial or complete interruption of transit of bowel contents

↑ Of luminal contents

↑ bowel secretion of H2O, Na+, Cl-

Nausea and Vomiting

↑ Bowel distension

↑ Bowel contractions

Colic

Continuous abdominal pain

Damage of intestinal epithelium, hypertensive state in the lumen

Hyperemia/edema
In intestinal wall

Inflammatory response
# Symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>Nausea / vomiting</td>
<td>68 - 100 %</td>
</tr>
<tr>
<td>Colicky pain</td>
<td>72 - 76 %</td>
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<tr>
<td>Continuous abdominal pain</td>
<td>92 %</td>
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<tr>
<td>Diarrhea</td>
<td>34 %</td>
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<tr>
<td>Constipation</td>
<td>13 %</td>
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<tr>
<td>Auteurs</td>
<td>Tumeur primaire</td>
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<tr>
<td>-----------------------</td>
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<tr>
<td>Lund et al, 1989</td>
<td>Ovaires</td>
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<td>Soo et al, 1988</td>
<td>Ca gynécologique</td>
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<td>Pictus et al, 1988</td>
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<td>Krebs et al, 1983</td>
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<table>
<thead>
<tr>
<th>Authors</th>
<th>Tumor Type</th>
<th>Operative mortality (%)</th>
<th>Other complications (%)</th>
<th>Survival (mo)</th>
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<td>Chan et al, 1992</td>
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<td>80</td>
<td>2 (median)</td>
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<td>44</td>
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<td>7 (mean)</td>
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<td>NR</td>
<td>11 (median)</td>
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<tr>
<th>Authors</th>
<th>Lary tumor</th>
<th>Operative mortality (%)</th>
<th>Other complications (%)</th>
<th>Survival (month)</th>
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Contraindications to surgery

**Absolute**

- Recent laparotomy demonstrating that further corrective surgery was not possible
- Previous abdominal surgery which showed diffuse metastatic cancer
- Involvement of proximal stomach
- Intra-abdominal carcinomatosis demonstrated radiologically with a contrast study revealing a severe motility problem
- Diffuse palpable intra-abdominal masses
- Massive ascites which rapidly recur after drainage

Contraindications to surgery

- Extra-abdominal metastases producing symptoms which are difficult to control
- Nonsymptomatic extensive extra-abdominal malignant disease
- Poor general performance status
- Poor nutritional status (marked weight loss/cachexia, marked hypoalbuminemia, low lymphocyte count)
- Advanced age in association with cachexia
- Previous radiotherapy of the abdomen or pelvis

### Medical symptomatic treatment

<table>
<thead>
<tr>
<th>Authors</th>
<th>Primary Tumor</th>
<th>Mean survival</th>
</tr>
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<tbody>
<tr>
<td>Ventafridda et al, 1990</td>
<td>Miscellaneous</td>
<td>13.4 days (2 - 50)</td>
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<tr>
<td>Fainsinger et al, 1994</td>
<td>Miscellaneous</td>
<td>18 days (2 - 41)</td>
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<tr>
<td>Isbister et al, 1990</td>
<td>Miscellaneous</td>
<td>29 days</td>
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<tr>
<td>Steiner et al, 1991</td>
<td>Miscellaneous</td>
<td>1.6 months (1 - 4)</td>
</tr>
<tr>
<td>Baines et al, 1985</td>
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<td>3.7 months (1 - 12)</td>
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Treatment of nausea

Anti-secretory drugs

- **Hyoscine butylbromide**: 40-120 mg/day sc, iv
- **Hyoscine hydrobromide**: 0.8-2.0 mg/day sc
- **Glycopyrrolate**: 0.1-0.2 mg tid sc or iv

- **Somatostatin analogue**
  - **Octreotide**: 0.2-0.9 mg/day sc

Anti-emetics

- **Prokinetic drug**
  - **Metoclopramide**: 60-240 mg/day sc, if partial obstruction and no colic

- **Neuroleptic drugs**
  - **Haloperidol**: 5-15 mg/day sc
  - **Methotrimeprazine**: 6.12-50 mg/day sc
  - **Prochlorperazine**: 25 mg 8 hourly pr
  - **Chlorpromazine**: 50-100 mg 8 hourly pr or im

- **Antihistamine drug**
  - **Cyclizine**: 100-150 mg/day sc or 50 mg 8 hourly pr
  - **Dimenhydrinate**: 50-100 mg sc prn
Somatostatin analogue: mechanism of action

- Pain
- Nausea
- Vomiting

Secretions
Distension
Epithelial Surface
Intestinal Content
Epithelial Surface
Distension

Somatostatin analogue

Mechanism of action:
- Decreases secretions
- Reduces distension
- Normalizes epithelial surface
**Other measures**

**Hydratation**

- 1000-1500 ml/24h sc or iv: ↓ nausea
- Preoperative iv hydratation IV

**Nasogastric tube**

- Emergency treatment of intestinal obstruction before surgery
- In case of failure of medical symptomatic treatment (upper intestinal obstruction), prefer gastrostomy (PEG), except if patient very near death

**Parenteral Nutrition**

- Only indicated in patients with slowly growing tumor, with Karnofsky Performance Status > 50

**Stents**

- Ex: Pyloric obstruction, obstruction of small intestine or colon
Schema of symptom construct

1. Production / construct

2. Perception

3. Expression

- Modulation
  - Cognitive status
  - Mood
  - Beliefs
  - Cultural
  - Biography

Bruera Cancer Treat Rev 1996;22(supp A):3-12
Total pain

Physical
- Functional capacity
- Fatigue, cachexia
- Sleep and recuperation
- Appetite, nausea, etc.

Psychological
- Apprehension, worries
- Grief, depression
- Pleasures, leisure
- Anxiety, anger
- Cognitive function

Social
- Communication with healthcare team
- Relationships with family and friends, capacity of giving
- Financial situation, insurance problems

Spiritual
- Personal value as a human being
- Meaning of life/illness/pain
- Religious faith
- Existential perspectives
Palliative care: a global perspective

The development of palliative care through effective and low cost approaches represents a priority in order to respond to the urgent needs of the sick and improve their quality of life.
Palliative care: a global perspective

There is a need to promote a public health approach in which comprehensive palliative care programs are integrated into existing healthcare systems and tailored to the specific cultural and social context of the target populations.
Foundation measures:
little cost, big effect
(Stjernswärd J. J PSM 2002;24(2)259)

Education
- Public, professionals
- Undergraduate education for doctors and nurses
- Postgraduate training
- Advocacy (policy makers, administrators, drug regulators)

Drug availability
- Changes in legislation to improve availability especially of cost effective opioids
  such as morphine sulfate tablets
  - Prescribing made easier and distribution, dispensing and administration improved

Governmental policy
- National policy emphasizing the need to alleviate unnecessary pain and suffering of the chronically and terminally ill
- Governmental policy integrating PC into the healthcare system
- Separate systems of care are neither necessary nor desirable
Palliative care: useful international organisations

- WHO Programme on Cancer Control

- EAPC (European Association for Palliative Care)  
  [www.eapcnet.org](http://www.eapcnet.org) and [www.eapcare.org](http://www.eapcare.org)

- International Association for Hospice and Palliative Care  
  [www.hospicecare.com](http://www.hospicecare.com)

- Hospice Information Service St Christopher’s Hospice  
  London  
  [www.hospiceinformation.co.uk](http://www.hospiceinformation.co.uk)
Palliative care: some references

- Oxford Textbook of Palliative Medicine 2003
- WHO guidelines on Cancer pain, opioid availability, symptom control and palliative care:
  - Cancer pain relief (1996)
  - Symptom relief in terminal illness 1998
  - Cancer pain relief and palliative care in children 1998
- Journal of Pain and Symptom Management 42(2) August 2002
- Edmonton Regional Palliative Care Program: [www.palliative.org](http://www.palliative.org)
  (useful contents about: clinical work, educational opportunities, informations for general public, links, research and literature)