

Practical tips for the management of difficult pain problems

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Stepwise approach to the management of difficult pain problems

1. Consider the role of primary therapies to address the underlying cause of the pain.
2. Titrate opioids up to maximal tolerated dose.
3. Manage side effects through appropriate drug therapy or by trials of alternative opioids.
4. Consider the role of adjuvant analgesics.
5. Consider regional anesthetic approaches.
6. Consider the role of invasive neuroablative interventions.
7. The use of sedation in the management of refractory pain at the end of life.

Step 1: Consider the role of primary therapies

- The assessment process may reveal a cause for the pain that is amenable to therapy that is directed at the cause.
- This therapy may improve comfort, function or duration of survival.
- Specific analgesic treatments are usually required as an adjunct to the primary therapy.

Radiotherapy

- Best evidence for:
 - painful bone metastases
 - epidural neoplasm
 - headache due to cerebral metastases

- In other settings use of radiotherapy is largely anecdotal.

Chemotherapy

- In responsive cancers, tumor shrinkage is generally associated with relief of pain.
- Some reports of analgesic clinical benefit even in the absence of significant tumor shrinkage.
 - Gemcitabine in Pancreatic cancer

Surgery

- Common indications
 - as obstruction of a hollow viscus
 - unstable bony structures
 - compression of neural tissues

- Locally advanced disease
 - toilet mastectomy
 - amputation of the effected limb
 - exenteration +/- sacrectomy in advanced pelvic tumors

- Endoprosthetic treatments with stents
 - esophageal, biliary, colonic and urethral obstructions

Antibiotic Therapy

- Antibiotics may be analgesic when the source of the pain involves infection.
- Clinical context
 - cellulitis
 - chronic sinus infections
 - pelvic abscess
 - pyonephrosis
 - osteitis pubis
- Occult infection
 - relatively common in head and neck cancer
 - fungating tumors

Radiofrequency tumor ablation

- Anecdotal literature

- Reported indications
 - presacral and pelvic tumor recurrences
 - osteoid osteoma
 - painful pancreatic cancer
 - renal and adrenal tumors
 - painful bony metastases including vertebral metastases

Methylmethacrylate vertebroplasty and acetabuloplasty

■ Vertebroplasty

- can result in rapid (1–3 days) disappearance of pain, with restoration of spinal stability.
- Indications:
 - osteolytic lesion of the vertebral body
 - no disruption of posterior wall
- Relatively contraindicated when there is epidural invasion by tumor.

■ Acetabuloplasty

- Anecdotal reports

Acetabuloplasty



Images reprinted by courtesy of Dr. G.C. Anselmetti
from <http://www.vertebroplastica.it>

Step 2: Titrate opioids up to maximal tolerated dose

Choices for 1st line therapy

1990

- Morphine

2010

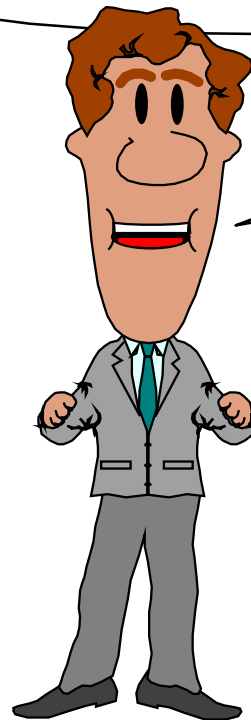
- Morphine
- Oxycodone
- Fentanyl
- Methadone
- Hydromorphone



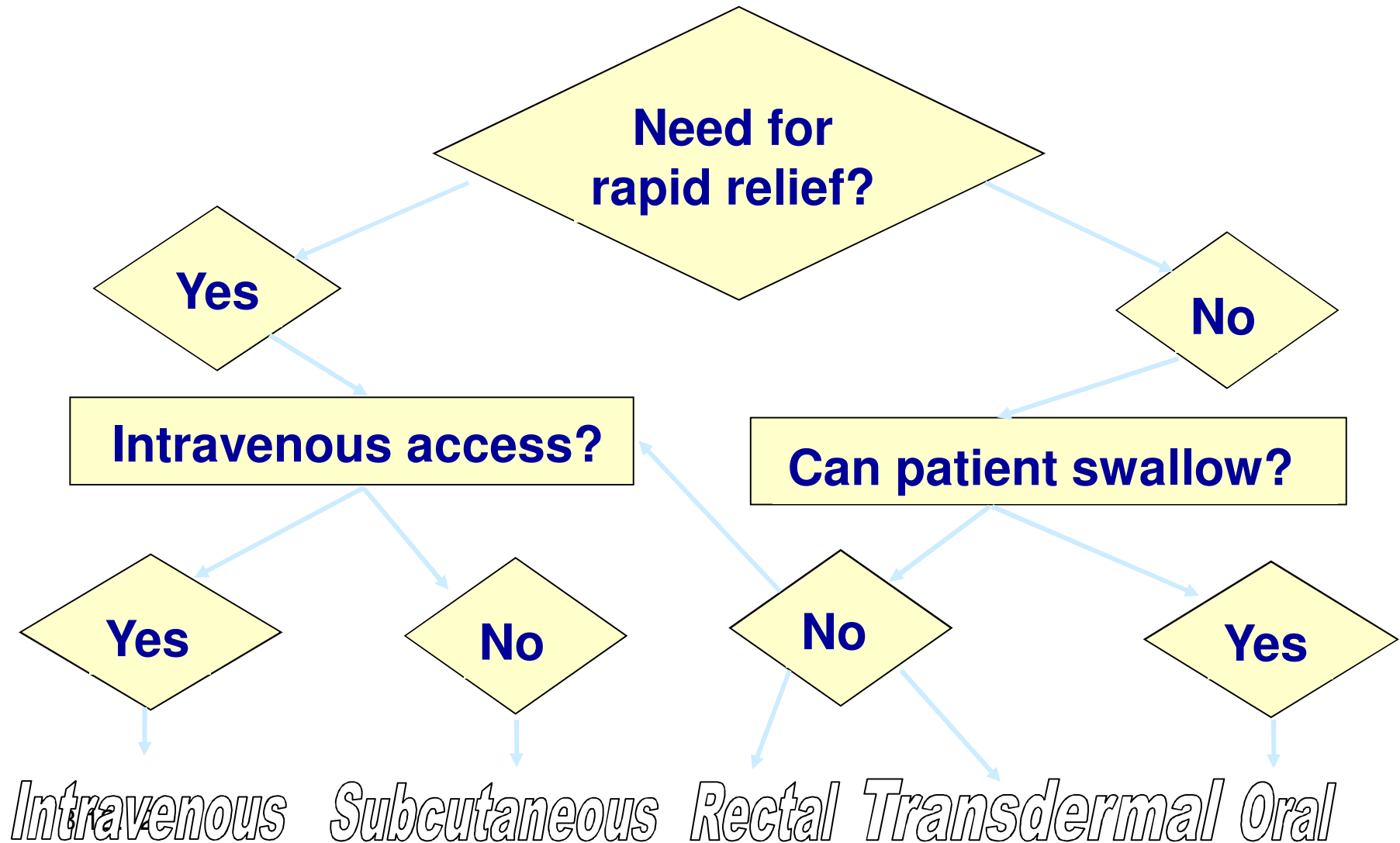
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

European Society for Medical Oncology

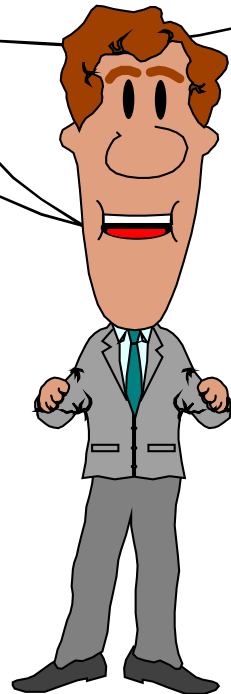
Opioids should be administered by the least invasive and safest route capable of providing adequate analgesia.



Algorithm for selection of route



Inadequate relief should be addressed through gradual escalation of dose until adequate analgesia or intolerable side effects supervene.



Dose escalations less than 30-50% are not likely to significantly improve analgesia.



The absolute dose is immaterial as long as the balance between analgesia and side effects remains favorable.



Step 3: Manage side effects through appropriate drug therapy or by trials of alternative opioids

Opioid-induced side effects

■ Gastrointestinal

- Constipation
- Nausea
- Vomiting

■ Central nervous system

- Drowsiness
- Hallucinations
- Myoclonus / seizures
- Respiratory depression

■ Cutaneous

- Itching

■ Urinary

- Urinary retention

Differential diagnosis

- Opioid-induced adverse effect
 - with initiation
 - dose-related

- New morbidity in a patient taking opioids
 - related to current disease
 - new pathology
 - Iatrogenic

WHEN a new adverse effect appears in a
previously stable patient...

SUSPECT that something new is going on

THINK related to current disease?
new pathology?
iatrogenic?

Common causes of co-morbidity

- Sepsis
- Metabolic events
 - Hypocalcaemia
 - Hyponatremia
 - Uremia
 - Liver failure
- Metastases
 - Brain
 - Leptomeningeal
 - Liver
- Drugs
 - Centrally acting
- Concurrent disease
 - Stroke
 - Cardiac Failure

Which approach?

- Reduce the dose?
- Treat the side effect?
- Switch opioid?

No data to indicate best practice!

Strategies to reduce opioid dose

- Add a non-opioid co-analgesic
 - NSAID
 - Dipyrrone

- Non-pharmacological approaches
 - Radiotherapy
 - Nerve block
 - Cognitive-behavioral

Central nervous system side effects

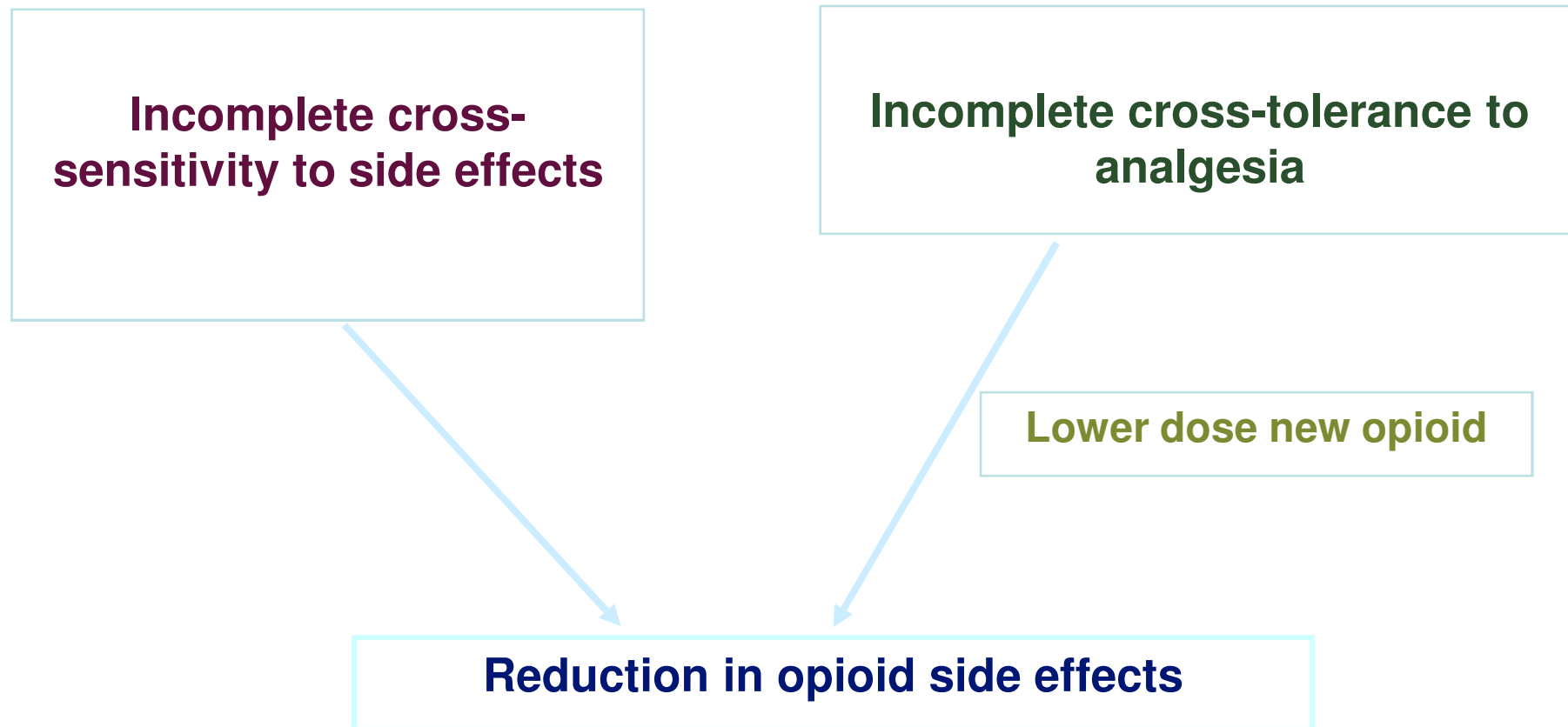
| | |
|-----------------------|-----------------------------------------------------|
| Drowsiness | Methylphenidate 0.5 mg x 2 Pemoline 18.75 mg x 2 |
| Hallucinations | Haloperidol 2.5 mg x 3 |
| Myoclonus | Clonazepam 0.5 mg x 2 |

Opioid Rotation (opioid switching)

■ Definition

- In setting of dose limiting adverse effects
- Substitution of one opioid for another
- Aim: to achieve equal or better analgesia with fewer adverse effects

Opioid rotation: Mechanism



Advantages

- **Minimizing polypharmacy**
 - **Often effective**

Disadvantages

- **Outcomes are variable and unpredictable**
 - some patients may have an unimproved or worse outcome
- **Needs patience and perseverance**
 - in one prospective survey, 20% of patients needed to undergo two or more switches until a satisfactory outcome was achieved

Equianalgesic Dose Table

| | Parenteral. | P.O. | Other information |
|----------------------------------------------------------------------------|-------------|-------|------------------------------------------------------------------------------------------------------------|
| Oxycodone | 7 | 20 | |
| Morphine | 10 | 20-30 | Rectal 20-30 |
| Hydromorphone | 2-3 | 7.5 | |
| Methadone | 1-3 | 2-6 | Morphine: Methadone dose ratio varies with dose 30-90mg 4:1 90-300mg 7:1 >300mg 10:1 |
| Fentanyl Transdermal System | | | |
| Empirically Transdermal fentanyl 100µg/h= 2-4 mg/h intravenous morphine | | | |

Step 4: Consider the role of adjuvant analgesics

Adjuvant analgesics

■ Neuropathic pain

- Corticosteroids
- Tricyclics
- Lidocaine Patches
- Anti-convulsants
 - Gabapentin
 - Pregabalin

- Second line
 - Mexilitine
 - Capsaicin cream
 - Baclofen

■ Bone pain

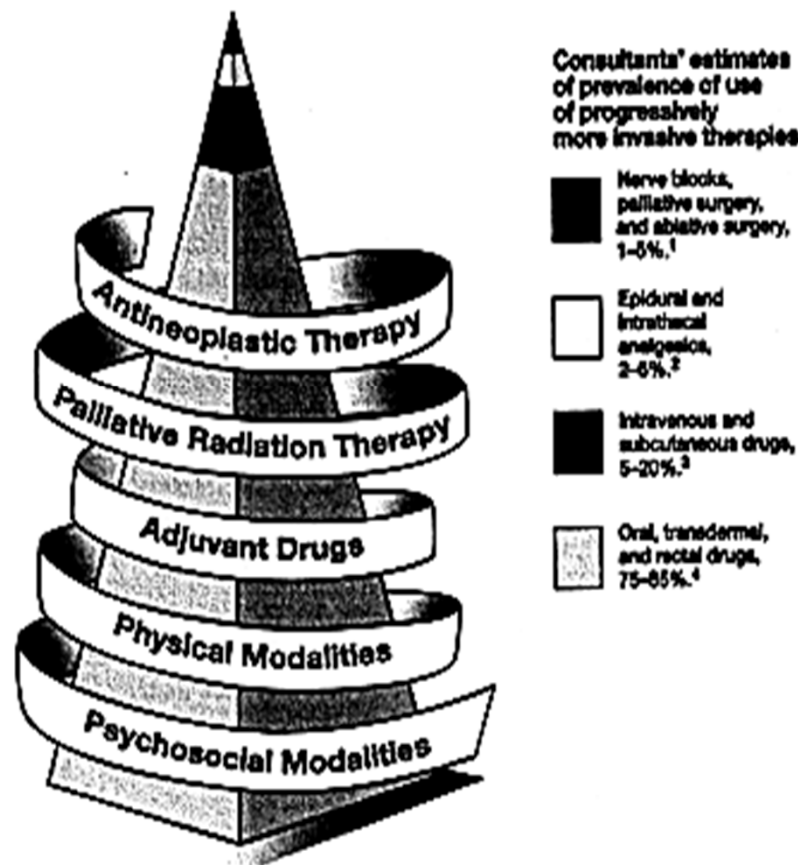
- Corticosteroids
- Bisphosphonates
- Calcitonin
- Radiopharmaceuticals
 - Strontium-89

Step 5: Consider regional anesthetic approaches

The place of Invasive Analgesic Therapies

- Systemic therapies sub-optimal
10-30%
- Anesthetic and neurosurgical approaches
 - may reduce requirement for systemically administered opioids to achieve adequate analgesia

Pain management strategies: a hierarchy



Epidural and intrathecal opioids

- Delivery of low opioid doses in the spinal cord may → lessen supraspinally-mediated adverse effects.
- One randomized trial Spinal therapy vs. Systemic
 - better analgesia and fewer adverse effects
- In general intrathecal is preferred to epidural administration
- Spinal coanalgesics
 - bupivacaine
 - clonidine

Intraventricular opioids

- A limited international experience
- Indications
 - upper body or head pain
 - severe diffuse pain
- Generally very well tolerated
- Schedules
 - intermittent injection
 - continual infusion

Regional local anesthetic infusions

- Intrapleural local anesthetics
 - chronic post-thoracotomy pain
 - head, neck, chest, arms and upper abdominal viscera

- Interscalene brachial plexus
 - localized upper limb pain

Step 6: Consider the role of invasive neuroablative interventions

Cautions

- Problematic literature
 - lack of uniformity in patient selection
 - inadequate reporting of previous analgesic therapies
 - inconsistencies in outcome evaluation
 - paucity of long-term follow-up

- Reported outcomes may not predict the outcomes of a procedure performed on a medically ill patient by a physician who has more limited experience with the techniques involved.

Consideration in selection of invasive approaches

1. The procedure most likely to be effective should be selected.
2. If there is a choice, choose the one with the fewest and least serious adverse effects.
3. Whenever possible, somatic neurolysis should be preceded by the demonstration of effective analgesia with a local anesthetic prognostic block.

Common invasive approaches

- Spinal Opioids
 - epidural
 - Intrathecal

- Celiac plexus Blockade
- Rhizotomy
- Cordotomy

Step 7: The use of sedation in the management of refractory pain at the end of life

“Refractory Symptoms”: Definition

A symptom which cannot be adequately controlled despite aggressive efforts to identify a tolerable therapy that does not compromise consciousness.

General considerations

- Procedure of last resort
- After expert consultation

Procedural Guidelines for Sedation

Original Article

 **PALLIATIVE
MEDICINE**

European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care

Palliative Medicine

23(7) 581–593

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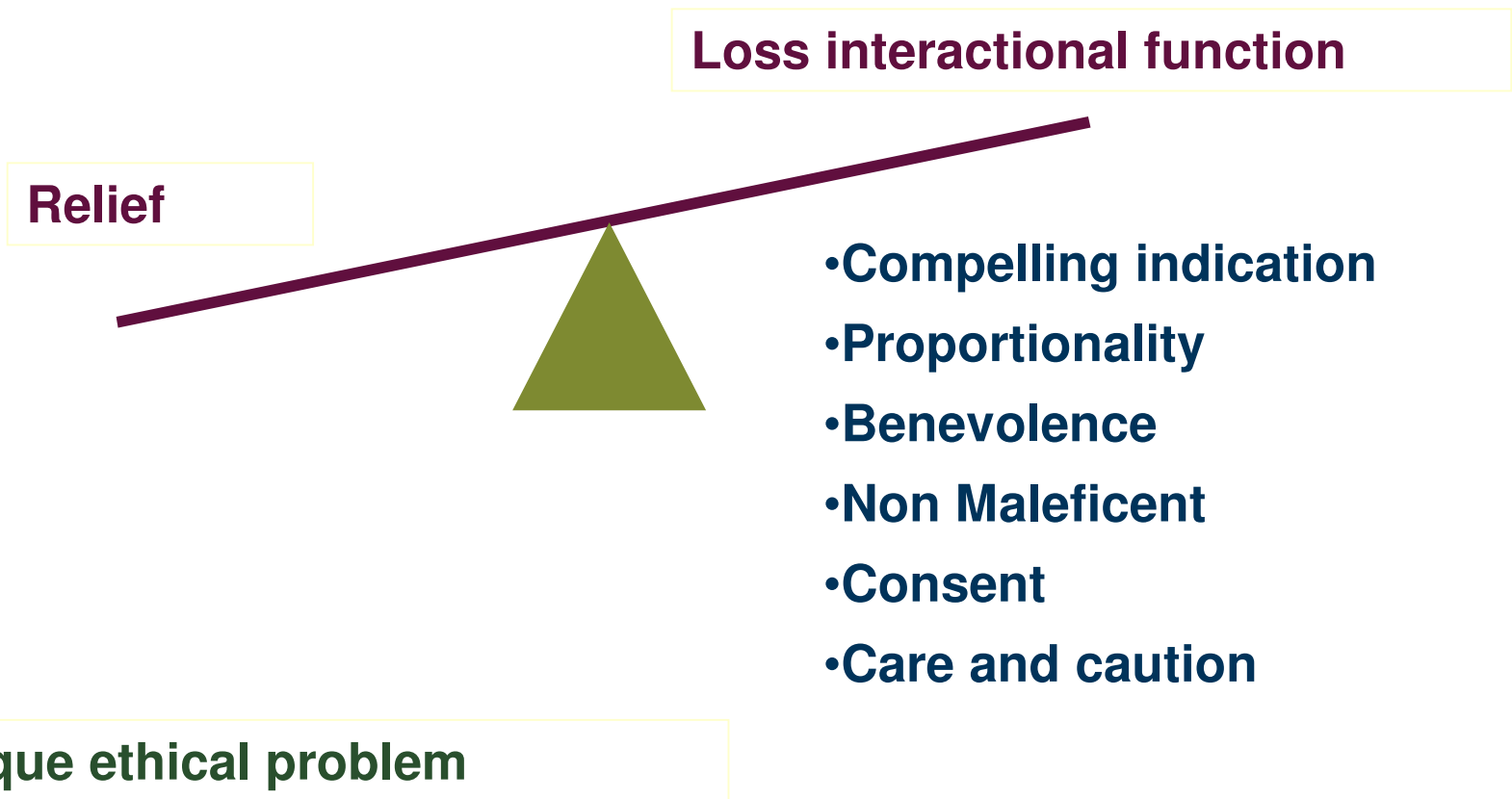
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Clinical (ethical) pragmatism : Sedation

Sedation for refractory suffering



Hydration and nutrition at end of life

■ Consensus

- invasive forms of nutrition of no medical value

■ No Consensus

- hydration at end of life