

Cancer Pain Management:

An Overview

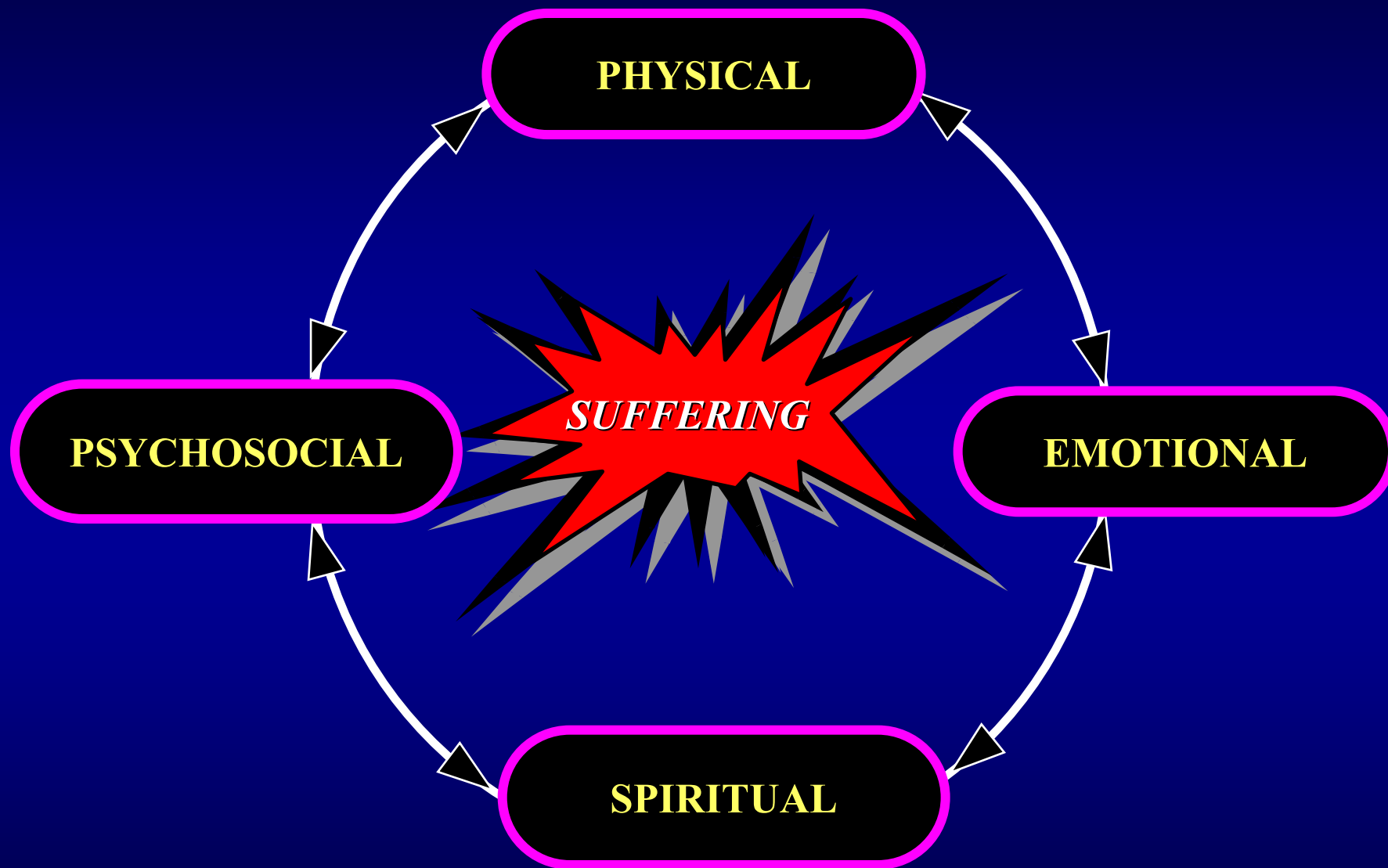
Dr. Mike Harlos

Medical Director, WRHA Palliative Care

Pain

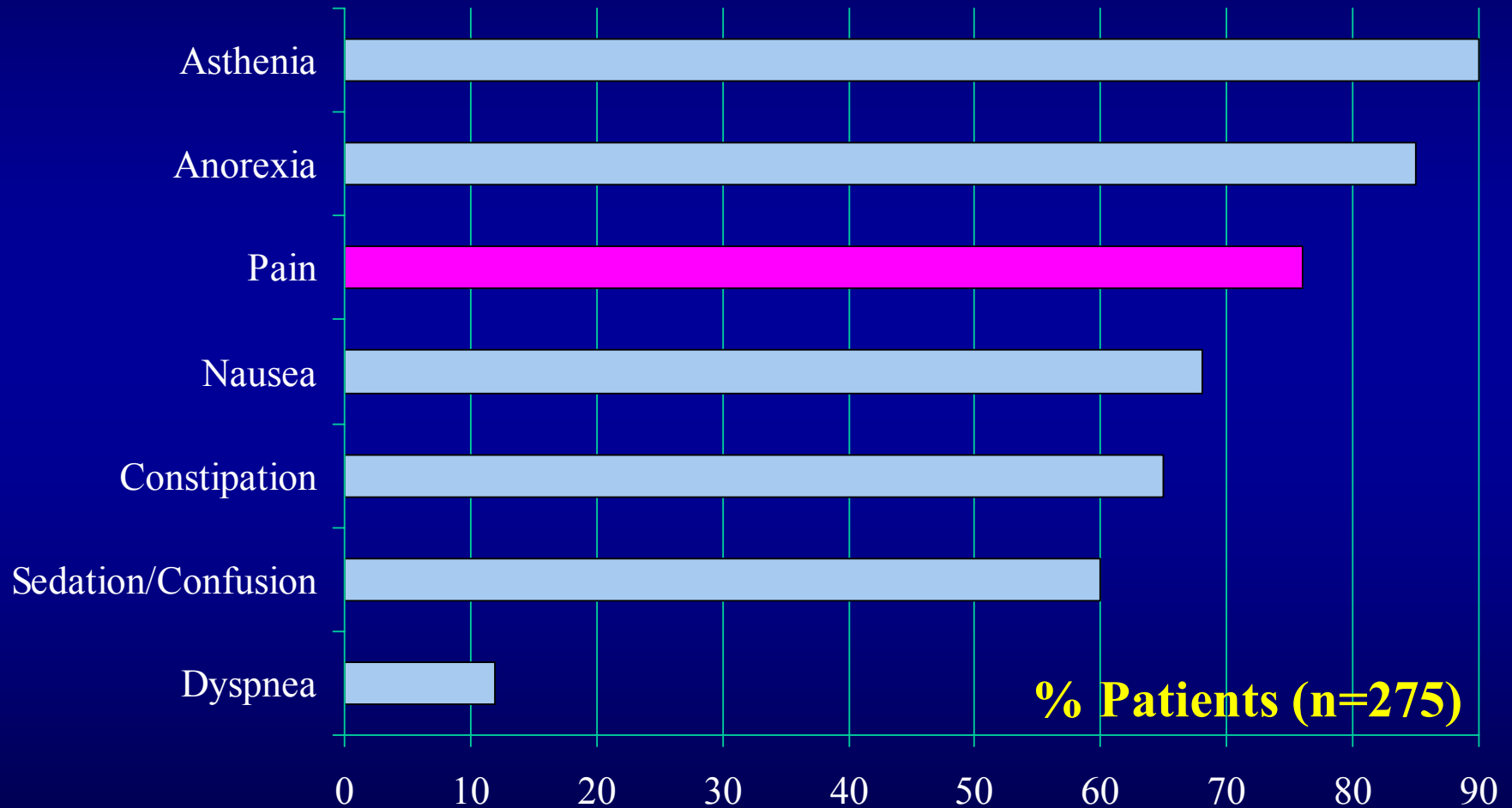
An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.

International Association for the Study of Pain



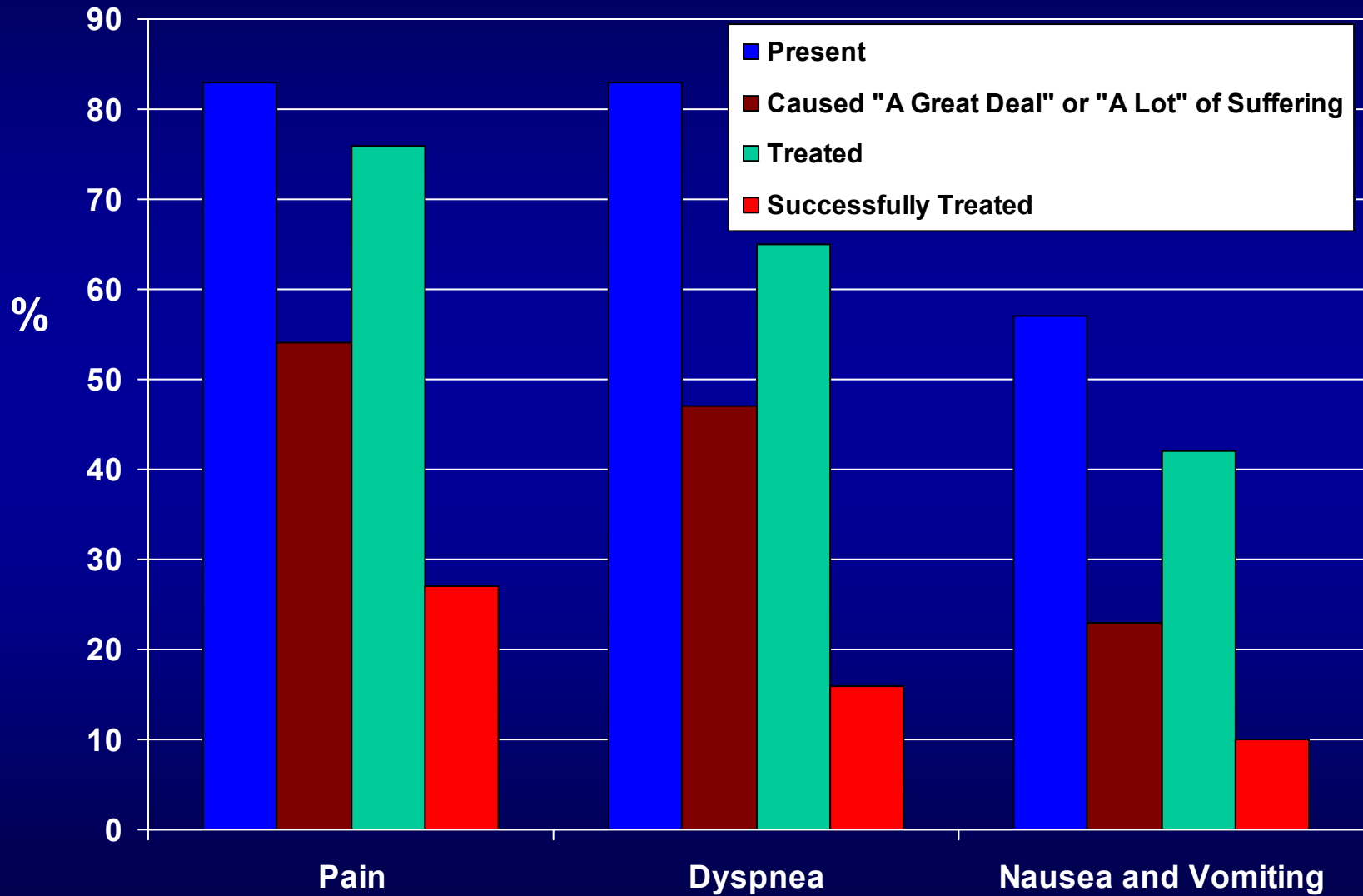
SYMPTOMS IN ADVANCED CANCER

Ref: Bruera 1992 "Why Do We Care?" Conference; Memorial Sloan-Kettering



Symptoms At The End of Life in Children With Cancer

Wolfe J. et al, NEJM 2000; 342(5) p 326-333



TYPES OF PAIN

NOCICEPTIVE

NEUROPATHIC

Somatic

- bones, joints
- connective tissues
- muscles

Visceral

- Organs –
heart, liver,
pancreas, gut,
etc.

Deafferentation

*Sympathetic
Maintained*

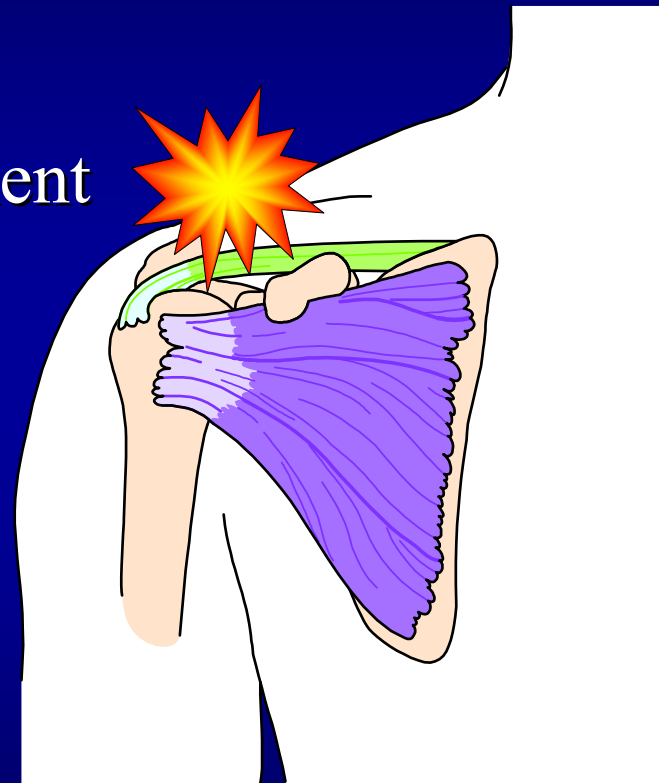
Peripheral

Somatic Pain

- Aching, often constant
- May be dull or sharp
- Often worse with movement
- Well localized

Eg/

- Bone & soft tissue
- chest wall





- bone is the most common site of tumour metastases

Primary Tumour	Bone Mets %
Breast	50 – 85
Prostate	60 – 85
Lung	64
Bladder	42
Kidney, Thyroid	28 - 60

Mundy GR. In: *Bone Remodeling and Its Disorders*. 1995:104-107.

Special Considerations in Bone Pain

- Spinal cord compression in vertebral mets:

Pain = earliest feature

- Risk of pathological fracture

Indications for prophylactic surgery in large, weight-bearing bones

- Cortical Lesions

- Destruction of $> 50\%$ of the cortical width
- Axial length of lesion $>$ diameter of the bone
 $> 2 - 3$ cm lesion

- Medullary lesions

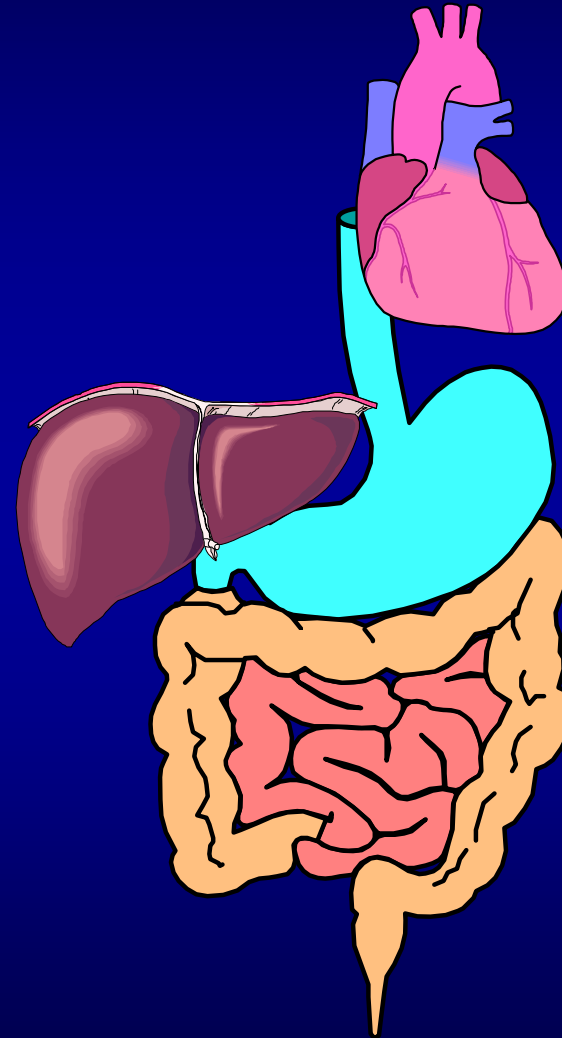
- Lesion $> 50\%$ of the medulla
- Pain unrelieved by radiotherapy

Visceral Pain

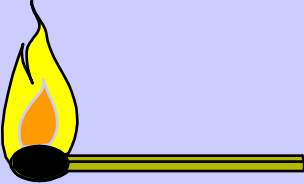
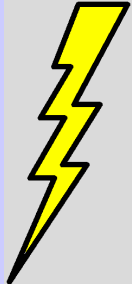
- Constant or crampy
- Aching
- Poorly localized
- Referred

Eg/

- CA pancreas
- Liver capsule distension
- Bowel obstruction



FEATURES OF NEUROPATHIC PAIN

COMPONENT	DESCRIPTORS	EXAMPLES
<p><i>Steady, Dysesthetic</i></p> 	<ul style="list-style-type: none"> • Burning, Tingling • Constant, Aching • Squeezing, Itching • <u><i>Allodynia</i></u> • <u><i>Hypersthesia</i></u> 	<ul style="list-style-type: none"> • Diabetic neuropathy • Post-herpetic neuropathy
<p><i>Paroxysmal, Neuralgic</i></p> 	<ul style="list-style-type: none"> • Stabbing • Shocklike, electric • Shooting • Lancing 	<ul style="list-style-type: none"> • trigeminal neuralgia • may be a component of any neuropathic pain

PAIN ASSESSMENT

- Description: severity, quality, location, temporal features, frequency, aggravating & alleviating factors
- Previous history
- Context: social, cultural, emotional, spiritual factors
- *Meaning*
- Interventions: what has been tried?

Assessment of Bone Pain

History:

- Continuous, localized, dull pain
- Increases with local pressure
- Incident pain

Physical:

- Local tenderness
- Neuro assessment, especially in vertebral mets (spinal cord compression)

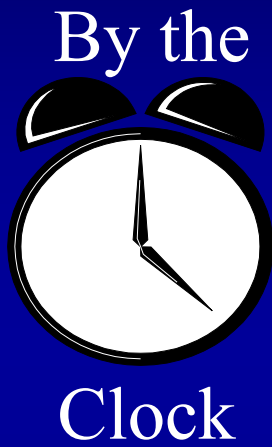
Investigations:

- Plain Xrays: specific but not sensitive
- Bone scan: sensitive (except myeloma);
False (+)ve rate 40 – 50%
- CT/MRI – when suspect spinal cord compression, or results of other investig. neg.

Medication(s) taken

- Dose
- Route
- Frequency
- Duration
- Efficacy
- Side effects

W.H.O. ANALGESIC LADDER



1
Non-opioid
+/- adjuvant

2
Weak opioid
+/- adjuvant

3
Strong opioid
+/- adjuvant

Pain persists or increases

STRONG OPIOIDS

- most commonly use:
 - morphine
 - hydromorphone
 - transdermal fentanyl (Duragesic®)
 - oxycodone
 - Methadone
- DO NOT use meperidine (Demerol®) long-term
 - active metabolite *normeperidine* → seizures

OPIOIDS and INCOMPLETE CROSS-TOLERANCE

- conversion tables assume full cross-tolerance
- cross-tolerance unpredictable, especially in:
 - high doses
 - long-term use
- divide calculated dose in $\frac{1}{2}$ and titrate

CONVERTING OPIOIDS

NB: Does not consider incomplete cross-tolerance

Medication	Approx. Equiv. Oral Dose (mg)
Morphine	10
Hydromorphone	2
Methadone	1
Codeine	60

CONVERTING OPIOIDS

NB: Does not consider incomplete cross-tolerance

Drug		Approximate Equipotency with Morphine (Morphine:Drug)
Hydromorphone		5:1
Oxycodone		1.5:1 to 2:1
Codeine		1:12
Methadone	<i>Daily Morphine Dose</i>	
	30 – 90 mg	3.7:1
	90 – 300 mg	7.75:1
	> 300 mg	12.75:1
Fentanyl		80:1 to 100:1 (for subcutaneous dosing of each)

TITRATING OPIOIDS

- dose increase depends on the situation
- dose ↑ by 25 - 100%

EXAMPLE: (doses in mg q4h)

Morphine	5	10	15	20	25	30	40	50	60
Hydromorphone	1	2	3	4	5	6	8	10	12

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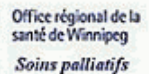
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- [Guideline for Estimating Prognosis](#) 
- [Flowchart: Nursing Management of Suspected Narcotization](#) 
- [Clinical Guideline: Anticipating And Preparing For Predictable Clinical Challenges In The Medical Care Of The Terminally Ill Person Wishing To Die At Home](#) 
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http://palliative.info/AnalgProt.htm Internet

Opioid Dosage Chart

OPIOID	ROUTE	DOSAGE STEPS (# mg every 4 hours)													
Morphine	po/pr/SL	5	10	15	20	30	40	60	80	100	130	160	200	240	280
	SQ	2.5	5	7.5	10	15	20	30	40	50	65	80	100	120	140
Hydromorphone	po/pr/SL	1	2	3	4	6	8	12	16	20	26	32	40	48	56
	SQ	0.5	1	1.5	2	3	4	6	8	10	13	16	20	24	28

NOTE: - Generally, in converting from one opioid to another, in order to address incomplete cross-tolerance divide the calculated equivalent dose by half and titrate up quickly if needed. However, under circumstances of poor pain control it may not be appropriate to reduce the converted dose in this manner.

DETAILS:

A registered nurse who has approval to use the protocol may, without contacting a physician:

- administer a breakthrough medication dose consisting of 50-100% of the q4h dose, up to q1h prn. If more than 3 doses of aggressive breakthrough medications are needed (eg. q1h dosing), the physician should be contacted to review options.

Comment: This dose not mean that breakthroughs *must* be given prior to moving to the next step of the Protocol (see next point below). It is to emphasize that if a circumstance has developed requiring aggressive breakthrough administration, that the patient should be reviewed.

- progress to the next level of the protocol up to once per 24 hours even without having given prior breakthrough doses



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- progress to the next level of the protocol up to once per 24 hours, even without having given prior breakthrough doses.

Comment: In general, it takes 3-5 half-lives to reach a steady state of a drug given on a regular dosing interval. (Most commonly, the dose interval is equal to the half-life). It would not make pharmacologic sense to keep increasing the regular q4h dose before the previous dose adjustment has reached steady state. The Protocol allows for generous administration of breakthrough opioids to address discomfort while awaiting the effect of a recent increase of the regular opioid dosing.

- change the route of administration as per the protocol table above.

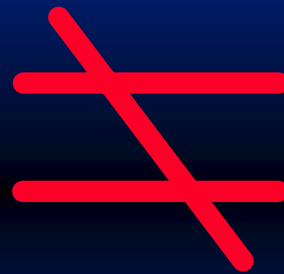
Consider decreasing the opioid dose by one increment using the Opioid Dosage Chart *if the pain control is adequate and:*

- The patient is drowsy and/or
- The respiratory rate persists between 8-10 per minute. If the respirations are below 8 per minute, the opioid is held and the physician called.

A physician must be contacted when any of the following present:

- Patient's respirations are less than 8 per minute;
- Patient's respirations persist between 8-10 per minute in spite of decreasing the opioid dose on the Analgesia and Dyspnea Protocol;
- There are persisting jerking movements, raising the possibility of opioid-induced myoclonus and neurotoxicity;
- The patient is both drowsy and in discomfort;
- The patient requires 3 or more of aggressive breakthrough medication, i.e. every 1 hour dosing;
- The patient develops mental disturbances;
- Dosage has reached the maximum dose on the Opioid Dosage Chart;
- In order to change opioid;
- Any time there is concern about administration of the protocol opioid.

TOLERANCE



**PSYCHOLOGICAL
DEPENDENCE /
ADDICTION**

**PHYSICAL
DEPENDENCE**

TOLERANCE

Inturrisi C, Hanks G. Oxford Textbook of Palliative Medicine 1993: Chapter 4.2.3

**A normal physiological
phenomenon in which
*increasing doses are required
to produce the same effect***

PHYSICAL DEPENDENCE

Inturrisi C, Hanks G. Oxford Textbook of Palliative Medicine 1993: Chapter 4.2.3

A normal physiological phenomenon in which a withdrawal syndrome occurs when an opioid is abruptly discontinued or an opioid antagonist is administered

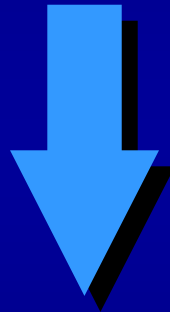
PSYCHOLOGICAL DEPENDENCE and ADDICTION

Inturrisi C, Hanks G. Oxford Textbook of Palliative Medicine 1993: Chapter 4.2.3

A pattern of drug use characterized by a continued craving for an opioid which is manifest as compulsive drug-seeking behaviour leading to an overwhelming involvement in the use and procurement of the drug

In chronic opioid dosing:

po / sublingual / rectal routes



reduce by 1/2

sq / iv / IM routes

Using Opioids for Breakthrough Pain

- Patient must feel in control, empowered
- Use aggressive dose and interval

Patient Taking Short-Acting Opioids:

- 50 - 100% of the q4h dose given q1h prn

Patient Taking Long-Acting Opioids:

- 10 - 20% of total daily dose given q1h prn
with short-acting opioid preparation

Management of Bone Pain

Pharmacologic treatment

- Acetaminophen
- Opioids
- NSAIDs: conventional & Cox-2 inhibitors
- Corticosteroids (not with NSAIDs)
- Bisphosphonates: pamidronate (Aredia[®]), clodronate (Bonafos[®]), zoledronate (Zometa[®])

Management of Bone Pain *ctd*

Radiation treatment

- Single (800 cGy) or Multiple fx (200 cGy x 3-5)
- Effective immediately
- Maximal effect 4 - 6 wks
- 60-80% pts get relief
- Strontium-89

Treatment of Neuropathic Pain

Pharmacologic treatment

- Opioids
- Steroids
- Anticonvulsants - *gabapentin*
- TCAs (for dysesthetic pain, esp. if depression)
- NMDA receptor antagonists: ketamine, dextromethorphan, methadone
- Anesthetics

Radiation therapy

Interventional treatment

- Spinal analgesia
- Nerve blocks

ADJUVANT DRUGS

- primary indication usually other than pain
- analgesic in some painful conditions
- enhance analgesia of opioids
- other roles:
 - treat opioid side effects
 - treat symptoms associated with pain

CORTICOSTEROIDS AS ADJUVANTS

- ↓ inflammation
 - ↓ edema
 - ↓ spontaneous nerve depolarization
- } ↓ tumor mass effects

CORTICOSTEROIDS: ADVERSE EFFECTS

IMMEDIATE	LONG-TERM
<ul style="list-style-type: none">• Psychiatric• Hyperglycemia• ↑ risk of GI bleed<ul style="list-style-type: none">➤ gastritis➤ aggravation of existing lesion (ulcer, tumor)• Immunosuppression	<ul style="list-style-type: none">• Proximal myopathy<ul style="list-style-type: none">** often < 15 days **• Cushing's syndrome• Osteoporosis• Aseptic / avascular necrosis of bone

DEXAMETHASONE: DOSING

- **minimal mineralcorticoid effects**
 - **po/iv/sq/?sublingual routes**
- **can be given once/day; often given bid – qid to facilitate titration**
- **typically administer as follows:**
 - » **4 mg qid x 7 days then**
 - » **4 mg tid x 1 day then**
 - » **4 mg bid x 1 day then**
 - » **4 mg once/day x 1 day then D/C**

Complementary / Alternative Therapies

- Acupuncture
- Cognitive/behavioral therapy
- Meditation/relaxation
- Guided imagery
- Herbal preparations
- Magnets
- Therapeutic massage

Opioid Side Effects

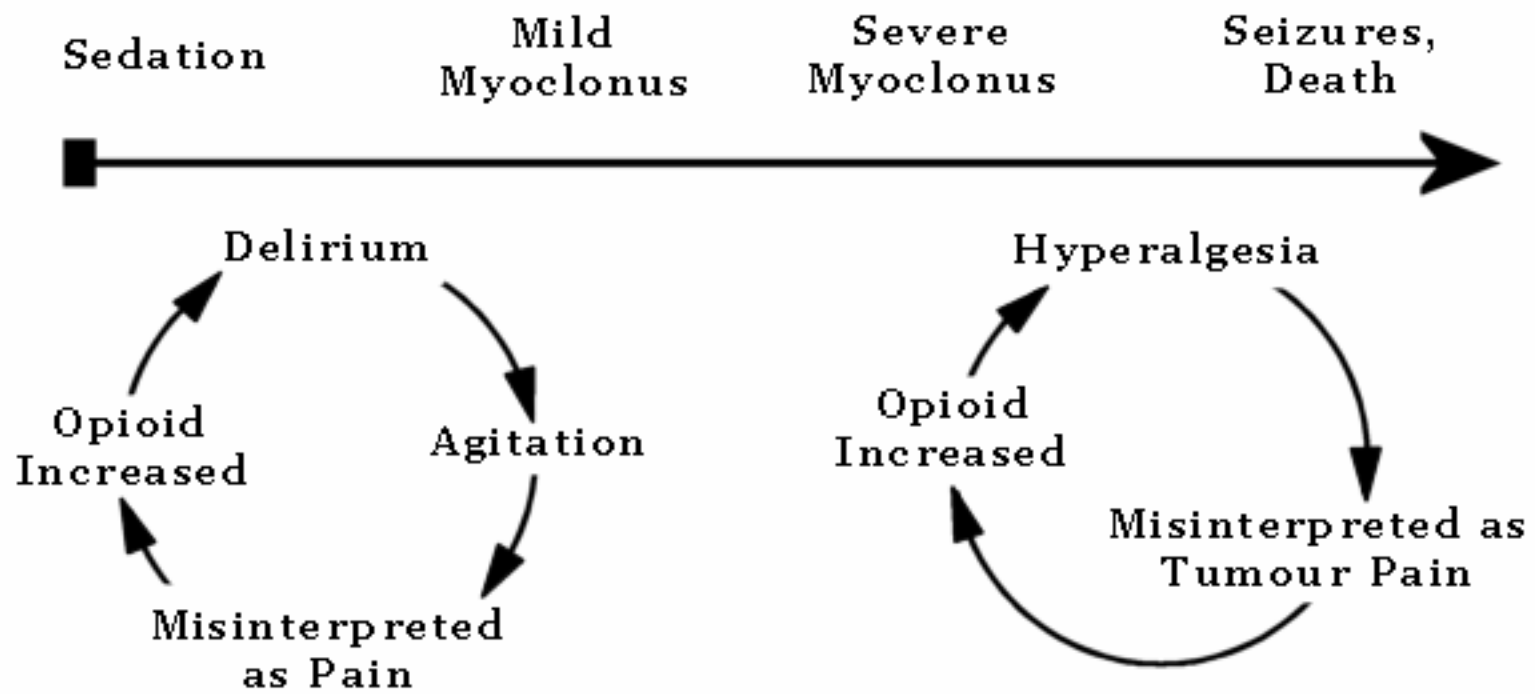
- Constipation
- Nausea/vomiting
- Urinary retention
- Itch/rash
- Dry mouth
- Respiratory depression
- Drug interactions
- Neurotoxicity: delirium, myoclonus → seizures

Opioid-Induced Neurotoxicity (OIN)

- Potentially fatal neuropsychiatric syndrome of:
 - Cognitive dysfunction
 - Delirium
 - Hallucinations
 - Myoclonus/seizures
 - Hyperalgesia / allodynia
- Increasing incidence – practitioners more comfortable and aggressive with opioids
- NMDA receptor involved
- Early recognition is critical

OIN: Recognition

- Myoclonus – twitching of large muscle groups
- Delirium
- Rapidly escalating dose requirement
- Pain “doesn’t make sense”; not consistent with recent pattern or known disease



OIN: Treatment

- Switch opioid (rotation) or reduce opioid dose
- Hydration
- Benzodiazepines for neuromuscular excitation

The Management of Incident Pain in Palliative Care

What is Incident Pain?

Pain occurring as a direct and immediate consequence of a movement or activity

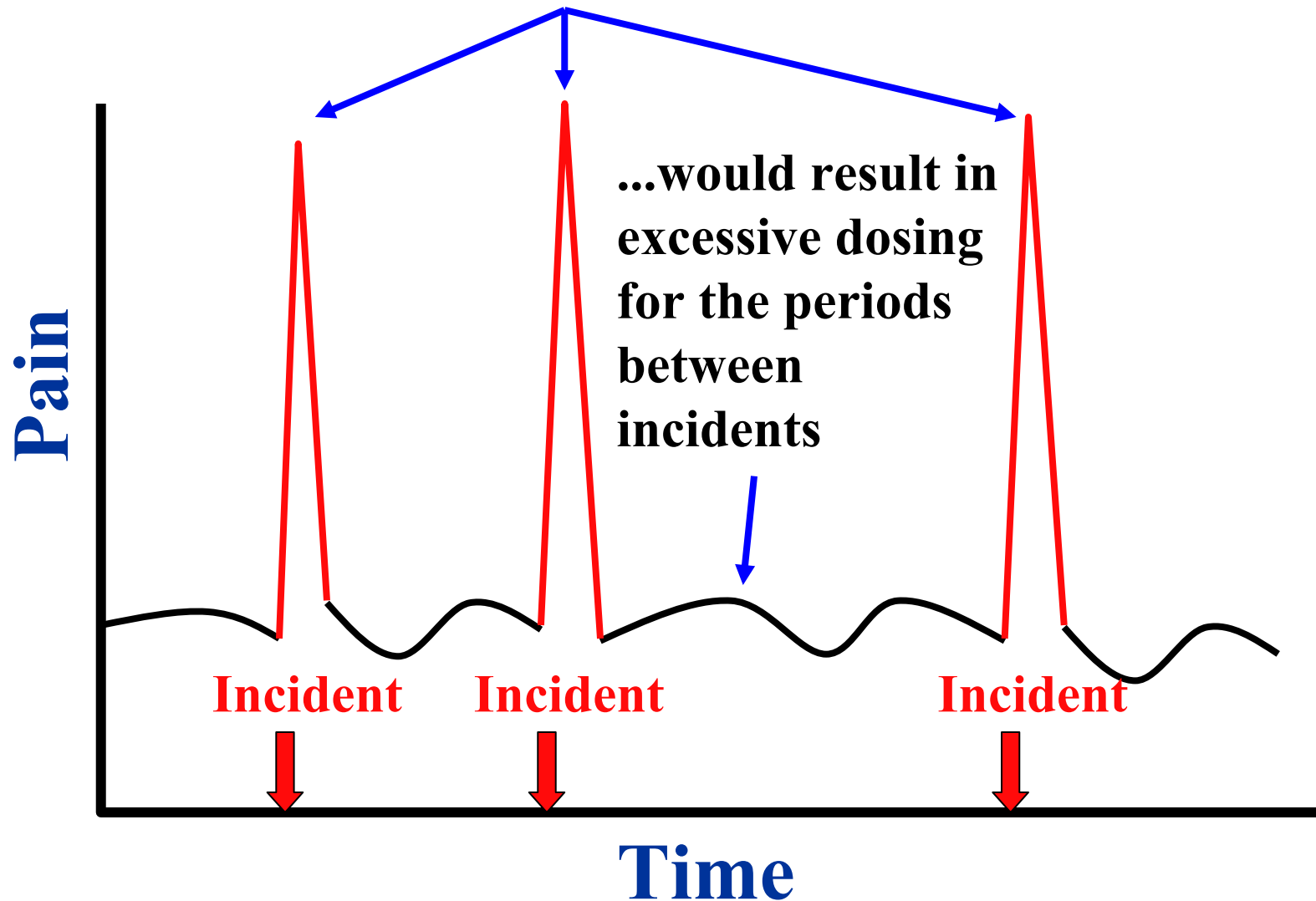
Circumstances In Which Incident Pain Often Occurs

- Bone metastases
- Neuropathic pain
- Intra-abdominal disease aggravated by respiration
 - » “incident” = breathing
 - » ruptured viscus, peritonitis, liver hemorrhage
- Skin ulcer: dressing change, debridement
- Disimpaction
- Catheterization

Barriers to Managing Incident Pain

- common opioids outlast painful stimulus
- opioid dose for incident pain may far exceed that needed for background pain control
- may be little warning of incident
- effective premedication before activity is time consuming

Having a steady level of enough opioid to treat the peaks of incident pain...



Considerations In Managing Incident Pain

- usually predictable
- stimulus is usually brief
- frequency of incidents may vary from several per minute to once per day or less.

Approach to Incident Pain

- **treat underlying problem**
 - » radiation Tx, chemotherapy
 - » bisphosphonates
 - » orthopedic intervention
 - » nerve blocks
- **ideal analgesic:**
 - » easily administered
 - » rapid onset
 - » short-duration of action
 - » in patient's control

Fentanyl and Sufentanil

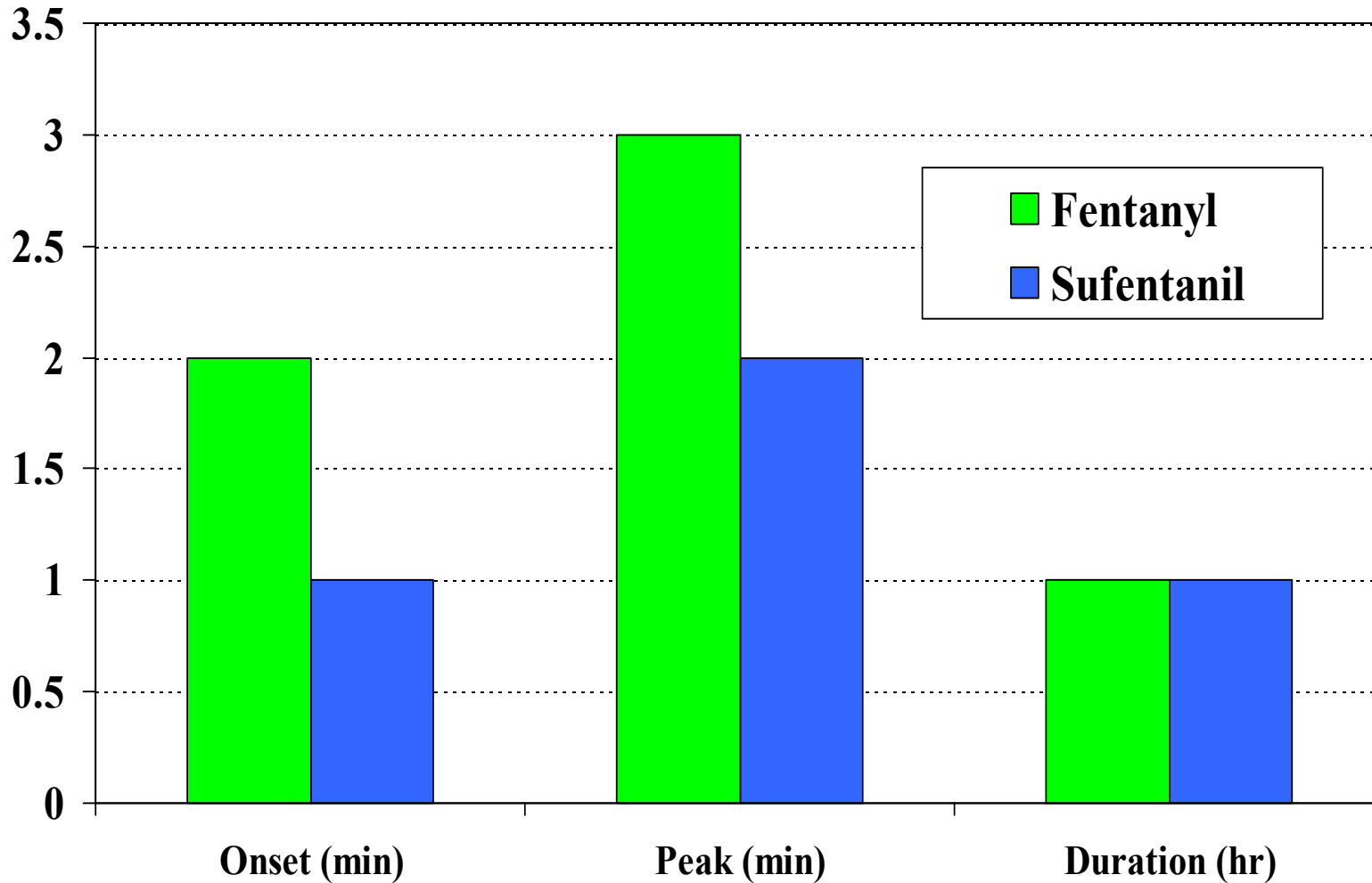
- synthetic μ agonist opioids
- highly lipid soluble →
 - » transmucosal absorption
 - » rapid redistribution, including in / out of CSF
- fentanyl \approx 100x stronger than morphine
- sufentanil \approx 1000x stronger than morphine

10 mg morphine

\approx 10 μ g sufentanil

\approx 100 μ g fentanyl

Comparison of Fentanyl and Sufentanil



INCIDENT PAIN PROTOCOL

Step #	Medication (50 µg/ml)	# Micrograms Sublingually
1	Fentanyl	50
2	Sufentanil	25
3	Sufentanil	50
4	Sufentanil	100

INCIDENT PAIN PROTOCOL ctd...

- **• fentanyl or sufentanil is administered SL 10 min. prior to anticipated activity**
- **• repeat q 10min x 2 additional doses if needed**
- **• increase to next step if 3 total doses not effective**
- **• physician order required to increase to next step if within an hour of last dose**
- **• the Incident Pain Protocol may be used up to q 1h prn**

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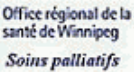
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Internet

Steps of the Incident Pain and Incident Dyspnea Protocol

Step	Medication	# micrograms SL (50 microgm/ml)
1	Fentanyl	50
2	Sufentanil	25
3	Sufentanil	50
4	Sufentanil	100 *

* A dose of 100 micrograms requires 2 ml of the 50 micrograms/ml preparation, which is a rather large volume to be absorbed transmucosally at once. It is recommended that it be given in two portions of 1 ml (50 micrograms) each, 10 - 15 minutes apart. The planned activity (dressing change, moving the patient, etc) should wait until 10 - 15 minutes after the second portion.

Application of the Incident Pain and Incident Dyspnea Protocol

1. The short acting opioid (fentanyl or sufentanil) is administered sublingually 10-15 minutes prior to anticipated activity. (See Incident Pain and Incident Dyspnea Protocol Table for dose) The patient is asked to try to hold the liquid under the tongue for about 10 minutes if possible without swallowing it.
2. If the initial dose appears to be insufficient, that same dose may be repeated up to two further doses, at 10-15 minute intervals. If a given dose is sufficient, the patient will typically appear drowsy 10 - 15 minutes following the dose. If this is not the case, or if the patient experiences discomfort during the planned activity, then repeat doses may be given up to a total of three as stated above.
3. Progression to the next step on the Incident Pain and Incident Dyspnea Protocol is undertaken at the discretion of the Registered Nurse who has the approval to use the Protocol, or the physician. All increases or decreases of doses MUST be written on the Physician's Order Sheet by the Registered Nurse or physician.
Increasing to the next step of the Incident Pain and Incident Dyspnea Protocol is undertaken if the maximum number of doses (three) is required to achieve comfort, or is insufficient to achieve comfort with activity. Increasing to the next step of the Incident Pain and Incident Dyspnea Protocol cannot be done within one hour of the last dose of fentanyl or sufentanil on the most recent implementation, except after contacting the physician. If the maximum number of doses (three) has been given, and the patient remains in discomfort with activity that must be undertaken presently, the physician should be contacted for consideration of immediately proceeding to the next step of the Incident Pain and Incident Dyspnea Protocol.
4. The Incident Pain and Incident Dyspnea Protocol may be used up to q 1h prn.