CLINICAL PEARLS IN SYMPTOM MANAGEMENT AND PALLIATIVE CARE

SURGICAL FOUNDATIONS SEMINAR
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OBJECTIVES

- Review the foundations of pain management
- Gain an approach to the use of opioids including dosing, titration, route of administration, and troubleshooting common pitfalls and side effects
- Learn a mechanistic approach to the use of antiemetics
- Overview of the philosophy of palliative care, dispel common myths and when to consider a palliative care consult

NOTE

- Equivalencies (e.g. hydromorphone is 5 times stronger than morphine) in this presentation are approximations and vary from person to person

- You will see slightly different equivalencies used in the literature

= Morphine 10 mg

2 oxycocet = 20 mg morphine

Oxycocet has 5 mg of oxycodone

Oxycodone is twice as strong as morphine

HOW MUCH EQUIVALENT ORAL MORPHINE IS IN TWO OXYCOCET/PERCOCET?

TYPES OF PAIN

- Nociceptive pain
- Neuropathic pain
- Complex and multidimensional concept with strong social and psychological components (“Total body pain”)

NOCICEPTIVE PAIN

Stimulation of intact nerve endings

- Mechanical
- Chemical

Two subtypes

- Somatic
  - Localized- may be deep
- Visceral
  - Poorly localized, colicky/intermittent
  - Radiates

NEUROPATHIC PAIN

Lesion/damage in PNS/CNS

Radiates

Positive symptoms

- Burning, lancinating, shooting
- Hyperalgesia, allodynia
- Constant

Negative symptoms

- Numb or wooden

TAKING A PAIN HISTORY

O- Onset

P- Provoking/palliating

- What have you tried? Did it help?

Q- Quality/quantity

R- Radiating

S- Severity

T- Timing

- Activity, meals, morning/evening

TAKING A PAIN HISTORY

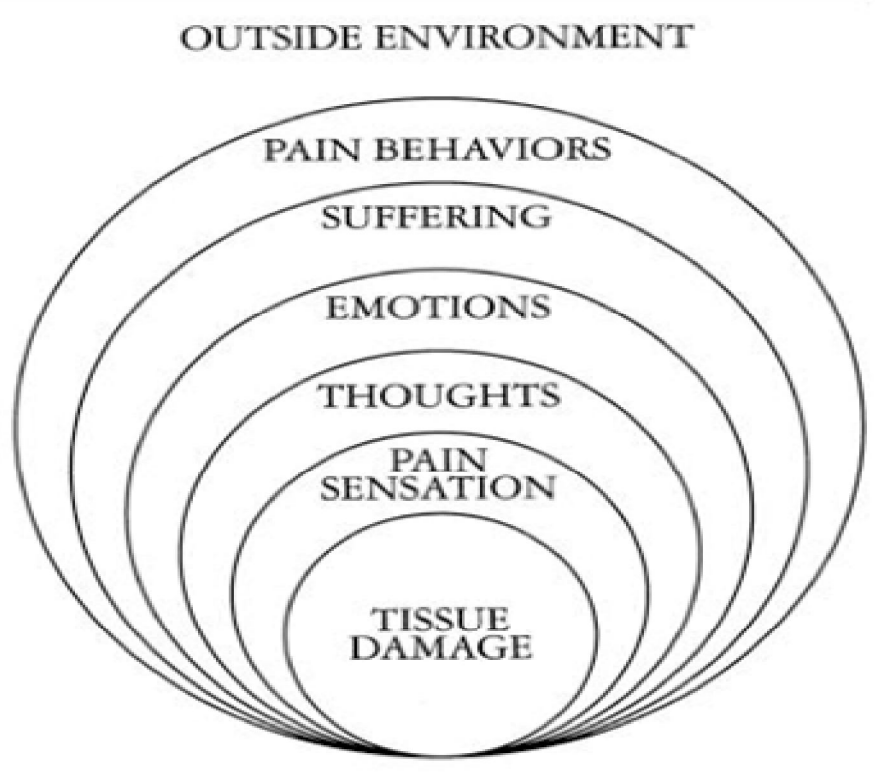
Screen for those at risk of opioid dependency

Known risk factors include:

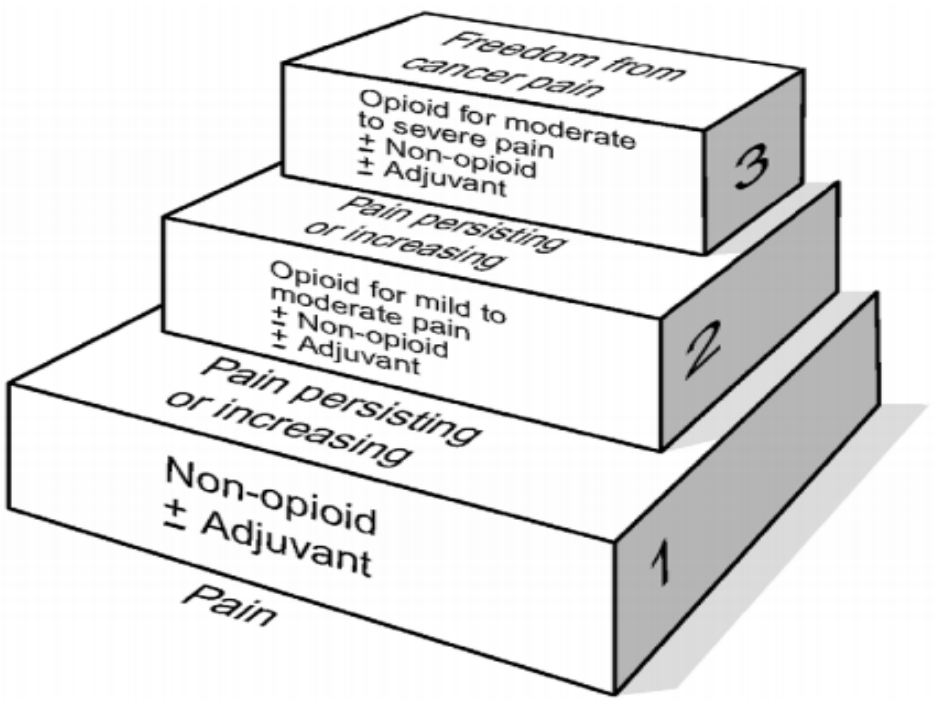
- family and personal history of substance abuse (prescription drugs, illegal drugs, alcohol)
- history of preadolescent sexual abuse (female)
- psychiatric history (ADD, OCD, bipolar, schizophrenia, depression)

TAKING A PAIN HISTORY

Psychiatric history and good psychosocial history also helps to flag “total pain”



WHO PAIN LADDER



LEVEL 1: MILD PAIN

Acetaminophen

- Standard upper limit for those without liver dysfunction is 4 g/day (consider going lower)
- 2 g/day in those with stable liver disease
- Most frequent drug named in accidental overdose
- Perceived safety and in many OTC medications with multiple active ingredients

LEVEL 1: MILD PAIN

NSAIDs:

- Good for inflammatory pain including bony metastases
- Poor choice in patients with renal dysfunction, history of GI ulcers/bleeds, or if anticipating long-term use
- Use the lowest possible dose for the shortest period of time; add PPI if using for over 1-2 weeks
- COX-2 may be lower risk in terms of GI side effects, but possible higher risk of cardiovascular events (MI, stroke)

LEVEL 1: MILD PAIN

Adjuvants

- including treating anticipatory or psychological pain which often includes non-pharmacological treatments such as biofeedback
- Agents targeting neuropathic pain (will discuss later)

OPIOIDS

- Weak: codeine, tramadol, tapentadol
- Strong: morphine, oxycodone, hydromorphone, fentanyl, etc.
- All exert their actions on mu-opioid receptors located both centrally and peripherally

OPIOID RECEPTORS

Mu

- Analgesia, euphoria, respiratory depression, reduced GI motility, dependence

Kappa

- Analgesia, sedation, dysphoria

Delta

- Analgesia, antidepressive effects, dependence

LEVEL 2: MILD TO MODERATE PAIN

Opioid for mild to moderate pain: e.g. codeine, tramadol

+/-non-opioid

+/-adjuvant

CODEINE

- Metabolized in the liver by CYP2D6
- Prodrug, converted to morphine
- Very constipating
- Up to 10% of population are poor metabolizers (e.g. T#3 no better than Tylenol alone)
- Up to 2% are extensive metabolizers (1.5x as potent)

CODEINE

- Unpredictable metabolism and perceived safety compared to stronger opioids = inadvertent overdoses – especially in children
- Hospital for Sick Children has taken codeine off its formulary

CODEINE

- **Morphine 1 mg oral=Codeine 10 mg oral**
- Tylenol #3/Lenoltec #3=325 mg acetaminophen, 30 mg codeine (=3 mg morphine equivalent)
- Why not just give morphine? (1/2 a 5 mg tablet = 2.5 mg)
- T#3s also have caffeine

Bottom line: There is no good reason to prescribe codeine, *especially Tylenol #3*

LEVEL 3: MODERATE TO SEVERE PAIN

OPIOID	ORAL TABLETS IR & CR	ORAL SYRUP	TRANSDERMAL PATCH	PARENTERAL IV/SC
MORPHINE	☑	☑		☑
OXYCODONE	☑			
HYDROMORPHONE	☑	☑		☑
FENTANYL			☑	☑

MORPHINE AND HYDROMORPHONE

- Both are metabolized by the liver
- **Morphine 5 mg = Hydromorphone 1 mg (i.e. hydromorphine is 5x stronger than morphine!)**
- Drugs and metabolites are significantly renally cleared
- General thinking is that hydromorphone's metabolites are less toxic but there is no good evidence to show this

MORPHINE AND HYDROMORPHONE

Both are available in various formulations

Oral: tablets and syrups, short and long (contin) acting

Parenteral:

- IV/SC is **2-3x** as strong as oral (e.g. morphine 2-3 mg PO= 1 mg IV/SC) and reaches peak effect **twice** as fast (30 minutes vs 60 minutes)

PRN dosing: Q1H – if pain is not better an hour after PRN – it won't get much better

STARTING DOSES FOR OPIOID NAÏVE PTS

GENERALLY START WITH ONLY PRN – BUT THESE ARE GOOD STARTING STANDING Q4H DOSES AS WELL

	Moderate Pain	Severe Pain
Frail (elderly, cachetic)	2.5 mg oral morphine 1 mg morphine IV/SC 0.5 mg oral hydromorphone 0.2 mg hydromorphone IV/SC	5 mg oral morphine 2 mg morphine IV/SC 1 mg oral hydromorphone 0.5 mg hydromorphone IV/SC
Robust	5 mg oral morphine 2 mg morphine IV/SC 1 mg oral hydromorphone 0.5 mg hydromorphone5 mg	10 mg oral morphine 5 mg morphine IV/SC 2 mg oral hydromorphone 1 mg hydromorphone IV/SC

MR. W, 88 Y.O MAN

- Type 2 diabetes, CAD and prior CABGx3, significant peripheral arterial disease
- Bed-ridden with significant dry gangrene of the toes
- Family brought him into hospital for uncontrolled pain, failure to cope
- Rates pain as 4/10, when moving around is 7/10
- Not a candidate for bypass and currently trying to decide on amputation
- Currently taking 1 g acetaminophen PO TID
- What would you prescribe for pain control?

MR. W, 88 Y.O MAN

- Any of the following would be reasonable:

1. morphine 2.5 mg PO Q1H PRN or morphine 1 mg IV/SC Q1H (Q30min) PRN
2. hydromorphone 0.5 mg PO Q1H PRN or hydromorphone 0.2 mg IV/SC Q1H (Q30min) PRN

I always give option of both – parenteral faster time to onset and good alternative if pt is n/v or agitated; oral is important if pt is likely to go home requiring opioids

OXYCODONE

Only available in oral formulations (no parenteral), more expensive

In Ontario, only Percocet/Endocet/Oxycocet (325 mg acetaminophen, 5 mg oxycodone) has ODB coverage

Oxycodone alone and OxyNEO are not covered unless under EAP, physician has Palliative Care Facilitated Access or patient has private insurance

Oxycodone 1 mg = Morphine 2 mg (i.e. oxycodone is 2x as strong as morphine)

MR. W, 88 Y.O MAN

- Currently taking oxyNEO 30 mg PO Q12H
- You want to take him off long-acting and convert him to standing doses of immediate release
- How do you do this?

DURATION OF ACTION

- For morphine, hydromorphone, and oxycodone it is ~4-5 hours
- So to convert from CR to IR, calculate the total daily dose and then find the equivalent Q4H dose

(divide by 6)

- oxyNEO 30 mg BID = 60 mg daily oxycodone = oxycodone 10 mg PO Q4H *standing*
- In renal or hepatic failure, increase to Q6-8H and start at a lower dose (don't even need CR in end-stage renal or hepatic dz, just use IR)

MR. W, 88 Y.O MAN

- If taking oxyNEO 30 mg PO Q12H
- What do you prescribe as his breakthrough dose?

BREAKTHROUGH OPIOID DOSING

oxyNEO 30 mg PO Q12H

2 rules you can follow:

1. 10% of the total daily standing dose
2. 50-100% of the equivalent Q4H dose

=6 mg oxycodone

→5 mg oxycodone Q1H PRN

=5-10 mg oxycodone Q1H PRN

(pick a number – don't leave a range)

TITRATION OF OPIOIDS

If a patient is using >4-6 breakthroughs a day, the base dose likely needs to be increased

2 rules:

1. Increase base dose by 25% of daily amount
2. Another rule is to calculate the total breakthroughs used in 24 hours and add it to the standing dose (not recommended)

*titrate up the standing dose of opioid **not more frequently than every 24 hours***

Opioid	PO Dose	IV/SC Dose
Codeine	100mg	--
Morphine	10mg	5mg
Oxycodone	5mg	--
Hydromorphone	2mg	1mg

PAIN

Would you change anything about these medications?

Hydromorph contin 9 mg BID

Hydromorphone 1 mg PO Q1H PRN – taking 8-9 breakthrough/day

The breakthrough dose is too low.

BREAKTHROUGH OPIOID DOSING

Hydromorph contin 9 mg PO BID

= 18 mg/24 hours

Going with Rule #1 (10% of total daily dose) =

18 mg x 10% = 1.8 mg = 2 mg

Breakthrough dose = hydromorphone 2 mg PO Q1H PRN

Going with Rule #2 (50-100% of the Q4H dose):

18 mg/6 = 3 mg PO Q4H

Breakthrough dose = hydromorphone 1.5-3 mg PO Q1H PRN

PARENTERAL BREAKTHROUGH DOSE FOR PT ON MORPHINE 10 MG PO Q4H STANDING

- Morphine 10 mg PO Q4H standing

= MEDD (morphine equivalent daily dosing) is 60 mg PO

= 30 mg IV/SC

- 10% is morphine 3 mg IV/SC Q1H PRN

Q4H STANDING DOSE OF PARENTERAL HYDROMORPHONE FOR A PT ON OXYNEO 40 MG Q12H

- oxyNEO 40 mg Q12H = 80 mg/24 hrs
- MEDD= 80 mg x 2 = 160 mg morphine PO in 24 hours
- 160/5 = 32 mg hydromorphone PO in 24 hours
- 32/2 = 16 mg hydromorphone IV/SC in 24 hours
- 16/6=2.67 mg =

<u>2.5 mg hydromorphone IV/SC Q4H PRN</u>

ROTATING OPIOIDS

- When rotating, ↓equivalent dosage by 25-50% to take into account incomplete cross-tolerance
- So in previous example, oxyNEO 40 mg BID = 2.5 mg hydromorphone Q4H standing

→decrease this *further* to 1.5 (or 2) mg Q4H IV/SC hydromorphone standing

- Tolerance and increasingly higher doses of opioids is common and expected and different from addiction

MR. S FEELS VERY ITCHY ON MORPHINE 20 MG PO Q4H STANDING. ROTATE HIM TO HYDROMORPHONE.

- Morphine 20 mg PO Q4H
- 20/5= 4 mg hydromorphone PO Q4H standing
- Reduce by 25-50% for incomplete cross-tolerance
- 2 or 3 mg hydromorphone PO Q4H standing – both are reasonable

CONTROLLED RELEASE

- When pt is on **stable** opioid regimen (parenteral or IR), then you can consider switching to contin/controlled release
- Hydromorphone 2.5 mg PO Q4H standing
- You want to switch to hydromorph contin/hydromorphone CR

CONTROLLED RELEASE

- Hydromorphone 2.5 mg PO Q4H standing

=2.5x6=15 mg daily hydromorphone

=15/2 = 7.5 mg hydromorphone PO Q12H

But, hydromorph contin/hydromorphone CR does not come in 7.5 mg – need to try 6 mg first, then 9 mg.

FENTANYL

- Transdermal patch is changed every 72 hours
- Patch conversion: fentanyl 25 mcg/hr =50 mg PO MEDD – there is *wide* variability in literature
- No known active metabolites so considered safer in ESRD (but still proceed with caution!)
- Absorption can vary based on body habitus, fever, etc.

WHEN SHOULD A FENTANYL PATCH BE CONSIDERED?

- NOT in unstable pain!
- When pain is stable but:
  - There is concern around renal impairment
  - Patient has difficulty swallowing
  - Intolerable side effect profile of other opioids (sedation, constipation)
  - Questionable GI absorption of opioids (especially CR formulation!)

FENTANYL

- Parenteral (Subcut) and sublingual(using parenteral) very useful for incident pain, 12.5-25 mcg starting doses
- Onset of action for fentanyl is fast (5-10 minutes) and it is cleared quickly (30-40 minutes)
- There are 2 quick-acting buccal tablets (Abstral and Fentora) – don't use them if you are not comfortable with opioids, not for opioid-naïve pts – starts at 100 mcg

HYDROMORPH CONTIN 18 MG PO Q12H TO FENTANYL PATCH

- HMc 18 mg x 2 = 36 mg hydromorphone/24 hr
- MEDD = 36 x 5 = 180 mg PO morphine/24 hr
- 180/50 x 25* = 90 mcg/hr fentanyl

this was because I use 25 mcg/hr fentanyl patch = 50 mg MEDD

Dose reduce for incomplete cross-tolerance gives a range of 45-67.5 mcg/hr

So 50 mcg/hr patch is a good start (will likely need to increase)

For breakthrough, continue to use previous BT, e.g. hydromorphone 4 mg PO or 2 mg IV/SC Q1H PRN

MISCELLANEOUS

- If a patient has ++GI pathology (e.g. previous resection, gut wall edema, etc.) be cautious around calculating equivalencies of controlled release opioids, may need to dose reduce significantly
- E.g. someone on hydromorph contin 18 mg BID may only end up needing 25 mcg/hr fentanyl patch or a much lower parenteral dose because gut absorption was so poor
- If pt is very anxious, consider making PRN intervals longer (e.g. Q2H) to avoid toxicity as pt may be "chemically coping"
- Write ALL your calculations in the chart – especially if complicated – then double and triple check

OPIOIDS: SIDE EFFECTS

- Expected side effects: nausea +/- vomiting, mild mental fog and fatigue, anticholinergic side effects such as dry mouth
- Most tend to improve after a few days except constipation

CONSTIPATION AND OPIOIDS

- Docusate is **NOT** helpful for opioid-induced constipation
- Start with Senna TT OD or BID → can up to 3-4 T BID
- Add on an osmotic agent:

  Lactulose 15-30 cc OD-BID (on ODB)

  or PEG3350 (Lax-a-day, Restoralax – Not on ODB)
- Other: suppositories, enemas, methylnaltrexone SQ

OPIOID-INDUCED NEUROTOXICITY

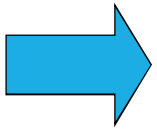
Myoclonus

Somnolence

Confusion / delirium

Hyperalgesia

Seizures



- Cut back on the dose (25-50%)
- IV fluids
- Look for underlying cause (e.g. AKI, infection)
- (Rotate to another opioid)

INTENT FOR ANALGESICS IS SHORT-TERM, BUT ON INITIATION USE BECOMES LONG-TERM

1997-2008. Ontario seniors age 66 and older reviewed

Low-risk short stay surgeries: cataract surgery, TURP, varicose vein stripping, laparoscopic cholecystectomy

Pre - surgery	7 Days Post-surgical Discharge	One Year after Surgery
Opioid Use	Opioid Use	Opioid Use
391,139 pts	27,636 pts	30,145 pts
0%, - all were opioid-naive	7.1 %	7.7%

Pre - surgery	7 Days Post-surgical Discharge	One Year after Surgery
NSAID Use	NSAID Use	NSAID Use
383,780 pts	1169 pts	30,080 pts
0%, - all were NSAID-naïve	0.3 %	7.8%

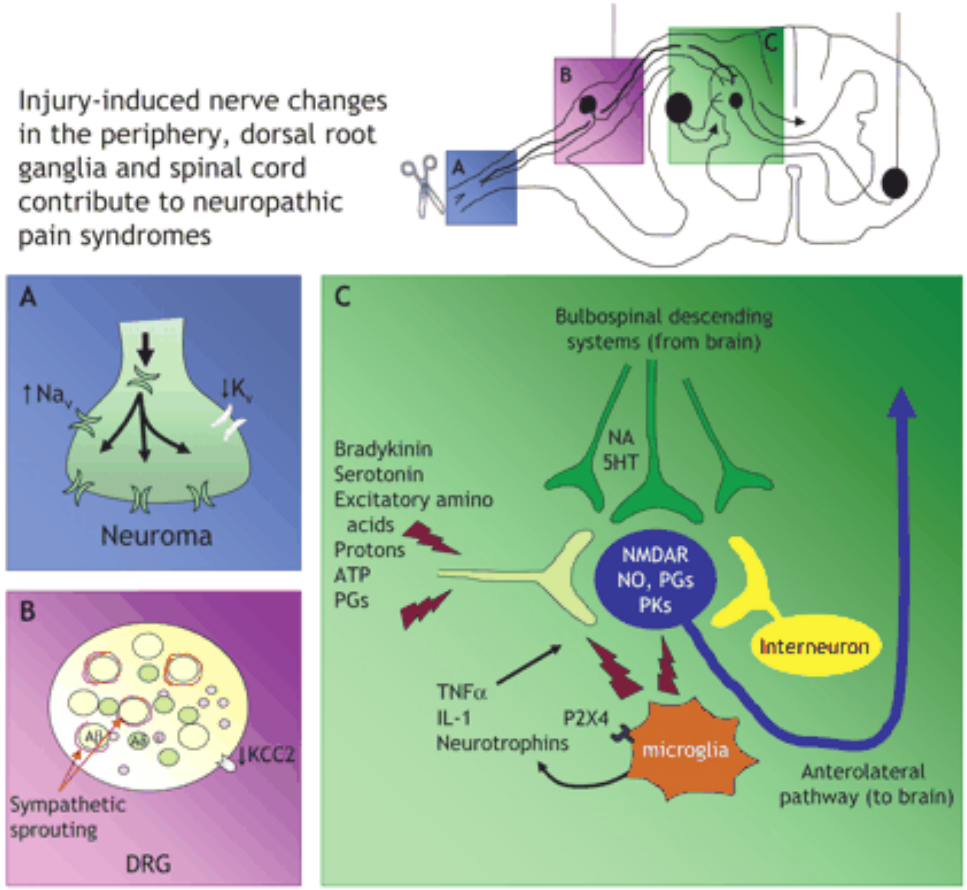
2012 Arch Intern Med(5):425-30. Long-term analgesic use after Low-Risk Surgery

Slide credit: Bruce Kennedy, Fraser Health

NEUROPATHIC PAIN

- Consider if characteristics include shooting or burning pain, hyperalgesia, allodynia
- Also consider if pain is not responding well to opioids
- First line adjuvants: TCAs, gabapentin/pregabalin, SNRIs (duloxetine, venlafaxine)

Injury-induced nerve changes in the periphery, dorsal root ganglia and spinal cord contribute to neuropathic pain syndromes



TRICYCLIC ANTIDEPRESSANTS

Cheap, once daily

Secondary amines better tolerated

- Nortryptiline
- Desipramine

Risks

- Anticholinergic side effects
- ?MI risk
- Suicide potential

Moderately effective for DN and post-herpetic neuralgia in multiple RCTs

- ~50% receive mild-mod benefit

Start at 25mg, increase by 25mg/d every week

SNRIS

Duloxetine beneficial in 3 RCTs of DN

- Few side effects
  - Nausea
- Start at 30mg/d, inc to 60mg/d after 1 week

Venlafaxine effective in many types of neuropathy

- Start at 37.5 or 75mg daily, increase by 75mg/d per week

GABAPENTINOIDS

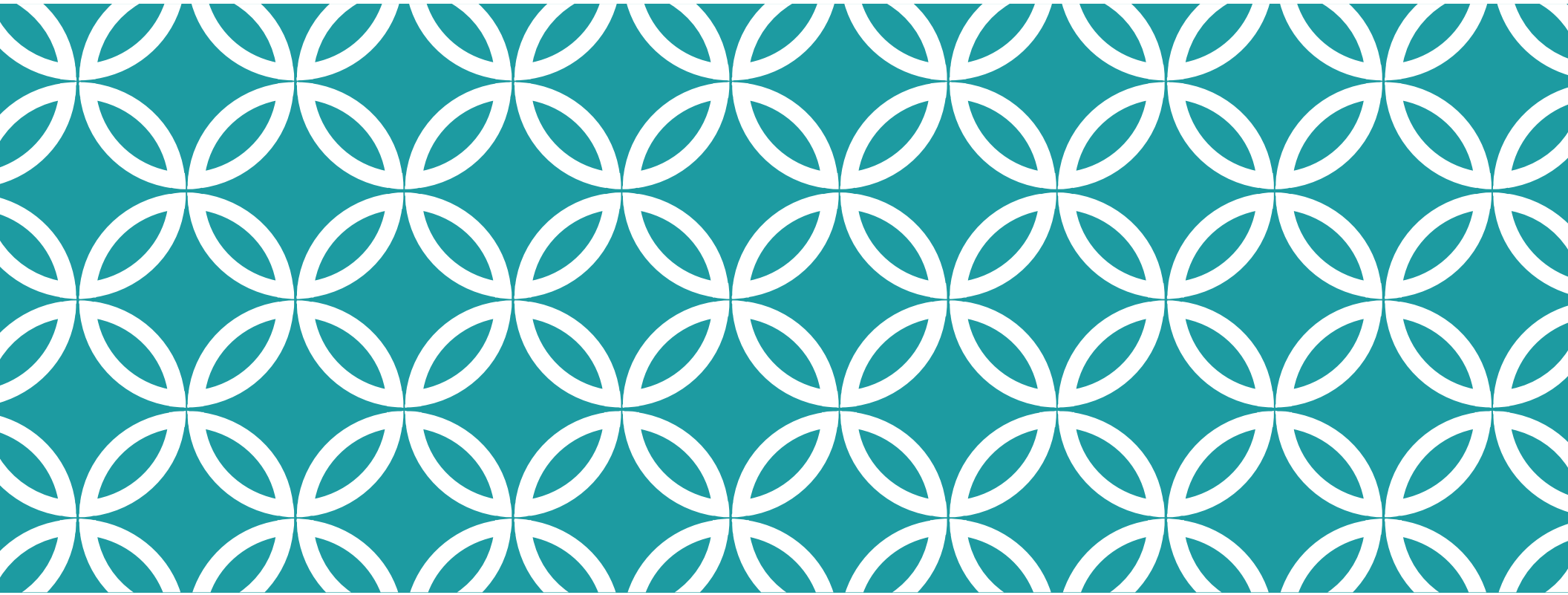
Prevent release of glutamate, norepi, sub. P

Gabapentin

- Effective in many types of NP
- Some vertigo/ataxia, somnolence
- Start 300-900/d, titrate up to 1.8-3.6g/d divided into TID/QID dosing

Pregabalin

- Effective in DN, PHN mostly
- Start 50 mg OD/BID, titrate to 150-300mg BID
- Easier to titrate, similar tolerability, ?faster
- Both pregab and gabapentin need dose adjustment for renal failure
- Pt can get myoclonic, confused on both → reduce dose

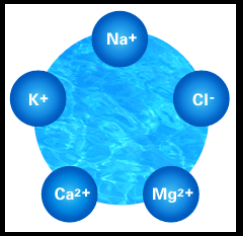


NAUSEA

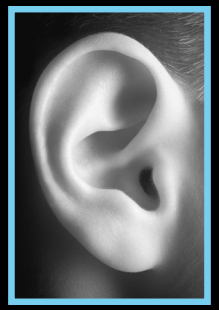
Serotonin

Ondansetron

Dopamine

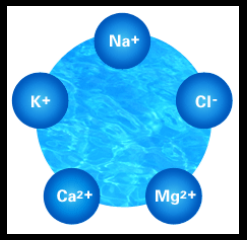


Histamine
Acetylcholine



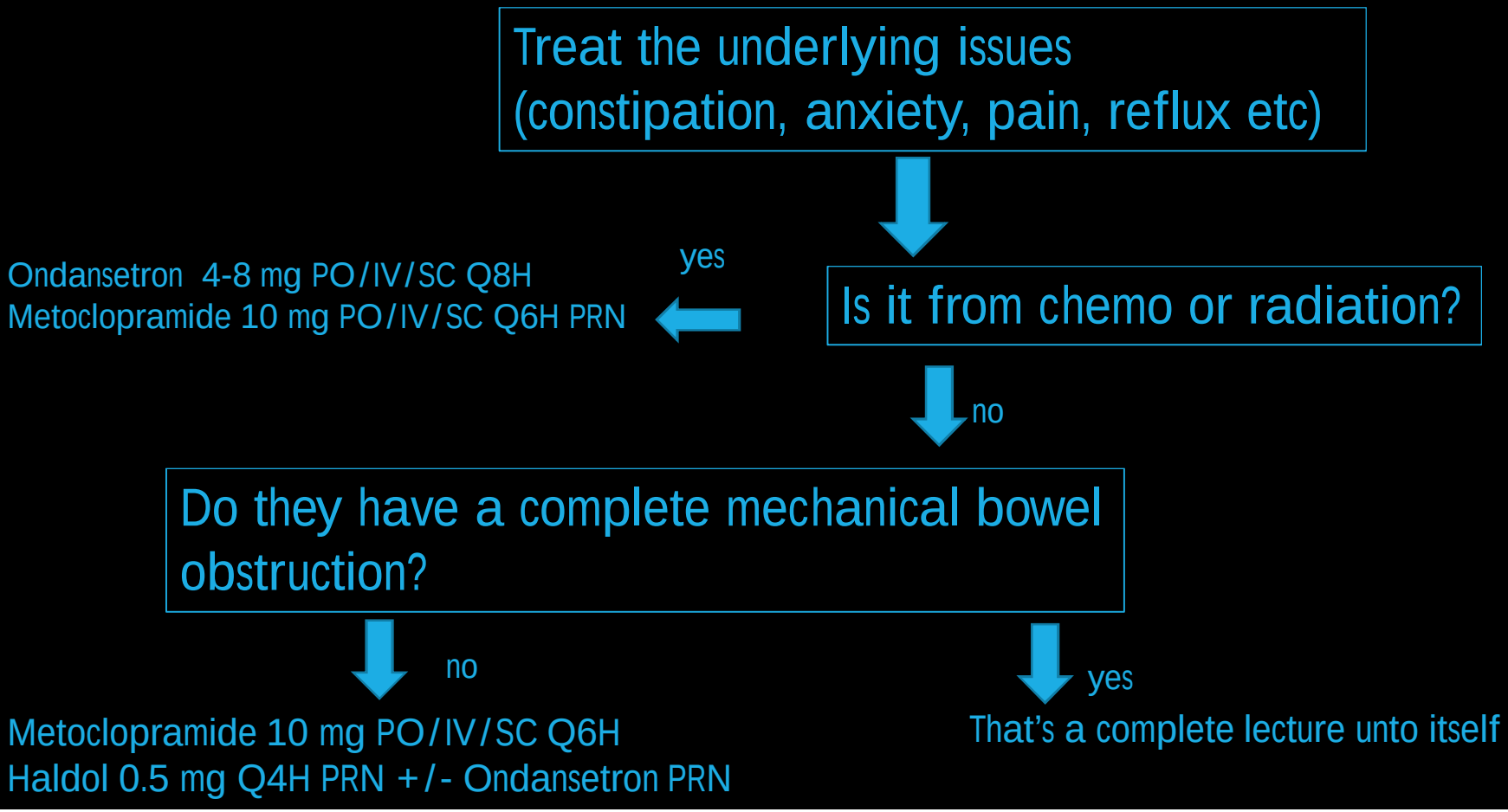
Dimenhydrinate
Scopolamine

Anti-dopamine Agents



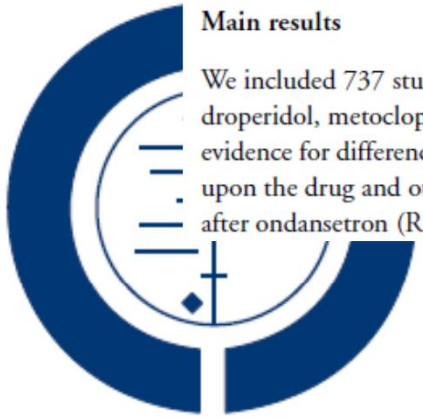
Central	Peripheral (i.e. prokinetic)	Mixed
~~Prochlorpromazine (Stemetil)~~ Haloperidol Methotrimeprazine (Nozinan)	Domperidone	Metoclopramide (Maxeran)

Irene's Super Simplistic Algorithm



Drugs for preventing postoperative nausea and vomiting (Review)

Carlisle J, Stevenson CA

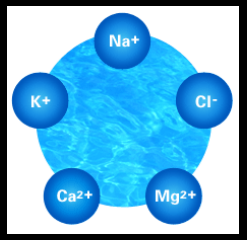


THE COCHRANE COLLABORATION®

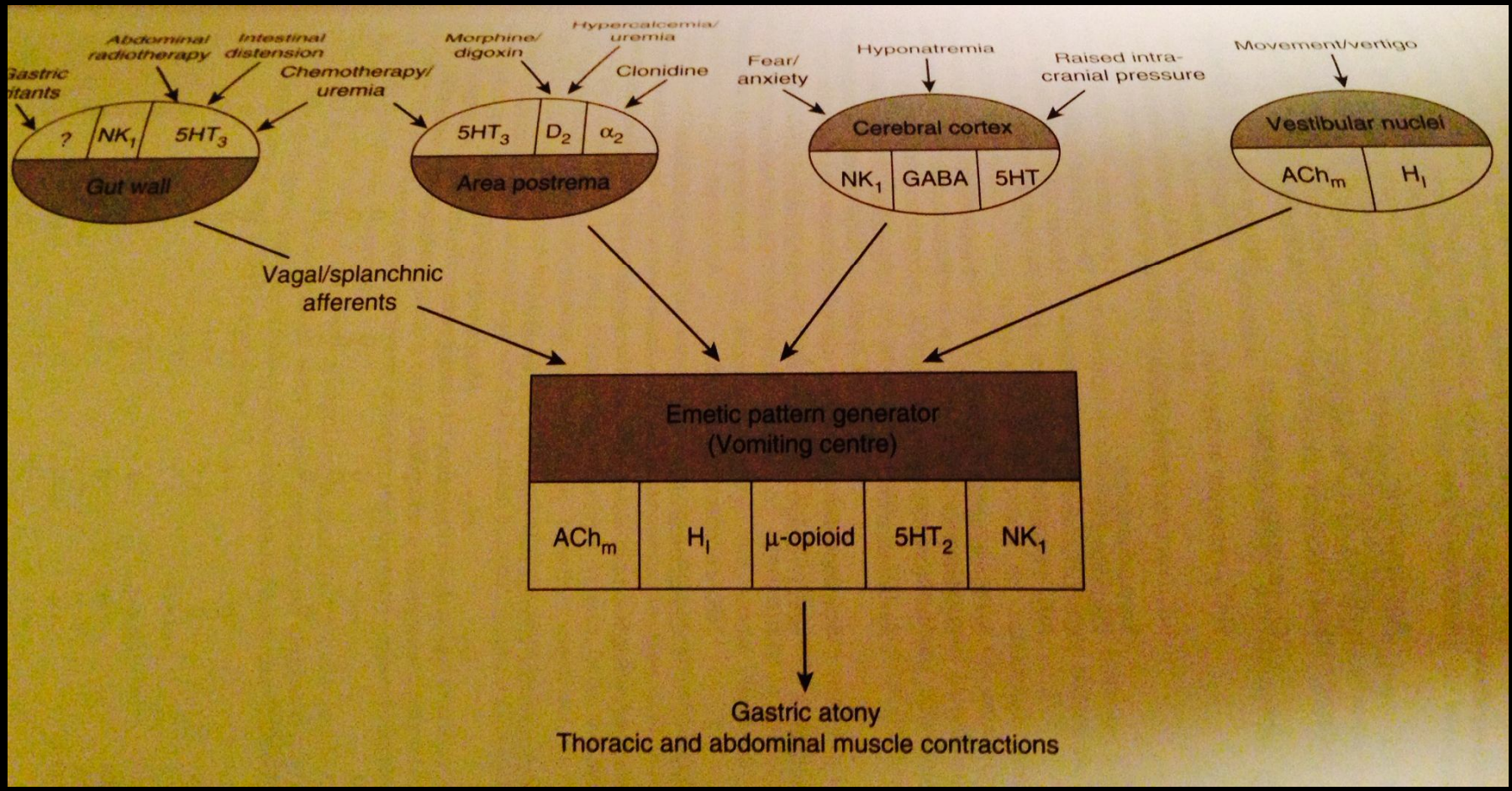
Main results

We included 737 studies involving 103,237 people. Compared to placebo, eight drugs prevented postoperative nausea and vomiting: droperidol, metoclopramide, ondansetron, tropisetron, dolasetron, dexamethasone, cyclizine and granisetron. Publication bias makes evidence for differences among these drugs unreliable. The relative risks (RR) versus placebo varied between 0.60 and 0.80, depending upon the drug and outcome. Evidence for side effects was sparse: droperidol was sedative (RR 1.32) and headache was more common after ondansetron (RR 1.16).

Notes about treating nausea



- Metoclopramide is a good first choice most of the time: acts both peripherally and centrally
- Needs dose reduction in renal impairment
- Main side effects/risks related to basal ganglia – EPS, Parkinsonism, akathisia
- Domperidone better in Parkinsonism – watch QTc
- If one anti-emetic doesn't work, add another that hits a different receptor
- Lots of other Rx possibilities: dexamethasone, cannabinoids, etc.


Gastric
itants
Abdominal radiotherapy
Intestinal distension
Chemotherapy/ uremia
?
NK1
5HT3
Gut wall
Morphine/ digoxin
Hypercalcemia/ uremia
Clonidine
5HT3
D2
α2
Area postrema
Fear/ anxiety
Hyponatremia
Raised intra-cranial pressure
Cerebral cortex
NK1
GABA
5HT
Movement/vertigo
Vestibular nuclei
AChm
H1
Vagal/splanchnic afferents
Emetic pattern generator (Vomiting centre)
AChm
H1
μ-opioid
5HT2
NK1
Gastric atony
Thoracic and abdominal muscle contractions

DISPELLING MYTHS IN PALLIATIVE CARE

- What is Palliative care?
- Palliative Care ≠ hastening death/withdrawal of care/End of Life Care
- Opioids and the Principle of Double Effect
- A brief primer on the palliative care landscape in Toronto (e.g. how do I send a patient to a palliative care unit or hospice?)

WHAT IS PALLIATIVE CARE?

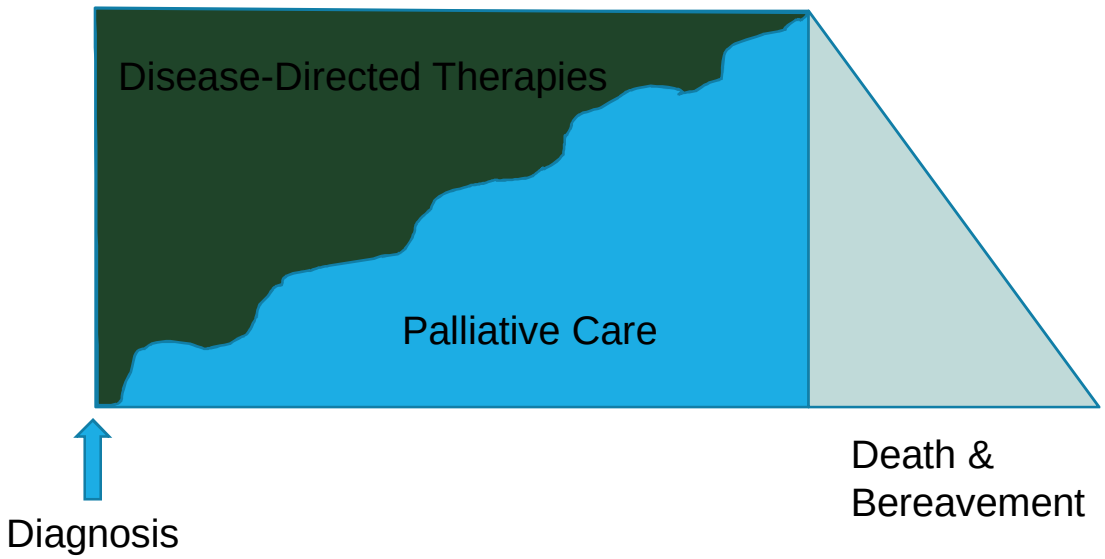
Medical care for people with serious illness and their families

Patients and families define it as being focused on improving quality of life

Appropriate at **any age,** for **any diagnosis**, at **any stage in a serious illness**, and provided together with curative and life-prolonging treatments

http://www.capc.org/tools-for-palliative-care-programs/marketing/public-opinion-research/2011-public-opinion-research-on-palliative-care.pdf

CONCEPTUAL SHIFT FOR PALLIATIVE CARE



PALLIATIVE CARE MODELS

Quality Improves	Costs Reduced
• Symptoms • Quality of Life • Length of Life • Family satisfaction • Family bereavement outcomes • MD satisfaction • Care matched to patient-centred goals	• Hospital costs decrease • Need for hospital, ICU, ED decreased • 30 day readmissions decreased • Hospital mortality decreased

Diane E. Meier. Palliative Care 2020: Matching Care to Frail Older Patient and Family Needs. 9th Annual Advanced Learning in Palliative Medicine Conference. Vancouver. 2013

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Palliative Care for Patients with Metastatic Non–Small-Cell Lung Cancer

Jennifer S. Temel, M.D., Joseph A. Greer, Ph.D., Alona Muzikansky, M.A., Emily R. Gallagher, R.N., Sonal Admane, M.B., B.S., M.P.H., Vicki A. Jackson, M.D., M.P.H., Constance M. Dahlin, A.P.N., Craig D. Blinderman, M.D., Juliet Jacobsen, M.D., William F. Pirl, M.D., M.P.H., J. Andrew Billings, M.D., and Thomas J. Lynch, M.D.

RESULTS

Of the 151 patients who underwent randomization, 27 died by 12 weeks and 107 (86% of the remaining patients) completed assessments. Patients assigned to early palliative care had a better quality of life than did patients assigned to standard care (mean score on the FACT-L scale [in which scores range from 0 to 136, with higher scores indicating better quality of life], 98.0 vs. 91.5; P=0.03). In addition, fewer patients in the palliative care group than in the standard care group had depressive symptoms (16% vs. 38%, P=0.01). Despite the fact that fewer patients in the early palliative care group than in the standard care group received aggressive end-of-life care (33% vs. 54%, P=0.05), median survival was longer among patients receiving early palliative care (11.6 months vs. 8.9 months, P=0.02).

CONCLUSIONS

Among patients with metastatic non–small-cell lung cancer, early palliative care led to significant improvements in both quality of life and mood. As compared with patients receiving standard care, patients receiving early palliative care had less aggressive care at the end of life but longer survival. (Funded by an American Society of Clinical Oncology Career Development Award and philanthropic gifts; ClinicalTrials.gov number, NCT01038271.)

THERE IS NO SUCH THING AS A "PALLIATIVE" PATIENT

- There is no intervention in and of itself that IS or IS NOT palliative
- It is the intent of the intervention that dictates whether it is palliative (e.g. it is not to reverse the underlying condition, but to improve quality of life)
- Surgery can be palliative
- Medications: e.g. reasonable to keep beta-blocker if pt can take and they have a history of tachyarrhythmia – may help symptoms; stop statin if life expectancy <1 year

OPIOIDS AND RESPIRATORY DEPRESSION

- Highest risk is inappropriate dosing in opioid naïve patients
- Use the starting doses and titration guidelines outlined – if in any doubt, “start low, go slow”

OPIOIDS FOR DYSPNEA

Dyspnea “derives from interactions among multiple physiological, psychological, social, and environmental factors, and may induce secondary physiological and behavioral responses”

It is a *subjective sensation*

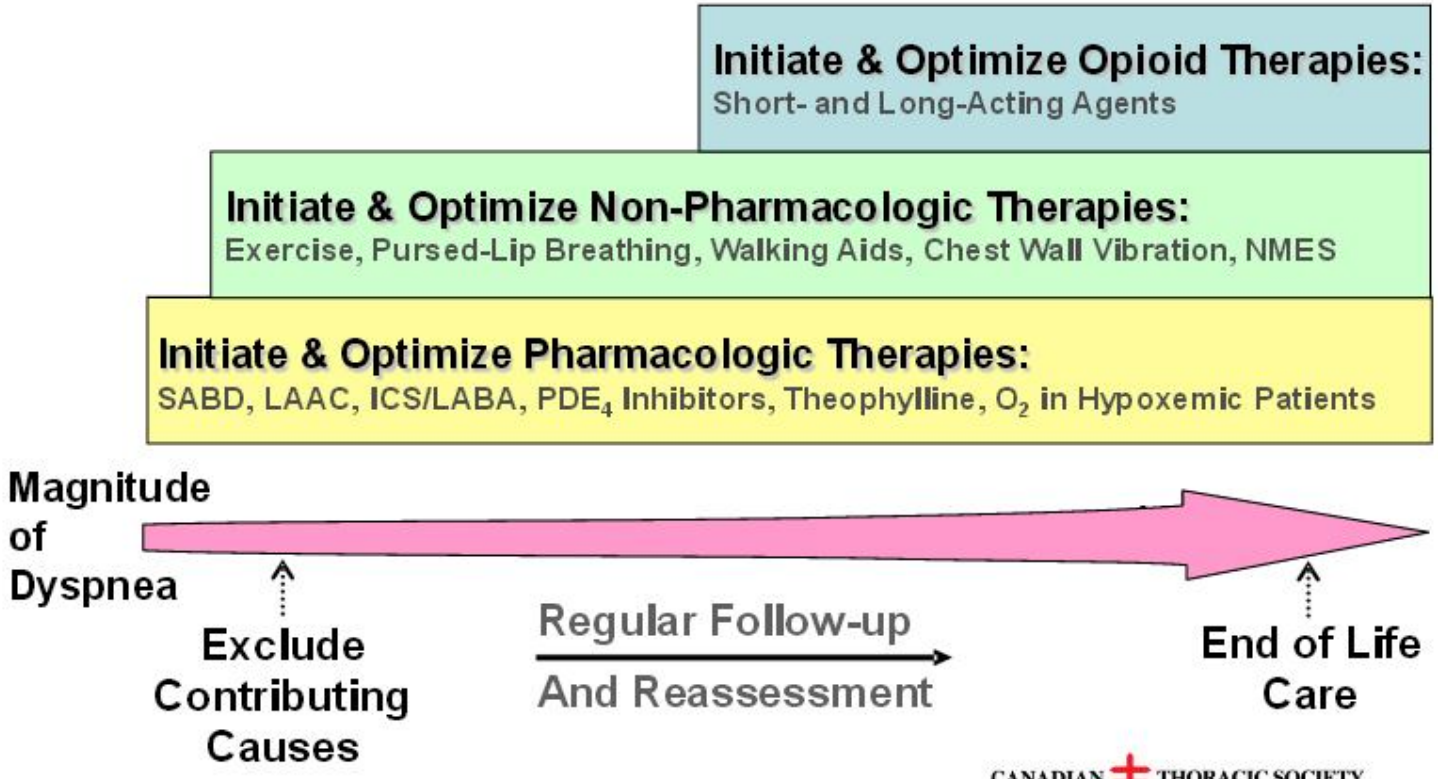
First line should always be to optimize or reverse underlying issues

Opioids are first line treatment for dyspnea refractory to condition-specific treatments → reduces the sensation of breathlessness

Canadian Respiratory Guidelines

COPD
Treatable. Preventable.

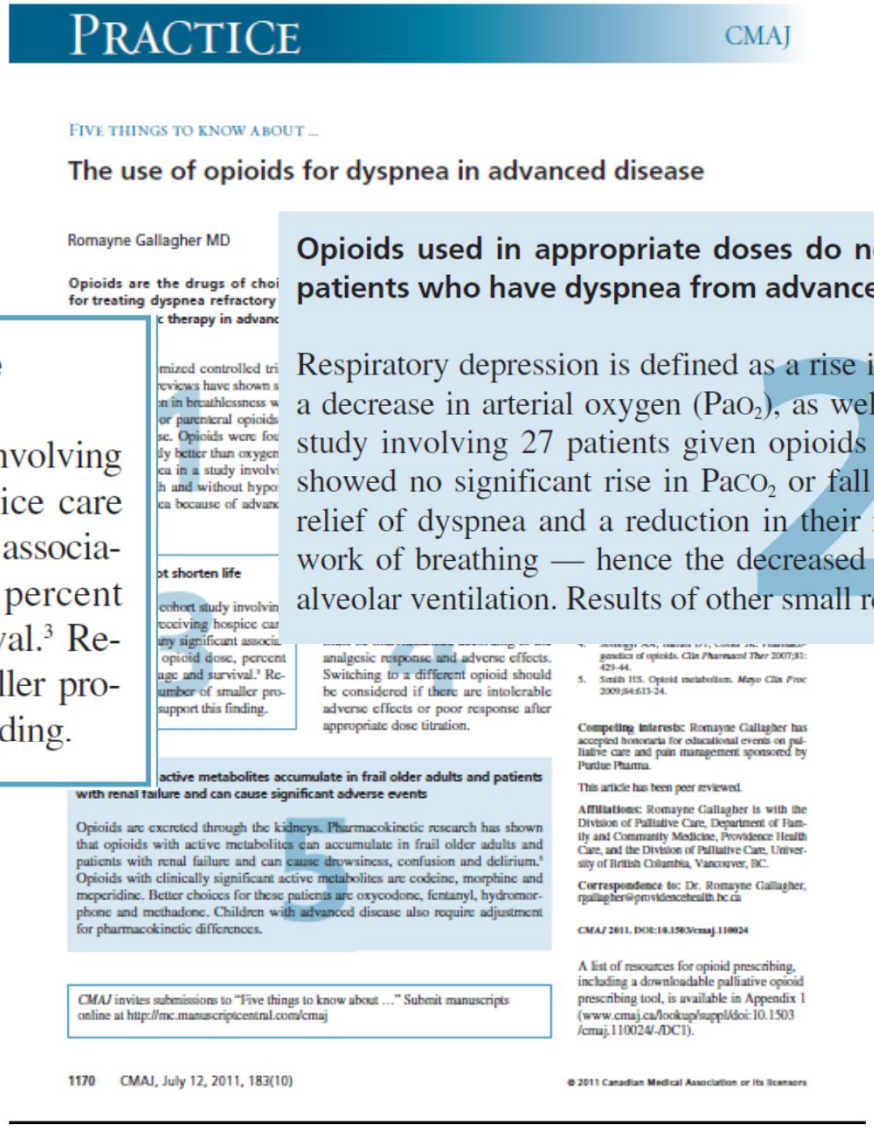
Comprehensive Approach to Management of Refractory Dyspnea in Advanced COPD



Marciniuk DD, et al. *Can Resp J* 2011; 18:69-78.

CANADIAN THORACIC SOCIETY
SOCIÉTÉ CANADIENNE DE THORACOLOGIE

DO OPIOIDS CAUSE RESPIRATORY DEPRESSION AND HASTEN DEATH?



PRACTICE CMAJ

FIVE THINGS TO KNOW ABOUT ...

The use of opioids for dyspnea in advanced disease

Romayne Gallagher MD

Opioids are the drugs of choi
for treating dyspnea refractory
c therapy in advanc

mized controlled tri
reviews have shown s
in breathlessness w
or parenteral opioids
se. Opioids were fou
ly better than oxygen
ca in a study involvi
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ohort study involvin
eceiving hospice car
ny significant associa
opioid dose, percent
age and survival.[3] Re-
umber of smaller pro-
support this finding.

analgesic response and adverse effects. Switching to a different opioid should be considered if there are intolerable adverse effects or poor response after appropriate dose titration.

active metabolites accumulate in frail older adults and patients with renal failure and can cause significant adverse events

Opioids are excreted through the kidneys. Pharmacokinetic research has shown that opioids with active metabolites can accumulate in frail older adults and patients with renal failure and can cause drowsiness, confusion and delirium.[4] Opioids with clinically significant active metabolites are codeine, morphine and meperidine. Better choices for these patients are oxycodone, fentanyl, hydromorphone and methadone. Children with advanced disease also require adjustment for pharmacokinetic differences.

CMAJ invites submissions to "Five things to know about ..." Submit manuscripts online at http://mc.manuscriptcentral.com/cmaj

1170 CMAJ, July 12, 2011, 183(10)

4. ... genetics of opioids. *Clin Pharmacol Ther* 2007;81:429-44.
5. Smith HS. Opioid metabolism. *Mayo Clin Proc* 2009;84:613-24.

Competing interests: Romayne Gallagher has accepted honoraria for educational events on palliative care and pain management sponsored by Purdue Pharma.

This article has been peer reviewed.

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CMAJ 2011. DOI:10.1503/cmaj.110024

A list of resources for opioid prescribing, including a downloadable palliative opioid prescribing tool, is available in Appendix 1 (www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.110024/-/DC1).

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Opioids used in appropriate doses do not cause respiratory depression in patients who have dyspnea from advanced disease

Respiratory depression is defined as a rise in arterial carbon dioxide ($PaCO_2$) and a decrease in arterial oxygen (PaO_2), as well as a decrease in respiratory rate. A study involving 27 patients given opioids for dyspnea from advanced disease showed no significant rise in $PaCO_2$ or fall in PaO_2. All patients had significant relief of dyspnea and a reduction in their respiratory rate.[2] Opioids reduce the work of breathing — hence the decreased respiratory rate — but do not affect alveolar ventilation. Results of other small retrospective studies support this.

Opioids do not shorten life

A prospective cohort study involving 725 patients receiving hospice care did not show any significant association between opioid dose, percent change in dosage and survival.[3] Results from a number of smaller prospective trials support this finding.

SOOO….WHEN DO I ASK FOR A PALLIATIVE CARE CONSULT?

Reason for Referral:

- ☐ Pain *(Choose one):*
  - ☐ *Malignant*
  - ☐ Post Herpetic Neuralgia
  - ☐ Non malignant, non Tx related Pain
  - ☐ Post Treatment Pain:
    - ☐ *Post Surgical*
    - ☐ *Post Chemotherapy*
    - ☐ *Post Radiation*
    - ☐ *Uncertain*
  - ☐ Decision Making
  - ☐ Discharge Planning
  - ☐ End of Life Care
- ☐ Symptom Management *(Choose one):*
  - ☐ *Anorexia (poor appetite)*
  - ☐ *Anxiety*
  - ☐ *Constipation*
  - ☐ *Delirium*
  - ☐ *Depression*
  - ☐ *Fatigue*
  - ☐ *Nausea/Vomiting*
  - ☐ *Secretions*
  - ☐ *Shortness of breath*
- ☐ Psychosocial/Family Support
- ☐ Other: _____

Referred From:

- ☐ Acute Pain Service
- ☐ B4ICU
- ☐ B5ICU
- ☐ Cardiac Surgery
- ☐ Cardiology
- ☐ CCU
- ☐ CRCU
- ☐ CVICU
- ☐ D4ICU
- ☐ Emerg
- ☐ ENT
- ☐ General Surgery
- ☐ Geriatric Medicine
- ☐ GI
- ☐ GIM
- ☐ Gyne Onc
- ☐ Haem Onc
- ☐ Holland Centre
- ☐ K1E
- ☐ Long Term Care
- ☐ Med Onc
- ☐ Nephrology
- ☐ Neurosurgery
- ☐ OP PCCT
- ☐ Orthopedics
- ☐ Psychiatry
- ☐ Rad Onc
- ☐ Rapid Response
- ☐ Respirology
- ☐ Rheumatology
- ☐ Surg Onc
- ☐ TLCPC
- ☐ Trauma
- ☐ Urology
- ☐ Vascular Surgery

TO ALL PALLIATIVE CARE PROVIDERS

(For the purpose of this Form, an individual refers to a patient or client)

Your submission of this form will be taken to explicitly mean that you have gained appropriate permission for release of the information contained to the agencies and services to whom you are submitting this. Please also include your Organization's Release of Information Form, if applicable.

Please complete this form as thoroughly as possible and PRINT clearly. Each referring agency, group or institution should decide which practitioner(s) is most appropriate to complete each section.

Individual's Last Name: _____ **First Name:** _____

Goals of Care/ Reason for Referral:

Type(s) of services requested	Urgency of response	Pages Required
☐ **Community Care Access Centre** (complete CCAC Medical Referral Form):	☐ 1-2 days ☐ 1 - 2 weeks	**Page 1-4**
☐ **Community Palliative Care Physician** (Specify Palliative Physician Team): Referral is for: ☐ Consultative care ☐ Primary care	☐ 1-2 days ☐ 1 - 2 weeks	**Page 1-3**
☐ **Hospice Program**: ☐ **Home Visiting** ☐ **Day Program** ☐ **Residential Hospice** (specify):	☐ 1-2 days ☐ 1 - 2 weeks ☐Future ☐ 1-2 days ☐ 1 - 2 weeks ☐Future	**Page 1-4**
☐ **Inpatient Palliative Care Unit** (List all units referred):	☐ 1-2 days ☐ 1 - 2 weeks ☐Future	**Page 1-4**
☐ **Other** (specify):	☐ 1-2 days ☐ 1 - 2 weeks ☐Future	**Page 1-4**

Please send directly to your desired hospice palliative care provider(s). Do not send to the Toronto Central Palliative Care Network.

[1] The Palliative Care Common Referral Form was originated from TPCLI (2004). This Form has been adapted from the Toronto Central Palliative Care Network Common Referral Form. Further uses of this Form are permitted, provided the original is unaltered.

COMMON ISSUES WITH PALLIATIVE CARE IN THE COMMUNITY

- Not all areas are covered by a home visiting palliative MD → don't guarantee anyone until you are sure
- All PCUs and hospices need a confirmed DNR status to activate the application (but not if it is only for backup)
- Different PCUs/hospices will accommodate slightly different interventions (e.g. some will and some will not provide HD, CPAP, bloodwork, IV) – again, don't assume

QUESTIONS?

Thanks!

Email: irene.ying@sunnybrook.ca