GOALS OF THERAPY:

- To prevent acute, delayed, and anticipatory nausea and vomiting
- To decrease incidence of nausea and vomiting (once it has occurred)
- To maintain quality of life
- To prevent complications related to nausea and vomiting

DEFINITIONS:

Acute	Occurs within 24 hours following chemo or radiation
Delayed	Starts after the first 24 hours following chemo or radiation
Anticipatory	A conditioned response to previous poorly controlled N&V
Breakthrough	Nausea and vomiting that occurs despite prophylaxis

MECHANISM OF NAUSEA AND VOMITING:

- Complex reflex coordinated by the vomiting centre in brain stem
- Stimulation of the vomiting centre from the chemoreceptor trigger zone (CTZ), vestibular system, GI tract
- CTZ not protected by blood-brain barrier

POTENTIAL CAUSES OF NAUSEA AND VOMITING:

CNS	Brain tumors, epilepsy
Drugs	Anesthetics, antibiotics, chemotherapy
GI	Obstruction
Infectious	Viral gastroenteritis
Metabolic	Hypercalcemia
Vestibular	Motion sickness
Radiation therapy	

DETERMINING THE LIKELIHOOD OF NAUSEA AND VOMITING:

Patient specific	• Female gender • Younger age (< 50 years) • No alcohol use • Anxiety • History of motion sickness/pregnancy

Chemotherapy related	• Emetogenic potential
	  ○ % of patients who will experience emesis if no prophylaxis given
	  ○ Treat for most emetogenic agent or use Hesketh algorithm
	• Dose and dosing regimen
	• Number of previous cycles

CONSIDER EMETOGENIC POTENTIAL:

- Newer chemotherapy agents may not have been evaluated for inclusion in the classification system
- Moderate emetogenic classification is quite broad and this could affect results of clinical trials evaluating antiemetics
- No two patients are exactly identical in incidence of CINV or response to treatment

NEUROTRANSMITTERS:

- Predominant receptors
  - Serotonin antagonists (5 HT3)
  - Neurokinin antagonists (NK1, substance P)
  - Dopamine antagonists
- Because multiple neurotransmitters are involved, multiple antiemetic medications may be useful

NON-PHARMACOLOGICAL STRATEGIES:

Dietary adjustments	• Small meals several times a day • Avoid foods high in fat or heavy aroma • Try dry starchy foods • Try ice chips and small sips of clear fluids • Avoid food preparation
Acupuncture/ Acupressure	• Evidence remains insufficient to make a recommendation for or against • Evidence conflicted for acupuncture, NO significant benefit for acupuncture wristbands
Ginger	• Evidence remains insufficient to make a recommendation for or against (conflicting evidence)

MONITORING PARAMATERS:

- Onset and duration of symptoms
- Timing of nausea, retching, vomiting
- Impact on the patient, e.g. weight loss
- Description of the vomiting episodes
- Other medications that the patient is taking
- Adherence to the treatment plan
- Assess hydration status (lab tests, e.g. electrolytes)
- Assess for hypercalcemia
- Physical exam for other symptoms such as orthostatic hypotension, abdominal symptoms
- Side effects of the anti-emetics

APPROACH TO TREATMENT & THERAPEUTIC TIPS:

- The goal is NO nausea or vomiting
- It is far easier to prevent CINV than to treat it
  - Regular doses > prn medications
  - Oral = IV (if vomiting, use PR)
- Anticipatory CINV is a conditioned response that only happens after a negative past experience
- Re-evaluate anti-emetic therapy for every cycle of chemotherapy
- Diphenhydramine is not a useful therapeutic agent for CINV, unless the pt has a vestibular component to their N&V (but avoid as a single agent)

PROPHYLACTIC REGIMENS:

	PRE	POST
Rare emetogenic	• Not usually required	• Prochlorperazine 10 mg po every 4-6 h PRN x 3-4 days • Metoclopramide 10-40 mg PO every 4-6 hours PRN x 3-4 days
Low emetogenic	• Dexamethasone 4-12 mg PO (preferred) • Prochlorperazine 10 mg PO • Metoclopramide 20-40 mg PO	• Dexamethasone 4 mg BID for up to 2-3 days • Prochlorperazine 10 mg PO every 4-6 hours PRN x 3-4 days • Metoclopramide 10-40 mg PO every 4-6 hours PRN x 3-4 days
	ACUTE	**DELAYED**

Moderate emetogenic	1. One 5-HT3 antagonist
	  • Ondansetron 8 mg PO/IV
	  • Granisetron 1 mg PO/IV
	2. Plus dexamethasone 8-20 mg PO
		1. Dexamethasone 4 mg PO evening of chemo, then 4 mg PO BID x 2-3 days
		2. One anti-emetic “as needed”
		  • Prochlorperazine 10 mg PO every 4-6 hrs PRN x 3-4 days
		  • Metoclopramide 10-40 mg PO every 4-6 hrs PRN x 3-4 days

High emetogenic	1. One 5-HT3 antagonist
	  • Ondansetron 8 mg PO/IV
	  • Granisetron 1 mg PO/IV
	  • Palonosetron 0.5 mg PO or 0.25 mg IV
	2. Plus dexamethasone 8-20 mg PO AND aprepitant 125 mg PO or Fosaprepitant 150 mg IV +/- olanzapine 10 mg PO
		1. Dexamethasone 4 mg PO evening of chemo, then 4 mg PO BID x 2-3 days AND aprepitant 80 mg PO daily x 2 days (if treating PO only) +/- olanzapine 10 mg PO days 2-4
		2. One anti-emetic “as needed”
		  • Prochlorperazine 10 mg PO every 4-6 hrs PRN x 3-4 days
		  • Metoclopramide 10-40 mg PO every 4-6 hrs PRN x 3-4 days

OPTIONS IN TREATMENT FAILURE:

- Increase dose of ondansetron (if applicable)
- Increase dose of dexamethasone or extend duration of treatment
- Olanzapine 2.5 – 5 mg PO BID
- Haloperidol 1 – 2 mg PO q4-6h or 1-3 mg IV q4-6 h
- Lorazepam 0.5 – 2 mg PO or SL q4-6 h if anticipatory N&V
- Nabilone: 0.5 mg PO BID and titrate to max 6 mg/day
- Prochlorperazine 25 mg PR q12h or 10 mg PO/IV q4-6h
- Metoclopramide 20-40 mg PO q4-6h or 1-2 mg/kg IV q3-4h +/- diphenhydramine 25 – 50 mg PO/IV q4-6 h
- Dimenhydrinate 100 mg PO q12h alternative with prochlorperazine 10 mg PO q12 h (for a q6h regimen)

PHARMACOLOGICAL TREATMENTS:

Serotonin antagonists	• Most common: **ondansetron,** granisetron, palonosetron • Pharmacare coverage not available for palonosetron • Most common side effects are headache, constipation, diarrhea ○ Severe side effects: prolonged QT (QTc) interval, cardiac dysrhythmias, torsades de pointes (5%)	
Corticosteroids	• Dexamethasone is most commonly used • Mechanism unknown • Effective in delayed nausea and v omitting • Common side effects: mood changes, increased appetite, GI irritation, fluid retention, weight gain	
Palonosetron/Netupitant	• Combination product: 300 mg netupitant and 0.5 mg palonosetron capsule once per cycle • In combination with dexamethasone for acute and delayed highly emetogenic CINV or moderately emetogenic CINV uncontrolled by a 5-HT3 receptor antagonist alone • NOT covered by BC Pharmacare	
Aprepitant/ Fosaprepitant	MOA	• Blockade of substance P NK_1 receptors in CNS
	PK	• Aprepitant: once daily oral dosing x 3 days • Fosaprepitant: one single IV dose • No dose adjustment in special populations
	Drug interaction potential	• CYP 3A4 inhibitor • Increases dexamethasone concentration • Ketoconazole increases aprepitant concentration • Decreased warfarin concentrations and INR
	Side effects	• Asthenia, fatigue • Constipation or diarrhea • Anorexia • Hiccups • Headache
Olanzapine	• Atypical antipsychotic with antiemetic properties • Targets dopamine, serotonin, adrenaline, histamine, muscarinic receptors • First line prophylaxis – recommended in a number of guidelines • NOT covered by BC Pharmacare for this indication • Side effects: somnolence, postural hypotension, constipation, dizziness, fatigue, dyspepsia, restlessness	
Cannabinoids	• Insufficient evidence to recommend medicinal cannabis for prevention of CINV • Insufficient evidence to recommend medicinal cannabis in place of nabilone • 2015 Cochrane meta-analysis concluded "cannabis-based medications *may be useful for treating refractory CINV*" ○ Methodologic limitations and further research is necessary	