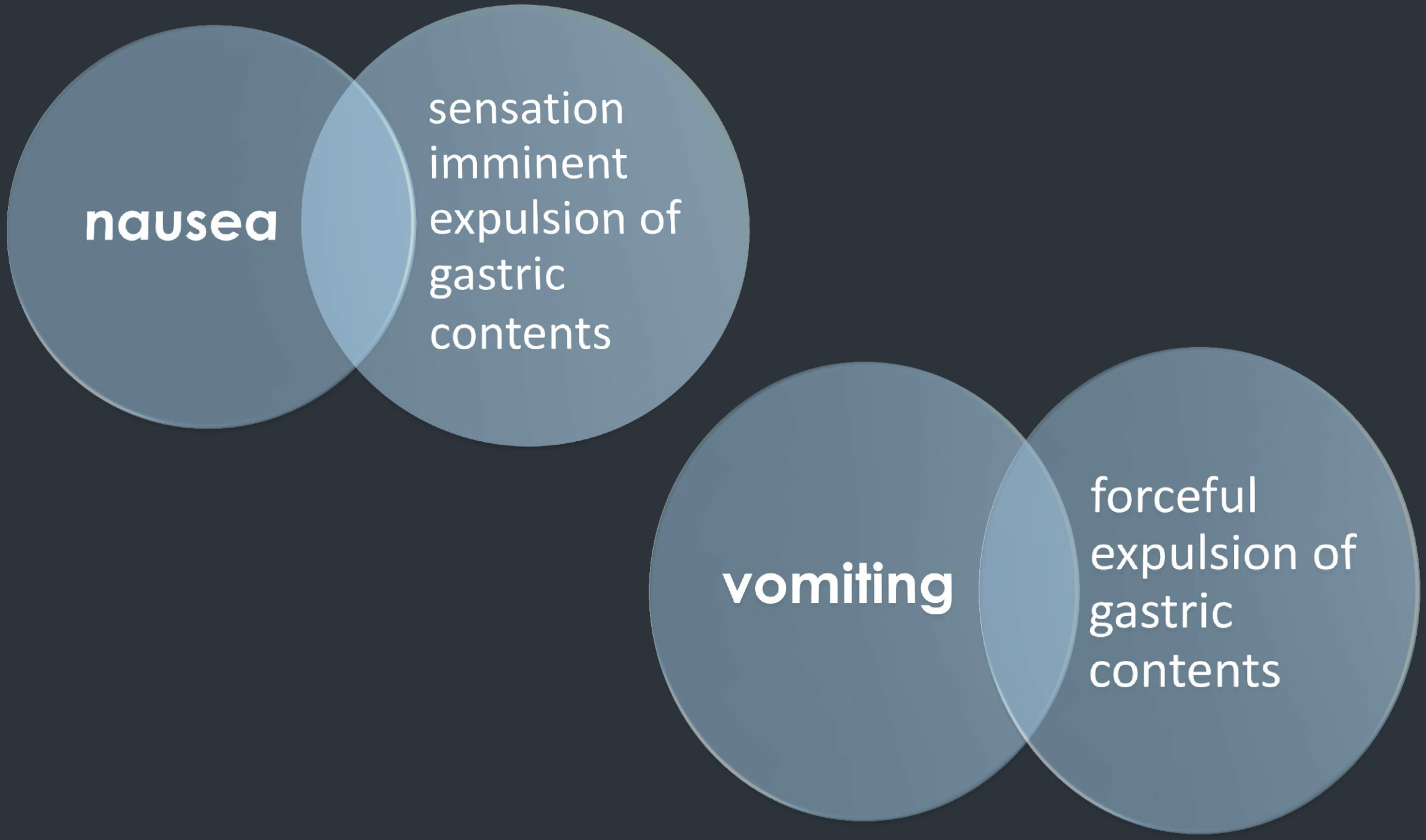
Nausea & Vomiting

Dr Eve Lyn TAN
Liverpool Hospital
NSW, AUSTRALIA


nausea
sensation imminent expulsion of gastric contents
vomiting
forceful expulsion of gastric contents

Prevalence…

Symptom Prevalence in Patients with Incurable Cancer: A Systematic Review

Saskia C.C.M. Teunissen, PhD, Wendy Wesker, MD, Cas Kruitwagen, MSc, Hanneke C.J.M. de Haes, PhD, Emile E. Voest, MD, PhD, Alexander de Graeff, PhD

- prevalence varies*, systemic review 2007 :
  - overall prevalence : nausea 30%, vomiting 20%
  - in last 1-2 weeks of life :
    - nausea 17%, vomiting 13%

July 2007 Volume 34, Issue 1, Pages 94–104

JPSM JOURNAL OF PAIN AND SYMPTOM MANAGEMENT
Advancing Palliative Care, Hospice, and Symptom Research

Case Study 1 – Mr PH

- 64 year old married man with worsening nausea & vomiting past 3 weeks
- background prostate cancer with bony-only metastasis

Mr PH's comorbidities & medications

- other co-morbidities : diabetes mellitus for past 12yrs, hypertension past 3yrs, gastro-esophageal reflux disease, osteoarthritis
- medications : paracetamol, sitagliptin, gliclazide, pantoprazole, amlodipine, vitamin D & fish oil, calcium supplementations, nil allergies

Other questions to ask Mr PH?

- number of vomits / day
- vomitus characteristics, appearance, amount, ?blood
- precipitants, relationship to foods, types of food, timing
- bowel function & if other associated symptoms – pain, dyspepsia, dysphagia, early satiety, ↓ oral intake, weight loss, fatigue, others
- what therapy for symptom has been tried? response?
- psychosocial impact?

Significant aspects of examination?

- haemodynamic stability & hydration status
- if any signs of anaemia, nutritional deficiency, organ failure, condition of mouth & disease
- chest & abdominal examination +/- PR examination

What is the value of history & physical examination?

ascertain type & likely cause(s)

ascertain severity & complications, impact on multiple domains & quality of life

assist with antiemetic choice, route, dose if drug approach required

assist to guide investigations, management

history & examination

potential complications

- dehydration & acute renal failure (pre-renal*)
- electrolyte disorders (↓K^+, ↑Na^+)
- acid-base imbalances (alkalosis)
- risk of oesophageal tears & haematemesis
- ↓ oral intake, weight loss, malnutrition, cachexia
- ↑ fatigue, lethargy
- ↓ **mood & psychological well-being**

other consequences

- if on palliative oral anti-cancer therapy
- can impact on other symptom control
  - eg. pain control, if on oral analgesia
- management of other medical conditions / comorbidities
  - eg. if on thyroxine for hypothyroidism, citalopram for depression, others

further reaching consequences

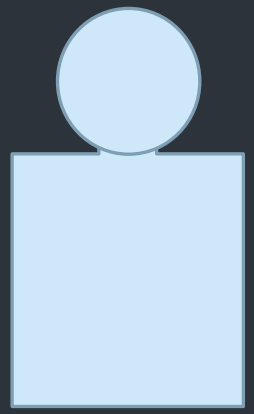
- psychosocial impact on family & friends
  - esp. given sociocultural as well as familial / personal meaning of fluids, food & meal sharing
    - often reflects love, affection & bonding*
  - potentially compounding distress, affecting relationships

potential impact on physical domain

potential impact on psychological domain

potential impact on family & friends

potential biochemical, organ, other complications



patient

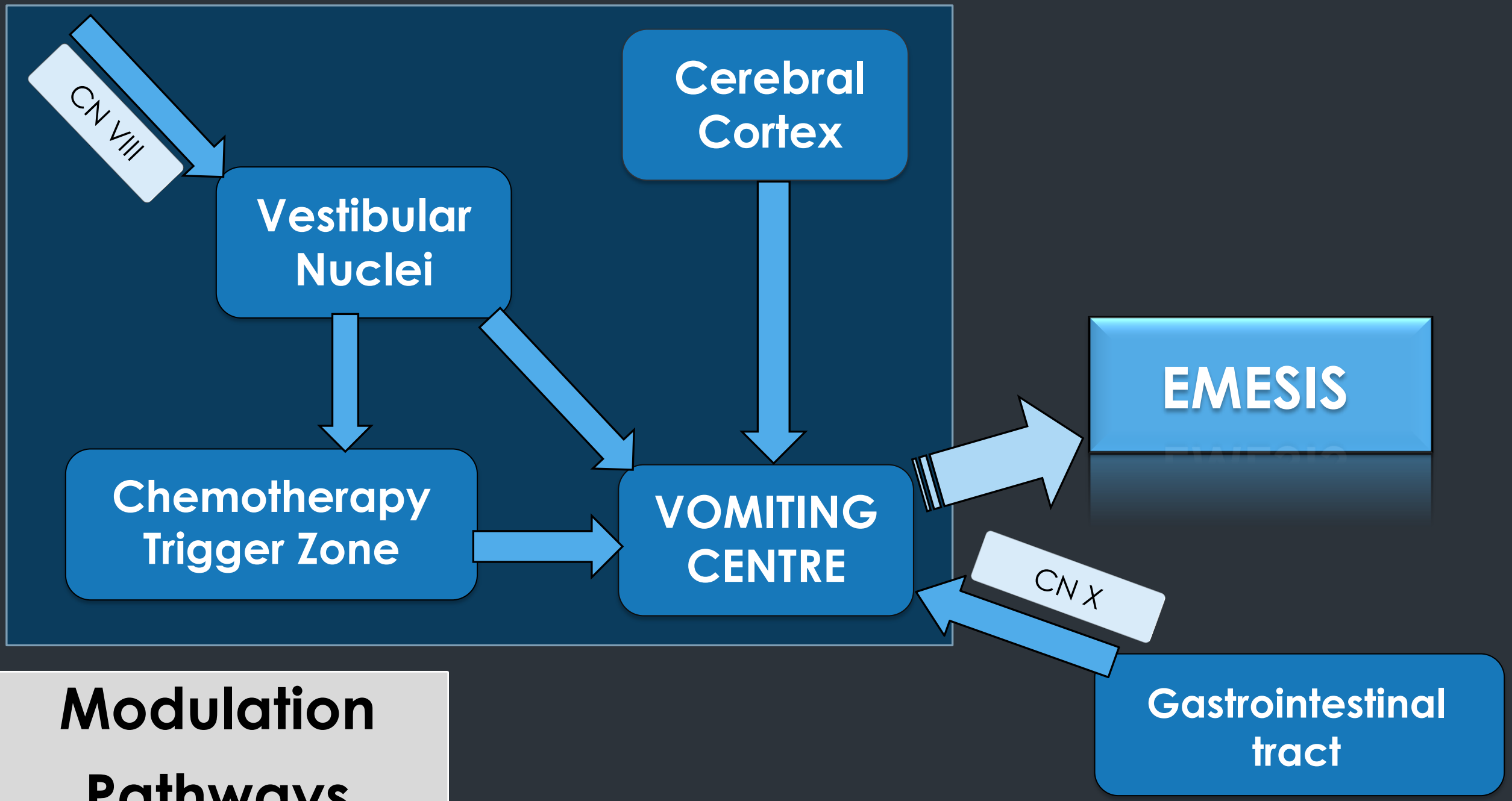
คนไข้

↓quality of life

potential impact on healthcare staff

Simplified pathophysiology

emetogenic pathway

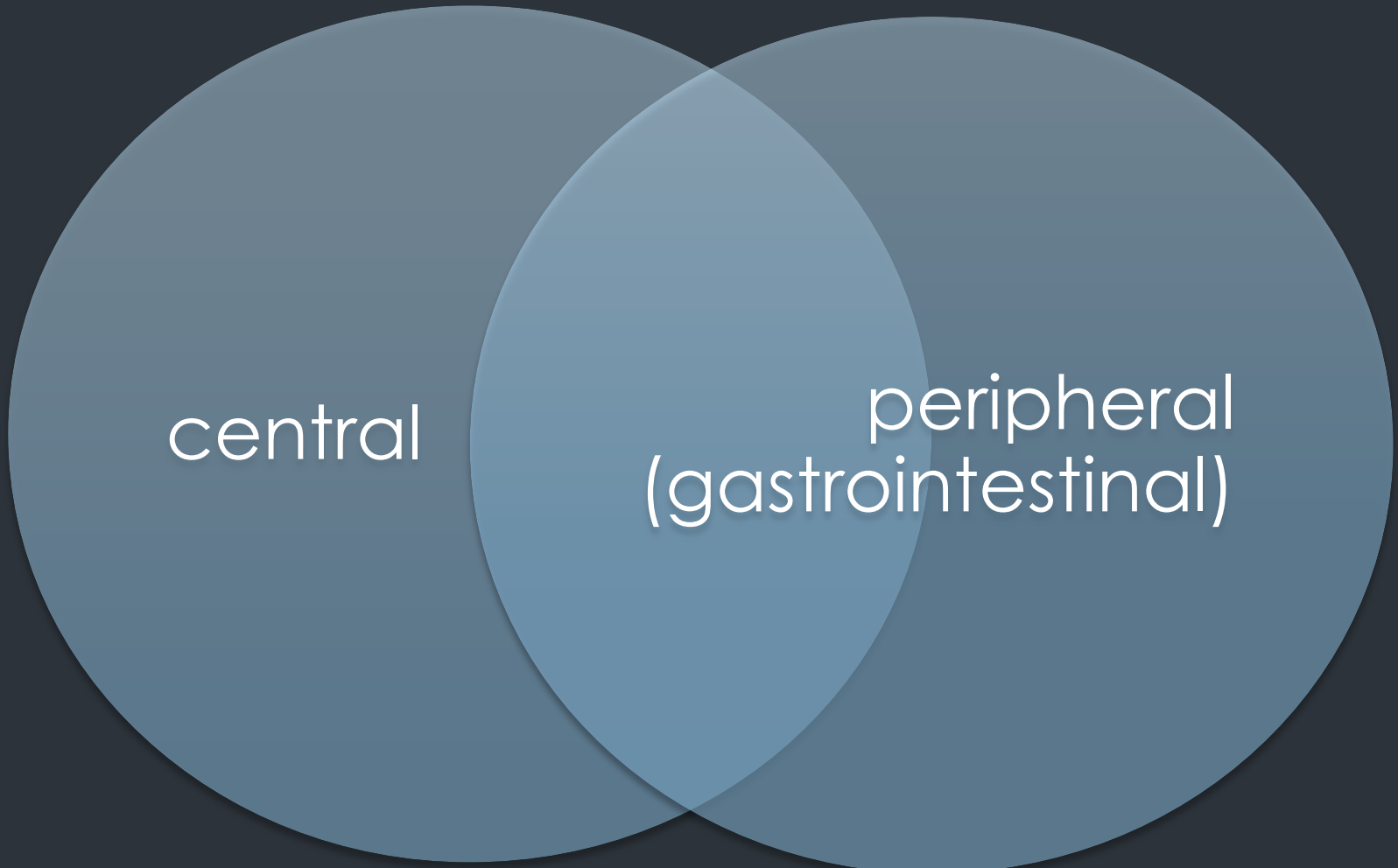


Modulation Pathways

Types of nausea & vomiting

peripheral or **central** or **both (mixed)**

Types of nausea & vomiting



Peripheral nausea & vomiting

elements on history to help distinguish :

- related to oral intake
- usually worse after eating, better after vomiting
- commonly associated with early satiety
- commonly intermittent
- always check bowels movements

Central nausea & vomiting

elements on history to help distinguish :

- not directly related to oral intake
- not worse after eating, not better after vomiting
- dry retching, commonly more constant
- precipitated by sight, smell, thought of food*
- possible associated symptoms eg. headaches, other neurological

Anticipatory nausea

- type of central nausea, occurs prior to or in response to conditioned stimuli (perceived to precipitate N&V)
- classic example : pre-chemotherapy
- related to anxiety
- use benzodiazepine :
  - eg. lorazepam oral or sublingual 0.5mg

TYPE of NAUSEA & VOMITING Characteristics	Peripheral	Central
precipitated by sight, smell or thoughts of food	NO	YES
worse after eating	YES	NO
better after vomiting	YES	NO

Why useful? potentially assist with cause(s)

- peripheral nausea & vomiting
  - typically gastrointestinal tract affected
- central nausea & vomiting
  - multiple stimuli / systemic insults which affect CNS
- **mixed peripheral & central nausea & vomiting**
  - likely combined aetiologies

Potential causes of peripheral N&V

- upper gastrointestinal :
  - gastroparesis, ‘gastric squash’
- lower gastrointestinal :
  - intestinal ileus
  - severe constipation
  - bowel obstruction (malignancy, adhesions)

Potential causes of central N&V

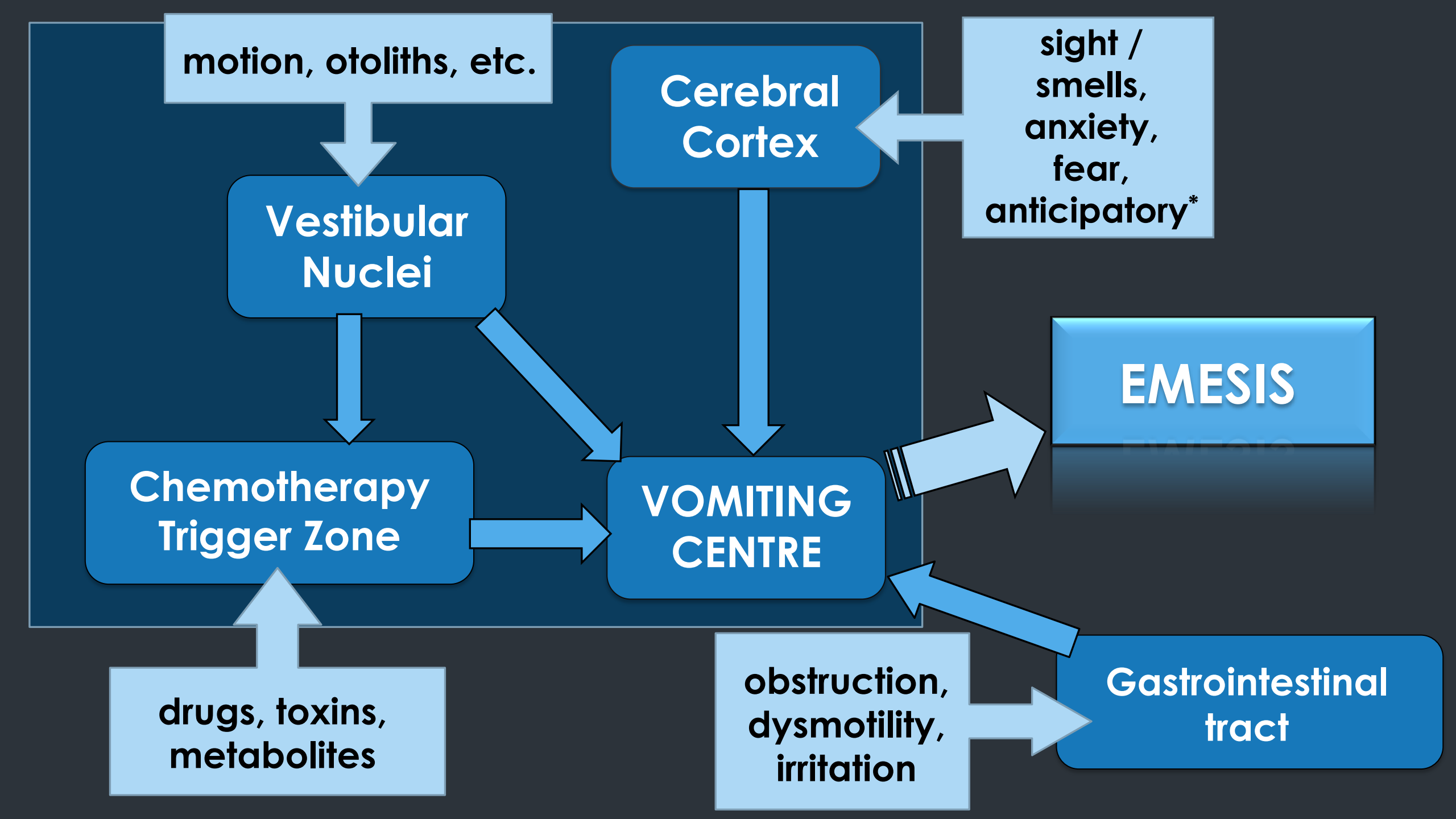
- systemic infection / organ failure / malignancy / autoimmune / immunological
  - underlying inflammation +/- tissue damage / necrosis, toxins, cytokines, etc.
  - eg. microbial infection, infarction, vasculitis, trauma, surgery, radiotherapy*
  - eg. organ failure (↓ clearance / accumulation toxins)

Potential causes of central N&V

- electrolyte / metabolic / endocrine disorders, medications +/- iilicit
  - eg. ↑ Ca^{2+}, chemotherapy, opioids, alcohol intoxication
- CNS / neurological pathology
  - eg. neoplasm (primary / secondary), stroke, CNS infection, hypertensive crisis, ↑ intracranial pressure
- **severe pain, anxiety**, others

Revisiting emetogenic pathway

site of action of various aetiologies / stimuli


motion, otoliths, etc.
Cerebral Cortex
sight / smells, anxiety, fear, anticipatory*
Vestibular Nuclei
EMESIS
Chemotherapy Trigger Zone
VOMITING CENTRE
drugs, toxins, metabolites
obstruction, dysmotility, irritation
Gastrointestinal tract

Mr PH - further history

- previous intermittent nausea now mostly constant throughout day
- dry-retches at times, least 4-5 vomits a day for past 3 days, medium yellowish vomits, no haematemesis
- worse after meals, better after vomiting, early satiety
- not bothered by smell or sight of food

Mr PH - further history

- unrelated to type of food, nil dysphagia / odynophagia / reflux
- upper abdominal spasm-like pain when dry-retching / vomiting otherwise nil pain issues
- bowels regular
- nil other symptom issues

Type of nausea & vomting in Mr PH?

- complete history taking, examination unremarkable apart from slight dry mucous membranes, recent routine bloods within normal limits

- **possible causes of Mr PH's nausea & vomiting?**
- **management of his nausea & vomiting?**

General Management

approach to nausea & vomiting

General management

- history & examination, ascertain impact
- appropriate investigations* & treat reversible aetiologies*
  - eg. constipation, antibiotics for infection
  - if receiving chemotherapy (or radiotherapy) and severe N&V, may require postphone / cease
    - liaise with medical (or radiation) oncologist

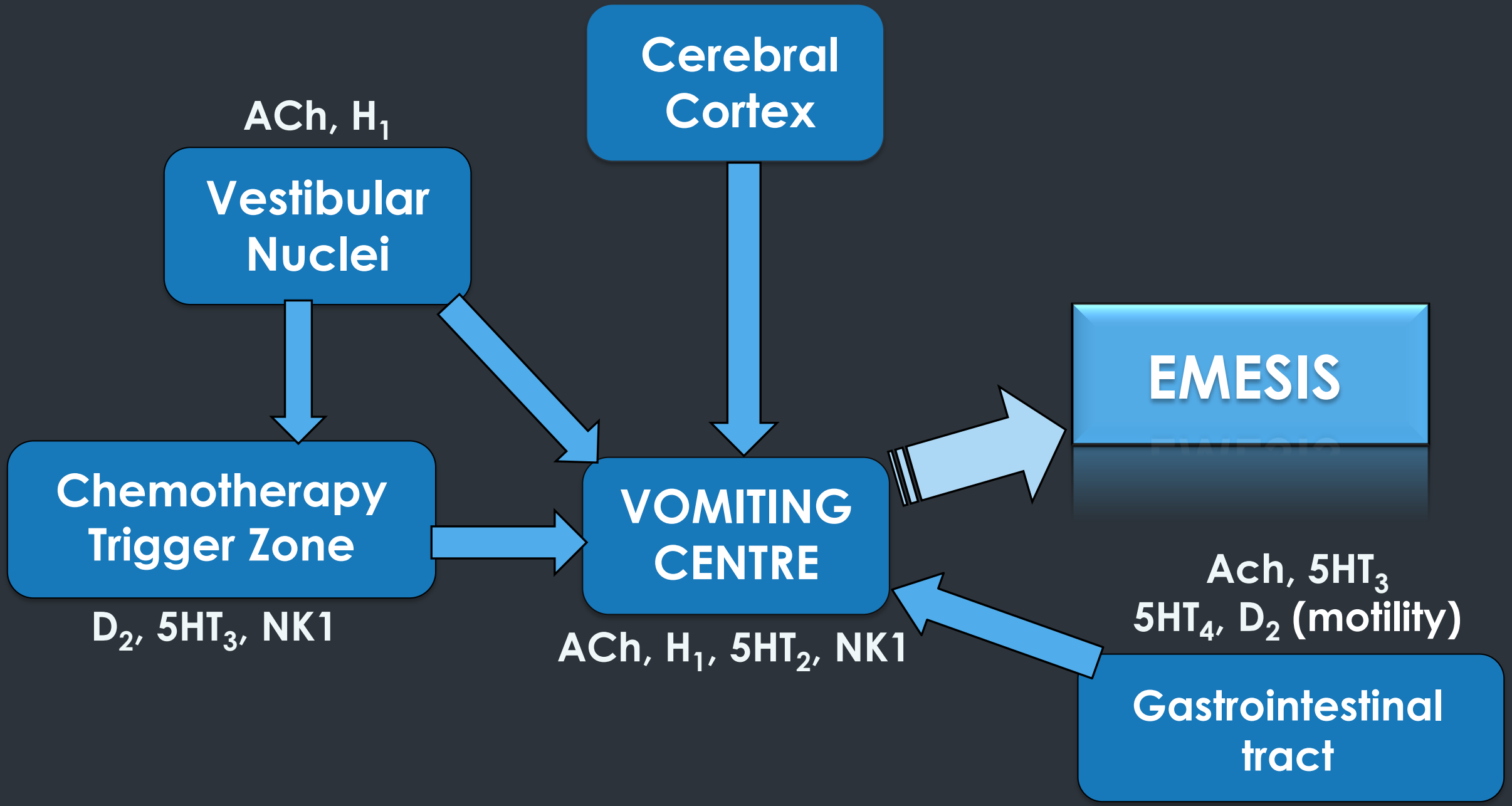
General management

- do not delay treating symptoms
  - select appropriate antiemetic(s), dose & route
- supportive measures*
  - fluid & electrolytes supplementation
  - psychosocial support

Pharmacology

Drugs with antiemetic properties

- dopamine antagonists
  - neuroleptics / antipsychotics
- antihistamines
- $5HT_3$-receptor antagonists
- substance P / NK1-receptor antagonists
- anticholinergics*
- steroids*
- benzodiazepines*


Cerebral Cortex
ACh, H_1
Vestibular Nuclei
EMESIS
Chemotherapy Trigger Zone
VOMITING CENTRE
D_2, $5HT_3$, NK1
ACh, H_1, $5HT_2$, NK1
Ach, $5HT_3$
$5HT_4$, D_2 (motility)
Gastrointestinal tract

Selected antiemetic agents

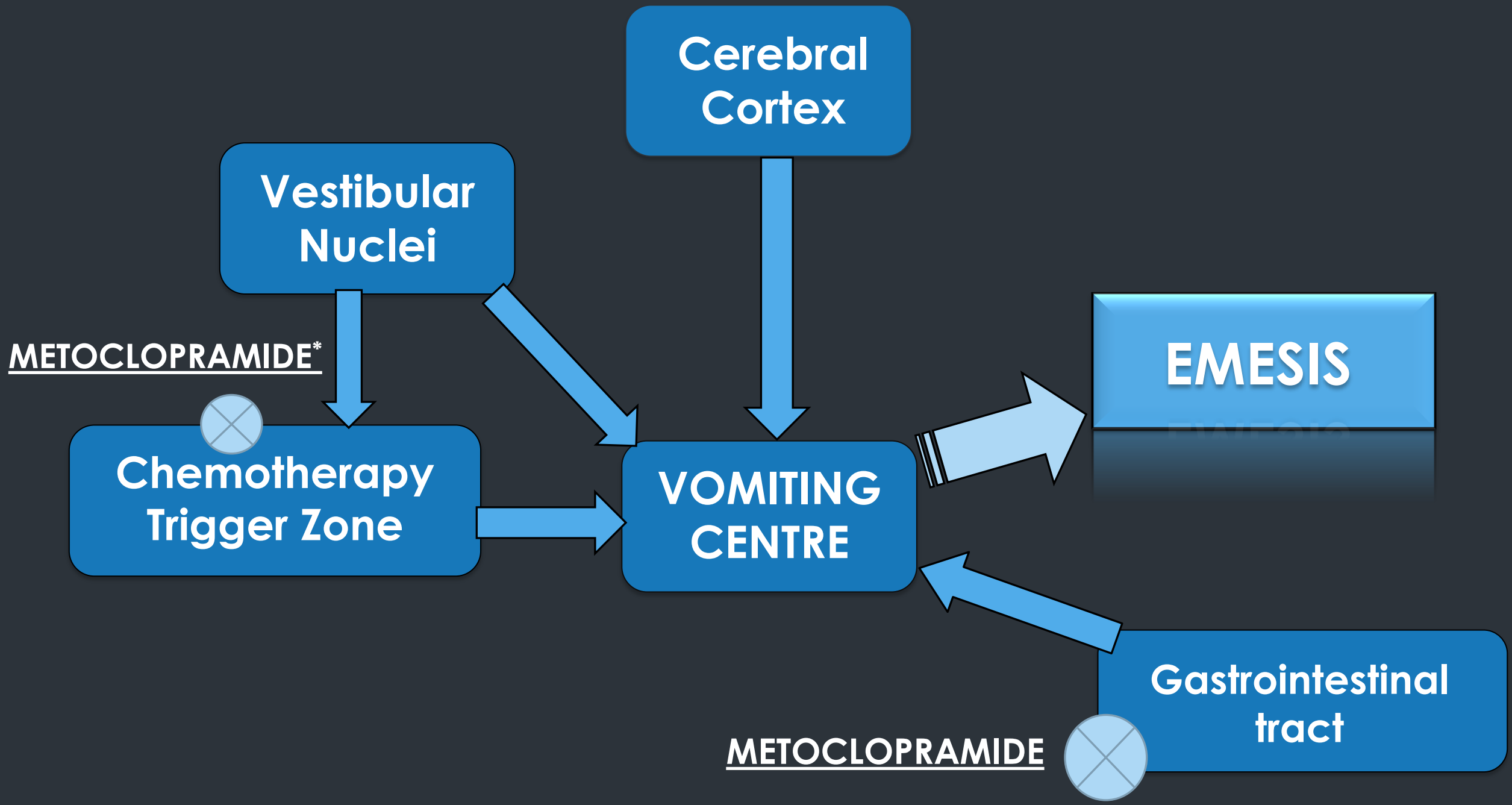
used in palliative care

metoclopramide (Maxolon™)

- commonly used anti-emetic agent
- dopamine antagonist, peripheral & central effects
- prokinetic promotes upper GI motility, caution in colicky abdominal pain, small bowel obstruction
- potential side-effects : extrapyramidal* SE (esp. ↑ risk in young female adults*), sedation in higher doses

metoclopramide

- start 10mg TDS-QID, oral / subcutaneous / IV / IM
- for earlier satiety, ½hr prior to main meals +/- bedtime
- may titrate to higher doses cautiously
  - (palliative care patients as high as 80-100mg/day in certain situations)


Cerebral Cortex
Vestibular Nuclei
METOCLOPRAMIDE*
Chemotherapy Trigger Zone
VOMITING CENTRE
EMESIS
Gastrointestinal tract
METOCLOPRAMIDE

haloperidol (Serenace™)

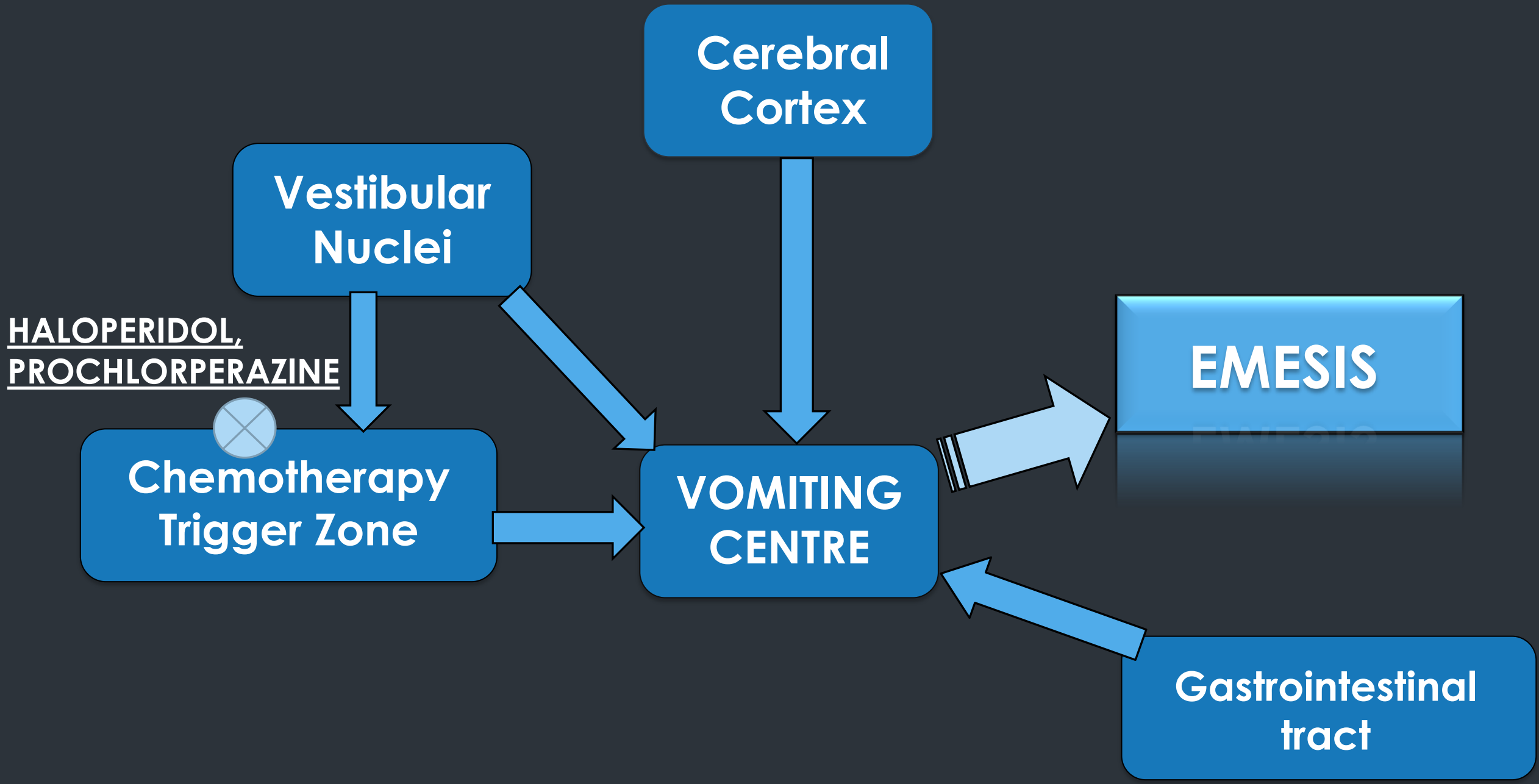
- centrally acting dopamine receptors antagonist
- avoid in Parkinson disease
- potential side effects :
  - not usually sedative unless high doses
  - extrapyramidal, neuroleptic malignant syndrome risk
  - possible increased risk of QTc interval prolongation*

haloperidol

- starting dose 0.5mg BD + PRN :
  - oral or subcutaneous
  - MAX dose commonly total 3-5mg per day* - usually limited by side effects or absence of further benefit
- usually no dose adjustment in renal / hepatic* failure
- caution in combined use with metoclopramide

prochlorperazine (Stemetil™)

- centrally acting dopamine receptors antagonist, potentially also helpful for vertigo
- avoid in Parkinson disease
- potential side effects :
  - CNS depression, EPSE eg. tardive dyskinesia
- starting dose : 5–10mg oral bd-tds OR 12.5mg IV/IM every 8 hours PRN

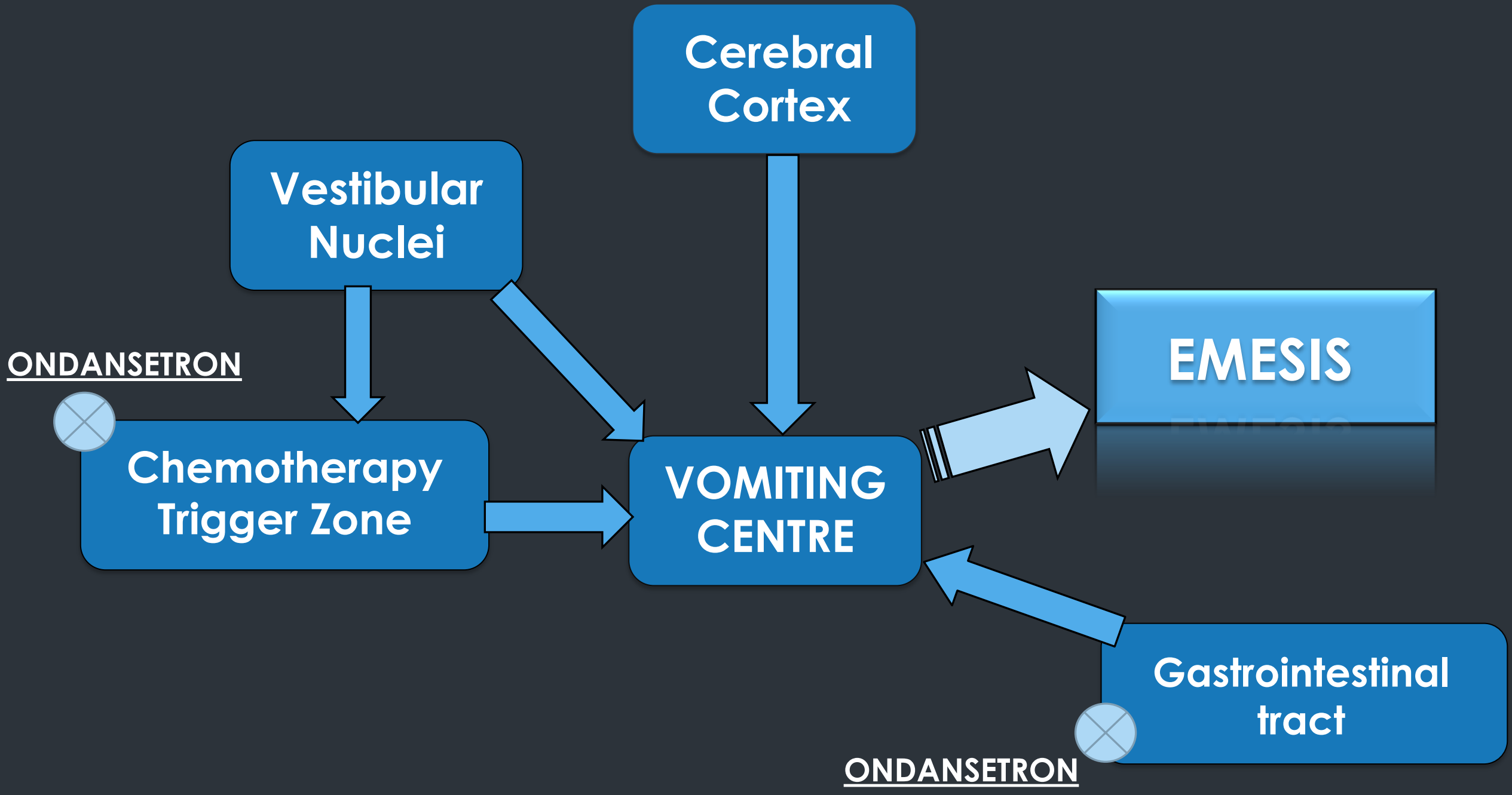

Cerebral Cortex
Vestibular Nuclei
HALOPERIDOL, PROCHLORPERAZINE
Chemotherapy Trigger Zone
VOMITING CENTRE
EMESIS
Gastrointestinal tract

other antiemetic

used in chemotherapy / radiation therapy

ondansetron

- chemotherapy / radiotherapy-induced nausea / vomiting, post-operative nausea / vomiting,
- rarely used in palliative care, relatively expensive
- serotonin $5HT_3$ receptor antagonist
- action centrally (CTZ) & peripherally (gut)
- potential side-effects :
  - constipation, esp. prolonged use, caution in ↑ QT_c


Cerebral Cortex
Vestibular Nuclei
ONDANSETRON
Chemotherapy Trigger Zone
VOMITING CENTRE
EMESIS
Gastrointestinal tract
ONDANSETRON

Evidence?

- poor quality evidence for various antiemetics in palliative care setting
- no published good quality evidence to date supporting practice of antiemetic selection based on aetiology / inferred mechanism over empirical
- currently controlled antiemetic trials for nausea unrelated to anti-cancer Tx – await results, conclusions

COMMON ANTIEMETICS	PREDOMINANT SITE OF ACTION	SPECIAL CONSIDERATIONS	SUBCUT ROUTE
METOCLOPRAMIDE	PERIPHERAL	PROKINETIC – EARLY SATIETY, HICCUPS	YES
HALOPERIDOL	CENTRAL	ANTIPSYCHOTIC, for AGITATION*	YES
PROCHLOPERAZINE	CENTRAL	POSSIBLE BENEFIT for VERTIGO	NO

Antiemetic therapy in Mr PH?

- peripheral (gastrointestinal) nausea & vomiting

- **likely diabetic gastroparesis**
- **management of his nausea & vomiting?**
- **reasonable 1st choice** : metoclopramide
  - peripherally acting antiemetic, prokinetic
  - 10mg tds IV / subcutaneous initially

summary - nausea & vomiting

- identify and ↓ or remove stimuli as well as factors for nausea & vomiting whenever appropriate
- choose reasonable antiemetic dosing, route
- institute supportive measures if required +/- review analgesia regimen & other po medications
- **MONITOR RESPONSE, ADVERSE EFFECTS**

FINAL WORDS – nausea & vomiting

identify and ↓ or remove stimuli as well as factors for nausea & vomiting whenever appropriate

- ascertain if peripheral and/or central types
- assist to elucidate likely cause(s) & thus direct :
- investigations and/or therapy
  - including treatment of reversible causes if appropriate for individual patient

FINAL WORDS – nausea & vomiting

choose reasonable antiemetic dosing, route

- **manage symptom using antiemetic therapy :**
  - suitable antiemetic selection, usually based on nausea & vomiting type, aetiology, response to previous antiemetics, availability
  - route - eg. parenteral if severe nausea, vomiting

FINAL WORDS – nausea & vomiting

institute supportive measures if required +/- review analgesia regimen & other po medications

- if already on regular oral opioids, consider if short-term replacement with parenteral opioid appropriate
- **institute supportive Mx* if appropriate**
  - eg. supplemental fluids, electrolyte replacement

FINAL WORDS – nausea & vomiting

MONITOR RESPONSE, ADVERSE EFFECTS

- **ongoing evaluation of response**
  - titrate antiemetic dosing, consider appropriate combination of agents, monitor for adverse effects

generally more antiemetic agents will become available with time, allowing for more options & flexibility

ขอบคุณ ค่ะ

THANK YOU

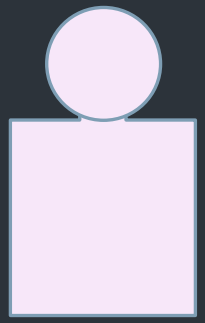
Another case study!

(in your own time, for further reading)

Case Study 2 – Ms RJ

- 41 year old accountant with gradually worsening nausea without vomiting, associated distress
- background of metastatic recurrent colorectal (caecal) cancer diagnosed 10 months ago, past right hemicolectomy 5yrs ago; known recurrent metastatic peritoneal, liver, lung, bony disease

Mrs RJ - further history



- recurrent malignant ascites only drained 2 days ago
- last chemotherapy 2 months ago, borderline suitability
- no significant comorbidities, for painful bony mets :
  - MS Contin 80mg bd, PRN morphine 25mg, laxatives
- nausea onset 3 months ago, nil improvement with cessation of chemotherapy or with ascites drainage

Mrs RJ - further history

- nausea constant, unrelated to meals, worse with smell of food, worse early morning prior to po intake
- recent am headache, nil other CNS symptoms
- bowels regular, nil other significant symptoms
- no subjective benefit with metoclopramide, prochlorperazine, promethazine

Mrs RJ - assessment & investigations

- examination : fairly unremarkable including neurological examination, urinalysis clear
- bloods tests :
  - essentially all normal including calcium level
- **reasonable antiemetic to trial?**

Antiemetic therapy in Mrs RJ?

- **reasonable antiemetic trial** - centrally acting antiemetic such as :
  - haloperidol 0.5mg nocte to bd

  or

  - cyclizine 12.5-25mg bd to tds
- as well as rescue antiemetic (PRN) available

Further investigations for Mrs RJ**?**

- other reasonable investigation :
  - CT brain (contrast) : normal
- Ms RJ then develops vague dizziness, headaches worse, nausea better with cyclizine, ↑ analgesia
- likely cause of central nausea & symptoms?

Mrs RJ – further investigations

- MRI brain organised :
  - confirms leptomeningeal disease
- dexamethasone 8mg mane & midday added (with omeprazole cover)
- referred to radiation oncology for consideration of whole brain radiotherapy

ขอบคุณ ค่ะ

THANK YOU