Nausea & Vomiting

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Introduction

Why Nausea and vomiting occur?

- Nausea and Vomiting are biological defence mechanisms.
- The major physiological function of emesis (vomiting) is to remove toxic or harmful substances from the body after ingestion.
- Nausea & Vomiting can also occur as a result of disease pathology [Cause, Mechanisms of development, morphologic changes, and the consequences of changes]

Vomiting is multifactorial in origin and can be caused by a range of stimuli, including:

- Ingesting poisonous substances & Infections - gastroenteritis
- Physiological - Pregnancy, Motion,
- Medical Interventions - Surgery, Chemotherapy & Radiotherapy
- Various drugs
- Central - Disgusting sights, smells or memories
The vomiting process

The process of emesis can be classified into 3 phases, nausea, retching and vomiting.

**Nausea** is described as an unpleasant sensation that immediately proceeds vomiting. A cold sweat, pallor, salivation, a noticeable disinterest in the surroundings, loss of gastric tone, duodenal contractions and the reflux of intestinal contents into the stomach often accompany nausea.

**Retching** follows nausea, and comprises laboured spasmodic respiratory movements against a closed glottis with contractions of the abdominal muscles, chest wall and diaphragm without any expulsion of gastric contents. Retching can occur without vomiting but normally it generates the pressure gradient that leads to vomiting.

**Vomiting** is caused by the powerful sustained contraction of the abdominal and chest wall musculature, which is accompanied by the descent of the diaphragm and the opening of the gastric-cardia. This is a reflex activity that is not under voluntary control. It results in the rapid and forceful evacuation of stomach contents up to and out of the mouth.
The vomiting reflex

Diaphragm

Stomach

Direction of muscular contractions  Flow of gastric contents
Complications are multidimensional!

- **Physical:**
  - Dehydration & renal failure
  - Electrolyte imbalance
  - Unable to take oral medication

- **Psychological:**
  - Anxiety
  - Reminder of illness

- **Social**
  - Isolating
  - Anti-social
  - Stress on carers

- **Spiritual**
  - Damaging to coping mechanisms
Multiple causes

1. Pain; pain medications & Pain medication S/E →
   Severe pain can induce N/V, Opioid, Constipation

2. Oro-pharyngeal Narrowing/ Plaques → Candida infection, sputum

3. GI narrowing due to internal compression →
   Internal Bleeding, Ulcers, Tumour growth,
   due to external Compression →
   Enlarged liver, pancreas, LN

4. Gastric Stasis → Motility disorders

5. Biochemical Causes → Renal Failure, Liver Failure, Hypercalcaemia

6. Central causes → ↑ ICP

7. Cancer Treatment Related → Acute / Delayed and Anticipatory N & V

8. Gastritis → NSAIDs / Steroid induced

9. Psychological / Emotional → Pain/Fear/Anger/Anxiety & Depression
N / V Can be multi-factorial: Example – ‘Cancer patient’

Cancer patient with ‘pain’ → Induces N/V;
Using Opioid → Induces N/V;
Opioid S/E → Constipation → Leads to N / V
Chemo / DXT → Induces acute nausea /delayed nausea

Anxiety of further chemo → Leads to ‘Anticipatory N /V’

Two Approaches → Mechanistic or Empirical

Mechanistic Approach
- Accurate identification of the cause
- Understanding of pharmacological mechanism
- Use of most effective drug
The emetic process—pathways of emesis and the neurotransmitters involved

Baines, M. J BMJ 1997;315:1148-1150
Vomiting Reflex

- Chemoreceptor Trigger Zone (area Prostema-4th ventricle)
- Vomiting Centre (Medulla)
- Stomach Small intestine
- Labyrinths

Factors which can cause nausea & vomiting:
- Surgery

Sensory input (pain, smell, sight)

Memory, fear, anticipation

- Higher cortical centres
- Chemotherapy
- Anaesthetics
- Opioids
- Chemotherapy
- Surgery
- Radiotherapy

Neuronal pathways
<table>
<thead>
<tr>
<th>Anti-emetic Medications &amp; Their functions</th>
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<tbody>
<tr>
<td><strong>Metoclopramide</strong></td>
</tr>
<tr>
<td>D&lt;sub&gt;2&lt;/sub&gt; Antagonist, 5HT&lt;sub&gt;3&lt;/sub&gt; at high doses + (5HT&lt;sub&gt;4&lt;/sub&gt; - gut)</td>
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<td><strong>Haloperidol</strong></td>
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<td>D&lt;sub&gt;2&lt;/sub&gt; Antagonist</td>
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<td><strong>Cyclizine</strong></td>
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<td>H&lt;sub&gt;1&lt;/sub&gt; Antagonist, Anticholinergic antagonist</td>
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<td><strong>Levomepromazine</strong></td>
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<td>D&lt;sub&gt;2&lt;/sub&gt; + H&lt;sub&gt;1&lt;/sub&gt; + 5HT&lt;sub&gt;2&lt;/sub&gt; Antagonist + Acetylcholine</td>
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<tr>
<td><strong>Ondansetron</strong></td>
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<tr>
<td>5HT&lt;sub&gt;3&lt;/sub&gt; Antagonist</td>
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<td><strong>Others used to for N / V</strong></td>
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<td>PPI / Lorazepam / Steroids</td>
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Metoclopramide and Domperidone

Both are

- Prokinetic Drugs
- Same doses / frequencies (10-20mg tid or qid)
- Same Receptor Activity

What is the difference?

- Metoclopramide is more potent than Domperidone in prokinetic activity
- Metoclopramide can cross the BBB & cause extra-pyramidal S/Es But Domperidone will NOT the BBB ➔ Therefore, safe with Parkinson disease or Patients with Neurological issues!
- Domperidone available as tablets/ suspension / Suppository
- Metoclopramide also available as injections
New Drugs - NK1 receptor antagonists ("aprepitant")

- Substance P (Neurokinin, NK) is widely distributed in the CNS
- There are NK receptor sub-types
- NK1 receptors are present in area postrema (CTZ), nucleus of the solitary tract (VC), and in GI tract
- NK1 receptors are also present in areas of brain responsible for regulation of affect and neurochemical responses to stress
NK1 receptor antagonists

**Animal studies:**
- Central depletion of Substance P blocks emetic action of central and peripheral triggers to emesis in ferrets.
- An identical effect is obtained with a specific NK₁ receptor antagonist.
- The anti-emetic effect of NK₁ receptor antagonists is lost if the drug cannot cross the blood-brain barrier.

**Human studies:**
- Chemotherapy produces a measurable rise in circulating substance P.
- NK₁ receptor antagonists stop Cisplatin related emesis
What Are the Key Questions to Ask When Assessing Nausea & Vomiting?

- **Causes**
  - Precipitating factors
  - Nausea only / vomiting only / both
  - Description of vomit
  - Associated symptoms of the likely causes especially Fullness / Satiety; Constipation; Abdominal pain; Headache

- **Severity of vomiting**
  - Frequency
  - Amount

- **Severity of nausea**
  - Continuous / intermittent
  - Effect on day to day activities
  - Visual analogue, verbal rating or numerical rating scale
Approach to Managing Nausea and Vomiting

- Is it Physiological or Pathological?
- Remove the cause
- Non-drug treatments
- Choose appropriate route
- Drug treatments: *Empirical vs. Mechanistic*
- The theory and the evidence
<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Causes</th>
<th>Clinical features</th>
<th>Helpful measures</th>
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<tbody>
<tr>
<td>Floppy stomach</td>
<td>Gastric motility failure caused by drugs or autonomic failure</td>
<td>Small volume, effortless vomit)</td>
<td>As for gastric stasis (Metoclopramide / Domperidone)</td>
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<td>May need nasogastric suction</td>
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<td>Ease compression e.g. paracentesis</td>
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<td>Gastric irritation</td>
<td>Gastritis or peptic ulceration</td>
<td>Epigastric pain, nausea, vomiting.</td>
<td>Avoid gastric irritant drugs.</td>
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<td>Treat with PPIs, H2 blockers</td>
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<td>Metoclopramide may help.</td>
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<td>Gastric outlet obstruction</td>
<td>Tumour, stricture</td>
<td>Projectile vomiting, rapid dehydration</td>
<td>Refer for surgical opinion</td>
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<td></td>
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<td></td>
<td>Dexamethasone can help to relieve blockage by tumour</td>
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<tr>
<td>Gastric stasis</td>
<td>Gastric motility failure caused by drugs or autonomic failure</td>
<td>Large volume vomiting, reflux, fullness, hiccups, brief nausea relieved by vomiting</td>
<td>Metoclopramide 10-20mg 6-hourly (start SC, then PO)</td>
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<td>Domperidone 10-20mg 6-hourly PO</td>
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<td>or 30-60mg 6-hourly PR</td>
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<tr>
<td>Intestinal obstruction</td>
<td>Tumour or adhesions</td>
<td>Nausea, vomiting, colic, distension.</td>
<td>Refer for surgical opinion</td>
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<td>Cyclizine 25-50mg 8 hourly (start SC → PO)</td>
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<td>Consider: radiotherapy or surgery</td>
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<td>Raised intracranial</td>
<td>Cerebral tumour, or hydrocephalus</td>
<td>Morning vomiting, little nausea, headache</td>
<td>Cyclizine 25-50mg 8 hourly (start SC → PO)</td>
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<tr>
<td>pressure</td>
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<td>Start Dexamethasone 8mg daily PO or SC</td>
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<tr>
<td>Squashed stomach</td>
<td>Gastric compression by ascites or tumour</td>
<td>Small volume vomit</td>
<td>As for gastric stasis (Metoclopramide / Domperidone)</td>
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<tr>
<td>Chemotherapy or DXT</td>
<td>Serotonin release in Gl tract)</td>
<td>Nausea, vomiting</td>
<td>Granisetron or Ondansetron according to local protocols. + Dexamethasone 4 to 8mg/day +/- NK 1 Blocker</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Toxins, high calcium, drugs, uraemia</td>
<td>Nausea, vomiting</td>
<td>Haloperidol 1 to 1.5 mg SC at bedtime.</td>
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<tr>
<td>Movement Related</td>
<td>Gastric distension, Motion Sickness, Otitis media, zoster, CP angle tumour</td>
<td>As for gastric stasis</td>
<td>As for gastric stasis (Metoclopramide / Domperidone)</td>
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<td></td>
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<td>Nausea on movement of head. Vertigo with nausea</td>
<td>Can try Hyoscine Hydrobromide (Kwells) or Cyclizine 25-50mg 8-hourly (start SC, then PO)</td>
</tr>
<tr>
<td>Psychological</td>
<td>Fear, anxiety</td>
<td>Nausea or vomiting in Specific situations</td>
<td>Reassurance, discussion</td>
</tr>
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<td>Vagal / viscera stimulation</td>
<td>Mucosal irritation or distension of viscera</td>
<td>Nausea, vomiting</td>
<td>Oxazepam 7.5 mg PO or Lorazepam 0.5mg PO</td>
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<tr>
<td>Persistent nausea and</td>
<td>Multiple causes or cause uncertain</td>
<td>Non-specific pattern of nausea and vomiting</td>
<td>Levomepromazine 2.5-5mg SC at bedtime.</td>
</tr>
<tr>
<td>vomiting</td>
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<td>Consider Dexamethasone 4mg in the morning</td>
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<td>Contact palliative care physician</td>
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Thank you