The management of Nausea and Vomiting

Incidence and patient perception

- Incidence in advanced cancer estimated between 40 and 70%
- Experienced by 59% of hospice patients
- Nausea ranked as the most feared side effect of chemotherapy by patients receiving treatment
- Vomiting ranked as third most feared side effect

Nausea

- Subjective experience
  - Hard to describe, wave like sensation at the back of the throat
- Sensation that immediately precede vomiting
  - Often represents a desire to vomit
- More prolonged and more difficult to control than vomiting
- Associated with a degree of anorexia or loss of appetite
- Patients are often pale, sweaty, cold, tachycardic, increased salivation
- For many patients nausea is more unpleasant than vomiting

Retching

- Attempt to vomit without expelling any material
- Commonly precedes vomiting
- Particularly uncomfortable and distressing in the absence of vomiting

Vomiting

- Involuntary defence mechanism used to expel toxic or harmful substances
- Rapid and forceful expulsion of stomach contents up and out of the mouth
  - Caused by powerful sustained contraction of the abdominal and chest wall muscles
- Vomiting is usually followed by lethargy and muscle weakness.
  - The patient may feel cold, shivery or experience muscular pains

The role of nausea and vomiting in health

- What is the role of nausea and vomiting in maintaining health?
- Are there any positive outcomes from nausea and vomiting?
- When do the negative consequences outweigh the positive?

Consequences of recurrent nausea and vomiting

- Reduced quality of life
- Reduced functional status
- Precipitate physiological complications
  - Fluid and electrolyte balance, malnutrition
- Increased hospitalisation
- Embarrassment and potential social isolation
- Jeopardize delivery of treatment
- Effect compliance with potentially beneficial treatment

Outcomes of effective management

- Positive effect on QOL
- Provide patients with a sense of control over their body and life
- Decrease anxiety and fear
- Decrease caregiver burden
- Decrease fatigue, anorexia and insomnia
- Increase physical, social and cognitive functioning
- Facilitate daily living activities

Management of nausea and vomiting

- Identify the cause of nausea and/or vomiting
- Identify the emetic pathway through which the cause triggers vomiting
- Select an antiemetic that is an agonist to the receptor identified
- Titrate and give regular, appropriately timed, antiemetics
- Monitor effect – consider adjuvant medications
- Treat reversible causes
- Support with non-pharmacological measures

Management decision making

- Consider whether treatment of the cause is appropriate, or whether the emphasis should be on treatment of symptoms.
- Take the following factors into account:
  - The stage of illness and the person's prognosis.
  - The person's wishes and those of carers and family.
  - The cause of the person's nausea or vomiting and whether it is reversible or untreatable.
  - The severity of nausea or vomiting and the presence of complications.
  - The urgency with which treatment is required.
  - The input of the multidisciplinary team.

Step one

- Identify the cause of nausea and/ or vomiting

Gastrointestinal (mechanical)

- Primary tumour – oesophagus, stomach, colorectal
- Constipation
- Changes in gut motility
- Bowel obstruction
- Ascites
- Hepatomegaly
- Treatment adhesions
- Reflux oesophagitis
- Peptic ulcer

Cerebral

- Fear/anxiety
- Changes in taste/smell
- Brain primary/ metastases
- Anticipatory – associated with chemotherapy
- Raised intracranial pressure

Biochemical/Metabolic

- Renal failure
- Electrolyte imbalance
- Liver failure
- Hypercalcaemia
- Tumour toxins

Treatment related

- Chemotherapy
- Radiotherapy
- Medication
  - Cerebral effect (e.g. opioids)
  - Gastrointestinal effect (NSAID’s, antibiotics)

Other causes of nausea and vomiting

- Polypharmacy
- Pain
- Oral candida
- Tenacious sputum (retching, not easily expectorated)

Assess the cause

- What might you include in an assessment of a patient experiencing nausea and vomiting ?

Assessment of cause – patient history

- Take a detailed history
  - how much, how often, when does it happen etc
  - characteristics – colour, volume
- Review drug treatments
- Abdominal examination (ascites, hepatomegaly, distension, bowel sounds)
- Investigate possibility of brain metastases if symptoms suggest
- Evaluate biochemical status (U&E's, Ca^{+} etc)
- Review drug treatments
- Recent pattern of bowel actions
  - Never forget constipation!

Step two

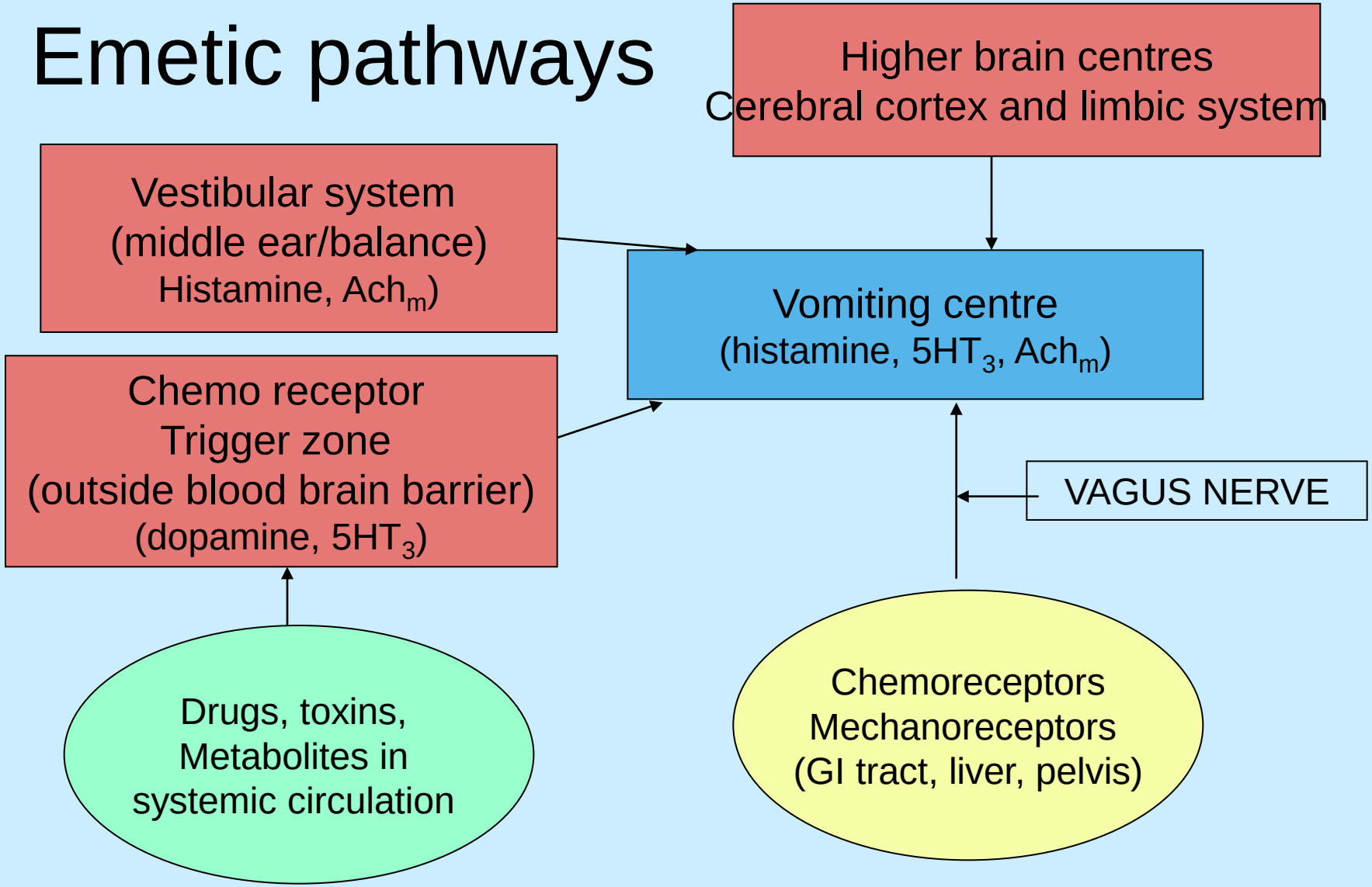
Identify the emetic pathway through which the cause triggers vomiting

Emetic pathways

- The vomiting centre co-ordinates the complex process of vomiting

- Stimulus for the vomiting centre to act carried by
  - The vagus nerve
  - Chemoreceptor Trigger Zone
  - Vestibular system (inner ear – balance and motion)
  - Higher brain centres – memories, sights and smells

Emetic pathways



Emetic pathways

- **Vagus nerve messages** are sent from

- Chemoreceptors in GI tract
  - Stimulated by toxic agents

- Mechanoreceptors in GI tract, abdomen and pelvis
  - respond to
    - Overdistension of the stomach and duodenum
    - Disordered patterns of gastric motility

Emetic pathways

- **Chemoreceptor trigger zone**
  - Situated on the fourth ventricle,

- Lies outside the blood/brain barrier and is bathed in the systemic circulation
  - Detects noxious substances in the systemic circulation and cerebrospinal fluid

Neurotransmitters and Receptors

- Send messages along the emetic pathways
- Each neurotransmitter acts on a specific receptor
  - Dopamine
    - CTZ, GI tract
  - Serotonin type 3 (5-HT_3)
    - CTZ, VC, GI tract
  - Histamines
    - VC, vestibular afferents
  - Muscarinic cholinergic
    - VC, vestibular afferents

Step three

Select an antiemetic that is an agonist to the receptor identified

Gastric stasis/delayed gastric emptying

- Causes
  - Ascites, hepatomegaly, tumour infiltration
- Clinical features
  - Epigastric fullness/ discomfort, early satiety, large volume infrequent vomits, nausea relieved by vomiting, vomitus contains undigested food, colicky pain
- Pathway
  - Gastric mechanoreceptors, vagus nerve to VC
- Antiemetics
  - Metoclopramide and Domperidone (Prokinetics)
    - Work at dopamine receptors on CTZ and GI tract
    - Increase peristalsis in upper GI tract

Chemically induced

- Causes
  - Drugs, metabolic abnormalities, toxins
- Clinical features
  - Nausea more prominent than vomiting and may be constant, vomiting may not relieve nausea
- Pathway
  - Stimulates dopamine and 5HT3 receptors in CTZ
- Antiemetics
  - Haloperidol (a butyrophenone) works at dopamine receptors at CTZ
  - Levomepromazine (a phenothiazine) works on dopamine and serotonin receptors at CTZ, histamine receptors at vomiting centre

Stretch/irritation of visceral/GI mucosa

- Causes
  - Liver metastases, constipation, bowel obstruction, tumour, ureteric obstruction
- Clinical features
  - Pain is often a feature, colic, altered bowel habit, nausea
- Pathway
  - Mechanoreceptors, vagus nerve, vomiting centre
- Antiemetics
  - Cyclizine, antihistamine working at Vomiting Centre
  - Levomepromazine (a phenothiazine) works on dopamine and serotonin receptors at CTZ, histamine receptors at vomiting centre

Raised intracranial pressure

- Causes
  - Cerebral tumour, infiltration of meninges, skull metastases
- Clinical features
  - Neurological signs (e.g. papiloedema, drowsiness), dizziness, headache
- Pathway
  - Direct stimulation of cerebral histamine receptor
  - Meningeal mechanoreceptors to vomiting centre
- Antiemetic
  - Cyclizine (antihistamine) works at Vomiting Centre
  - Levomepromazine (a phenothiazine) with dopamine and 5HT3 properties at VC and CTZ
  - Dexamethasone – anti-inflammatory properties

Cortical

- Causes
  - Anxiety, anticipatory nausea, pain
- Clinical features
  - Intermittent nausea and vomiting, associated anxiety
- Pathway
  - Central pathway stimulaiton fo the vomting centre

Chemotherapy related

- Ematogenic potential of specific drugs need to be identified
  - Is related to dose, route and frequency
  - Age of patient (worse in young),
  - Gender (worse in women),
  - History of motion sickness (worse if yes),
  - Poor emetic response to previous chemotherapy
  - History of alcohol intake (less in those with history of chronic drinking)

Chemotherapy related

- High to moderate ematogenic potential
  - Serotonin ($5HT_3$) receptor antagonists
    - Graniestron, ondansetron

- Serotonin is released in response to “insults” including chemotherapy and abdominal radiotherapy
- Graniestron and other $5HT_3$ antagonists block the transmission of the message to vomit through the vagus nerve pathway

Substance P antagonist!

- Substance P
  - a protein involved in transmitting nerve messages to the vomiting centre
  - Acts on neurokinin-1 receptors that are found in the vomiting centre in the brain
- Chemotherapy (and other causes) result in substance P activating the neurokinin-1 receptors, resulting in feelings of sickness.
- Aprepitant blocks the neurokinin-1 receptors in the brain and stops substance P from acting on them
- Aprepitant is used to **prevent** acute and delayed sickness that can be caused by chemotherapy
- In chemotherapy related N&V it is given alongside graniestron and dexamethasone as part of a three day regimen around each cycle of chemotherapy
- Emend capsules should be swallowed whole.
  - Lots of side effects, contra-indications and interactions

Antiemetics and chemotherapy

Emetic risk	**Acute Rx**	**Delayed Rx**
High (<90%)	5HT3 (graniestron) + Dexamethasone	Dexamethasone + 5HT3 or domperidone or metoclopramide
Moderate (30-90%)	5HT3 (graniestron) + Dexamethasone	Dexamethasone + 5HT3 or domperidone or metoclopramide
Low (> 30)	Domperidone	Domperidone prn

Antiemetics and chemotherapy

- Most side effects occur when the patient is at home
  - Essential to provide clear information on antiemetic use and self care measures
- Patient expectations need to be explored prior to chemotherapy
  - May have negative expectations from media, family and friends etc
  - Anticipatory nausea and vomiting can develop particularly if patient has a negative experience

However, life isn't that simple!!!

- There is much overlap between the neurotransmitters
  - different antiemetic agents can be effective for treating multiple causes of nausea.
- Some anti-emetics are broad spectrum working at multiple receptor sites
  - the selection of anti-emetics is not as evidence based as this talk has suggested!
- The causes of nausea and vomiting are often multifactorial or are unknown in the patient with cancer, particularly in terminal illness
- More than one antiemetic may be needed for symptom control

Antiemetic selection

- Caution is needed to avoid drugs that are incompatible or that block the action of another drug being used
  - e.g. metoclopramide and graniestron can cause cardiac arrhythmias
  - e.g. cyclizine and metoclopramide block
- When more than one antiemetic is given use a combination of drugs with different actions
  - e.g. cyclizine and haloperidol

Step four

Titrate and give regular,

appropriately timed, antiemetics using an appropriate route

Administration

- Give antiemetics at appropriate times
  - Identify pattern of occurrence
  - If patient able to eat time before meals
- Consider syringe driver
  - For vomiting of more than 24 hours duration
  - Moderate to severe nausea unresponsive to oral antiemetics for more than 48 hours
  - Reduces need for multiple injections
  - Ensures continuous level of drug absorbed

Step five

Monitor effect – consider adjuvant medications

Assessment

- Essential to identify degree of problem and effectiveness of treatment
- Nurses and patients assessments of patient problems rarely match (Florin 2005)

- Components of assessment should include
  - Frequency, duration, severity, associated distress
  - Alleviating factors, medication used
  - Impact on well being and QOL

Assessment

- Assessment tools may be useful
- Nausea a subjective experience
  - Only the patient is aware of severity
  - Patient self assessment most appropriate method

- Nausea and vomiting a multidimensional phenomena that requires a multidimensional tool
- Timing of assessments important
  - Should be ongoing and capture the range of experience (patterns, effect of interventions)
  - Unreliability of retrospective recall

Issues around assessment tools

- No tools have been extensively evaluated in palliative care settings
  - Further work is required to validate and develop approaches suitable for this group of patients
- Range of tools exist
  - E.g. VAS, numeric rating scales, verbal categorical scales e.g. likert (strongly agree to strongly disagree)
- Each approach has positive and negative elements
  - e.g. some patients find VAS difficult to use, the interpretation of words varies between patients (e.g. severe, moderate)
- Any tool may be problematic for patients who are unwell
  - Or experiencing side effects of anti-emetics

Monitor for side effects

- Metoclopramide
  - Extrapyramidal effects
    - Facial and skeletal muscle spasms and oculogyric crises
- 5HT3 receptor antagonists (e.g. graniestron)
  - Headache, constipation, fatigue, dry mouth, dizziness
- Levomepromazine
  - Sedation, Extrapyramidal effects

Monitor for side effects

- Haloperidol
  - Extrapyramidal effects, sedation, dry mouth, constipation, difficulty with micturition, arrhythmias
- Cyclizine
  - Drowsiness, blurred vision, dry mouth, constipation, difficulty with micturition, arrhythmias

Consider adjuvant medications

- Corticosteroids (dexamethasone)
  - Used widely in chemotherapy induced n&v
  - Reduces peri-tumour oedema and can relieve compression and pain
  - Useful in raised intracranial pressure
- Benzodiazepines
  - Reduce anxiety, particularly useful in anticipatory nausea and vomiting
- Octreotide
  - Reduces gastric secretion in intestinal obstruction

Step six
Treat underlying cause

- Primary tumour
- Constipation
- Bowel obstruction
- Ascites
- Peptic ulcer
- Fear/anxiety
- Brain primary/ metastases
- Anticipatory – associated with chemotherapy
- Hypercalcaemia
- Electrolyte imbalance
- Medication
  - Review medication
  - Check levels where appropriate (e.g. digoxin, phenytoin, carbemazepine)
- Polypharmacy
- Pain
- Oral candida

Step seven

Support with non-pharmacological measures

Behavioural strategies

- Progressive muscle relaxation and guided imagery
  - Decrease anxiety and feelings of distress
  - Work as distraction, focusing on neutral or relaxing images
  - Promote feelings of control and reduce feelings of helplessness
  - Easily learned, no side effects, cheap, mobile
- Cognitive behavioural therapy
  - Helping to improve patients perspectives of the symptom and their ability to control it, teaching problem solving skills
- Hypnosis
  - Emerging evidence but needs better evaluation e.g.
    - (Sherwood et al 2005, Richardson 2006, Wilkinson 2008)

Acupressure and acupuncture

- Based on theory that energy travels along pathways called meridians
- These can become blocked by imbalances in the body
- Applying pressure at certain points can release imbalance by stimulating or easing the energy flow

Acupressure

- Two points associated with nausea and vomiting
  - Nei-guan point (P6) – pericardium meridian
    - anterior surface of forearm
  - Three miles (ST36) – stomach meridian
    - Below knee lateral to the tibia
- A recent study found that patients who used a programme of acupressure at P6 following chemotherapy had significantly less nausea than patients in placebo and usual care groups

Supportive care – Nutrition

- Food has important physical and psychological significance
- Interventions must be appropriate to patient situation and wishes
- Absence of nutrition can provoke family conflict (Souter 2005)

Hydration

- Should be considered if the prognosis is likely to be measured in weeks and frequency of vomiting inhibits oral hydration

- In terminal care artificial hydration should be considered if it helps to promote patient comfort
  - (e.g. thirst, confusion caused by dehydration)
- Potential effects need to be carefully considered for each patient
- Need for consultation and effective communication with family

Supportive care

- Oral hygiene
  - Frequent exposure of oral mucosa and teeth to acidic stomach contents can decrease oral hygiene and comfort
  - Regular mouthcare essential

- Bucket, tissues and water
  - “a decent sized bowl is essential to avoid the distress of soiling clothes and bed linen” Regnard & Hockley

Social isolation

- Vomiting is a distressing and unsociable act
- For many patients the embarrassment and indignity that results from unresolved nausea and vomiting may be as distressing as the physical problems experienced (Campbell and Hately 2000)
- Essential to consider issues of privacy and dignity
- Recognising the physical and psychological distress associated with nausea and vomiting is fundamental to nursing care

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