

Anti-emetic Drugs

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Vomiting

- ▶ **Useful vomiting** occurs as a **protective mechanism** for eliminating irritant and harmful substances from the upper GIT
- ▶ **Pregnancy, motion sickness, cancer therapy**, etc.....
- ▶ The act of emesis is controlled by **vomiting center in medulla**, which receive stimuli from various sources:
 - Chemoreceptor trigger zone (CTZ)
 - vestibular system (motion sickness)
 - periphery (irritation of pharynx & gut, MI, biliary or renal stones)

Classification of antiemetic drugs

- ▶ **Dopamine D2 receptor antagonists:**
Metoclopramide, domperidone, haloperidol, phenothiazines (chlorpromazine, prochlorperazine)
- ▶ **5HT3-receptor antagonist:** ondansetron
- ▶ **Antimuscarinics:** hyoscine
- ▶ **H1-receptor antagonists:** meclizine, cyclizine, dimenhydrat
- ▶ **Others:** corticosteroids, cannabinoids, benzodiazepines

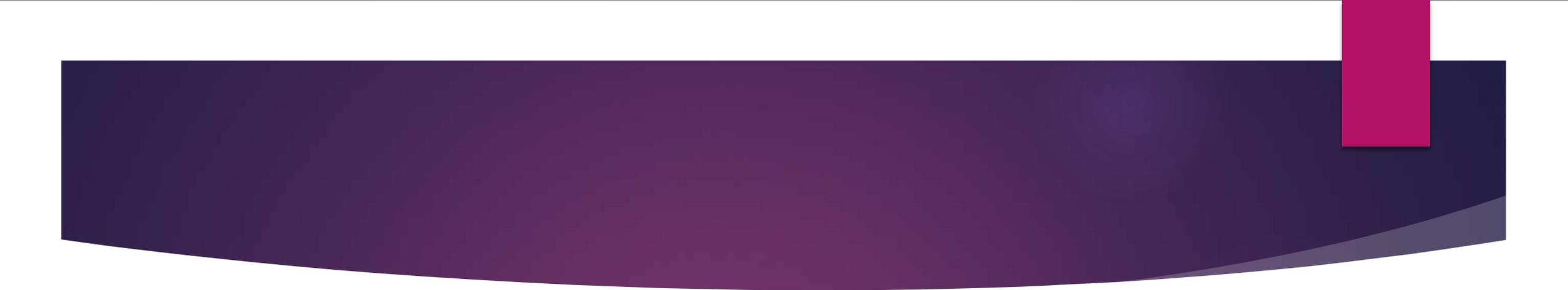
Metoclopramide

- ▶ Clopram, plasil
- ▶ Acts **centrally** by **blocking dopamine D2 receptors in CTZ**, and
- ▶ **peripherally** by **enhancing action of acetylcholine at muscarinic nerve ending in the gut**, it raises tone of lower esophageal sphincter, relax pyloric antrum, increases peristalsis and emptying of stomach
- ▶ Therefore, it is used to **empty stomach** before **emergency anaesthesia and labour**
- ▶ **Half-life 4 hrs**

Therapeutic Uses

- ▶ N & V associated with GI disorders, cytotoxic drugs, radiotherapy
- ▶ In migraine
- ▶ **Used as pro-kinetic agent** (enhances gastric emptying and intestinal motility)



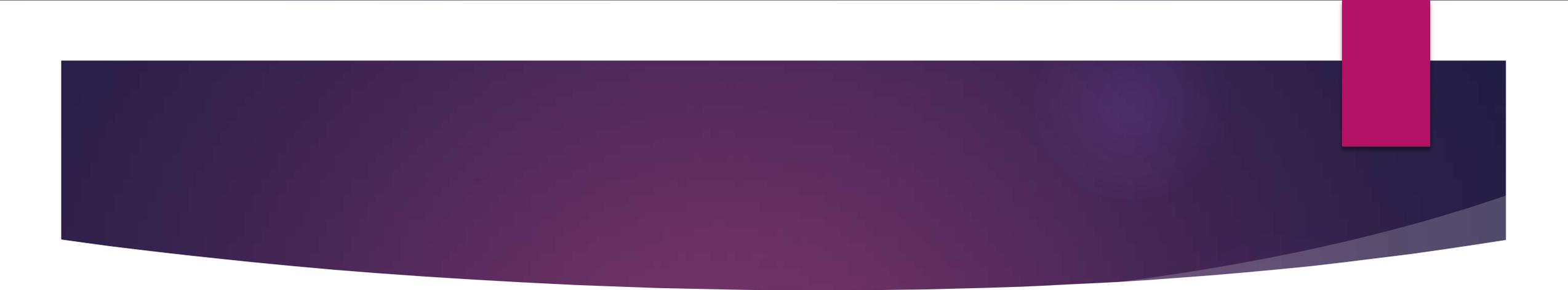
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- ▶ **Side effects:**
 - ▶ **Extrapyramidal dystonia** due to dopamine receptor antagonists (facial spasm), mainly in children and young adults
 - ▶ **Stimulate prolactin release** causes **gynecomastia and lactation**
 - ▶ Diarrhea
 - ▶ **Long-term use;** tardive dyskinesia mainly in elderly

Domperidone

- ▶ **Motilat, motilium**
- ▶ Is selective **dopamine D2-receptor antagonist**
- ▶ Unlike metoclopramide, it does not pose acetylcholine-like effect
- ▶ Less risk of adverse effects because it does not readily penetrate BBB
- ▶ Useful in patients in treatment of with N & V, bloating in patients with dyspepsia
- ▶ May cause **gynecomastia and galactorrhea**

Ondansetron

- ▶ **Zofran**
- ▶ Is a selective **5HT₃- receptor antagonist**
- ▶ Highly effective against **N & V induced by cytotoxic agents and radiotherapy**
- ▶ **Anticancer treatment release serotonin (5HT)** from enterochromaffin cells in the gut mucosa (where resides more than 80% of serotonin in the body), thereby **activating specific receptors in gut and CNS to cause to emesis**

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- ▶ Is given **before cancer chemotherapy by iv injection, followed by oral up to 5 days**
 - ▶ Half-life 5 hrs
 - ▶ **Side effects:** constipation, headache

Motion sickness

- ▶ Is more **easily prevented than cured**
- ▶ It is due to **over-stimulation of the vestibular system**
- ▶ It is common on a rough sea
- ▶ **H1-receptor antagonists:** meclizine, cyclizine, dimenhydrate
- ▶ **Prophylaxis** with antiemetic is best taken **1 hour before motion**
- ▶ Once motion has started, **oral administration of drugs fail, IM or SC or rectal route are required**
- ▶ Alternatively, **hyoscine as dermal patch is given**

Vomiting due to cytotoxic drugs

- ▶ **Cisplatin** is highly emetic
- ▶ **Ondansetron** is highly effective as is **dexamethasone**
- ▶ Lorazepam is useful adjuvant, may cause **sedation, dysphoria**
- ▶ **In sever vomiting, ondansetron plus dexamethasone** with or without lorazepam
- ▶ **Metoclopramide** may be substituted for **ondansetron**

Vomiting in pregnancy

- ▶ This reaches a peak at **10-11 weeks**, resolve by **13-14 week** of gestation
- ▶ **Histamine H1-receptor antagonist** or **phenothiazide**
- ▶ **Hyperemesis gravidarum** requires IV fluids and multivitamins supplements

Vertigo

- ▶ **Antimuscarinics** and **phenothiazines** are preferred
- ▶ **Cyclizine** or **prochlorperazine** is used to relieve an **acute attack**
- ▶ **Betahistine** (histamine analogue) is used for **improving blood circulation to the inner ear** in **Meniere's syndrome**, cinnarizine is also used