Gastrointestinal drugs

Antacids and other antiulcer drugs

Antacids (usually containing aluminium or magnesium compounds) can often relieve symptoms in ulcer dyspepsia and in non-erosive gastro-oesophageal reflux; they are also sometimes used in non-ulcer dyspepsia but the evidence of benefit is uncertain. Antacids are best given when symptoms occur or are expected, usually between meals and at bedtime, 4 or more times daily; additional doses may be required up to once an hour. Conventional doses for example 10 ml 3 or 4 times daily of liquid magnesium–aluminium antacids promote ulcer healing, but less well than antisecretory drugs (such as an H_2 -receptor antagonist); proof of a relationship between healing and neutralizing capacity is lacking. Liquid preparations are more effective than solids.

Aluminium- and **magnesium-containing** antacids (for example aluminium hydroxide, and magnesium hydroxide), being relatively insoluble in water, are long-acting if retained in the stomach. They are suitable antacids for most purposes. Magnesium-containing antacids have a laxative effect whereas aluminium-containing antacids may be constipating.

H_2 -receptor antagonists heal gastric and duodenal ulcers by reducing the secretion of gastric acid as a result of histamine H_2 -receptor blockade; they can also relieve gastro-oesophageal reflux disease. High doses of H_2 -receptor antagonists have been used in the Zollinger–Ellison syndrome, but a proton-pump inhibitor is now preferred.

Maintenance treatment with low doses has largely been replaced in *Helicobacter pylori* positive patients by eradication regimens (see below). Maintenance treatment may occasionally be used for those with frequent severe recurrences and for the elderly who suffer ulcer complications.

Treatment of undiagnosed dyspepsia with H_2 -receptor antagonists may be acceptable in younger patients but care is required in older people because their symptoms may be caused by gastric cancer.

H_2 -receptor antagonist therapy can promote healing of NSAID-associated ulcers (particularly duodenal). Treatment also reduces the risk of acid aspiration in obstetric patients at delivery (Mendelson syndrome).

PEPTIC ULCER

Ulcer disease is caused by peptic ulceration that involves the stomach, duodenum, and lower oesophagus. General and inexpensive measures like introducing healthy life-style, stopping smoking and taking antacids should be promoted. The possibilitiy of malignant disease should be considered in all patients over the age of 40 years who are suspected of having an ulcer.

Gastric and duodenal ulcers are healed by 4–8 weeks treatment with H_2 -receptor antagonists but there is a high rate of relapse (greater than 70% over 2 years) requiring maintenance therapy. Relapses can be prevented very sucessfully by eradicating *Helicobacter pylori* which is causally associated with most peptic ulcers (except

those related to NSAID use). Eradication of *H. pylori* reduces the relapse rate to about 4–8%. This is undoubtedly cost-effective compared to the alternatives of long-term maintenance therapy with low-dose H_2 -receptor antagonists or repeated treatment of recurrent ulcers. It is recommended that the presence of *H. pylori* is confirmed before starting eradication treatment, particularly for gastric ulcers. The urea breath test is used widely to test for *H. pylori* , but it may produce false negative results if used soon after proton pump inhibitors or antibacterials. Eradication regimens are based on a combination of an acid-reducing ('antisecretory') drug and antibiotics.

The following model eradication regimen is suggested on the basis of its efficacy and simplicity (only doses suitable for adults are shown):

- **omeprazole** 40 mg daily for 1 week
- plus
- **metronidazole** 400 mg three times daily for 1 week
- plus
- **amoxicillin** 500 mg three times daily for 1 week

The decision on choosing an eradication regimen for a particular country should take into account local resistance to antibacterials, cost and availability of the necessary drugs.

NSAID-ASSOCIATED ULCERS

Gastrointestinal bleeding and ulceration may occur with NSAID use. To avoid this, emphasis should be on stopping NSAID use but this is not always possible. A proton pump inhibitor may be considered for protection against NSAID-associated gastric and duodenal ulcers. An H_2 -receptor antagonist may be effective for protection against NSAID-associated duodenal ulcers only.

Patients who must continue NSAID therapy after ulcer development may take high-dose H_2 -receptor antagonists concomitantly, but ulcers tend to heal more slowly with H_2 -receptor antagonists if NSAIDs are continued. A proton-pump inhibitor such as omeprazole is more effective but it is also more expensive.

In patients who can discontinue NSAID therapy after ulcer development, treatment with an H_2 -receptor antagonist is effective, but a treatment period of up to 8 weeks may be necessary. A proton pump inhibitor usually produces the most rapid healing. After healing, continued prophylaxis is required.

DYSPEPSIA

Dyspepsia covers pain, fullness, early satiety, bloating, or nausea. It can occur with gastric and duodenal ulceration and gastric cancer but most commonly it is of uncertain origin.

Patients with non-ulcer dyspepsia should be advised to avoid smoking, alcohol and aggravating foods, and to eat small regular meals to aid digestion. Non-ulcer dyspepsia tends to be self-limiting but antacids and H_2 -receptor antagonists are often used to suppress gastric acid.

Effective treatment is important in the presence of severe oesophageal ulceration to prevent longer term complications such as oesophageal stricture and carcinoma.

GASTRO-OESOPHAGEAL REFLUX DISEASE

Gastro-oesophageal reflux disease (including non-erosive gastro-oesophageal reflux and erosive oesophagitis) is characterized by symptoms which include heartburn, acid regurgitation, and sometimes difficulty in swallowing (dysphagia); oesophageal inflammation (oesophagitis), ulceration, and stricture formation may occur and there is an association with asthma.

The management of gastro-oesophageal reflux disease includes drug treatment, lifestyle changes and, in some cases, surgery. Initial treatment is guided by the severity of symptoms and treatment is then adjusted according to response.

For mild symptoms of gastro-oesophageal reflux disease, initial management may include the use of antacids. H_2 -receptor antagonists suppress acid secretion and they may relieve symptoms and permit reduction in antacid consumption. Severe symptoms initially require a short-course of a proton-pump inhibitor.

ZOLLINGER–ELLISON SYNDROME

Management of Zollinger–Ellison syndrome requires high dose H_2 -receptor antagonist treatment. The proton pump inhibitors are more effective particularly for cases resistant to other treatment but they are more expensive.

Aluminium hydroxide

Tablets , aluminium hydroxide 500 mg

Oral suspension , aluminium hydroxide 320 mg/5 ml

Uses:

ulcer and non-ulcer dyspepsia; gastro-oesophageal reflux; hyperphosphataemia

Contraindications:

hypophosphataemia; undiagnosed gastrointestinal or rectal bleeding; appendicitis; porphyria

Precautions:

impaired renal function and renal dialysis (Appendix 4); hepatic impairment (Appendix 5); constipation; dehydration; fluid restriction; gastrointestinal disorders associated with decreased bowel motility or obstruction; **interactions:** Appendix 1

Dosage:

Dyspepsia, gastro-oesophageal reflux, *by mouth* , **ADULT** 1–2 tablets chewed 4 times daily and at bedtime *or* 5–10 ml suspension 4 times daily between meals and at bedtime; **CHILD** 6–12 years 5 ml up to three times daily

Hyperphosphataemia, *by mouth* , **ADULT** 2–10 g daily in divided doses with meals

Patient Advice. Do not take other medicines within 2–4 hours of aluminium hydroxide preparations. May be taken with water to reduce constipating adverse effects

Adverse effects:

constipation; intestinal obstruction (large doses); hypophosphataemia with increased bone resorption, hypercalciuria and risk of osteomalacia (patients on low phosphate diet or prolonged therapy); hyperaluminaemia—resulting in osteomalacia, encephalopathy, dementia, microcytic anaemia (in chronic renal failure treated with aluminium hydroxide as phosphate-binding agent)

Magnesium hydroxide

Oral suspension , magnesium hydroxide equivalent to magnesium oxide 550 mg/10 ml

Uses:

ulcer and non-ulcer dyspepsia; gastro-oesophageal reflux

Contraindications:

severe renal impairment

Precautions:

renal impairment (Appendix 4); hepatic impairment (Appendix 5); **interactions:** Appendix 1

Dosage:

Dyspepsia, gastro-oesophageal reflux, *by mouth* , **ADULT** 5–10 ml repeated according to patient's needs

Adverse effects:

diarrhoea; in renal impairment—hypermagnesaemia resulting in loss of deep tendon reflexes and respiratory depression, with other symptoms including nausea, vomiting,

flushing of skin, thirst, hypotension, drowsiness, confusion, muscle weakness, bradycardia, coma and cardiac arrest

Ranitidine

Ranitidine is a representative H_2 -receptor antagonist. Various drugs can serve as alternatives

Tablets , ranitidine (as hydrochloride) 150 mg

Oral solution , ranitidine (as hydrochloride) 75 mg/5 ml

Injection (Solution for injection), ranitidine (as hydrochloride) 25 mg/ml, 2-ml ampoule

Uses:

benign gastric and duodenal ulceration, gastro-oesophageal reflux, Zollinger–Ellison syndrome, other conditions where gastric acid reduction is beneficial

Contraindications:

porphyria

Precautions:

hepatic impairment (Appendix 5); renal impairment (Appendix 4); pregnancy (Appendix 2); breastfeeding (Appendix 3); middle-aged or older patients and those whose symptoms change—may mask gastric cancer; **interactions:** Appendix 1

Dosage:

Benign gastric and duodenal ulceration, *by mouth* , **adult** 150 mg twice daily *or* 300 mg at night for 4–8 weeks, up to 6 weeks in chronic episodic dyspepsia, and up to 8 weeks in NSAID-associated ulceration (in duodenal ulcer 300 mg can be given twice daily for 4 weeks to achieve a higher healing rate); maintenance, 150 mg at night; **CHILD** (peptic ulcer) 2–4 mg/kg twice daily, maximum 300 mg daily

Benign gastric and duodenal ulceration, reflux oesophagitis, Zollinger–Ellison syndrome, *by intramuscular injection* , **adult** 50 mg every 6–8 hours *or by slow intravenous injection* , 50 mg diluted to 20 ml and given over at least 2 minutes, may be repeated every 6–8 hours *or by intravenous infusion* , 25 mg/hour for 2 hours, may be repeated every 6–8 hours

Duodenal ulceration associated with*H. pylori* , see notes above

Prophylaxis of NSAID-induced duodenal ulcer, *by mouth* , **adult** 150 mg twice daily

Reflux oesophagitis, *by mouth* , **adult** 150 mg twice daily *or* 300 mg at night for up to 8 weeks, or if necessary 12 weeks (moderate to severe, 150 mg 4 times daily for up to 12 weeks); long-term treatment of healed oesophagitis, 150 mg twice daily

Zollinger–Ellison syndrome, *by mouth* , **adult** 150 mg 3 times daily; up to 6 g daily in divided doses has been used

Gastric acid reduction (prophylaxis of acid aspiration) in obstetrics, *by mouth* , **adult** 150 mg at onset of labour, then every 6 hours; surgical procedures, *by intramuscular or slow intravenous injection* , **adult** 50 mg 45–60 minutes before induction of anaesthesia (intravenous injection diluted to 20 ml and given over at least 2 minutes), *or by mouth* , 150 mg 2 hours before induction of anaesthesia, and also, when possible on the preceding evening

Prophylaxis of stress ulceration, **adult** initial *slow intravenous injection* of 50 mg diluted to 20 ml and given over at least 2 minutes *then by continuous intravenous infusion* , 125–250 micrograms/kg per hour (may be followed by 150 mg twice daily *by mouth* when oral feeding commences)

Adverse effects:

diarrhoea and other gastrointestinal disturbances, headache, dizziness, rash, tiredness, acute pancreatitis, bradycardia, AV block, confusion, depression; rarely hallucinations (particularly in the elderly or the very ill), hypersensitivity reactions (including fever, arthralgia, myalgia, anaphylaxis), blood disorders (including agranulocytosis, leukopenia, pancytopenia, thrombocytopenia), hepatitis, tachycardia, agitation, visual disturbances, erythema multiforme, alopecia, gynaecomastia and impotence

Antiemetic drugs

Metoclopramide has antiemetic properties and also stimulates upper gastrointestinal motility. Metoclopramide is effective against nausea and vomiting associated with gastrointestinal disorders or migraine, following surgery and chemotherapy and is also effective against radiation-induced nausea and vomiting. Combining metoclopramide with corticosteroids (such as dexamethasone) can improve its antiemetic effect in chemotherapy-induced nausea and vomiting. Metoclopramide may be useful in the management of gastro-oesophageal reflux and gastroparesis, as well as preoperatively in the prevention of aspiration syndromes. It is also used to facilitate intubation of the small bowel during radiographic examinations. Metoclopramide is **not** effective in the prevention or treatment of motion sickness.

Metoclopramide may cause acute dystonic reactions with facial and skeletal muscle spasms and oculogyric crises. These reactions are most common in the young (especially girls and young women) and the elderly; they occur shortly after the start of treatment and subside within 24 hours of drug withdrawal.

Promethazine is a phenothiazine that in addition to D2 dopaminergic blockade has pronounced histamine H_1 and muscarinic receptor blocking properties. It is effective in the prevention and treatment of vertigo and motion sickness. Promethazine may be

useful in the prevention and treatment of postoperative and drug-induced nausea and vomiting. It has limited effect on chemotherapy-induced mild to moderate emesis.

Metoclopramide hydrochloride

Tablets , metoclopramide hydrochloride 10 mg

Injection (Solution for injection), metoclopramide hydrochloride 5 mg/ml, 2-ml ampoule

Uses:

nausea and vomiting in gastrointestinal disorders and treatment with cytotoxics (section 8.2) or radiotherapy; gastro-oesophageal reflux; gastroparesis; premedication and postoperatively; aid to gastrointestinal intubation; nausea and vomiting in migraine (section 7.1)

Note. In children (and in some countries, patients under 20 years) use restricted to severe intractable vomiting of known cause, vomiting of radiotherapy and chemotherapy, aid to gastrointestinal intubation, premedication

Contraindications:

gastrointestinal obstruction, haemorrhage or perforation; 3–4 days after gastrointestinal surgery; convulsive disorders; phaeochromocytoma

Precautions:

elderly, children and young adults; hepatic impairment (Appendix 5); renal impairment (Appendix 4); may mask underlying disorders such as cerebral irritation; avoid for 3–4 days after gastrointestinal surgery; pregnancy (Appendix 2); breastfeeding (Appendix 3); Parkinson disease; epilepsy; depression; porphyria; **interactions:** Appendix 1

Dosage:

Nausea and vomiting, gastro-oesophageal reflux, gastroparesis, *by mouth or by intramuscular injection or by slow intravenous injection* (over 1–2 minutes), **ADULT** 10 mg 3 times daily; **young ADULT** 15–19 years (under 60 kg) 5 mg 3 times daily; **CHILD** up to 1 year (up to 10 kg) 1 mg twice daily, 1–3 years (10–14 kg) 1 mg 2–3 times daily, 3–5 years (15–19 kg) 2 mg 2–3 times daily, 5–9 years (20–29 kg) 2.5 mg 3 times daily, 9–14 years (30 kg and over) 5 mg 3 times daily (usual maximum 500 micrograms/kg daily, particularly for children and young adults)

Premedication, *by slow intravenous injection* , **ADULT** 10 mg as a single dose

Aid to gastrointestinal intubation, *by mouth or by intramuscular injection or by slow intravenous injection* , **ADULT** 10–20 mg as a single dose 5–10 minutes before examination; **young ADULT** (15–19 years), 10 mg; **CHILD** under 3 years 1 mg, 3–5 years 2 mg, 5–9 years 2.5 mg, 9–14 years 5 mg

Note. High dose metoclopramide with cytotoxic chemotherapy, see section 8.2

Adverse effects:

extrapyramidal symptoms (especially in children and young adults; see notes above); tardive dyskinesias on prolonged use; hyperprolactinaemia; drowsiness, restlessness, dizziness, headache, diarrhoea, depression, hypotension and hypertension reported; rarely, neuroleptic malignant syndrome; rashes, pruritus, oedema; cardiac conduction abnormalities following intravenous administration; rarely methaemoglobinaemia (more severe in G6PD deficiency)

Promethazine hydrochloride

Tablets , promethazine hydrochloride 10 mg, 25 mg

Elixir (Oral solution), promethazine hydrochloride 5 mg/5 ml

Injection (Solution for injection), promethazine hydrochloride 25 mg/ml, 2-ml ampoule

Uses:

nausea, vomiting, labyrinthine disorders, motion sickness; premedication (section 1.3)

Contraindications:

porphyria

Precautions:

prostatic hypertrophy; urinary retention; glaucoma; hepatic disease (Appendix 5); epilepsy; elderly and children (more susceptible to adverse effects); pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions:** Appendix 1

Skilled tasks. May impair ability to perform skilled tasks, for example operating machinery, driving

Dosage:

Nausea and vomiting (including postoperative), *by mouth or by intramuscular injection or by slow intravenous injection* (diluted to 2.5 mg/ml in water for injection), **ADULT** 12.5–25 mg, repeated at intervals of not less than 4 hours (usual maximum, 100 mg in 24 hours)

Motion sickness, prevention, *by mouth* , **ADULT** 20–25 mg at bedtime on night before travel, repeated on day of travel if necessary; **CHILD** 2–5 years, 5 mg at night and on day of travel, if necessary; 5–10 years, 10 mg at night and on day of travel, if necessary

Dilution and administration. Intravenous injection, according to manfacturer's directions

Adverse effects:

drowsiness, dizziness, sedation (but paradoxical stimulation may occur, especially with high doses or in children and elderly); headache, psychomotor impairment; urinary retention, dry mouth, blurred vision, gastrointestinal disturbances; hypersensitivity reactions; rashes, photosensitivity reactions; jaundice; blood disorders; cardiovascular adverse effects—after injection; venous thrombosis at site of intravenous injection; pain on intramuscular injection

Antihaemorrhoidal drugs

Haemorrhoids are enlarged or varicose veins of the tissues at the anus or rectal outlet. They are the most frequent cause of rectal bleeding. Anal and perianal pruritus, soreness and excoriation occur commonly in patients suffering from haemorrhoids, fistulas and proctitis. Careful local toilet with attention to any minor faecal soiling, adjustment of the diet to avoid hard stools, the use of bulk-forming materials such as bran and a high residue diet are helpful.

Soothing preparations containing mild astringents such as bismuth subgallate, zinc oxide and hamamelis with lubricants, vasoconstrictors or mild antiseptics, in the form of topical ointments, creams and suppositories, are used to provide symptomatic relief. Local anaesthetics are included in some preparations to relieve pain. Corticosteroids may be combined in such preparations (but should only be used after exclusion of infection); they are suitable for occasional short-term use, but prolonged use can cause atrophy of the anal skin.

Local anaesthetic, astringent and anti-inflammatory drug

Ointment or suppository

Uses:

short-term symptomatic treatment of hemorrhoids

Anti-inflammatory drugs

Ulcerative colitis and Crohn disease are inflammatory diseases of the intestinal tract.

ULCERATIVE COLITIS

Acute attacks of ulcerative colitis require treatment with local corticosteroids such as **hydrocortisone** in the form of suppositories or retention enemas. Because of the risk of intestinal perforation, rectal administration of hydrocortisone must be used with extreme caution in patients with severe ulcerative disease and should not be given to such patients without conducting a thorough proctological examination. More extensive disease requires oral corticosteroid treatment and severe extensive or fulminant disease needs hospital admission and intravenous corticosteroid administration; other therapy may include intravenous fluid and electrolyte replacement, blood transfusion, and possibly parenteral nutrition and antibiotics.

The aminosalicylate **sulfasalazine** is useful in the treatment of symptomatic disease. It also has value in the maintenance of remission in ulcerative colitis for which corticosteroid treatment is unsuitable because of adverse effects. In resistant or frequently relapsing cases azathioprine 2–2.5 mg/kg daily (section 8.1) given under close supervision may be helpful. Laxatives are required to facilitate bowel movement when proctitis is present. Antimotility drugs such as codeine and antispasmodic drugs should not be used in active ulcerative colitis because they can precipitate paralytic ileus and megacolon. Diarrhoea resulting from reduced bile salt absorption may improve with colestyramine. General nutritional care and appropriate supplements are essential. High-fibre or low-residue diets should be used as appropriate. Irritable bowel syndrome during remission of ulcerative colitis requires avoidance of a high-fibre diet and possibly treatment with an antispasmodic (see section 17.5).

CROHN DISEASE

Treatment of Crohn disease of the colon is similar to that of ulcerative colitis. In small bowel disease **sulfasalazine** may have marginal benefit. Symptoms and inflammation associated with disease exacerbation are suppressed by oral corticosteroids such as prednisolone. **Metronidazole** may be beneficial in the treatment of active Crohn disease particularly with perianal involvement, possibly through its antibacterial activity. Other antibacterials should be given if specifically indicated (for example, sepsis associated with fistulas and perianal disease) and for managing bacterial overgrowth in the small bowel. General nutritional care and appropriate supplements are essential.

Hydrocortisone

Hydrocortisone retention enema is a representative rectal corticosteroid preparation (other than suppository). Various formulations can serve as alternatives

Hydrocortisone rectal preparations are complementary drugs

Suppositories , hydrocortisone acetate 25 mg

Retention enema (Rectal solution), hydrocortisone 100 mg, 60-ml bottle

Uses:

ulcerative colitis, proctitis, proctosigmoiditis; anaphylaxis (section 3.1); skin (section 13.3); adrenocortical insufficiency (section 18.1)

Contraindications:

use of enemas in bowel obstruction, bowel perforation, or extensive fistulas; untreated infections

Precautions:

proctological examination required before treatment; systemic absorption may occur (see section 18.1); prolonged use should be avoided; pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions:** Appendix 1

Dosage:

Ulcerative colitis, proctitis, *by rectum* (suppositories), **ADULT** 25 mg twice daily for 2 weeks; may be increased to 25 mg 3 times daily *or* 50 mg twice daily in severe cases; in factitial proctitis treatment may be required for 6–8 weeks

Ulcerative colitis, ulcerative proctitis, ulcerative proctosigmoiditis, *by rectum* (retention enema), **ADULT** 100 mg at night for 21 days or until clinical and proctological remission; if no clinical and proctological improvement after 21 days, discontinue; treatment for 2–3 months may be required for proctological remission; when used for more than 21 days, discontinue gradually using 100 mg every other night for 2–3 weeks

Adverse effects:

local pain or burning sensation; rectal bleeding (reported with use of enema); exacerbation of untreated infections; suppositories may stain fabrics; systemic adverse effects (section 18.1)

Sulfasalazine

Sulfasalazine is a representative aminosalicylate. Various drugs can serve as alternatives

Tablets , sulfasalazine 500 mg

Suppositories , sulfasalazine 500 mg

Retention enema (Rectal solution), sulfasalazine 3 g, 100-ml bottle

Uses:

ulcerative colitis; Crohn disease; severe rheumatoid arthritis (section 2.4)

Contraindications:

hypersensitivity to salicylates or sulfonamides; child under 2 years; porphyria; intestinal or urinary obstruction; severe renal impairment

Precautions:

renal impairment (Appendix 4); hepatic impairment; G6PD deficiency; slow acetylator status; monitor blood counts and liver function initially and at monthly intervals for first 3 months; monitor kidney function initially and at intervals during treatment; history of allergy; pregnancy and breastfeeding (Appendices 2 and 3); **interactions:** Appendix 1

Blood disorders. Patients should be advised to report any unexplained bleeding, bruising, purpura, sore throat, fever or malaise occurring during treatment; blood count should be performed and sulfasalazine stopped immediately if there is suspicion or evidence of blood disorder

Dosage:

Ulcerative colitis, *by mouth* , **ADULT** 1–2 g 4 times daily in acute attack until remission, reducing to maintenance dose of 500 mg 4 times daily; **CHILD** over 2 years, 40–60 mg/kg daily in acute attack, reducing to maintenance dose of 20–30 mg/kg daily

Active Crohn disease, *by mouth* , **ADULT** 1–2 g 4 times daily in acute attack until remission occurs; **CHILD** over 2 years, 40–60 mg/kg daily in acute attack

Ulcerative colitis, Crohn colitis, *by rectum* (suppositories, used alone or in conjunction with oral therapy), **ADULT** 0.5–1 g morning and evening after a bowel movement; *by rectum* (retention enema), **ADULT** 3 g at night retained for at least an hour; **CHILD** not a suitable formulation

Adverse effects:

nausea, exacerbation of colitis; diarrhoea, loss of appetite, fever, blood disorders (including Heinz body anaemia, megaloblastic anaemia, leukopenia, neutropenia, thrombocytopenia); hypersensitivity reactions (including rash, urticaria, Stevens-Johnson syndrome (erythema multiforme), exfoliative dermatitis, epidermal necrolysis, pruritus, photosensitization, anaphylaxis, serum sickness, interstitial nephritis, lupus erythematosus-like syndrome); lung complications (including eosinophilia, fibrosing alveolitis); ocular complications (including periorbital oedema); stomatitis, parotitis; ataxia, aseptic meningitis, vertigo, tinnitus, alopecia, peripheral neuropathy, insomnia, depression, headache, hallucinations; kidney reactions (including proteinuria, crystalluria, haematuria); oligospermia; rarely acute pancreatitis, hepatitis; urine may be coloured orange; some soft contact lenses may be stained

Antispasmodic drugs

The smooth muscle relaxant properties of anticholinergic (more correctly termed antimuscarinic) and other antispasmodic drugs may be useful in dyspepsia, irritable bowel syndrome, and in diverticular disease. The gastric antisecretory effects of conventional anticholinergic drugs are of little practical significance since dosage is limited by atropine-like adverse effects. Moreover they have been superseded by more powerful and specific antisecretory drugs, including the histamine H_2 -receptor antagonists.

Anticholinergics that are used for gastrointestinal smooth muscle spasm include **atropine** and hyoscine butylbromide.

Atropine sulfate

Atropine sulfate is a representative antispasmodic drug. Various drugs can serve as alternatives

Tablets , atropine sulfate 600 micrograms

Uses:

dyspepsia, irritable bowel syndrome, diverticular disease; premedication (section 1.3); mydriasis and cycloplegia (section 21.5); poisoning (section 4.2.3)

Contraindications:

angle-closure glaucoma; myasthenia gravis; paralytic ileus; pyloric stenosis; prostatic enlargement

Precautions:

children, elderly and Down syndrome (increased risk of adverse effects); gastro-oesophageal reflux; diarrhoea; ulcerative colitis; acute myocardial infarction; hypertension; hyperthyroidism; cardiac insufficiency, cardiac surgery—conditions characterized by tachycardia; pyrexia; pregnancy (Appendix 2); breastfeeding (Appendix 3); **interactions:** Appendix 1

Dosage:

Dyspepsia, irritable bowel syndrome, diverticular disease, *by mouth* , **ADULT** 0.6–1.2 mg at night

Adverse effects:

constipation; transient bradycardia (followed by tachycardia, palpitations and arrhythmias); reduced bronchial secretions, urinary urgency and retention; dilatation of pupils with loss of accommodation, photophobia, dry mouth, flushing and dryness of skin; occasionally confusion (particularly in the elderly), nausea, vomiting and giddiness

Laxatives

A balanced diet, including adequate fluid intake and fibre is of value in preventing constipation.

Before prescribing laxatives, it is important to be sure that the patient is constipated and that the constipation is not secondary to an underlying undiagnosed complaint. It is also important that the patient understands that bowel habit can vary considerably in frequency without doing harm. For example some people consider themselves constipated if they do not have a bowel movement each day. A useful definition of constipation is the passage of hard stools less frequently than the patient's own normal pattern and this should be explained to the patient since misconceptions about bowel habits have led to excessive laxative use which in turn has led to hypokalaemia and an atonic non-functioning colon.

Laxatives should generally be avoided except where straining will exacerbate a condition such as angina or increase the risk of rectal bleeding as in haemorrhoids. Laxatives are of value in drug-induced constipation, for the expulsion of parasites after anthelminthic treatment and to clear the alimentary tract before surgery and radiological procedures. Prolonged treatment of constipation is rarely necessary except occasionally in the elderly.

There are many different laxatives. These include **bulk-forming laxatives** which relieve constipation by increasing faecal mass and stimulating peristalsis, **stimulant laxatives** which increase intestinal motility and often cause abdominal cramp, **faecal softeners** which lubricate and soften impacted faeces and **osmotic laxatives** which act by retaining fluid in the bowel by osmosis. **Bowel cleansing solutions** are used before colonic surgery, colonoscopy or radiological examination to ensure that the bowel is free of solid contents; they are **not** a treatment for constipation.

Senna

Senna is a representative stimulant laxative. Various drugs can serve as alternatives

Tablets , total sennosides (calculated as sennoside B) 7.5 mg

Uses:

constipation; acts in 8–12 hours

Contraindications:

intestinal obstruction; undiagnosed abdominal symptoms

Precautions:

avoid prolonged use unless indication for prevention of faecal impaction; breastfeeding (Appendix 3)

Dosage:

Constipation, *by mouth* , **ADULT** 2–4 tablets, usually at night; initial dose should be low, then gradually increased; **CHILD** over 6 years, half the adult dose in the morning (on doctor's advice)

Adverse effects:

abdominal discomfort; atonic non-functioning colon and hypokalaemia (with prolonged use or overdosage)

Drugs used in diarrhoea

Acute diarrhoeal diseases are a leading cause of childhood morbidity and mortality; frail and elderly patients are also at risk. In adults acute diarrhoea is the most frequent

health problem of travellers to developing countries and is increasingly common among HIV-infected persons. Assessment and correction of dehydration and electrolyte disturbance is the priority in all cases of acute diarrhoea. Symptomatic relief (section 17.7.2) in adults may be warranted in some cases but antidiarrhoeals should never be used in children since they do not reduce fluid and electrolyte loss and may cause adverse effects.

Diarrhoea persisting for longer than a month is known as chronic diarrhoea. A mild malabsorption syndrome, tropical enteropathy, is apparent in most healthy indigenous populations of tropical countries. However the majority of cases of chronic diarrhoea have non-infectious causes including gluten-sensitivity, inherited metabolic disorders or inflammatory bowel disease.

Bloody diarrhoea is usually a sign of invasive enteric infection and should be treated with an appropriate anti-infective agent.

Oral rehydration

Acute diarrhoea in children should always be treated with oral rehydration solution according to plan A, B or C as shown. Severely dehydrated patients must be treated initially with intravenous fluids until they are able take fluids by mouth. For oral rehydration it is important to administer the solution in small amounts at regular intervals as indicated below.

Treatment of dehydration: WHO recommendations

According to the degree of dehydration, health professionals are advised to follow one of 3 management plans.

Plan A: no dehydration. Nutritional advice and increased fluid intake are sufficient (soup, rice, water and yoghurt, or even water). For infants aged under 6 months who have not yet started taking solids, oral rehydration solution must be presented before offering milk. Mother's milk or dried cow's milk must be given without any particular restrictions. In the case of mixed breast-milk/formula feeding, the contribution of breastfeeding must be increased.

Plan B: moderate dehydration. Whatever the child's age, a 4-hour treatment plan is applied to avoid short-term problems. Feeding should not therefore be envisaged initially. It is recommended that parents are shown how to give approximately 75 ml/kg of oral rehydration solution with a spoon over a 4-hour period, and it is suggested that parents should be watched to see how they cope at the beginning of the treatment. A larger amount of solution can be given if the child continues to have frequent stools. In case of vomiting, rehydration must be discontinued for 10 minutes and then resumed at a slower rate (about one teaspoonful every 2 minutes). The child's status must be re-assessed after 4 hours to decide on the most appropriate subsequent treatment. Oral rehydration solution should continue to be offered once dehydration has been controlled, for as long as the child continues to have diarrhoea.

Plan C: severe dehydration. Hospitalization is necessary, but the most urgent priority is to start rehydration. In hospital (or elsewhere), if the child can drink, oral

rehydration solution must be given pending, and even during, intravenous infusion (20 ml/kg every hour by mouth before infusion, then 5 ml/kg every hour by mouth during intravenous rehydration). For intravenous supplementation, it is recommended that compound solution of sodium lactate (see section 26.2) is administered at a rate adapted to the child's age (infant under 12 months: 30 ml/kg over 1 hour then 70 ml/kg over 5 hours; child over 12 months: the same amounts over 30 minutes and 2.5 hours respectively). If the intravenous route is unavailable, a nasogastric tube is also suitable for administering oral rehydration solution, at a rate of 20 ml/kg every hour. If the child vomits, the rate of administration of the oral solution should be reduced.

Oral rehydration salts

Glucose salt solution

sodium chloride	2.6 g/litre of clean water
sodium citrate	2.9 g/litre of clean water
potassium chloride	1.5 g/litre of clean water
glucose (anhydrous)	13.5 g/litre of clean water

When glucose and sodium citrate are not available, they may be replaced by

sucrose (common sugar)	27 g/litre of clean water
sodium bicarbonate	2.5 g/litre of clean water

NOTE. The solution may be prepared either from prepackaged sugar/salt mixtures or from bulk substances and water. Solutions must be freshly prepared, preferably with recently boiled and cooled water. Accurate weighing and thorough mixing and dissolution of ingredients in the correct volume of clean water is important. Administration of more concentrated solutions can result in hypernatraemia

CHOLERA.. In cases of cholera, oral rehydration salts containing a higher concentration of sodium may be required to prevent hyponatraemia

Uses:

dehydration from acute diarrhoea

Precautions:

renal impairment

Dosage:

Fluid and electrolyte loss in acute diarrhoea, *by mouth* , **ADULT** 200–400 ml solution after every loose motion; **INFANT** and **CHILD** according to Plan A, B or C (see notes above)

Adverse effects:

vomiting—may indicate too rapid administration; hypernatraemia and hyperkalaemia may result from overdose in renal impairment or administration of too concentrated a solution

Antimotility drugs

Opioids such as codeine are used in the symptomatic relief of uncomplicated, acute diarrhoea in adults but not in young children. They act on opioid receptors in the gut wall and decrease bowel motility. In dehydration, fluid and electrolyte replacement (section 17.7.1) are of primary importance.

Codeine phosphate

Drug subject to international control under the Single Convention on Narcotic Drugs (1961)

Tablets , codeine phosphate 30 mg

Uses:

short-term symptomatic relief of acute diarrhoea in adults; pain (section 2.2)

Contraindications:

children; conditions where inhibition of peristalsis should be avoided; abdominal distension; acute diarrhoeal conditions such as ulcerative colitis or antibiotic-associated colitis; acute respiratory depression

Precautions:

tolerance or dependence may occur with prolonged use; elderly and debilitated patients; hepatic impairment (Appendix 5); renal impairment (Appendix 4); pregnancy (Appendix 2); breastfeeding (Appendix 3); **overdosage:** see section 4.2.2; **interactions:** Appendix 1

Dosage:

Symptomatic relief of acute diarrhoea, *by mouth* , **ADULT** 30 mg 3–4 times daily

Adverse effects:

nausea, vomiting, constipation, drowsiness; respiratory depression and hypotension (large doses); dependence; difficulty with micturition; ureteric or biliary spasm; dry mouth, sweating, headache, facial flushing, vertigo, bradycardia, tachycardia, palpitations, hypothermia, hallucinations, dysphoria, mood changes, miosis, decreased libido or potency, rash, urticaria, pruritus; convulsions (large doses).