Therapeutic Drug Guidelines
Kiribati Ministry of Health
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Book 3
Gastrointestinal and Respiratory

Adapted from the draft prepared for the Fiji National Drug and Therapeutic Committee by Prof Gill Shenfield in July 2007
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1. Drugs used in gastrointestinal disease

1.1. Antacids and acid suppressants

1.1.1. Antacids
- Only antacid in the Kiribati EDL is magnesium trisilicate
- Frequent high doses of antacids are generally not recommended for long-term use
- Other antiulcerants are more reliable and have more convenient dosing

1.1.2. Histamine H2-receptor antagonists
- Structurally related to histamine and more potent at blocking H2-receptors (present mainly in the gastric mucosa) than the more widespread H1-receptors. The only one in the Kiribati EDL is ranitidine
- Ranitidine is well absorbed orally, but absorption is reduced by antacids
- Plasma half-life is short but the duration of action is longer and allows for once- or twice-daily dosing for peptic ulcers
- Twice-daily dosing preferred for reflux
- Renally excreted, so dose reductions may be required in significant renal impairment
- No clinically significant interactions or effects on liver metabolism
- Adverse effects uncommon but it can occasionally cause severe liver toxicity, blood dyscrasias and skin rashes
- For peptic ulcer disease due to Helicobacter pylori, ranitidine used in combination with antibiotics for a 1- to 2-week period

1.1.3. Proton pump inhibitors
Proton pump inhibitors (PPIs) inhibit the enzyme hydrogen/potassium adenosine triphosphatase, thus suppressing acid secretion irrespective of the stimulus to acid production.
Inhibition of acid secretion by PPIs, although of slower onset, is greater and more sustained than with histamine H2-receptor antagonists.
Healing of erosive oesophagitis and peptic ulcers is superior with PPIs compared with histamine H2-receptor antagonists or other antiulcerants.
Oral omeprazole is available on the Kiribati EDL.
- For peptic ulcer disease due to Helicobacter pylori, PPIs are used in combination with antibiotics for a 1- to 2-week period

1.2. Laxatives
- Laxatives can be classified as bulk-forming, osmotic, stool-softening, or stimulant.
- Paraffin and glycerol are lubricant laxatives but probably work by a combination of osmotic, stool-softening or stimulant effects.
- Bulk-forming laxatives include natural products such as bran, ispaghula husk and hydrophilic colloids.
- Increased fibre in the diet can also act as a bulk-forming laxative.
- Bulk-forming laxatives need to be taken with adequate fluid to be effective.
• Bulk-forming laxatives are better at prevention of constipation than treatment of established constipation. They are therefore best used in circumstances where constipation would be expected, e.g. the elderly, people confined to bed, patients taking regular opioids.

Lactulose is a potent osmotic laxative available in Kiribati, mainly used in the management of hepatic encephalopathy. It can be used in the treatment of intractable constipation in children and in adults with opiate induced constipation. Not absorbed from the small intestine and so largely reaches the colon intact. In the colon, lactulose is metabolised by colonic bacteria to lactic acid, short-chain carboxylic acids and its constituent monosaccharides. The end result is a change in osmotic pressure that increases stool water content. Lactulose frequently produces flatulence and abdominal cramps when first used. It can also cause diarrhoea, nausea, anorexia and electrolyte disturbances.

• Bisacodyl, coloxyl and senna are all colon stimulants which may be given orally or as a suppository
  • Mode of action of colonic stimulants is not known, but they may stimulate the enteric nervous system, thus increasing motility
  • Major adverse effects are abdominal colic and cramps
  • Frequent use can lead to significant hypokalaemia due to excessive electrolyte secretion into the colon

1.3 Antidiarrhoeals

The most commonly used antidiarrhoeal drugs are opioid derivatives, in which the adverse effect of the opioid (constipation) is being exploited.

1.3.1 Codeine
Codeine is available as the 30mg tablet in the Kiribati EDL.
It is an analgesic with the side effect of slowing gut motility.
A naturally occurring opioid but only has analgesic effects because about 10% is converted to morphine in the liver.
Action on the gut is probably produced by both codeine and morphine.
Codeine shares all the properties of other opioids, including the potential for dependence.

1.3.2 Diphenoxylate
An opioid derivative that is not currently on the Kiribati EDL.

1.4 Antiemetics

Often used prophylactically to counteract the emetic adverse effects of other drugs, especially opioids in chronic pain relief or palliative care. However, care should be taken with this practice as all the commonly used antiemetics can themselves cause significant adverse effects.

Drugs available in the Kiribati EDL are metoclopramide, prochlorperazine and promethazine.

1.4.1 Metoclopramide
  • Stimulates motility of the upper gastrointestinal tract, increasing gastric emptying rate and reducing small intestinal transit time
  • An antagonist at dopamine receptors in the central nervous system
• Well absorbed orally but undergoes significant first-pass metabolism. Its elimination half-life is approximately 4 hours
• Can produce sedation and acute dystonic and dysphoric reactions
• Acute dysphoric reactions can occur after a single dose and are more common in the young. Acute dystonic reactions, including oculogyric crisis, are also more common in children and young adults (particularly females) and are due to individual sensitivity or excessive dosing. Penetration of the drug across the blood-brain barrier is higher in young people than mature adults
• Long-term use of metoclopramide can cause tardive dyskinesia, particularly in the elderly
• Can change rate of absorption of other drugs through its effect on gastric motility

1.4.2 Prochlorperazine and promethazine
• Are phenothiazine derivatives and have antipsychotic as well as antiemetic properties
• Major antiemetic effect is centrally mediated, probably by blockade of dopamine receptors

Adverse effects
• Common adverse effects of prochlorperazine include postural hypotension and sedation
• Has additive sedative affects with alcohol, benzodiazepines, opioids and other central nervous system depressants
• Acute extrapyramidal reactions, although uncommon, are the most important adverse effect. Such reactions are more common in the young and can occur after a single dose
• Prolonged use of prochlorperazine can cause the adverse effects associated with phenothiazines, including drug-induced parkinsonism

1.5 Drugs used in inflammatory bowel disease

1.5.1 Aminosalicylates
5-aminosalicylic acid (5-ASA) is an agonist of peroxisome proliferator-activated receptor-γ (PPAR-γ).
• Are drugs that deliver 5-ASA to the luminal surface of the terminal small bowel and colonic mucosa reduce the frequency of relapse and control mild inflammation in ulcerative colitis
• May be of some benefit in active Crohn’s colitis but the evidence is weak

Sulfasalazine is a conjugate of sulfapyridine and 5-ASA. The sulfapyridine component of sulfasalazine is absorbed and metabolised in the liver, but little of the 5-ASA is absorbed.
• About 10% to 15% of patients are unable to take sulfasalazine because of its adverse effects, most of which are due to sulfapyridine, and many of which are dose-related.
• It should not be used in patients with a known sensitivity to sulfonamides.
• The most common adverse effects are epigastric pain, nausea, skin rashes, headache, reversible male infertility and macrocytosis.
• More severe but less common effects include haemolytic anaemia, blood dyscrasias, diarrhoea, hepatitis, pneumonitis, Stevens-Johnson syndrome and encephalitis, all of which may be fatal.

Sulfasalazine is not currently available in Kiribati.

1.5.2 Corticosteroids
Used principally to induce remission in both Crohn’s disease and ulcerative colitis

Prednisolone and hydrocortisone are in the Kiribati EDL.
Dosing of systemic corticosteroids

- Lowest dose possible to achieve the desired clinical response should be used
- Low doses are used to produce an anti-inflammatory effect while high doses are needed to produce immunosuppression
- Prednisolone is generally given as a single daily dose in the morning to mimic the natural cortisol peak
- Dosing in the evening often results in sleep disturbances

Dose reduction (tapering)

- The hypothalamic-pituitary-adrenal axis is suppressed by glucocorticoid therapy
- Treatment with prednisolone at doses greater than 5 mg for longer than 2 weeks can be sufficient to cause adrenal suppression
- Tapering of the dose is required to avoid both adrenal insufficiency and also rebound in symptoms, which may occur with sudden cessation
- Rate of reduction depends on the dose level, duration of treatment and underlying disease state

Adverse effects

Systemic corticosteroid treatment inevitably results in adverse effects if the dose and/or duration of treatment are sufficient, because most are dose-related biological effects of the hormone.

Table 1 Important complications of corticosteroids

<table>
<thead>
<tr>
<th>Glucocorticoid</th>
<th>Mineralocorticoid</th>
</tr>
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<tbody>
<tr>
<td>gastrointestinal effects (e.g. dyspepsia, risk factor for peptic ulceration, gastrointestinal bleeding)</td>
<td>hypertension</td>
</tr>
<tr>
<td>growth retardation</td>
<td>hypokalaemic alkalosis</td>
</tr>
<tr>
<td>immunosuppression, risk of infections</td>
<td>sodium-retaining effects</td>
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<tr>
<td>metabolic effects (e.g. diabetes, hypertriglyceridaemia)</td>
<td></td>
</tr>
<tr>
<td>myopathy</td>
<td></td>
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<tr>
<td>ocular effects, particularly increased intraocular pressure and cataracts</td>
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<tr>
<td>osteoporosis</td>
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<tr>
<td>pituitary-adrenal suppression</td>
<td></td>
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<tr>
<td>psychological disturbances (e.g. euphoria, depression, paranoid psychosis)</td>
<td></td>
</tr>
<tr>
<td>skin atrophy</td>
<td></td>
</tr>
<tr>
<td>weight gain and redistribution of fat</td>
<td></td>
</tr>
</tbody>
</table>

1.5.3 Azathioprine and mercaptopurine

Azathioprine, a prodrug of mercaptopurine, and mercaptopurine itself are used to treat inflammatory bowel disease in patients whose disease is refractory to other therapies or who have frequent relapses. These are not available in Kiribati

1.5.4 Methotrexate

Methotrexate is an inhibitor of dihydrofolate reductase, and is cytotoxic at high doses. The mechanism of its beneficial action in Crohn’s disease is unknown, but may involve inhibiting inflammatory cell activation and cytokine release. Response to therapy is seen over several months. Currently not available consistently in Kiribati through the EDL.
1.5.5 Metronidazole

- Has a role in perineal Crohn’s disease
- Common adverse effects include nausea, diarrhoea and metallic taste
- Can cause a disulfiram-like reaction with alcohol, so alcohol should be avoided during treatment
- Can cause paraesthesiae and peripheral neuropathy, especially when used for long periods or in high doses

1.6 Drugs used in liver disease

Corticosteroids are the main treatment options available in Kiribati for autoimmune chronic hepatitis.

Lactulose (see above) is used in the management of hepatic encephalopathy. It may also be used in the treatment of intractable constipation.

2. Nausea and vomiting

Effective treatment of nausea and vomiting usually depends on correction of the underlying cause, including medications, metabolic disturbances, abdominal or intracranial pathology. These causes should be considered and excluded with appropriate investigations.

There is no universally effective antiemetic as none of the available drugs antagonise all the receptor sites involved in the emetic response.

2.1 Motion sickness

Motion sickness is an autonomic syndrome similar to that which accompanies vertigo, except that it is due to real motion, not an illusion of motion. Anticholinergics and antihistamines are the drugs of first choice for prophylaxis of motion sickness. Dopamine antagonists (e.g. metoclopramide) are usually ineffective.

For prophylaxis, use:

- Promethazine 25 mg (child 2 to 5 years: 5 to 6.25 mg; child 6 to 10 years: 10 to 12.5 mg) orally, 1 to 2 hours before travel

These drugs offer reasonable protection but may produce sedation and impair vigilant performance.

For treatment, use:

- Promethazine 25 to 50 mg orally, then 25 mg 8- to 12-hourly, up to 100 mg in 24 hours (child greater than 2 years: 0.125 to 0.3 mg/kg orally, 6-hourly, up to 100 mg in 24 hours)

Do not drive after taking this drug.

2.2 Vestibular disturbances

For patients with an acute attack of vertigo (e.g. vestibular neuritis), use:

- Prochlorperazine 12.5 mg IM, immediately, followed 6 hours later if required by prochlorperazine 5 to 10 mg orally, as a single dose

Alternatively, use:
• Prochlorperazine 5 to 10 mg orally, 3 to 4 times daily

OR

• Promethazine 10 to 25 mg IM or slow IV, then 10 to 25 mg orally, IM or slow IV, 8- to 12-hourly for 48 hours if required

Anticholinergic effects and dystonic reactions may complicate acute use of these drugs. Long-term symptomatic treatment of chronic dizziness or vertigo with these drugs is not good practice. Tardive dyskinesia, Parkinsonism, jaundice, agranulocytosis and skin reactions are all potential complications. Chronic use, particularly in elderly patients with vague nonvertiginous dizziness, should therefore be avoided if possible.

2.3 Pregnancy

Nausea is one of the most common symptoms of early pregnancy, being reported by approximately 70% to 80% of pregnant women. Vomiting occurs in about 50% of pregnancies and is severe enough to require admission to hospital for correction of dehydration and electrolyte imbalance (hyperemesis gravidarum) in about 1% of pregnancies. The treatment of most patients is nonpharmacological. Reassurance of a good prognosis and dietary modification (small, frequent, high-carbohydrate, low-fat meals) are important.

Ginger (in doses equivalent to 1 to 2 g of powdered ginger daily) may have some efficacy in relieving nausea and vomiting associated with pregnancy.

For severe nausea, with or without vomiting, use:

• metoclopramide 10 mg orally, 3 times daily (category A)

PLUS

• pyridoxine 25 mg orally, 4 times daily (uncategorised)

If unsuccessful, use:

• Prochlorperazine 5 mg orally, 3 times daily (category C)

OR

• Promethazine 25 mg orally, 3 times daily (category C)

For patients unable to tolerate oral medication, use:

1. Metoclopramide 10 mg IM or slow IV (category A)

OR

2. Prochlorperazine 25 mg rectally (category C)

OR

2. Prochlorperazine 12.5 mg IM (category C)

2.4 Drug-induced nausea and vomiting

Many drugs e.g. opiates and digoxin can cause nausea and vomiting. If possible, cease or reduce the dose of the offending drug. If necessary, use:

• Metoclopramide 10 mg (5mg in the elderly) orally or IM or IV, 4- to 6-hourly as required

Sometimes a prophylactic antiemetic is given routinely with an opioid analgesic. However, since antiemetics can themselves cause adverse effects, this should only be done where vomiting would be particularly harmful (e.g. after upper abdominal or intraocular surgery), in patients unable to protect their airways, or in patients known to vomit excessively after opioids.
3. Disorders of the oesophagus

3.1 Gastro-oesophageal reflux
Symptoms of gastro-oesophageal reflux or heart burn are extremely common. Most individuals have occasional symptoms, usually following dietary indiscretions and some have daily symptoms. If symptoms significantly impair the quality of life, either due to frequency (twice per week or more) or severity, the person is considered to be suffering from gastro-oesophageal reflux disease (GORD).

3.1.1 Treatment of mild intermittent symptoms
Non drug treatment
For treating mild intermittent symptoms (once or less per week), the avoidance of precipitating foods may be all that is required. Anecdotal evidence suggests limiting alcohol, high fat meals, chocolate and coffee may be beneficial. Reduced intake of citrus fruits (e.g. oranges, grapefruits and lemons), tomato products, spicy foods and carbonated beverages may also be of some benefit. Other advice may include:

- Cessation of smoking if applicable
- Small frequent meals
- Most fluid intake between meals rather than with meals
- Avoidance of lying down after eating (by sitting upright or taking a walk instead)
- Avoidance of eating or drinking for at least 2 to 3 hours before bedtime
- Elevation of bed head (for nocturnal symptoms)
- Weight reduction if appropriate

If symptoms persist in spite of the above measures:

GIVE:
- Magnesium trisilicate 10 to 20 mL orally, as required

In those patients with severe reflux in whom symptoms persist:

GIVE:
- Ranitidine 300 mg orally, once daily as required

If symptoms persist, increase dose to:
- Ranitidine 300mg orally bd

Patients with GORD rarely need endoscopy but there are some ‘Alarm symptoms’ and clinical history which might indicate more serious disease. Endoscopy should be considered in the following situations:

### Alarm symptoms
- Severe anaemia
- Dysphagia/odynophagia (difficult/painful swallowing)
- Haematemesis and/or melaena
- Vomiting
- Weight loss

### Significant history
- Short history of symptoms
- Severe/frequent symptoms
- Change in symptoms
- Older age
3.1.2 Gastro-oesophageal reflux in pregnancy
Symptoms of gastro-oesophageal reflux are common in pregnancy and existing symptoms are often exacerbated. There is evidence to recommend small, frequent and low-fat meals.

3.1.3 Gastro-oesophageal reflux in children
Regurgitation is common in infants less than 6 months old and tends to improve with age. It is considered pathological when it leads to complications such as oesophagitis, haematemesis, aspiration, and apnoea or growth failure. Irritability may occasionally be related to gastro-oesophageal reflux and oesophagitis.

Most infants with otherwise uncomplicated gastro-oesophageal reflux do not require specific therapy. Breast feeding is the best way to avoid the problem. Where it is thought necessary, simple measures should be used:

- Position the infant on its side when sleeping or feeding
- Slightly elevate the head of the cot
- Thicken feeds with mashed root vegetables or very soft cooked rice

The consistency should be similar to runny custard. Expressed breast milk may be mixed with thickened food and given by bottle.

Metoclopramide should not be used in childhood reflux disease as it has been associated with significant dystonic reactions.

4. Helicobacter pylori, NSAIDs and peptic ulcer disease

*Helicobacter pylori* and nonsteroidal anti-inflammatory drugs (NSAIDs) e.g. ibuprofen, indomethacin and including aspirin, are the 2 most important risk factors for peptic ulcer disease and upper gut bleeding.

The prevalence of infection is higher in older people, those with lower socioeconomic status and the institutionalised. The likelihood of infection is related most strongly to living conditions in childhood (when most acquisition occurs) and is more frequent in family members of an infected person and where there is a family history of peptic ulcer disease or gastric cancer.

4.1 *H. pylori* gastritis and symptoms

Most people infected with *H. pylori* are asymptomatic but infection confers a lifetime risk of peptic ulcer disease of 15% to 20%, and of gastric cancer of up to 2%. All people infected develop active chronic gastritis, although there is an inconstant relationship between the presence of *H. pylori* gastritis and symptoms. Thus, gastritis is a pathological, not a clinical diagnosis.

Unlike patients with ulcers, only a minority of people with *H. pylori* gastritis and symptoms (nonulcer dyspepsia) will have sustained relief of their symptoms after eradication therapy. Therefore it should not be given routinely.

4.2 *H. pylori* and peptic (duodenal and gastric) ulcer disease

Most duodenal ulcers and about two-thirds of gastric ulcers have been attributed to *H. pylori* infection. NSAID use accounts for most other ulcer disease.

Epigastric pain or discomfort, often relieved by antacids, is the most common presentation and may be accompanied by nausea, vomiting and heartburn. There is considerable overlap with symptoms of other upper
gastrointestinal disorders, particularly nonulcer dyspepsia or gastro-oesophageal reflux and dual pathology with ulcer and reflux may occur.

There are a number of circumstances where eradicating *H. pylori* may confer benefit, by reducing current or long-term risks of ulcer or cancer. The indications for eradication therapy in current consensus guidelines are summarised below.

### Indications to treat *H. pylori* infection

<table>
<thead>
<tr>
<th>Indication</th>
<th>Benefits of treatment</th>
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<tbody>
<tr>
<td>Endoscopically proven duodenal or gastric ulcers</td>
<td>heals ulcers and reduces relapse</td>
</tr>
<tr>
<td><em>H. pylori</em> associated gastric ulcers</td>
<td>heals ulcers and reduces relapse</td>
</tr>
<tr>
<td>Mucosa associated lymphoma</td>
<td></td>
</tr>
<tr>
<td>Severe chronic dyspepsia</td>
<td>may reduce symptoms and long-term risks of peptic ulcer disease and gastric cancer</td>
</tr>
<tr>
<td>NSAID and aspirin users with evidence of bleeding or very severe symptoms</td>
<td>reduces risks of peptic ulcer disease and gastric bleeding</td>
</tr>
<tr>
<td>patients requiring long-term acid suppression</td>
<td>reduces progression of intestinal metaplasia</td>
</tr>
<tr>
<td>close relatives of patients with gastric cancer</td>
<td>reduces long-term risk of gastric cancer</td>
</tr>
</tbody>
</table>

Metronidazole-resistant *H. pylori* has been noted in many overseas countries but currently there is no evidence it occurs in Kiribati.

For first line therapy use:
- **Ranitidine 300mg orally once daily (nocte) x 14 days PLUS**
- **Amoxycillin 500mg orally every 8 hours x 14 days PLUS**
- **Metronidazole 400mg orally every 8 hours x 14 days**

Another regimen with higher efficacy (slightly more expensive) but with better compliance is:
- **Omeprazole 20mg orally 12 hourly x 14 days PLUS**
- **Amoxycillin 500mg 8 hourly x 14 days PLUS**
- **Metronidazole 400mg orally 8hourly x 14 days**

For patients hypersensitive to Penicillin, substitute Amoxycillin with:
- **Tetracycline 500mg every 6 hours**

### 4.3 NSAID-induced ulcers

Of the NSAIDs available on the Kiribati EDF only indomethacin and regular, high dose aspirin are major risk factors.

Low-dose aspirin use for cardiovascular disease does increase the risk of peptic ulcer but not sufficiently to require eradication therapy unless there is evidence of bleeding.

### 5. Biliary and pancreatic disorders

#### 5.1 Biliary colic

Patients presenting with severe upper abdominal pain and who have gallstones on ultrasound usually require narcotic analgesia for pain control and consideration for subsequent laparoscopic or open cholecystectomy.
USE:
• Morphine 10 to 15 mg IM, 3- to 4-hourly
OR
• Morphine 0.1 mg/kg IV, titrated to effect, followed by morphine 0.05 to 0.1 mg/kg/hour IV, by continuous infusion

5.2 Acute cholecystitis

Patients with acute cholecystitis usually present with upper abdominal pain and fever. They require narcotic analgesia and antibiotics.

Where possible, do culture and sensitivity tests. Surgery may be indicated in addition to antibiotics.

Enterobacteriaceae, enterococci and anaerobes are usual pathogens.

Empirical treatment:
• Ampicillin 1g IV 6 hourly for 10-14 days
  PLUS
• Gentamicin 240mg IV once daily for 10-14 days (maintenance dose adjusted for renal function)
  PLUS
• Metronidazole 500mg suppository PR 12 hourly for 10-14 days OR less severe cases: 400mg orally 8 hourly

5.3 Ascending cholangitis

Ascending cholangitis is usually associated with Gram-negative sepsis and prompt antibiotic treatment, after collection of blood cultures, is essential. If biliary obstruction persists, urgent drainage should be undertaken.

GIVE:
• Antibiotics as for cholecystitis

Unrelieved biliary obstruction may potentiate aminoglycoside toxicity for courses longer than 72 hours. This effect occurs almost exclusively in patients with initial bilirubin levels above 85 micromol/L.

5.4 Acute pancreatitis

Acute pancreatitis is diagnosed by a combination of suggestive clinical features and a plasma amylase concentration that is usually at least 5 times greater than the upper limit of the reference range. Most episodes of acute pancreatitis are due to prolonged excessive alcohol use, are associated with gallstones (particularly bile duct stones), or are idiopathic.

The mortality is approximately 5% and is largely restricted to patients with severe necrotising pancreatitis.

Factors associated with an adverse outcome include:
• Advanced age
• Obesity (body mass index greater than 30)
• Hypotension
• A high white cell count, hypoxaemia
• Impaired renal function
• Hypocalcaemia
• Hyperglycaemia
- Elevated lactate dehydrogenase (LDH) levels
- Low albumin levels
- A grossly elevated ESR

The degree of elevation of the amylase or the lipase levels is not an adverse prognostic indicator.

Pain is associated with all grades of severity of pancreatitis.

Pancreatitis may rarely be induced by drugs.

E.g. azathioprine, carbamazepine, corticosteroids, enalapril, erythromycin, frusemide, hydrochlorothiazide, mercaptopurine, oestrogens, opioids, paracetamol, rifampicin, sodium valproate, sulphasalazine and tetracycline.

Management

Mild to moderate pancreatitis

Non drug treatment

In mild to moderate pancreatitis, cease oral fluids and food. Administer intravenous fluids with careful monitoring of hydration and urine output.

In the absence of complicating factors (e.g. acute cholecystitis) adequate analgesia is the mainstay of management. There is no evidence to support the belief that morphine causes biliary spasm.

GIVE:

- Morphine 10 to 15 mg IM, 3- to 4-hourly

If vomiting is a significant problem, insert a nasogastric tube. If antiemetic drugs are needed, use:

- Metoclopramide 10 mg IM or slow IV, 8-hourly as required
  OR
- Prochlorperazine 12.5 mg IM or IV, 4- to 8-hourly lipase levels as required

Food can be re-introduced when pain subsides.

Severe pancreatitis

Patients with severe pancreatitis should be managed in high-dependency or intensive therapy units with facilities for central venous pressure monitoring, arterial monitoring and ventilatory assistance. Therapy, in addition to that for mild pancreatitis, may include the following:

- aggressive fluid replacement involving infusion of large volumes to maintain intravascular volume
- parenteral nutrition
- insulin for the treatment of acute diabetes
- infusion of calcium gluconate for the rare patient with symptomatic hypocalcaemia

5.5 Chronic pancreatitis

Chronic alcohol use is the most common cause of chronic pancreatitis. Hyperlipidaemia and hypercalcaemia should be excluded as primary causes for pancreatitis and imaging should be undertaken to exclude pseudocyst formation.

The presence of pancreatic calcification on either plain abdominal X-ray or computerised tomography is diagnostic of chronic pancreatitis but is not necessarily present in all individuals.

Common complications of chronic pancreatitis are pain, malabsorption and diabetes.

Pain in chronic pancreatitis

In the management of pain in chronic pancreatitis:
• Cessation of alcohol is essential and may be all that is required to control pain

If this is insufficient, analgesia as in the World Health Organization analgesic ‘3-stage ladder’ for chronic pain can be instituted.

6. Liver disorders

6.1 Drug-induced liver disease

Drug-induced liver dysfunction is under diagnosed. A careful history of medications (both prescribed and non-prescription) and traditional herbal, and other, treatments or dietary supplements should be taken in any patient with symptoms suggestive of liver dysfunction and/or with abnormal liver function tests.

In most cases the cause is an unpredictable hypersensitivity or immunologic response which is not dose-related, and can occur at variable times after exposure (or re-exposure) to the drug.

• Drugs and herbal medications can cause either predominantly hepatocellular (elevated ALT and AST) or cholestatic injury (elevated ALP and bilirubin) or a mixed picture. They can also cause both acute and chronic liver abnormalities

• Examples of drugs and herbal medications known to cause hepatocellular toxicity are paracetamol (usually in overdose), black cohosh, kava (alcoholic extract or tablets) and NSAIDs

• Many drugs (e.g. enalapril, nitrofurantoin, phenytoin and the sulfonamides) cause a mixed pattern of liver dysfunction.

In nearly all cases the liver abnormalities resolve on cessation of the offending agent.

6.2 Acute hepatitis

Acute viral hepatitis

General management principles

Acute viral hepatitis may be caused by hepatitis A, B, C, D or E, or occasionally by cytomegalovirus and Epstein-Barr virus.

General supportive care forms the basis of treatment.

Sedatives and nonsteroidal anti-inflammatory drugs should be avoided and patients should be advised to cease alcohol until liver function tests (LFTs) return to normal. The oral contraceptive pill may prolong jaundice and should be ceased until the patient recovers.

Severe liver failure is a rare complication of acute hepatitis and such patients need intensive monitoring of liver function (International Normalised Ratio—INR—{the “prothrombin time”} is the most sensitive marker) and supportive medical care.

Acute hepatitis B

Ninety-five per cent of immunocompetent adults infected with hepatitis B acutely will clear the virus and become hepatitis B surface antigen (HBsAg) negative and hepatitis B surface antibody (HBsAb) positive. Less than 1% will develop fulminant hepatic failure.
Acute hepatitis C

Very few cases of acute hepatitis C are recognised, because significant symptoms or signs, such as jaundice, are absent in the majority of cases.

6.3 Chronic viral hepatitis

Chronic viral hepatitis is a major cause of end-stage liver disease and hepatocellular carcinoma. It is most often caused by hepatitis B (HBV) or hepatitis C (HCV). A small number of individuals with hepatitis B are co-infected with hepatitis D.

Hepatitis A and E never progress to chronic disease.

6.4 Acute alcoholic hepatitis

Alcohol excess can lead to either acute or chronic liver disturbance.

Cessation of alcohol intake is the major goal of therapy and will lead over time to stabilisation and/or improvement in liver function.

Acute alcoholic hepatitis is usually characterised by high fever, hepatic pain and tenderness and can be associated with encephalopathy. Wbc and aminotransferase (AST), are elevated. Nutritional support including enteral therapy has been shown to be beneficial.

Clinical trials have demonstrated that in a select group of subjects with encephalopathy due to severe acute alcoholic liver failure, prednisolone can lead to a reduction in mortality.

6.5 Complications of liver disease

6.5.1 Cirrhosis

Regardless of aetiology, chronic liver disease may progress to cirrhosis and portal hypertension with the development of specific complications requiring intervention.

The haemodynamic changes of cirrhosis result in fluid retention and ascites, which become progressively more difficult to control as liver disease severity worsens. Patients with ascites are at risk of further complications such as spontaneous bacterial peritonitis and hepatorenal syndrome.

Portal hypertension commonly results in the development of oesophageal varices, which may rupture causing severe gastrointestinal bleeding.

Hepatic encephalopathy may result from severe liver failure, but may also develop in patients with large spontaneous portosystemic shunts although with relatively preserved hepatic synthetic function.

Osteoporosis and vitamin D deficiency are commonly associated with cirrhosis. Patients with cirrhosis have an annual risk of development of hepatocellular carcinoma of 2% to 5%.

6.5.2 Ascites

Development of ascites

In cirrhosis, ascites occurs because of elevated pressures in the portal vein (portal hypertension), low plasma concentrations of albumin and enhanced renal retention of sodium.

Large-volume ascites is usually obvious on physical examination, but smaller amounts are often only visible on imaging.

Cirrhotic ascites has the characteristics of a transudate with a substantial difference (greater than 11 g/L) between the serum and ascitic concentrations of albumin.

The presence of an exudate suggests the possibility of complications such as spontaneous bacterial peritonitis or hepatocellular carcinoma.

Ascites may develop progressively as liver disease worsens or suddenly as a result of new complications such as portal vein thrombosis, hepatocellular carcinoma or other malignancy. Patients with new-onset ascites or a
sudden deterioration should therefore be fully evaluated for such an underlying precipitant or a complication such as spontaneous bacterial peritonitis.

The aim of treatment is to improve symptoms, not to completely remove the ascites.

**Mild ascites**
Patients with mild ascites should be advised to take a salt-reduced diet (aiming for 50 to 100 mmol sodium per day) and, if possible, be counselled by a dietitian.

If ascites is causing abdominal discomfort or distension,

**GIVE:**
- Spironolactone 25 to 100 mg orally, daily in the morning
  (Monitor serum electrolytes and renal function)

**Moderate to severe ascites**
Patients with moderate to severe ascites should be able to be managed as outpatients provided there are no other complicating factors. In some circumstances, patients may require admission to hospital for bed rest, daily weighing, and monitoring of serum electrolytes and renal function. A sample of ascitic fluid should be examined to exclude spontaneous bacterial peritonitis.

**GIVE:**
- Spironolactone 100 mg (child: 2 mg/kg up to 100 mg) orally, daily for 1-2 weeks
  
  **THEN**
  - Increasing by 100 mg/day (child: 2 mg/kg/day up to 100 mg/day) every 4 to 7 days as required, to a maximum of 400 mg (child: 8 mg/kg up to 400 mg) orally, daily

In patients without significant peripheral oedema, weight loss should not exceed 1 kg/day.

If spironolactone alone is ineffective, **ADD:**
- Frusemide 40 mg orally, daily in the morning

Diuretics may precipitate hyponatraemia, changes in potassium levels and renal impairment. Frequent monitoring of electrolytes and renal function is therefore required with appropriate dos adjustment.

In patients with tense or refractory ascites, symptoms can be improved and hospital stays shortened by the drainage of large volumes of ascitic fluid—large-volume paracentesis (e.g. 5 to 10 L over 1 to 6 hours).

Care should be taken in patients with renal impairment due to the risk of precipitating hepatorenal syndrome.

It is essential to ensure an adequate intake of protein (1 to 1.5 g protein/kg/day has been recommended). Oral nutritional supplementation may be required.

**Intractable ascites**
Intractable ascites involves repeated paracentesis with the maximum tolerated dose of diuretics

**6.5.3 Spontaneous bacterial peritonitis**

**Diagnosis**
Spontaneous bacterial peritonitis (SBP) occurs in up to 20% of patients with ascites admitted to hospital.

SBP should be suspected when ascites increases in severity, particularly in the presence of fever, abdominal pain, abdominal tenderness and worsening encephalopathy.

The diagnosis is confirmed by an ascitic tap.

The diagnosis is established when the absolute white cell count of the ascitic fluid is greater than 500/mm³ and/or the neutrophil count is greater than 250/mm³ (neutrophilic ascites). Bacteria are rarely detected on Gram stain and the fluid should be cultured for 5 to 7 days although cultures are positive in only a minority of patients.

The causative organisms are most often enteric Gram-negative bacilli such as *Escherichia coli*, although *Streptococcus pneumoniae*, other streptococci and enterococci are encountered. Anaerobes are uncommon. Patients with culture-negative neutrophilic ascites should be treated as having SBP.
Treat patients with SBP, until culture results are available, with:

- **Ceftriaxone 1 g (child: 25 mg/kg up to 1 g) IV, daily**

Continue therapy until clinical signs of infection have resolved (usually for 5 to 10 days).

### 6.5.4 Bleeding oesophageal varices

Varices are enlarged submucosal, portosystemic veins that develop in response to portal hypertension. The only symptom is gastrointestinal bleeding.

The mortality from an acute bleed varies from 20% to 40%.

Patients should be referred urgently to surgeons for endoscopy and appropriate procedures.

#### Primary prevention of bleeding

Nonselective beta blockers reduce the risk of bleeding, probably due to reflex splanchnic vasoconstriction secondary to a fall in cardiac output.

**GIVE:**

- **Propranolol 20 mg orally, twice daily** - titrating up to 80 mg orally, twice daily (aim to reduce heart rate by 25% of the resting rate or to 60 bpm, whichever is the more rapid)

### 6.5.5 Hepatic encephalopathy

Hepatic encephalopathy is a syndrome of neuropsychiatric symptoms and signs which may develop in severe liver disease. These include changes in intellect, personality and emotions, sleep disturbances, and disorientation in time and space. A flapping tremor strongly supports the diagnosis of encephalopathy. Eventually coma may occur.

Encephalopathy occurs in both acute fulminant hepatic failure and in chronic liver disease, usually cirrhosis.

Contributors to encephalopathy include elevated blood concentrations of ammonia, high concentrations of false neurotransmitters (e.g. octopamine), and changes in the sensitivity of the brain to inhibitory neurotransmitters such as gamma-aminobutyric acid. Ammonia and false neurotransmitters are largely derived from gut bacteria and are at high concentrations in encephalopathy because of shunting of blood from the portal to the systemic circulation.

#### Management

##### Acute hepatic encephalopathy

Medical treatment of encephalopathy includes the recognition and correction of precipitating factors including renal impairment, gastrointestinal bleeding, infections and electrolyte disturbances.

Encephalopathy may be aggravated by sedatives and opioid analgesics.

Current drug therapy for encephalopathy reduces the absorption of toxic amines by decreasing numbers of colonic bacteria or by lowering the colonic pH.

For severe acute encephalopathy:

**GIVE:**

- **Lactulose 30 mL (child: 1 mL/kg up to 30 mL) orally, 1- to 2-hourly initially to induce a rapid laxative effect**

When a laxative effect has been achieved, reduce the dosage to:

- **Lactulose 30 mL (child: 1 mL/kg up to 30 mL) orally, 3 to 4 times daily**

Adjust the dose subsequently to produce 2 or 3 soft stools per day. In unconscious patients or patients who cannot swallow, lactulose may be given rectally or by nasogastric tube.

In the absence of a readily identifiable precipitant, empirical treatment for infection should be given:
• Ceftriaxone 1 g (child: 25 mg/kg up to 1 g) IV, daily

Chronic hepatic encephalopathy
For chronic encephalopathy, use:
• Lactulose 30 mL (child: 1 mL/kg up to 30 mL) orally, 3 to 4 times daily to produce 2 or 3 soft stools per day

Patients with chronic liver disease commonly suffer from significant malnutrition therefore protein restriction is not recommended.
Protein is usually withheld for the first 24 to 48 hours in acute severe encephalopathy but the protein intake should be progressively increased to normal as recovery occurs.

7. Constipation

Definition and aetiology
• No objective definition of constipation because of great individual variation in normal bowel habit
• Implies a diminished frequency of bowel motions and/or the passage of small hard stools
• Normal frequency of bowel motions varies from 3 times per day to twice per week
• Constipation is very common in the elderly (especially if immobile) and in patients on long term treatment with morphine

A person may complain of constipation if:
• Defecation occurs less frequently than usual
• Stools are harder than usual
• Defecation causes straining
• There is a sense of incomplete evacuation.

The major lifestyle factors that may contribute to constipation are:
• Inadequate dietary fibre
• Inadequate fluid intake
• Inappropriate bowel habits (ignoring the call to defecate)
• Inadequate activity/exercise

Some drugs may cause constipation, e.g.:
• amitriptyline
• chlorpromazine
• iron tablets
• opioids e.g. codeine, morphine
• prochlorperazine
• promethazine
• verapamil

Changing or stopping these drugs may be all that is required to restore normal bowel function.
Constipation in adults

Diet and lifestyle
Adults, especially if ambulant and otherwise healthy, should be encouraged to control their bowel activity by attention to diet and exercise. The diet should contain adequate amounts of fibre and adequate fluid to avoid dehydration. The fibre content of the diet should be increased gradually to avoid adverse effects such as bloating or flatulence.

Sources of fibre include:

- Vegetables especially green and leafy
- Corn, legumes e.g. lentils (dhali)
- Cassava, dalo, kumala, breadfruit
- Fruits with a skin especially pawpaw
- Wholegrain cereals and bread
- Nuts, grains, brown rice and seeds

Patients should be encouraged to drink 7 or 8 glasses of water a day –more on very hot days.

Physical exercise has been shown to reduce intestinal transit time and is believed to stimulate regular bowel movements.

Bulking agents
Bulk forming agents increase bulk and moisture in the stool. This then stimulates colonic activity. Rapid increases in dosage can result in flatulence and distension.

Osmotic agents
These work by drawing water into the gut lumen and hence increasing the water content of stools. They should be taken with fluid, preferably fruit juice to augment the osmotic effect. They work within 2 to 48 hours.

Bowel stimulants
These stimulate intestinal motility and can cause abdominal cramps. They should take effect within 6-12 hours and should not be used long term.

- Available in Kiribati EDL - bisacodyl suppository-5mg and 10mg- and tablet 5mg

Stool Softeners
These are not effective as sole treatment but can be useful if used in combination with other agents such as bowel stimulants.

Constipation in the older person
Bulking agents are effective for the ambulant elderly, whereas osmotic and stimulant laxatives are needed for those who are bed bound and those on opioids.

Laxatives should be prescribed whenever opioids are used. Agents of choice include combined stool softener with stimulant and osmotic laxatives.

If symptoms suggest impaction, and this is confirmed by rectal examination, enemas and suppositories may be needed to clear the rectum at the start of a bowel management program, especially if the person is bed bound.

Therapy should be tailored to suit individual patients, making one change at a time and allowing adequate time for this to have an effect (1 to 2 weeks) before instituting further changes.
Constipation in children
Frequency of bowel action varies widely in infants. Normal breastfed infants can pass a stool after each feed, or only once every 7 to 10 days. Bottle-fed infants and older children normally have a bowel action at least every 2 days.

Constipation in children can cause abdominal pain, reduced appetite and irritability. It may present with soiling due to overflow incontinence.

Management
- Education of parents and child with positive encouragement for passing stool
- Regular toileting (2 to 3 times daily, ensuring that the child can sit comfortably with feet supported)
- High-fibre diet
- Adequate fluid intake
- Adequate exercise

8. Diarrhoea

Diarrhoea is a term generally understood to mean an increased frequency of liquid or semi liquid stools. However the word means different things to different people and it is important to establish just what patients mean when they complain of diarrhoea.

Deviations from an individual’s usual pattern may be more important than the number of bowel motions per day.

The mechanisms that result in diarrhoea are varied and include increased secretion or reduced absorption of fluid and electrolytes by cells of the intestinal mucosa, and exudation due to inflammation of the intestinal mucosa. The former results in watery diarrhoea with loss of fluid and electrolytes. The latter leads to the presence of inflammatory cells and overt or occult blood in the stools.

Diarrhoea is a non-specific symptom of a wide range of gastrointestinal disorders, including viral, bacterial and protozoal gastrointestinal infections, adverse drug reactions, lactose intolerance, irritable bowel syndrome, spurious diarrhoea (constipation with overflow), inflammatory bowel disease, gastrointestinal malignancy and a variety of malabsorption syndromes. Diarrhoea can also be a manifestation of many systemic diseases, including thyrotoxicosis, diabetes and scleroderma.

All patients presenting with diarrhoea should be questioned about the relationship between symptoms and changes in medications.

8.1 Drugs commonly causing diarrhoea
- Antibiotics
- Colchicine
- Cytotoxic agents
- Laxatives (including secret use)
- Magnesium-containing antacids
- Metformin
- Nonsteroidal anti-inflammatory drugs

In children, it is important to remember that other conditions, such as infections (urinary tract) or surgical emergencies (appendicitis, intussusception) can cause acute vomiting and diarrhoea.

8.2 Infectious gastroenteritis
8.2.1 Viral infections

Adults

Most episodes of acute diarrhoea are due to viral infections, non-invasive bacteria or protozoa. Investigation or antibiotic therapy is not required in the normal host unless there is suspicion of an outbreak which requires preventive measures, or evidence to suggest invasion with a bacterial pathogen (e.g. persistent fever, bloody diarrhoea or rigors).

Adequate rehydration is the main treatment. If watery diarrhoea persists some form of electrolyte containing solution may be required.

**DRINK**
- At least 2-3 litres every 24 hours

Even in the presence of severe diarrhoea, water and salt continue to be absorbed by active sodium-glucose–coupled transport in the small intestine. Oral replacement solutions are effective if they contain balanced quantities of sodium, potassium, glucose and water.

Proprietary soft drinks and fruit juices are inadequate treatment for individuals in whom dehydration poses a significant risk (e.g. infants, children, the elderly and patients with renal disease).

**Children**

Most episodes of acute diarrhoea and vomiting are caused by a self-limiting viral infection, usually rotavirus. Children and infants in particular may rapidly become dehydrated during an episode of gastroenteritis.

Dehydration can cause death if not treated effectively
- Breastfeeding should be continued and increased where possible.
- Oral Rehydration Solution (ORS UNICEF) should be given

During the first 4 hours GIVE:

<table>
<thead>
<tr>
<th>Age*</th>
<th>Up to 4 months</th>
<th>4 months up to 12 months</th>
<th>12 months up to 2 years</th>
<th>2 years up to 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>&lt; 6kg</td>
<td>6-&lt;10 kg</td>
<td>10-&lt;12 kg</td>
<td>12-19 kg</td>
</tr>
<tr>
<td>Amount ORS in ml</td>
<td>200-400</td>
<td>400-700</td>
<td>700-900</td>
<td>900-1400</td>
</tr>
</tbody>
</table>

* Use the child’s age only when you do not know the weight. The approximate amount of ORS required (in ml) can also be calculated by multiplying the child’s weight (in kg) by 75.

- If profuse watery diarrhoea persists admit the child urgently to hospital
- Vitamin A should be administered to children with severe diarrhoea
- There is evidence to support the use of zinc supplements also

Antimotility drugs are never indicated for management of acute diarrhoea in infants and children.

Antimotility drugs may be of symptomatic benefit in adults with mild or moderate acute diarrhoea. Their most valuable role is in short-term control of symptoms during periods of maximum social inconvenience (e.g. travel and work).

They are contraindicated in patients with severe or bloody diarrhoea, where there is a possibility of invasive organisms, and in patients with severe inflammatory bowel disease because of the risk of toxic megacolon.

If an antimotility drug is considered appropriate, GIVE, if available:
• Loperamide 4mg orally initially, followed by 2mg orally after each unformed stool up to 16mg a day

8.2.2 Bacterial infections
Most cases of bacterial diarrhoea in adults and older children are self-limiting and do not require antibiotic therapy (e.g. *Campylobacter jejuni*, *Salmonella* species, enteropathogenic/enterotoxigenic *Escherichia coli*). The principal aim of treatment is to achieve and maintain adequate hydration. *Shigella* is common and may need antibiotics.

**Shigella** (moderate and severe dysentery only)
For moderate cases:
- Chloramphenicol 500mg orally / IV 6 hourly for 7 days
  OR
- Ciprofloxacin 500mg orally every 12 hours for 7 days (dose adjustment in renal impairment)

For severe cases:
- Ciprofloxacin IV 200mg (dose adjustment in renal impairment) every 12 hours for 7 days
  OR
- Ceftriaxone 2g IV once daily for 7 days

**Salmonella enteritis**
Antibiotic therapy is not generally advisable. Indicated in immunosuppressed or elderly people. Treat as for typhoid fever (see later) or based on antibiotics sensitivity for 5 days.

**Campylobacter enteritis**
Antibiotics are unnecessary in most cases. In severe cases:
- Erythromycin 500mg orally 6 hours for 7-10 days
  OR
- Ciprofloxacin 500mg 12 hourly for 7-10 days

Empirical Therapy
As for *shigella*

**Typhoid /paratyphoid fever**
Check sensitivity pattern with microbiologist. For empirical therapy:
- Chloramphenicol 500-750mg orally 6 hours for 14 days
  OR
- Amoxycillin 1g orally 8 hourly for 14 days

If the organism is found to be resistant to the above, change to:
- Ciprofloxacin 500mg orally 12 hours for 14 days

**Cholera**
Is not endemic in Kiribati but sporadic cases have come into the country when visitors arrive from endemic areas.

**Rehydration** is the basis of treatment.
Antibiotic therapy reduces the volume and duration of diarrhoea. USE:
- Doxycycline 100 mg (child greater than 8 years: 2.5 mg/kg up to 100 mg) orally, 12-hourly for 3 days
  OR
- Ciprofloxacin 1 g (child: 25 mg/kg up to 1 g) orally, as a single dose

For pregnant women and children, instead of doxycycline use:
• Amoxycillin 250 mg (child: 10 mg/kg up to 250 mg) orally, 6-hourly for 5 days
Antibiotic-resistant strains are now common in some regions. In the event of clinical failure, treatment should be guided by sensitivity results.

8.2.3 Antibiotic-associated diarrhoea
In most cases of antibiotic-associated diarrhoea, no pathogen is identified. *Clostridium difficile* is responsible in a minority of cases.

- Cease treatment with any antibiotic likely to be causing the symptoms

For mild cases:
- Observe patients after stopping antibiotic.

For moderate cases consider:
- **Metronidazole 400mg orally 8 hours for 7-10 days**

For severe and relapsing cases:
- **Metronidazole as above** and if no progress (and the drug is available)
- **Vancomycin 125mg orally 6 hourly for 7-14 days**

The emergence of Vancomycin resistant enterococci makes it essential to reserve vancomycin for severe cases unresponsive to Metronidazole. Currently not on the Kiribati EDL.

Contact Pharmacist-in-charge regarding preparation of oral vancomycin.

8.3. Parasitic Infections.

**Intestinal Amoebiasis**
- **Metronidazole 800mg 8 hourly for 6-10 days**
  
  For hepatic involvement, metronidazole should be continued for 14 days.

**Giardiasis (Giardia lamblia or intestinalis)**
Treatment of patients with asymptomatic passage of giardia cysts is unwarranted.

For symptomatic patients, use:
- **Metronidazole 400mg orally 8 hourly for 7 days**
  
  (Child: 10 mg/kg (up to 400mg) orally, daily for 3 days)

If the above treatment fails, repeat the primary course or use a longer course of metronidazole.

**Worms (Helminths)**

Hookworm, roundworm, threadworm & whipworm:
- **Mebendazole 100mg orally twice daily x 3 days**

Mebendazole should not be used in the 1st trimester of pregnancy or in children under 6 months of age. In such cases Pyrantel can be used.
- **Pyrantel 20mg/kg up to 750mg orally single dose, repeat after 7 days if heavy infection**

8.4 Chronic diarrhoea

Chronic diarrhoea is a symptom of a large number of gastrointestinal disorders, including the irritable bowel syndrome, diverticular disease, spurious diarrhoea (constipation with overflow), inflammatory bowel disease, malabsorption, drugs, chronic infections and gastrointestinal malignancy.

Diarrhoea can also be a manifestation of many systemic diseases, such as thyrotoxicosis, diabetes and scleroderma.
Investigation and management is guided by the nature of the diarrhoea; whether it is watery, contains blood or is suggestive of steatorrhoea. Management is usually directed at the underlying cause rather than at the symptom of diarrhoea. However, antimitotility drugs are sometimes useful for control of symptoms when treatment of the underlying cause is ineffective or if the cause is unknown.
9. Irritable bowel syndrome

Irritable bowel syndrome (IBS) is a common condition. Its aetiology and pathogenesis are not known but altered bowel motility, visceral hypersensitivity and psychosocial factors all contribute to symptoms.

The diagnosis is based on the presence for at least 12 weeks (not necessarily consecutive) in the preceding 12 months of unexplained abdominal discomfort or pain with at least 2 of the following 3 features:

- Pain is relieved by defecation
- Onset of pain is associated with a change in bowel frequency—either diarrhoea or constipation
- Onset of pain is associated with a change in the form of the stool—loose, watery or pellet-like

It is important to exclude other conditions and some features of irritable bowel syndrome require further consideration and/or investigation:

<table>
<thead>
<tr>
<th>Age of onset more than 40 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history of:</td>
</tr>
<tr>
<td>bowel cancer</td>
</tr>
<tr>
<td>coeliac disease</td>
</tr>
<tr>
<td>inflammatory bowel disease</td>
</tr>
</tbody>
</table>

Clinical symptoms/signs:
- abnormality on examination of abdomen
- anaemia
- fever
- nocturnal diarrhoea
- persistent mouth ulcers
- rectal bleeding
- significant weight loss
- steatorrhoea
- vomiting or severe pain

There is limited evidence to support the efficacy of therapies commonly used to treat patients with IBS.

Many patients report some benefit from complementary or alternative medicines. It is particularly important to take a history of ingestion of complementary or alternative therapies in IBS, as use is so common.

Dietary therapy

There is no standard diet which suits all patients and increasing dietary fibre is not always beneficial. Some food components may contribute to symptoms. These should be identified for each patients and appropriate dietary advice given.

Pharmacological therapies

There is no agent which works effectively in all patients.

Diarrhoea-predominant IBS

Exacerbations of diarrhoea in adults may be controlled in the short term by intermittent use of antidiarrhoeal agents.

The use of codeine-containing compounds to control diarrhoea is to be discouraged because of the risk of dependence.

- Loperamide may be effective in the short-term
**Constipation-predominant IBS**

Treatment of constipation-predominant IBS is similar to the treatment of constipation in general. Initial treatment should be to increase fibre and fluid intake and encourage regular exercise. Laxatives may be added as necessary but use of stimulant laxatives should be discouraged and prolonged use of any laxative should be avoided if possible.

**10. Diverticular disease**

**Diverticulosis**

Diverticula are herniations of the colonic mucosa through the muscle layer of the large bowel. Most occur in the sigmoid and descending colon, but any part of the large bowel can be affected. Right-sided diverticular disease affects younger patients.

The incidence of diverticula increases with age, and is usually asymptomatic. A few patients develop colicky lower abdominal pain or an irregular bowel habit, commonly alternating constipation and diarrhoea.

- There is no good evidence that a high-fibre diet makes any difference to symptoms
- Maintaining a soft stool is the primary strategy to prevent development of diverticulitis

**Diverticulitis**

Diverticulitis occurs when a diverticulum becomes inflamed. Clinical outcomes range from a sub clinical local inflammation to generalised peritonitis associated with perforation.

It usually presents as left lower quadrant pain, often with an associated alteration to bowel habit, and fever. Rebound tenderness suggests a degree of peritoneal involvement.

**Mild diverticulitis**

Seventy-five per cent of episodes of diverticulitis will be uncomplicated and do not need hospital admission. These patients should commence a soft diet and remain on this while symptomatic.

For mild infection GIVE:

- **Amoxycillin 500mg 8-hourly for 5 to 10 days**
- **Metronidazole 400 mg orally, 12-hourly for 5 to 10 days**

For patients with immediate penicillin hypersensitivity use:

- **Metronidazole 400 mg orally, 12-hourly for 5 to 10 days**
- **Trimethoprim+sulfamethoxazole 160+800 mg orally, 12-hourly for 5 to 10 days**

Fewer than 30% of patients with diverticulitis will have a second episode.

**Severe or complicated diverticulitis**

Patients with significant systemic features (high fever, marked rebound), or those with mild disease who fail to respond to outpatient management, should be admitted to hospital.

- Bowel rest, with IV fluids and IV antibiotics should be started
Where possible, do culture and sensitivity tests. Surgery may be indicated in addition to antibiotics. Enterobacteriaceae, enterococci and anaerobes are usual pathogens. *Strep anginosus* (milleri) is sometimes isolated in which case high dose Penicillin G will be required.

Empirical treatment:

- **Ampicillin 1g IV 6 hourly for 10-14 days**
  PLUS
- **Gentamicin 240mg IV once daily for 10-14 days (maintenance dose adjusted for renal function)**
  PLUS
- **Metronidazole 500mg suppository PR 12 hourly for 10-14 days OR less severe cases: 400mg orally 8 hourly**

For *streptococcus anginosus*

- **Penicillin G 1.8g (3 mega unit) every 4 hours for 21 days**

**Surgical management of diverticulitis**

Acute surgical intervention should be considered in the following circumstances:

- Peritonitis associated with perforation
- Abscess, not amenable to percutaneous drainage
- Bowel obstruction

If a fistula has formed between a diverticulum and an adjacent organ, elective repair is indicated.

**11. Inflammatory bowel disease**

Ulcerative colitis and Crohn’s disease are chronic, relapsing inflammatory diseases of the gut that may be associated with a range of extra-intestinal manifestations. Both appear to be very uncommon in Kiribati and they are not further discussed in these guidelines.

**12. Ileostomies and colostomies**

An ileostomy is a permanent or temporary opening of the distal small bowel onto the surface of the abdomen. Adaptation to loss of the absorptive function of the colon occurs over a period of weeks following creation of an ileostomy.

Ileostomy losses may be as high as 2000 mL per day in the first few days and patients can rapidly become dehydrated, especially in hot weather; children are particularly at risk.

- **Salt supplements and/or intravenous replacement fluids and electrolytes may be necessary.**

Fluid losses usually decrease to 750 to 1000 mL per day or less, over approximately 6 weeks. The volume of stoma output is related to the site of the stoma—the more proximal the stoma, the higher the output.

A colostomy is a permanent or temporary opening of the colon onto the surface of the abdomen. A sigmoid colostomy is formed from the sigmoid colon, a descending colostomy from the descending colon and similarly for transverse and ascending colostomies. The output of a colostomy is also affected by adaptation, becoming more formed over several weeks.
### Management of problems associated with ileostomies and colostomies

<table>
<thead>
<tr>
<th>Problem</th>
<th>Possible causes</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin irritation</td>
<td>leakage around the appliance</td>
<td>re-size appliance opening</td>
</tr>
<tr>
<td></td>
<td>inflamed hair follicles due to shaving</td>
<td>use waxing/scissors to keep hairs short, shave with an electric shaver</td>
</tr>
<tr>
<td></td>
<td>use of harsh soaps or disinfectants around the stoma</td>
<td>Use water or cleansing agents provided by the ostomy manufacturers. Do not use disinfectants</td>
</tr>
<tr>
<td></td>
<td>frequent removal of the appliance</td>
<td>avoid unnecessary changes</td>
</tr>
<tr>
<td></td>
<td>cellulitis/candidiasis (thrush)</td>
<td>skin/wound swab—antibiotic therapy may be required</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>unrelated diarrhoeal illness</td>
<td>identify and treat cause</td>
</tr>
<tr>
<td></td>
<td>drug adverse effect</td>
<td>monitor fluid and electrolyte status and supplement fluids and electrolytes</td>
</tr>
<tr>
<td></td>
<td>Food</td>
<td>review medications</td>
</tr>
<tr>
<td>Bleeding</td>
<td>vigorous cleaning of stoma</td>
<td>advise gentle cleaning</td>
</tr>
<tr>
<td></td>
<td>proximal gastrointestinal bleeding</td>
<td>medical review</td>
</tr>
<tr>
<td>Reduced stoma output</td>
<td>fibrous foods</td>
<td>reduce intake of fibrous foods</td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td>treat as any constipation</td>
</tr>
<tr>
<td></td>
<td>bowel obstruction</td>
<td>surgical review</td>
</tr>
<tr>
<td>Surgical complications</td>
<td>parastomal abscess, hernia, prolapse, retraction or stenosis</td>
<td>surgical review</td>
</tr>
</tbody>
</table>

### 13. Disorders of vitamin and mineral metabolism

Although some people regularly take over-the-counter vitamin and mineral supplements, there is very little evidence for this practice in the general population. There are some groups in the community who are at a greater risk of developing micronutrient deficiency due to inadequate intake: pregnant women, the elderly, vegans, individuals with a high alcohol intake and individuals consuming inadequate amounts of fruits and vegetables. Supplementation of appropriate nutrients may be beneficial in such individuals.

#### Vitamin deficiencies

**Vitamin A deficiency**

Vitamin A deficiency is common in the developing world. The most important effects of vitamin A deficiency are night blindness, complete blindness and xerophthalmia.

In Kiribati, lactating mothers and their children may be vitamin A deficient. For this reason it is recommended that children, who present with measles or severe dehydration, should be given vitamin A supplements if child has not received any supplement in the past 6 months.

**GIVE**

- 9 months up to 12 months  
  Vitamin A capsules 50,000 IU orally stat
- 1 to 5 years  
  Vitamin A capsule 100,000 IU orally stat
All adults and children should be encouraged to include foods which are rich in vitamin A in their diet e.g.:

- preformed vitamin A (retinol): only in animal-derived foods such as liver, butter, cheese, whole milk, egg yolk and fish
- provitamin A carotenoids including beta-carotene: found in green leafy vegetables and orange/yellow-coloured fruits and vegetables (e.g. carrot, pumpkin, kumela, apricot, peach, pawpaw, mango, red capsicum)

**Vitamin B₁ (Thiamine) deficiency**

Thiamine (vitamin B₁) deficiency is a significant problem with excessive alcohol use. Peripheral neuropathy is the mildest and most common manifestation of deficiency. For treatment and prevention of deficiency:

**GIVE**

- Thiamine HCl 500 mg orally, daily

Wernicke’s encephalopathy is a life-threatening complication of thiamine deficiency characterised by ophthalmoplegia, ataxia and confusion. Immediate therapy is required to minimise irreversible neurological damage with progression to Korsakoff’s psychosis.

If patients who consume large amounts of alcohol need to be given glucose, this should be accompanied by thiamine, as glucose metabolism may further deplete thiamine stores and precipitate.

**GIVE:**

- Thiamine HCl 100 to 200 mg IV, daily for 3 days

**FOLLOWED BY**

- Thiamine 500 mg orally, daily

Patients known to be heavy drinkers should be encouraged to eat some or all of the following foods rich in vitamin B₁:

- Yeast extract (e.g., Marmite, Vegemite)
- Wheat germ, wheat bran, nuts
- Liver, kidney, lean pork
- Wholemeal flour, wholemeal breads, sesame seeds

**Vitamin B₁₂ deficiency**

Dietary vitamin B₁₂ binds to intrinsic factor in the upper gastrointestinal tract and the complex is absorbed in the terminal ileum. It is essential for haematopoiesis and deficiency of vitamin B₁₂ causes megaloblastic anaemia. Vitamin B₁₂ also has a role in the maintenance of myelin in the nervous system. Severe deficiency causes degeneration of the spinal cord, which may be irreversible, and can also lead to peripheral neuropathy, optic atrophy and dementia.

Vitamin B₁₂ deficiency is usually caused by the absence of intrinsic factor (e.g. pernicious anaemia or gastrectomy), or by resection or disease of the terminal ileum. Milder vitamin B₁₂ deficiency can result from a combination of inadequate dietary intake, poor gastric mixing and small bowel bacterial overgrowth, particularly in the elderly. Pure dietary deficiency is rare, and is usually only seen in strict vegans.

If vitamin B₁₂ deficiency is associated with severe anaemia or neurological symptoms, vitamin B₁₂ should be administered in high doses without delay. Various regimens have been reported but a total dose of 3 to 10 mg should be administered over 2 to 4 weeks:
GIVE:

- Hydroxocobalamin 1 mg IM, on alternate days for 2 weeks

OR

- Hydroxocobalamin 1 mg IM, twice weekly for 3 weeks

After the first injection, malaise usually improves within 2 days while the reticulocyte count peaks at about 7 days. Serum iron falls after 1 to 2 days in some patients who may need iron supplements. Potassium supplements may also be required. The haemoglobin normally increases by about 10 g/L per week. The neuropathy improves slowly with therapy but some patients will have residual defects, particularly those with a long history of neurological symptoms.

If macrocytic or megaloblastic anaemia is identified vitamin B₁₂ MUST be given before folate to avoid precipitating peripheral neuropathy.

Most patients with vitamin B₁₂ deficiency require maintenance therapy for life.

GIVE:

- Hydroxocobalamin 1 mg IM, once every 3 months

Dietary Vitamin B₁₂ is only contained in foods of animal origin:

- Offal (liver, kidney), lean meat
- Oysters, fish, seafood
- Eggs, milk
- Fortified soy milk

**Folate deficiency**

Folate or folic acid is widespread in the diet, but is particularly susceptible to destruction during cooking. Absorption of folate occurs primarily from the duodenum and jejunum. Deficiency can occur due to malabsorption drugs such as methotrexate and sulfasalazine, and haematological conditions associated with an increased cell turnover.

Deficiency of folate causes megaloblastic anaemia but not neurological symptoms. Dietary deficiency is not uncommon, particularly among the elderly and those with excessive alcohol use.

**Pregnancy** is a common cause of deficiency as the requirement for folate doubles. An adequate intake of folate during the early part of pregnancy has been shown to reduce the risk of neural tube defects. All women planning a pregnancy are advised to consume a diet adequate in folate and/or take a supplement containing:

- Folic acid 5 mg orally, daily from at least 1 month prior to conception (if possible) and in the first 3 months of pregnancy

Patients with deficiency should be advised to eat increased quantities of the following foods:

- Yeast extract (e.g. Marmite, Vegemite)
- Green leafy vegetables
- Whole grains, peas, nuts, food cooked with fortified flour
- Avocado, offal (liver, kidney, heart)

Ongoing supplementation is recommended if requirements remain elevated and/or dietary intake remains inadequate.

Iron deficiency is common in adults, including women of childbearing age, and children in Kiribati—often associated with hookworm infestation.

Deficiency in these groups may also be the result of marginal dietary intake combined with high physiological requirements. The importance of adequate dietary intake of iron should be explained in such cases. There is a much higher rate of iron deficiency in infants and toddlers where high cows’ milk intake is encouraged or
allowed. Even in the absence of anaemia, iron deficiency produces adverse effects including fatigue and immune dysfunction. Impaired cognitive development has been found in children who become frankly anaemic due to iron deficiency.

Proven iron deficiency in other groups is almost always due to pathological blood loss, usually from the gastrointestinal tract. These patients should be investigated for sources of gastrointestinal bleeding.

In adults GIVE:

- **Ferrous sulfate 200-600mg orally once daily**
  (Should be continued for 3-6 months to replenish iron stores)

In children or the elderly who have difficulty swallowing GIVE:

- **Ferrous sulfate elixir 200 mg/5 mL) 15 to 30 mL (child: 0.3 to 0.5 mL/kg) orally, once daily**
- **For children with severe deficiency, up to 1 mL/kg daily in 2 to 3 divided doses may be needed, and should be continued for 3 months after the haemoglobin has returned to normal to replenish stores**

  An iron overdose can be fatal in a child and supplements should be stored in a locked cabinet.

Adverse effects such as nausea, bloating, constipation and diarrhoea may be minimised by introducing therapy in a gradual manner. Patients should be warned that oral iron supplements cause black stools.

Foods with high iron content include:

- **Haem sources (most absorbable):**
  - lean red meat, offal (liver, kidney, heart), chicken, fish

- **Nonhaem sources:**
  - leafy green vegetables,
  - iron-fortified breakfast cereals, wholemeal bread,
  - legumes, eggs, cocoa, dried fruit

**Zinc**

Zinc deficiency is associated with reduced growth in children, alopecia, diarrhoea, delayed sexual maturation, impaired appetite, impaired immune function and an eczematous skin rash especially on the face and in body flexures. Deficiency is usually due to inadequate intake in food.

GIVE children:

- **Up to 6 months 10mg daily for 10-14 days**
- **6 months and over 20 mg daily for 10-14 days**
14. Pregnancy and breastfeeding

Pregnancy

Prescribed medication
A drug can have more than one harmful effect on the foetus. Individual effects depend on the time of foetal exposure to the drug.

During the first 2 weeks after fertilisation and prior to full implantation, the embryo is thought to be resistant to any teratogenic effects of drugs. This is because there is no direct communication between maternal and embryonic tissue until after the placenta starts to form.

The critical period with respect to teratogenic effects is during organogenesis. This starts at about 17 days after conception and is complete by 60 to 70 days. Exposure to certain drugs during this period (17 to 70 days) can cause major birth defects.

Some drugs can interfere with functional development of organ systems (e.g. central nervous system, integumentary system, and cardiovascular system) in the second and third trimesters and produce serious consequences.

Breastfeeding

Prescribed medication
The benefits of breastfeeding are sufficiently important to recommend that breastfeeding be discontinued or discouraged only when there is substantial evidence that the drug taken by the mother will be harmful to the infant and that no therapeutic equivalent can be given. Most drugs are only excreted to a minimal extent in breast milk, and in most cases the dosage to which the infant is ultimately exposed is very low and well below the therapeutic dose level for infants.

For these reasons the time of dosing in relation to breast feeding does not matter.

There are few drugs that are totally contraindicated while breastfeeding.

Gastrointestinal drug use in pregnancy and breastfeeding

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pregnancy category</th>
<th>Breastfeeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>amoxycillin</td>
<td>safe</td>
<td>compatible</td>
</tr>
<tr>
<td>ampicillin</td>
<td>safe</td>
<td>compatible, may cause diarrhoea in infant</td>
</tr>
<tr>
<td>antacids</td>
<td>safe</td>
<td>compatible</td>
</tr>
<tr>
<td>bisacodyl</td>
<td>safe</td>
<td>compatible</td>
</tr>
<tr>
<td>calciferol</td>
<td>Probably safe</td>
<td>caution, monitor infant plasma calcium levels</td>
</tr>
<tr>
<td>calcium carbonate</td>
<td>Probably safe</td>
<td>compatible</td>
</tr>
<tr>
<td>ceftriaxone</td>
<td>safe</td>
<td>compatible, may cause diarrhoea in infant</td>
</tr>
<tr>
<td>cephalothin</td>
<td>safe</td>
<td>compatible, may cause diarrhoea in infant</td>
</tr>
<tr>
<td>codeine</td>
<td>safe</td>
<td>compatible in occasional doses</td>
</tr>
<tr>
<td>dexamethasone</td>
<td>safe</td>
<td>compatible</td>
</tr>
<tr>
<td>erythromycin</td>
<td>safe</td>
<td>compatible, may cause diarrhoea in infant</td>
</tr>
<tr>
<td>Folic acid</td>
<td>safe</td>
<td>compatible</td>
</tr>
<tr>
<td>hydrocortisone</td>
<td>safe</td>
<td>compatible</td>
</tr>
<tr>
<td>hydroxocobalamin</td>
<td>safe</td>
<td>compatible</td>
</tr>
<tr>
<td>iron preparations</td>
<td>safe</td>
<td>compatible</td>
</tr>
<tr>
<td>lactulose</td>
<td>Probably safe</td>
<td></td>
</tr>
<tr>
<td>magnesium trisilicate</td>
<td>safe</td>
<td>compatible</td>
</tr>
<tr>
<td>methotrexate</td>
<td>teratogenic</td>
<td>avoid</td>
</tr>
<tr>
<td>metoclopramide</td>
<td>safe</td>
<td>compatible</td>
</tr>
<tr>
<td>metronidazole</td>
<td>safe</td>
<td>compatible, avoid high single-dose therapy</td>
</tr>
<tr>
<td>Drug</td>
<td>Compatibility Status</td>
<td>Note</td>
</tr>
<tr>
<td>-----------------------</td>
<td>----------------------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>Safe</td>
<td>Compatible</td>
</tr>
<tr>
<td>Paraffin liquid</td>
<td>Safe</td>
<td></td>
</tr>
<tr>
<td>Prednisolone</td>
<td>Safe</td>
<td>Compatible</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>Safe, caution, observe infant for drowsiness</td>
<td></td>
</tr>
<tr>
<td>Promethazine</td>
<td>Safe</td>
<td>Compatible in single dose</td>
</tr>
<tr>
<td>Psyllium</td>
<td>Safe</td>
<td>Compatible</td>
</tr>
<tr>
<td>Pyridoxine</td>
<td>Safe</td>
<td>Compatible in therapeutic doses</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>Safe</td>
<td>Compatible, crosses into breast milk but not known to be harmful</td>
</tr>
<tr>
<td>Rehydration salts</td>
<td>Safe</td>
<td>Compatible</td>
</tr>
<tr>
<td>Senna</td>
<td>Safe</td>
<td>Compatible</td>
</tr>
<tr>
<td>Thiamine</td>
<td>Safe</td>
<td>Compatible in therapeutic doses</td>
</tr>
</tbody>
</table>
PART 2 Respiratory

1 Drugs Used in Respiratory Diseases

1.1 Beta2 receptor stimulating drugs (Beta2 agonists)

Stimulation of beta2-receptors on airway smooth muscle relaxes the muscle resulting in bronchodilation. All beta2 agonists may also stimulate beta1-receptors. Beta1-receptor stimulation (e.g. tachycardia) is more likely to occur following systemic absorption or following inhalation of relatively large doses.

The preferred route of administration for beta2 agonists is by inhalation which causes bronchodilation with low doses, minimising systemic adverse effects.

Adverse effects:
- Tachycardia (which can also lead to paroxysmal tachyarrhythmias, such as atrial fibrillation or paroxysmal supraventricular tachycardia), tremor, headaches, muscle cramps, insomnia, and a feeling of anxiety and nervousness
- In high doses (e.g. tablets, intravenous and emergency nebulisation) all beta2 agonists can cause hypokalaemia and hyperglycaemia

1.2 Short-acting beta2 agonists

Salbutamol is the only drug in this class in the Kiribati EDL and is available in puffers, inhalation solution, syrup and tablets and as a combination formulation with beclomethasone for inhalation.

- A fast-acting bronchodilator; the effects are evident within 5 minutes and last for about 3 hours.
- Used to relieve bronchoconstriction
- Often referred to as a reliever (blue puffer) medication

Precautions:
- Regular and frequent use of salbutamol without appropriate attention to other aspects of respiratory illness is inadvisable
- Attention to an asthma management plan, monitoring of symptoms and lung function and preventive therapy are important when salbutamol is used in the regular management of airways disease
- Should be reserved for intermittent symptom relief rather than regular treatment of asthma
- High-volume, regular use may indicate that the underlying disease process is poorly controlled, warranting modification of other aspects of drug therapy
- The use of one or more canisters per month is associated with a greater risk of hospital admission

1.3 Adrenaline

- Is available in Kiribati as a 1mg/mL solution for subcutaneous injection
- Has combined beta and alpha-adrenergic effects
- Should be used only in severe asthma not responding to inhaled beta-agonists in whom corticosteroids have already been started
- Will cause tachycardia and tremor and dose rate should be reduced if pulse exceeds 120/min
1.4 Xanthines (Aminophylline)

- Mechanism of action is not well understood
- Xanthines may relax smooth muscle, stimulate respiration and increase diaphragm contractility
- Aminophylline, a derivative of theophylline, administered intravenously, is in the Kiribati EDL
- Aminophylline should be reserved for severe acute asthma failing to respond to standard management. In adults a dose not exceeding 250 mg should be given over 5-10 minutes. The slow rate is critical if severe side effects are to be avoided
- Aminophylline has little effect in patients with chronic obstructive airways disease and should only be tried when other treatment has failed to control symptoms adequately (e.g. a trial of short-acting bronchodilators), or in patients who are unable to use inhaled therapy

Adverse effects, interactions and precautions:
- Nausea and vomiting, insomnia, cardiac arrhythmias, seizures, and hypokalaemia may occur with both oral theophylline and excessive doses of parenteral aminophylline

1.5. Corticosteroids

- Widely used in the treatment of asthma and other respiratory diseases to reduce bronchial inflammation and hyper responsiveness
- Reduce synthesis and secretion of inflammatory mediators (such as prostaglandins and leukotrienes) and cytokines, which are involved in the pathogenesis of asthma
- Used in the management of both acute severe asthma and the preventive management of asthma
- The Kiribati EDL contains oral prednisolone, hydrocortisone and dexamethasone, for injection and beclomethasone dipropionate given by inhalation

1.5.1 Inhaled corticosteroids

Beclomethasone dipropionate
- Used as preventive (brown puffer) therapy in asthma
- Has a delayed onset of clinical effect and should be used regularly
- Not sufficiently potent nor sufficiently rapid in effect to be of use in acute severe asthma

Adverse effects, interactions and precautions
- Does not generally produce systemic adverse effects until large doses are administered
- In adults, doses at which systemic adverse effects appear are greater than 500 to 750 micrograms daily of beclomethasone
- In children, doses at which systemic adverse effects may become manifest are those greater than 400 micrograms daily
- The possibility of cataracts should be considered, particularly in those receiving therapy of extended duration
- The lowest effective dose should always be used

Concern about inhaled corticosteroids impairing long-term growth in children should not prevent their use in asthma. Studies are inconclusive and the risk of continued poor asthma control probably exceeds any effect on growth.

With low inhaled doses adverse effects are uncommon, but include hoarse voice and oral and oesophageal Candida albicans infection (candidiasis/thrush).

Patients should be advised to rinse their throat and mouth with water and spit out after inhalation.
1.5.2 Oral corticosteroids

Oral prednisolone

- Well absorbed and eliminated by liver metabolism
- Plasma half-life approximately 3 hours; however, the biological action is prolonged for up to 24 hours
- Lowest dose possible to achieve the desired clinical response should be used
- Usually given as a short course lasting several days to weeks with the aim of disease control without exposing the patient to the corticosteroid for a long enough period for significant adverse effects to develop
- Given as a single daily dose in the morning to mimic the natural cortisol peak. Dosing in the evening often results in sleep disturbances

Dose reduction (tapering)

- The hypothalamic-pituitary-adrenal axis is suppressed by glucocorticoid therapy
- Treatment with prednisolone at doses of 5-10mg for longer than 2 weeks can be sufficient to cause adrenal suppression
- Tapering of the dose is required to avoid both adrenal insufficiency and also rebound in symptoms, which may occur with sudden cessation

Adverse effects

- Systemic corticosteroid treatment inevitably results in adverse effects if the dose and/or duration of treatment are sufficient, because most are dose-related biological effects of the hormone

<table>
<thead>
<tr>
<th>Glucocorticoid</th>
<th>Mineralocorticoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>gastrointestinal effects (eg dyspepsia, risk factor for peptic ulceration, gastrointestinal bleeding)</td>
<td>hypertension</td>
</tr>
<tr>
<td>growth retardation</td>
<td>hypokalaemic alkalosis</td>
</tr>
<tr>
<td>immunosuppression, risk of infections</td>
<td>sodium-retaining effects</td>
</tr>
<tr>
<td>metabolic effects (eg diabetes, hypertriglyceridaemia)</td>
<td></td>
</tr>
<tr>
<td>myopathy</td>
<td></td>
</tr>
<tr>
<td>ocular effects, particularly increased intraocular pressure and cataracts</td>
<td></td>
</tr>
<tr>
<td>osteoporosis</td>
<td></td>
</tr>
<tr>
<td>pituitary-adrenal suppression</td>
<td></td>
</tr>
<tr>
<td>psychological disturbances (eg euphoria, depression, paranoid psychosis)</td>
<td></td>
</tr>
<tr>
<td>skin atrophy</td>
<td></td>
</tr>
<tr>
<td>weight gain and redistribution of fat</td>
<td></td>
</tr>
</tbody>
</table>

1.5.3 Parenteral corticosteroids

- **Hydrocortisone** is used intravenously for the acute treatment of asthma. The exact time course of action is not well established, but response takes at least some hours to develop
- Oral prednisolone 25mg is equivalent to IV hydrocortisone 100mg
- Prednisone is converted to prednisolone in the liver and should be used in the same dose as prednisolone
- Moderate- to high-dose oral corticosteroids may be as effective as parenteral corticosteroid treatment for the management of acute asthma

Adverse effects:
• Very few acute adverse effects are seen, but psychoses, mood changes, hypokalaemia and hyperglycaemia can occur

1.6. Expectorants

The clinical use of expectorants is controversial as their efficacy is still the subject of debate. Expectorants reduce the viscosity of respiratory tract secretions and facilitate the removal of accumulated mucus by ciliary action and coughing. By increasing respiratory tract secretions, expectorants may also soothe the dry, irritated tissues and, in so doing, may reduce the urge to cough. They may also make a dry, unproductive cough more productive.

In children (or adults) a pleasant and moderately effective treatment is hot water with honey and lemon with ginger. Adults may prefer to sip hot water. Hydration may be the mechanism of any therapeutic benefit of expectorants.

Bromhexine tablets and elixir are available on the Kiribati EDL but do not have impressive data on efficacy to support their presence.

1.7. Antihistamines

Histamine and many other inflammatory mediator compounds are released from mast cells during type 1 (IgE-mediated) allergic reactions. Histamine released in this way stimulates H1-receptors, which contributes to redness, swelling, itching, sneezing, runny nose, nasal congestion, red eyes.

Promethazine is available on the Kiribati EDL

Adverse effects, interactions and precautions:
• May affect psychomotor performance and the ability to drive motor vehicles or to operate heavy machinery
• Patients must be advised of this
• Potentiates the effect of other CNS depressants (e.g. alcohol)
• Promethazine also has anticholinergic activity and may produce dry mouth, blurred vision, constipation and urinary retention
• May lead to a drying effect throughout the respiratory tract and a thickening of bronchial mucus
• Should not be used where anticholinergic activity may be contraindicated (e.g. in patients with narrow angle glaucoma or prostatic hypertrophy)

1.8 Use of respiratory drugs in competitive sport

Many drugs used in the management of respiratory illnesses may be banned or restricted in competitive sport. Examples include some bronchodilators, corticosteroids and decongestants.

The following drugs in the Kiribati EDL have been permitted for use in national and international sporting competition by patients with asthma:

• Salbutamol
• Beclomethasone
• Prednisolone (when used out of competition)

It is recommended that athletes contact their national sporting organisation before taking medication. In many cases written notification is needed via an Abbreviated Therapeutic Use Exemption form. The International Olympic Committee (IOC) <http://www.olympic.org> requires that athletes wishing to take asthma medications during the games have either significant bronchodilator response or a positive bronchial challenge test.
1.9 Drug-induced lung disease

The number of drugs that have been shown to damage the respiratory system continues to grow. Drugs from the same pharmacological category tend to induce the same adverse effects. A thorough medication history should be undertaken and an adverse reaction considered in the differential diagnosis of unexplained lung disease.

Examples of drugs that can cause lung disease

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchospasm</td>
<td>beta blockers, contrast media, nonsteroidal anti-inflammatory drugs</td>
</tr>
<tr>
<td>Cough</td>
<td>angiotensin converting enzyme inhibitors</td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td>methotrexate, nitrofurantoin</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>propranolol, bromocriptine, , nitrofurantoin</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>hydralazine, isoniazid, , phenytoin</td>
</tr>
</tbody>
</table>

2. Inhalation devices—puffers, spacers, nebulisers

Many respiratory drugs are delivered topically to the airway by inhalational devices.

- The effect on the airways is rapid with minimal systemic adverse effects
- Devices available for drug delivery are metered dose inhalers (MDIs, "puffers"), spacers and nebulisers
- Errors of technique occur with all devices
- It is important to check patient technique at each review

2.1 Metered dose inhalers (MDIs) /Puffers

Care of these devices is important:

- Need to be washed regularly to avoid blockage
- Shake the device every time it is used
- If there appears to be very little liquid inside the canister when shaken, it is time to replace it
- Technique is critical

Up to 70% of patients use an incorrect technique with a puffer, resulting in inadequate drug delivery to the lungs.

- Check patient technique and demonstrate the correct technique (if necessary) at every opportunity
- Puffer should be held upright with the mouthpiece at the bottom. This allows an accurate dose to be dispensed
- Starting at the end of a normal expiration, the puffer should be actuated once, at the same time as a slow deep inspiration through the mouth is undertaken. At the end of the slow deep inspiration, the breath should be held for approximately 10 seconds

Common mistakes when using puffers include:

- Failing to coordinate the puffer actuation with the start of the inspiration
- Inspiring too rapidly
- Closing the mouth and then inspiring through the nose after actuation of the puffer
- Actuating the puffer more than once during the inspiration
2.2 Spacer devices

Spacers hold the aerosol cloud, which is produced from an MDI, in a confined space and allow subsequent inhalation over a longer period.

Spacer devices have a valve system, which can help patients who have problems with coordination. Useful in decreasing the oropharyngeal deposition of medication and increasing the proportion of the dose delivered to the lung.

With inhaled corticosteroids, spacers are an important means of reducing candidiasis and dysphonia. Inhalation of aerosol from the spacer should commence as soon after actuation as possible to minimise deposition in the spacer and loss of drug. One actuation of MDI per inhalation is recommended.

Spacer devices with MDI in appropriate doses may be substituted for nebulised medication during asthma exacerbations:

- **4 to 10 inhalations of standard dose short-acting beta₂ agonists can produce a similar bronchodilator effect to standard nebulised doses**

Spacers should be washed before initial use and at least monthly thereafter:

- Use warm water with kitchen detergent
- Leave to drain (without rinsing) and allow to dry before use
- A cloth should not be used to dry the spacer, as this can produce an electrostatic charge causing drug particles to adhere to the walls of the spacer
- Before using the spacer, it should be ‘primed’ by actuating 3 to 5 doses of drug; this minimises fluctuations in dose due to variation in electrostatic charge

**Spacer devices (Figure 1)**

**Technique**
Correct use of a spacer is:

- Shake the MDI before use
• Insert MDI, mouthpiece down, into the spacer
• Actuate the MDI
• Inhale slowly and deeply from the spacer (starting as soon after actuation as possible)
• Hold breath for 10 seconds

Two modifications may be applicable for children.

Take 4 to 6 tidal breaths to inhale the aerosol
Use a face mask adapter to inhale from the spacer (infants and young children)

2.3 Nebulisers

There is a tendency to overuse this expensive form of drug delivery. The inhalation, via a large-volume spacer, of 4 to 10 separate actuations from a standard beta2 agonist MDI, provides an equivalent bronchodilator effect to that achieved by nebulisation.

Nebulisation aims to produce an aerosol from a solution of drug in a bowl. This may be done using a simple pump or, if electricity is unavailable, an oxygen cylinder. In children with asthma oxygen, if available, may be the better choice.

Technique

Nebulisers produce reasonable aerosols with a flow of at least 8 L per minute. The nebuliser fill volume should be 2.5 to 5 mL of solution, which will usually achieve nebulisation of about 80% of the contents within the first 5 to 10 minutes. If nebulisation is incomplete after 10 or 15 minutes, the nebuliser might be blocked or cracked, or the pump may be faulty. Pumps should be serviced, and filters changed regularly —every 6 to 12 months depending on the amount of use.

Use of devices in children

MDIs with a spacer and mask can be used in children younger than 2 years of age. MDIs alone require a reasonable amount of coordination; do not use without a spacer.

2.4 Oxygen Therapy

Oxygen is essential for human metabolism and lack of oxygen is generally fatal within 5 to 6 minutes. Oxygen has almost no adverse effects in the acute situation and should not be withheld if there is any suggestion of it being needed.

Use oxygen therapy for:
• Respiratory arrest
• Hypoxia of any cause
• Acute asthma attack
• Exacerbation of chronic obstructive airway disease (COPD)

Oxygen therapy should be monitored with pulse oximetry and blood gas estimation if available. Aim to achieve an oxygen saturation of at least 95%. Humidification of oxygen is not necessary.

2.4.1 Methods of Oxygen Delivery

a) Intranasal Catheters

• Should be used with an oxygen flow rate of between 1 and 4 litres/minute (1 – 2L/min in children). Higher flow rates cause drying of the nasal mucosa and are uncomfortable
• Should only be used in patients with mild hypoxia or cardiac failure or myocardial ischaemia
• Do not provide a high enough oxygen concentration for patients with significant hypoxia, carbon monoxide poisoning, shock or cardiac arrest

b) Plastic Face Masks

• These provide oxygen concentrations of between 35 and 70%
• The oxygen flow rate should be set between 4 and 15 litres/minute
• Do not use face masks with an oxygen flow rate less than 4 litres/minute
• This method of oxygen delivery is suitable for patients with moderate hypoxia or shock

c) Tight Fitting Face Masks (eg. Laerdal, CPAP masks)
These devices can provide oxygen concentrations close to 100%.
They should be used in patients with severe hypoxia or with cardiac arrest.

**Adverse Effects of Oxygen**

Patients with COAD and elevated carbon dioxide levels may have a hypoxia-dependent respiratory drive. In these patients, oxygen causes hypoventilation and an increase in the carbon dioxide level. This is far less dangerous than hypoxia itself.

In emergency, hypoxia must be corrected - problems with carbon dioxide retention can be handled later. Do not hesitate to give oxygen to hypoxic patients with chronic obstructive airway disease.

NOTE: If arterial blood gases are available, then they should be measured before the commencement of oxygen to establish the baseline.

### 3. Pulmonary function testing

Plays a role in:

- Assessing breathlessness, asthma and other chronic chest disorders
- Monitoring response to treatment
- Assessing fitness for surgery

The results are reported in relation to reference values and whether they fall within the normal range for an individual of that age and gender.

Available tests measure expiratory air flow.

#### 3.1 Peak expiratory flow (PEF)

- Uses a portable PEF meter and can be valuable in assessing the diurnal variability of airflow obstruction (a characteristic feature of asthma), as well as the response to therapy. The technique is simple and can be performed as part of the asthma management plan
- Patients in Kiribati often have their own peak flow meters but these are not routinely available within the hospitals. There is need for the test to be available
- The apparatus needs disposable mouth pieces

**Technique is important:**

- Insert disposable tube firmly into the monitor
- Hold a few centimetres from the mouth
- Take in and hold as deep a breath as possible
- Put tube into mouth and close lips firmly around it
- Blow into tube as hard, fast and long as possible
- Rest for 30 seconds
- Repeat above steps twice
- Record best result

#### 3.2 Spirometry

- Measures the forced expiratory volume in one second (FEV1) and compares it with the forced vital capacity (FVC)
- Asthma and COAD are characterized by an FEV1/FVC ratio of less than 0.7, which may improve after bronchodilator treatment
- Is a useful aid to diagnosis in asthma and COAD
- Is useful in monitoring response to treatment
- Is not currently available in Kiribati

A normal spirogram trace is depicted below showing the measurements derived from it

![Spirogram Trace]

Normal spirogram tracing showing the points of measurement of FEV1 and FVC: volume exhaled is on the vertical axis, time on the horizontal.

3.3 Pulse oximetry

Pulse oximetry measures oxyhaemoglobin saturation (SaO2) by applying a clip containing light-emitting diodes to the finger or earlobe. The method is non-invasive, is available in Tungaru Hospital and can provide very helpful information in the diagnosis of severity of respiratory disease. It can also be helpful in assessing progress in the management of acute asthma and respiratory failure.

4. Asthma

4.1 General
- A common chronic inflammatory disorder of the airways
- The chronic inflammation increases airway hyper responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or in the early morning
- Episodes are usually associated with widespread but variable airflow obstruction that is reversible either spontaneously or with treatment.
- Management includes prevention of attacks, treatment of acute attacks and, where necessary, long term medication which works best with strict adherence

All patients, both adult and children, should be given an asthma plan which needs frequent review and repetition to ensure full understanding by the patient or parents.
It is essential that they understand the difference between the blue reliever puffers (MDIs) and the brown preventer puffers.

Prevention of attacks

It may be possible to prevent or reduce the severity of attacks by:

- Avoidance of trigger factors where possible e.g. known allergens, tobacco smoke, stress
- Appropriate management of acute exacerbations
- Appropriate management of infections
- Appropriate long-term medication use with an individual patient management plan
- Regular assessment by lung function tests
- Avoidance of drugs that can cause bronchoconstriction e.g. beta blockers, aspirin, ibuprofen and indomethacin
- Paracetamol is rarely a problem and is the analgesic of choice for asthmatics

4.2 Treatment of an acute attack of asthma

This must always be treated as a serious emergency

Severity is estimated by clinical assessment, measurement of peak expiratory flow rate (PEFR) and by pulse oximetry.

Pulse rate may also be helpful in indicating severity of an attack:

- Mild <100
- Moderate 100-120 (children 100-200)
- Severe >120  (children >200)

Wheezing is an unreliable indicator of the severity of an asthma attack and may be absent in a severe attack. In severe asthma the patients will lack sufficient air flow to perform lung function tests

Cyanosis indicates life-threatening asthma.

All patients with moderate or severe asthma should be given oxygen.

Patients with severe asthma should be managed in an intensive care unit if possible and may occasionally require intubation and mechanical ventilation.

ADULTS:

Oxygen

- Give oxygen via face mask if moderate or severe asthma

Beta-adrenergic Agonists

- Use beta-adrenergic agonists to reverse bronchospasm. In very severe asthma intravenous salbutamol may be useful in addition to nebulised
- Give salbutamol 5 mg by nebulizer with oxygen and repeat every 30 minutes if necessary (or give continuously in severe asthma)

OR

- Give salbutamol by puffer using spacer (up to 50 puffs) if nebulisers are not available
- PLUS if very severe
- Give salbutamol 5 microgram/kg intravenously (to a maximum of 250 microgram) over one minute then commence an infusion at 5 microgram/kg per hour

NOTE: Continuous nebulized salbutamol is probably as effective as intravenous

Corticosteroids

Steroids reduce inflammation of the airways. Their effects are delayed for at least 4 hours but they are important to prevent relapse. Oral steroids are as effective as those given parenterally in most patients.

GIVE:

- Hydrocortisone 200 mg intravenously then 100mg six hourly
Other Drugs
Aminophylline provides no additional benefit to optimal doses of beta-adrenergic agonists. It has a number of undesirable side effects including seizures, ventricular tachycardia, hypokalaemia and vomiting. Routine use in asthma is not recommended. However, it may be of benefit in patients with severe asthma who require hospitalisation. A loading dose is given to patients who are not taking oral theophylline:
GIVE:
- Aminophylline 5 mg/kg (to a maximum of 250 mg) intravenously over 5-10 minutes

Adrenaline does not appear to have any advantage over salbutamol. It may be used as a last resort or when intravenous access or nebulisers are not available:
GIVE:
- 1:1000 adrenaline 0.5 - 1 mL subcutaneously

NOTE: Adrenaline may be given down the endotracheal tube - the dose is 5 times the intravenous dose and it should be diluted in 10 mL of normal saline.

CHILDREN

Oxygen
- Give oxygen via face mask to all children with asthma

Beta-adrenergic Agonists
- Use beta-adrenergic agonists to reverse bronchospasm. In very severe asthma intravenous salbutamol may be useful in addition to nebuliser.
- Give salbutamol 2.5 mg by nebulizer with oxygen to children 5 years of age or under, or give 5 mg by nebulizer to children over 5 years and repeat every 30 minutes if necessary (or give continuously in severe asthma)
PLUS if very severe
- Give salbutamol 5 micrograms/kg intravenously (to a maximum of 250 micrograms) over one minute and then infuse 5 micrograms/hr

NOTE: Intravenous salbutamol may be more effective than continuous nebulized in young children with severe asthma.

Corticosteroids
Steroids reduce inflammation of the airways. Their effects are delayed for at least 4 hours but they are important to prevent relapse. Oral steroids are as effective as those given parenterally in most patients.
GIVE:
- Hydrocortisone 1 - 4 mg/kg intravenously to a maximum of 200 mg then every six hourly
OR
- Give dexamethasone 0.2 mg/kg i.v. or i.m. to a maximum of 8 mg
OR
- Give prednisolone (prednisone) 1 mg/kg orally to a maximum of 50 mg daily

Other Drugs
Aminophylline provides no additional benefit to optimal doses of beta-adrenergic agonists. It has a number of undesirable side effects including seizures, ventricular tachycardia, hypokalaemia and vomiting. Routine use in asthma is not recommended. However it may be of benefit in patients with severe asthma.

A single dose may be given to patients who are not taking oral theophylline:
- Give aminophylline 5 mg/kg (to a maximum of 250 mg) intravenously over 5 minutes

Adrenaline does not appear to have any advantage over salbutamol. It may be used in severe asthma as a last resort or when intravenous access is not available:
- Give 1:1000 adrenaline 0.1 mL/kg intramuscularly or subcutaneously to a maximum of 0.5 mL

4.3 After an acute attack

Adults
All patients will need follow up and some form of ongoing therapy:

- Review trigger factors to identify the possible cause of the attack
- Discuss avoidance measures
- Start or adjust the patient’s maintenance therapy
- Design or adjust the patient’s asthma action plan
- Review adherence to prescribed medication regimen

**Mild Episodic**

Patients may only need to use:

- Salbutamol puffer 1-2 puffs prn up to 8 puffs a day (with spacer for children or adults with poor coordination)

They should all be advised of the symptoms of an acute attack and told to seek medical advice if their need to use the puffer increases or they are using more than 8 puffs a day

OR if unable to use a puffer with or without a spacer:

- Salbutamol tablets 4mg 6-8 hourly

**Moderate Persistent**

- Salbutamol puffer 1-2 puffs prn up to 8 puffs a day. (with spacer for children or adults with poor coordination)

OR if unable to use a puffer with or without a spacer

- Salbutamol tablets 4mg 6-8 hourly

AND

- Beclomethasone dipropionate by inhalation 100 microgram bd

**Severe Persistent**

If symptoms persist or deteriorate

- Continue any existing oral therapy and inhaled salbutamol

AND consider

- Using a spacer with 5-10 puffs inhaled over 5-10 minutes every 2 hours
- If available give nebulised salbutamol 5mg over 10 minutes 2-4 hourly
- Increase beclomethasone dipropionate dose to 200 microgram bd

If symptoms persist start:

- Prednisolone 25-50mg orally daily for 1-2 weeks

If response is good tail off the prednisolone over 10 days

A few patients with severe asthma will need:

- Prednisolone 5-7.5mg orally long term

**Children**

All should have followed up and some form of ongoing therapy and asthma plan:

- Review trigger factors to identify the possible cause of the attack
- Discuss avoiding trigger factors.
- Start or adjust the patient’s maintenance therapy
- Design or adjust the patient’s asthma action plan
- Prescribed medication regimen - review adherence/compliance

**Mild Episodic**

GIVE:

- Salbutamol puffer 1-2 puffs prn up to 8 puffs a day (with spacer)
Parents should be advised of the symptoms of an acute attack and told to seek medical advice if their need to use the puffer increases or they are using more than 8 puffs a day, OR if child aged 1-5 and unable to use a puffer with or without a spacer.

**Moderate Persistent**
- Salbutamol puffer 1-2 puffs prn up to 8 puffs a day (with spacer)
  - AND for children over 6 and/or able to use an inhaler with a spacer
- Beclometasone dipropionate 50-100 microgram bd

For children under 6 and/or unable to use an inhaler with spacer GIVE
- **Prednisolone 1mg/Kg a day for 3 days and review**

If unable to reduce or cease prednisolone refer to a paediatrician

**Severe Persistent**
If symptoms persist or deteriorate:
- **Continue any existing oral therapy and inhaled salbutamol**
  - AND give if possible:
    - 5-10 puffs salbutamol inhaled using a spacer over 5-10 minutes every 2 hours
    - If available give nebulised salbutamol 5mg over 10 minutes 2-4 hourly
    - Increase beclometasone dipropionate dose to 100 microgram bd
  - OR for children unable to inhale with a spacer:
    - **Prednisolone 2mg/kg orally daily for 1-2 days**

If none of the above treatments produce improvement the patient should be referred urgently to the on-call paediatrician

### 4.4 Review and education

All patients need an asthma management plan. Parents should hold one and understand it for their asthmatic children. It should be reviewed at clinic attendances whether in hospital or at Health Centres.

**Important! Adherence (compliance)**
- If asthma control is poor despite apparently adequate treatment, consider poor adherence/compliance. As patients feel better there is a risk they will reduce or fail to continue their medication. Discourage this

#### 4.4.1 Asthma management plan for - health professionals to follow

In the management of asthma, both patients and health professionals should use the same framework of management and similar terminology. To facilitate this, a 6-point management plan\(^1\) has been proposed:

- Assess asthma severity
- Achieve best lung function
- Maintain best lung function: identify and avoid trigger factors
- Maintain best lung function: optimise medication program
- Develop an asthma action plan
- Educate and review regularly

#### 4.4.2 Asthma action plan - for patients and their families

All patients should have an asthma action plan—in written form—that outlines how to:

- Recognise symptoms of asthma deterioration
- Start treatment
- Reach medical attention

Action plans may be based on peak expiratory flow (PEF) measurements or asthma symptoms or both. Plans should be simple, individualised and based on 2 to 4 action points.

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\(^1\) By the Thoracic Society of Australia and New Zealand, The Royal Australian College of General Practitioners, the Pharmaceutical Society of Australia and the Asthma Foundations, through the National Asthma Council.
All patients with asthma should know how to obtain prompt medical assistance

The principles of asthma action plans are:

- Increase the dose and frequency of inhaled beta2 agonist
- Increase the dose of inhaled corticosteroid or commence prednisolone if the patient is already on a high dose of inhaled corticosteroid
- Obtain prompt medical attention
- In an emergency, immediate use of a high-dose inhaled short-acting beta2 agonist (e.g. salbutamol 6 to 10 inhalations by MDI or 5 mg by nebuliser) and transfer to an emergency department (preferably by an ambulance that carries supplemental oxygen)

Asthma action plans must be individualised

5. Chronic obstructive airways disease (COAD)

- Is characterised by airflow obstruction that is not fully reversible
- Is, in most cases, progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases, most commonly cigarette smoke
- Usually some combination of:
  - emphysema, where the lung parenchyma is structurally damaged, with destruction of alveolar septa and formation of abnormally enlarged airspaces
  - airway damage with airway wall thickening and narrowing of the airway
  - chronic bronchitis which is defined clinically as a cough productive of sputum, occurring on a daily basis for 3 months in each of 2 consecutive years
- Some patients may have bronchodilator responsiveness whether or not they have a history of asthma
- Dyspnoea of COAD is frequently associated with cough, sputum production, and recurrent respiratory infection and wheezing, which may only be evident during infective exacerbations. Typically, the dyspnoea has developed insidiously over several years and it may be the patient’s only symptom

COAD affects middle-aged and older people, and cigarette smoking is the major causative factor. The figure illustrates the accelerated decline in lung function caused by smoking.
Smoking and loss of forced expiratory volume in 1 second (FEV₁)

The differences between the lines illustrate effects that smoking, and stopping smoking, can have on the FEV₁. This figure shows the rate of loss of FEV₁ for one particular susceptible smoker; other susceptible smokers will have different rates of loss, thus reaching ‘disability’ at different ages.

† = death, the underlying cause of which is irreversible chronic obstructive pulmonary disease, whether the immediate cause of death is respiratory failure, pneumonia, cor pulmonale or aggravation of other heart disease by respiratory insufficiency

This figure was first published in Fletcher C, Peto R. The natural history of chronic airflow obstruction. BMJ 1977;1:1645-8 and is reproduced by permission of the BMJ Publishing Group.

The spirometric abnormalities associated with COAD are a reduction in post bronchodilator forced expiratory volume in 1 second (FEV₁), and a reduction in the FEV₁/forced vital capacity (FVC) ratio to less than 70% (i.e. an obstructive pattern).

5.1 Management

Smoking cessation is the only intervention that has been shown to improve the natural history of COAD; to prevent deterioration it is vital that the patient stops smoking (see figure).

Bronchodilators

- Bronchodilators are recommended for the relief of wheezing and shortness of breath.
- Bronchodilators can improve the FEV₁, FVC and exercise tolerance

GIVE:

- Salbutamol 100 to 200 micrograms MDI by inhalation, up to 4 times daily

Use a large-volume spacer; this improves lung deposition of the aerosol.
In patients who are unable to use an MDI (with or without a spacer),

**USE:**
- Salbutamol 4mg orally up to 8 hourly as tolerated

**Corticosteroids for long-term treatment of COAD**

Only 10% of patients with stable COAD benefit in the short term from corticosteroids and only a trial of therapy will show who they are.

**Inhaled corticosteroids**

Benefits are not seen in patients with COAD who continue to smoke cigarettes.

Inhaled corticosteroids should be prescribed for patients:
- With an FEV₁ less than or equal to 50% predicted
- Who have documented evidence of responsiveness to inhaled corticosteroids (on PEF or spirometry)
- Who have had 2 or more exacerbations requiring treatment with antibiotics or oral corticosteroids in a 12-month period

**GIVE:**
- Beclomethasone dipropionate 300 to 400 micrograms by inhalation, twice daily
  Monitor response with PEF.

Patients who do not suffer frequent exacerbations should be assessed after about 6 weeks of treatment. Because of the potential risks of long-term corticosteroid use, only those patients in whom clear objective benefit has been obtained should continue with treatment. Inhaled corticosteroid doses should be gradually reduced to the minimum dose that maintains subjective benefit.

Oral corticosteroids are not recommended for maintenance therapy in COAD.

Management of pulmonary hypertension and cor pulmonale—should follow the guidelines for Congestive Heart Failure (see Cardiovascular Guidelines)

There is insufficient evidence to recommend prophylactic antibiotic therapy in the management of stable COAD.

**5.2 Acute Exacerbation of COAD**

Exacerbation of chronic obstructive airways disease (COAD) is a common problem in emergency medicine. The response of COAD to treatment is generally slower than that of asthma and most patients require admission.

- **Give oxygen to maintain saturation greater than 92%**. Although administration of oxygen can cause an elevation in arterial carbon dioxide levels in a few patients, this is far less of a problem than hypoxia itself.
- **For mildly hypoxic patients oxygen via an intranasal catheter will be sufficient while those with more severe hypoxia may require oxygen via a face mask. Use the lowest flow rate necessary to maintain an adequate arterial oxygen saturation.**

CAUTION: In patients with CO₂ retention, oxygen saturation should be maintained between 90 – 95%.

- **Give salbutamol 5 mg via nebulizer every 2 to 4 hours**
- If a nebuliser is not available use puffers with a spacer
- **Give hydrocortisone 200 mg intravenously every 6 hours**
  OR
- **Give prednisolone 40 mg orally daily**

Many exacerbations of chronic obstructive airways disease (COAD) are due to viral infection or noninfective causes and antibiotics are only occasionally indicated.

Antibiotics have been shown to be effective only when all 3 cardinal symptoms of acute bacterial exacerbations are present: increased dyspnoea, increased sputum volume and sputum purulence.

When indicated,
- **Give amoxycillin 500 mg orally or ampicillin 500mg intravenously every 8 hours**
OR if penicillin hypersensitive
  • Give erythromycin 500 mg orally every 6 hours for 5-7 days

6. Upper Respiratory tract infections

6.1 Acute sore throat

Most are viral. Simple analgesia plus adequate hydration will be adequate treatment.

Features suggesting bacterial infection include:
  • Fever >38 degrees Celsius
  • Tender cervical nodes
  • Tonsillar swelling or exudates
  • No cough

If likely bacterial:
  • Give Penicillin V 500 mg orally 12-hourly for 10 days
  OR
  • Benzathine penicillin 1.2 mega units IM as a single dose

Amoxicillin is not a preferred antibiotic as it has too wide a spectrum. If hypersensitive to penicillin:
  • Give Erythromycin 500 mg orally 12 hourly for 10 days
  OR
  • Erythromycin 250 mg orally 6-hourly for 10 days

It is important to complete the course to prevent rheumatic fever which is still common in Kiribati.

6.2 Acute bacterial otitis media

This is either bacterial or viral and normally resolves in a few days with some pain relief.

If symptoms persist or there is pus draining from the ear:
  • Give amoxycillin 500 mg orally 8-hourly for 7 days

If penicillin hypersensitive:
  • Give doxycycline 100 mg orally 12-hourly for 7 days
  OR
  • Tetracycline 500 mg orally 6-hourly for 7 days

6.3 Acute sinusitis

Follows an upper respiratory infection in up to 5% of cases

Indications for antibiotics are:
  • Persistent mucopurulent discharge
  • Facial pain
  • Tenderness over the sinuses
  • Poor response to decongestants
  • Give amoxycillin 500 mg orally 8-hourly for 7 days

If penicillin hypersensitive, give:
  • Tetracycline 500 mg 6-hourly
  OR
  • Doxycycline 100 mg. Orally 12-hourly for 7 days

6.4 Croup

A viral infection of the upper airway which affects children from the ages of 6 months to 3 years. It is
characterised by fever, a harsh cough, a hoarse voice and stridor. Children who have stridor while at rest or who have signs of respiratory distress (i.e. suprasternal retraction, tachypnea, restlessness) should be admitted. Pulse oximetry is useful – an oxygen saturation of 93% or less while breathing air is an indication for admission. Most cases of croup are mild and self-limited.

**Mild croup**
These patients will have stridor only with exertion or crying and no signs of respiratory distress. Avoid exposure to cold air. Give paracetamol for fever.

- **Give paracetamol 20 mg/kg every 4 hours**

**Moderate croup**
These patients will have stridor at rest and some signs of respiratory distress but oxygen saturation should be greater than 90% on air.

- **Give oxygen to maintain an oxygen saturation greater than 93%**
- **Give dexamethasone 0.6 mg/kg intramuscularly as a single dose**

**Severe croup**
These patients will have signs of marked respiratory distress plus hypoxia or cyanosis. Admission to an intensive care unit is desirable and intubation may be necessary.

- **Give oxygen to maintain an oxygen saturation greater than 93%**
- **Give dexamethasone 0.6 mg/kg intramuscularly as a single dose**
  - PLUS
    - **Give nebulised adrenaline, 0.5 ml/kg of 1: 1000 solution or 0.05 ml/kg of a 1% solution diluted with saline to a volume of 2.5 ml**

NOTE: Patients who fail to respond to nebulized adrenaline may require endotracheal intubation. Nebulized adrenaline provides only temporary relief of airway obstruction lasting 1 to 2 hours. Patients should be closely observed after this period for recurrence of obstruction.

**6.4 Acute Epiglottitis**
Epiglottitis is a **medical emergency** and failure to provide prompt treatment may be fatal.

- Due to infection of the epiglottis with Haemophilus influenzae bacteria.
- Mainly affects children between the ages of 3 and 8 years but is occasionally seen in adults
  - characterised by fever, inspiratory and expiratory upper airway noises, a severe sore throat, dysphagia and drooling
- Patient looks very unwell
- Very high risk of acute airway obstruction

All patients should be referred immediately to an anaesthetist and admitted to an intensive care unit. Attempting to view the throat or otherwise upsetting the child may cause airway obstruction and should be avoided. Keep the patient sitting up.

**GIVE:**
- **Ceftriaxone 100 mg/kg stat then 50mg/kg intravenously daily**
  - OR
  - **Chloramphenicol 40 mg/kg stat then 25mg/kg intravenously daily**

Early transfer to oral therapy is desirable.

**7. Lower Respiratory Tract Infections**

**7.1 Acute bronchitis**
In an immunocompetent adult or child, acute bronchitis is most often viral and does not require antibiotic therapy. Randomized controlled trials show that antibiotic therapy provides no overall benefit to the patient and may cause harm.

If sputum is voluminous and purulent, with fever, secondary bacterial infection is assumed:

- **Amoxicillin 500mg orally 8 hours for 5-7 days**
- **Doxycycline 100mg orally 12 hours for 7 days**
- **Tetracycline 500mg orally 6 hours for 5-7 days OR**
- **Erythromycin 500mg orally 6 hours for 5-7 days**

### 7.2 Acute exacerbation of chronic bronchitis

Treat as for Acute Bronchitis above.

### 7.3 Pneumonia

#### 7.3.1 Community acquired

A common condition, may present late in Kiribati. In otherwise healthy patients it is usually caused by single micro-organisms such as *Streptococcus pneumoniae*, *H influenzae*, *Mycoplasma pneumoniae*, *Chlamydia*

In immunocompromised patients (diabetics, in the elderly or patients with co-existent illness (e.g. cancer, liver disease, heart failure or renal failure), a broad-spectrum antibiotic cover may be required.

1. **Mild Disease**
   - Amoxicillin 500mg orally 8 hours for 7-10 days OR
   - Procaine Penicillin 3.6g (4 mega units) IM daily for 7-10 days
   - Tetracycline 500mg orally 6 hourly for 7-10 days OR
   - Doxycycline 100mg orally 12 hours for 7-10 days

2. If hypersensitive to penicillin or Mycoplasma or Chlamydia suspected:
   - Erythromycin 500mg orally 6 hourly for 10-14 days OR
   - Doxycycline 100mg orally 12 hours for 10-14 days

3. **Moderate Disease**
   - Penicillin G 1200mg (2 mega unit) IV 6 hours for 7-10 days
   - Chloramphenicol 1g IV 6 hourly X 7 – 10 days

   If the clinical response to parenteral therapy is satisfactory, high dose oral therapy may be substituted after a few days:
   - **Amoxycillin 0.5 – 1Gm. orally 8 hourly**
   - **Chloramphenicol 0.5g-1g orally 6 hours, for patients on chloramphenicol IV**

4. **Severe Disease**
   - In adults, severe pneumonia should be suspected if the following features are present:
     - Respiratory rate > 30 per minute
     - PaO2 < 60mmHg or SaO2 < 90% on room air
     - PaCO2 > 50mmHg on room air
     - Chest X-ray evidence of bilateral involvement or involvement of multiple lobes
     - Increase in size of chest X-ray opacity by 50% or more within 48 hours of admission.
     - Requirement for mechanical ventilation or inspired oxygen >35% to maintain SaO2> 90%
     - Haemodynamic compromise:
       - Systolic blood pressure < 90mmHg
       - Diastolic blood pressure < 60mmHg
       - Recent deterioration in renal function
       - White blood cell count <4 or >30 x 10⁹/L
Empirical:
- **Penicillin G 1200mg (2 mega unit) IV 6 hourly PLUS**
- **Cloxacillin 2g IV 6 hours  PLUS**
- **Gentamicin 4-6 mg/Kg IV once daily (maintenance dose adjusted according to renal function)**

If severe or no response then the following may be added:
- **Erythromycin 500mg 6 hourly**

If hypersensitive to penicillin:
- **Ceftriaxone 2g IV daily PLUS**
- **Erythromycin 0.5-1g IV (slow infusion over 1 hour) 6 hourly**

Definitive therapy should be instituted based on bacteriological data.

If *Streptococcus anginosus* is proven
- **Penicillin G 3-4mega (1800-2400mg) IV 6 hourly x 21 days**

If *Pseudomonas aeruginosa* is proven
- **Piperacillin 4g IV 6 hourly PLUS**
- **Gentamicin 240mg IV once daily (to be adjusted for renal function)**

If *Staphylococcus, aureus* is proven
- **Cloxacillin 2g IV 6 hourly for 3 to 4 weeks (oral therapy can be substituted once patient’s condition is stabilized)**

7.3.2 Hospital acquired pneumonia
Pneumonia that was not present at time of admission, and develops after 48 hours of hospitalization. It is usually due to Gram-ve organisms.

**GIVE:**
- **Cloxacillin 1g IV 6 hourly for 14-21 days PLUS**
- **Gentamicin 240mg IV once daily for 14-21 days (maintenance dose adjusted for renal function)**
  PLUS
- **Metronidazole 400mg PO 8 hourly or PR 500mg 12 hourly x 14-21 days**

**Immunosuppressed patients**
Pneumonia may be recurrent and due to unusual organisms. A microbiologist or physician should be consulted regarding diagnosis and treatment.

7.4 Bronchiectasis
A disease characterised morphologically by the permanent dilation of bronchi and bronchioles, and clinically by recurrent or persistent bronchial infection and cough with sputum.

**Management**
Generally accepted that keeping the airways as free of secretions as possible is an important part of the management but not supported by evidence from clinical trials.

Ideally refer to a physiotherapist experienced in the area.

For patients with significant airflow obstruction, nebulised bronchodilators may assist with clearing secretions.

**GIVE:**
- **Salbutamol 100 to 200 micrograms MDI by inhalation, up to 4 times daily**

In patients who are unable to use an MDI (with or without a spacer)

**USE**
- **Salbutamol 4mg orally up to 8 hourly as tolerated**

The effect of these agents may be monitored by self reported symptoms or by PEF.

**Infection**
If sputum becomes infected it is important to give antibiotics as early as possible.
(a) Mild Disease
- Amoxycillin 500mg orally 8 hours for 7-10 days

(b) Severe Disease
- Chloramphenicol 500mg 6 hourly orally / IV for 7-10 days

Alternatives:
- Amoxycillin 500mg orally 8 hours for 7-10 days PLUS
- Metronidazole 400mg orally 8 hours for 7-10 days OR
- Doxycycline 100mg 12 hourly for 7-10 days (as a single agent)

7.5 Lung abscess

Usually develop either as a result of the aspiration of organisms in patients with dental caries, or as a consequence of severe necrotising pneumonia.

Patients with altered conscious states (e.g. from anaesthesia, or alcohol intoxication, or postictal) and/or with swallowing difficulties are at particular risk.

Septic emboli are occasionally a cause in intravenous drug users, often with right-sided endocarditis.

Management
- Adequate drainage of the infected material
- Appropriate antibiotics
- Identify the causal organism
- If there is a possibility of a foreign body (e.g. a tooth, a peanut), then bronchoscopy is appropriate

GIVE:
- Penicillin G 2 mega units IV 6 hourly PLUS
- Cloxacillin 2g IV 6 hourly PLUS
- Metronidazole 400mg orally 8 hours

Gentamicin should be added if aspiration is likely cause of the abscess.

7.6 Management of parapneumonic effusion and empyema

If there is clinical suspicion of a parapneumonic effusion, this should be confirmed by chest X-ray, and the fluid sampled and cultured.

As with any collection of pus, adequate drainage is the most important aspect of management.

GIVE:
- Penicillin G 2 mega units IV 6 hourly PLUS
- Cloxacillin 2g IV 6 hourly PLUS
- Metronidazole 400mg orally 8 hours

8. Interstitial lung disease

In addition to infection by viruses, bacteria and fungi (the pneumonias), cardiogenic oedema, and fibrotic reaction to accumulation of nonorganic dust particles (the pneumoconioses), there are also many conditions in which the lung interstitium becomes inflamed, infiltrated or fibrosed.

They are characterised by a restrictive pattern on spirometry testing.

Spirogram showing restrictive ventilatory defect
The diagnosis is dependent upon:

- A typical history of slowly progressive breathlessness over months to years
- Basal crackles on chest auscultation
- Typical basal and peripheral reticular shadowing on X-Ray or computerised tomography of the lungs
- Typical restrictive lung function abnormalities

There is little that can be done to improve the poor prognosis of most interstitial fibrosing processes. The main principles are to:

- Identify and remove the causative factor, e.g. in the industrial exposure types or drug-related forms
- Avoid further exposure to potentially harmful inhaled or ingested agents
- Stop smoking
- Make a trial of corticosteroids, with or without an immunosuppressive agent such as azathioprine. This should only be attempted with specialist supervision

8.1 Drug-induced interstitial lung disease

Eosinophilic reactions

Lung parenchymal interstitial eosinophilic infiltration gives breathlessness and sometimes a cough; the patient may also wheeze (suggesting an airway component as well). A maculopapular rash occurs frequently. There may be pyrexia. An immunological reaction is the likely cause.

Drugs that may be implicated include:

- Antibiotics {nitrofurantoin, penicillins, sulfonamides (including co-trimoxazole), tetracyclines}
- Anti-inflammatory drugs (aspirin, sulfasalazine)
- Cytotoxic drugs (methotrexate)
- Antipsychotics and antidepressants (chlorpromazine, imipramine)
- Anticonvulsants (carbamazepine, phenytoin)

For treatment, identification and removal of the drug is paramount.

In severe or moderately severe cases, judged on clinical criteria, a short course of prednisolone can be given:

- Use prednisolone 20 to 40 mg orally, daily for 2 weeks
9. Tuberculosis

Kiribati has a continuing problem with, mainly, pulmonary tuberculosis. An immunization program aims to reach all children with BCG but this still remains a problem especially on the outer islands. Cases of the disease are detected at clinical presentation and a contact tracing program will begin in late 2007.

Diagnosis is made by sputum smear. Directly Observed Treatment Short course (DOTS) is being implemented with new workers serving Tarawa and others to be recruited.

At present (August 2007) there is one known case with multi-drug resistant organisms and two co-infected with HIV.

The WHO guidelines are followed for the detection and management of tuberculosis.

- Standard short-course therapy
- **Isoniazid 300 mg. orally daily for 6 months PLUS**
- **Rifampicin 600 mg. (<50 kg: 450 mg) orally daily for 6 months PLUS**
- **Pyrazinamide 2 G (<50 kg: 1.5 G) orally, daily for 2 months PLUS**
- **Ethambutol 15 mg/kg orally, daily for two months**
- **Pyridoxine 25 mg orally, daily is given as a routine with the above**
- All medication should be given together in a single daily dose 30 minutes before breakfast

Pregnancy and breastfeeding

Most anti-TB drugs are safe in pregnancy except streptomycin which can cause foetal ototoxicity. All the drugs are compatible with breast-feeding.

**Oral contraceptives**

Rifampicin induces enzymes which metabolise oral contraceptives. Another form of contraception is desirable.

**Liver function**

Check before commencement of treatment. If there is elevation of AST/ALT levels monitor regularly during treatment. Streptomycin and ethambutol do not affect liver function tests.

**Renal impairment**

Streptomycin and ethambutol require dose adjustment as they cumulate in renal impairment.

**HIV infection**

Prolong short course to 9 months.

Chemoprophylaxis with isoniazid 300 mg daily with pyridoxine 25mg should be given to:

- Recent tuberculin converters, especially if contacts of cases
- Children and adults <35 years with strongly positive tuberculin reactions
- Immunosuppressed patients with previously treated inactive TB
- Children born to mothers with active TB

10. Pregnancy and respiratory drugs

The first trimester of pregnancy is the major period of danger for teratogenic effects of drugs.
Some drugs can interfere with functional development of organ systems and the central nervous system in the second and third trimesters.

There is no convincing evidence that any of the drugs commonly used to treat respiratory disorders cause particular problems during pregnancy.

Attacks of asthma during pregnancy may reduce the amount of oxygen available to the foetus, so it is particularly important that asthma is well controlled. If this is achieved, asthma has no important effects on pregnancy, labour or the foetus. Severe exacerbations should be treated promptly with conventional therapy. Most asthma medications are safe to use during pregnancy.

### 11. Breastfeeding and respiratory drugs

Breastfeeding should be continued unless there is substantial evidence that the drug taken by the mother will be harmful to the infant and that no therapeutic equivalent can be given.

Most drugs are excreted only to a tiny extent in breast milk and in most cases the dose to which the infant is exposed is very low and well below the therapeutic dose level for infants. In most situations, drugs cross the placenta more efficiently than they pass into breast milk.

For these reasons the time of dosing in relation to breast feeding does not make much difference.

Inhalation drugs have particular advantages for breastfeeding mothers because their effects may be achieved without reaching high plasma concentrations. This reduces the likelihood of significant penetration into breast milk.

**Respiratory drugs in pregnancy and breastfeeding**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Status in Pregnancy</th>
<th>Use in breastfeeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminophylline</td>
<td>Safe</td>
<td>use with caution; monitor infant for irritability</td>
</tr>
<tr>
<td>Beclomethasone dipropionate</td>
<td>safe because inhaled</td>
<td>safe</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>Safe</td>
<td>safe</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>Safe</td>
<td>safe</td>
</tr>
<tr>
<td>Promethazine</td>
<td>may cause foetal drowsiness</td>
<td>safe in single dose</td>
</tr>
<tr>
<td>Salbutamol</td>
<td>Safe</td>
<td>safe</td>
</tr>
</tbody>
</table>