but patients may also experience pain in either arms, left shoulder, back, neck or stomach. This is accompanied by dyspnoea, sweating, stomach discomfort (indigestion or heartburn), nausea and vomiting. Depending on the extent and location of ischaemia, patients may be dizzy (hypotensive due to myocardial failure or dysrhythmias). Sympathetic activation (sweating), radiating pain, referred pain, nausea and vomiting are typical of visceral pain (see the next section).

The restoration of adequate myocardial oxygenation is the mainstay of treatment. This is done by increasing arterial partial pressure of oxygen (PO_2), increasing coronary blood flow, and decreasing myocardial oxygen demand. These steps limit cardiac muscle damage and reverses ischaemic pain. However, early pain control is important in decreasing myocardial oxygen demand as it decreases the stress response.

Supplemental oxygen is usually administered as soon as possible. IV morphine is analgesic, anxiolytic, decreases blood pressure and suppresses the stress response. These effects decrease oxygen demand. Concurrent management includes nitrates, antihypertensives, antiplatelet agents and interventions to restore myocardial perfusion.

Morphine sulphate has been shown to be very effective at suppressing acute cardiac ischaemic pain. It is titrated at a dose of 50 µg/kg every 5 minutes. Keep in mind that morphine delays the antiplatelet effect of ticagrelor.

Acute cardiac pain due to pericarditis is somatic pain, as opposed to ischaemic pain, and is best treated with NSAIDs.

Acute abdominal pain

A wide spectrum of conditions present with acute abdominal pain. These conditions may be due to abdominal pathology (intra- or extraperitoneally), radiating or referred pain from extra-abdominal pathology, or systemic conditions presenting with abdominal pain. Therefore, it is once again important to not only manage the pain, but also consider anatomical, physiological (including functional disturbances and psychological) and pharmacological factors (including toxins), as well as conducting appropriate investigations before deciding on the management (intervention).

Abdominal pain can have its origin intra-abdominally (intra- or extraperitoneally) or extra-abdominally. Pain can radiate or refer from the abdomen to extra-abdominal regions, for example, to the right shoulder (the gallbladder, liver or right diaphragm), to the back (stomach, pancreas, retroperitoneal blood or kidney) and to the groin (kidneys and ureters). Conversely, pain due to extra-abdominal pathology can radiate or refer to the abdomen, for example, MI, pericarditis, testicular pathology, pleural pathology (pneumonia or PE), herpes zoster (may

present like gallbladder pain), among others. Functional disturbances also present with acute abdominal pain, for example, irritable bowel syndrome (IBS).

Acute abdominal pain can be caused by a wide range of systemic conditions, including the following:

- Infections and infestations: gastroenteritis, typhoid, tuberculosis, malaria, intestinal parasites
- Metabolic diseases: ketoacidosis, uraemia, porphyria, hypercalcaemia
- Haematologic and immunological: sickle cell crisis, haemolytic crisis, retroperitoneal haemorrhage in patients on anticoagulants, enlarged lymph nodes, intestinal angioedema (C1 esterase deficiency, ACEI)
- Toxins: corrosive substances, arsenic, heavy metals (lead and mercury), spider and snake poison
- Neurologic disease: substance withdrawal syndromes, abdominal migraine, IBS, toxin-mediated peripheral neuropathy (heavy metals)

Acute abdominal pain due to abdominal pathology usually begins as visceral pain, but becomes somatic once the parietal peritoneum is affected. Visceral pain can be acute or chronic, and is classically colicky in nature. Local inflammation results in progression to typical acute somatic pain, with localisation of the affected area and progression to the clinical picture of peritonism.

Pathology causing acute abdominal pain is often accompanied by nausea and vomiting. Similar to abdominal pain, nausea and vomiting are caused by a wide range of conditions. The afferent input for nausea, the nausea centre, and the vomiting centres are responsible for the symptoms of nausea and vomiting.

The *nucleus tractus solitarius (NTS)* can be regarded as the 'nausea centre' and the *dorsal motor nucleus of the vagal nerve* forms the so-called 'vomiting centre'. The NTS is a cluster of afferents where various central and peripheral afferents converge. From here a common efferent pathway enters the dorsal motor nucleus of the vagal nerve, which coordinate the autonomic (sweating and salivation) and somatic (contraction of the diaphragm, abdominal wall and retroperistalsis of the stomach and oesophagus) phenomena of the act of vomiting.

The NTS receives input from the following centres:

- The chemoreceptor trigger zone is stimulated by toxins, drugs (several, including opioids) and metabolic derangement (ketoacidosis, uraemia, hypoxia and ketoacidosis). This stimulus is mediated by serotonin and dopamine. These causes are treated with serotonin-3-receptor (5-HT3) antagonists (ondansetron, granisetron) or dopamine antagonists (droperidol, metoclopramide, prochlorperazine, promethazine).
- Extramedullary brain structures, such as vestibular and cerebellar (motion sickness), olfactory, taste, cortex (emotion, severe pain), brain trauma and increased ICP. These are mediated by

acetylcholine and histamine. Nausea due to these stimuli is treated with the antimuscarinics (hyoscine, promethazine) and the H1 blockers (promethazine, cyclizine).

- GI visceral afferents from the GIT (vagal or sympathetic afferents) are stimulated by GI irritation (mucosal irritation, i.e. acid, alkali or bacterial toxins, distention, spasm, peritoneum) and are mediated by 5-HT3 and dopamine receptor stimulation. It is treated with 5-HT3 and dopamine antagonists.
- Extragastrointestinal stimulation (hepatobiliary [biliary colic]), peritoneum, heart, genitourinary (kidney colic, torsion or an ovary of ovarian cyst) is mediated by serotonin and treated with 5-HT3 blockers.

The management of abdominal pain consists of the management of the primary cause, as well as of the pain, hypermotility (spasm/colic), and nausea and vomiting.

This discussion is limited to conditions where urgent or emergency management is not considered, for example, bowel obstruction or GI haemorrhage.

Pharmacological treatment usually consists of analgesics and antispasmodics. Apart from atropine and glycopyrrolate, the antimuscarinic agent *hyoscine butylbromide* is the only injectable antispasmodic available in South Africa for management of GI, biliary (including the sphincter of Oddi) and genitourinary colic (renal colic). The dose is 0.2 mg/kg IVI or SC 6–8-hourly.

Renal colic

Kidney stones do not cause pain until these obstruct the ureter. Ureter obstruction causes the renal capsule to stretch and the smooth muscle in the ureter to spasm. These events activate the release of prostanoids and serotonin which cause colic pain, and nausea and vomiting, respectively. There is also a decrease in renal function. The severe pain usually requires a combination of drugs. NSAIDs, such as ketorolac, form the mainstay of treatment. An opioid is added as second-line drug. Paracetamol is of less value in this setting. NSAIDs do not aggravate nausea and vomiting and patients need fewer rescue analgesics than those receiving opioids.

Lignocaine can be used for intractable renal colic pain not responding to NSAIDs and opioids. Lignocaine 120 mg in 100 ml normal saline is infused IV over 10 minutes. A lignocaine-morphine combination is also useful: morphine sulphate 0.1 mg/kg plus lignocaine 1.5 mg/kg over 2–4 minutes.

When NSAIDs are contraindicated, an IV opioid with IV paracetamol must be used. An antispasmodic may be added. Patients presenting with renal colic are usually admitted to hospital for further management.

Biliary colic

Biliary colic is characterised by colic pain in the right hypochondrium, spreading to the epigastrium and back.

Obstruction of the biliary tree may occur in the left or right hepatic duct, common hepatic duct, cystic duct or common bile duct. The common bile duct is joined by the pancreatic duct after which it opens into the duodenum through the sphincter of Oddi. Obstruction can be caused by gallstones, fibrosis due to previous stones and cholangitis, malignancy, parasites, external pressure, as well as spasm of the sphincter of Oddi. Proximal and incomplete obstructions are often asymptomatic. Acute complete obstruction of the cystic or common bile duct is usually caused by a gallstone and may be intermittent, but may also require urgent exploration or cholecystectomy.

Acute obstruction of the cystic or common bile causes increased pressure in the gallbladder and intrahepatic bile ducts. *Mucosal irritation and contraction* of the smooth muscle in the walls of these ducts cause the release of *prostanoids*, which are responsible for colic pain and *serotonin*, which causes nausea and vomiting.

Prolonged obstruction (approximately one day) causes cholecystitis and cholangitis, which is characterised by the Charcot's triad (biliary colic, rigours and jaundice). Biliary colic may be intermittent. A stone that obstructs the outlet of the gallbladder may fall back into the gallbladder and the pain will subside. Stones in the common bile duct may be passed into the duodenum, or cause intermittent obstruction in the duct or at the sphincter of Oddi. A gallstone may cause obstruction of the pancreatic duct, causing pancreatitis.

Biliary colic should be referred for imaging, which will direct further management. The trend is to perform a laparoscopic cholecystectomy on an urgent basis. Protracted biliary colic is best managed by urgent laparoscopic cholecystectomy.

An NSAID is the first-choice treatment. NSAIDs have the same efficacy as opioids and significantly reduce the proportion of patients with severe complications. They are as effective as opioids, do not increase the tone of the sphincter of Oddi, do not cause nausea and vomiting, and prevent progression to cholecystitis.

If NSAIDs are used, it should be given parenterally since nausea and vomiting may make oral medication ineffective. Any parenteral NSAID may be used, but the following have been used in trials:

- Diclofenac 75 mg IMI
- Ketorolac 60 mg IMI, or 30 mg IVI

Besides pethidine and butorphanol, no reference could be found regarding the use of any other opioids in the management of biliary colic pain. These drugs were compared to an NSAID, and since these do not have any advantage over NSAIDs, it is not recommended but may be used in patients in whom NSAIDs are contraindicated.

Regarding the influence of opioids on the tone of the sphincter of Oddi: pethidine may decrease the tone, morphine may increase the tone, and tilidine does not affect the tone and may be used. The increase in tone caused by morphine is reversed by naloxone. The efficacy of the smooth muscle relaxant *hyoscine bromide* is inferior to that of NSAIDs.

Dysmenorrhoea

Primary dysmenorrhoea is explained by an overproduction of prostanoids in the endometrium when progesterone levels decline. A non-selective NSAID is the first-line treatment in the management of pain of dysmenorrhoea. Several of these agents are effective and are better than paracetamol. No reference regarding the use of opioids could be found.

Posttraumatic pain

Everybody, including babies, children, fit athletes and the frail elderly, is vulnerable to trauma. Trauma patients do not only differ in age, but also with regards to the type of trauma, comorbid conditions and medications – including analgesics. These factors must be considered when treating their pain.

Initial therapy for significant trauma pain is best achieved by the titration of IV opioids. Morphine sulphate remains the most widely-used agent, but adverse effects such as nausea and vomiting, hypotension, respiratory depression and oversedation occur commonly. The dose is 50 µg/kg every 5 minutes until the VAS is $\leq$ 3/10.

NSAIDs are effective analgesics in the trauma setting. These should preferably be administered IV, but IMI administration may be necessary if IV access is not available. NSAIDs (non-selective and selective COX-2 inhibitors) are generally safe, but should not be used in patients at risk of haemorrhage; that is CNS injury, head and neck injury, vascular injury, patients with premorbid diseases such as GI ulcers and bleeding diathesis (e.g. liver disease), antiplatelet agents, and anticoagulants. These should not be used in patients at risk of renal failure (hypovolaemia, the elderly, use of ACEIs, ARAs and diuretics) and IV paracetamol is preferable in these patients.

NSAIDs are usually continued after hospital discharge in an oral formulation either alone or in combination with an opioid derivative, such as codeine. *Topical NSAIDs* in gel or patch form are useful and decrease systemic analgesic requirements.