

## REVIEW ARTICLE

# Interpleural block – part 2

R. M. Dravid<sup>1</sup> and R. E. Paul<sup>2</sup>

*1 Consultant Anaesthetist, Kettering General Hospital, Kettering General Hospital, Rothwell Road, Kettering NN16 8UZ, UK*

*2 Specialist Registrar, Oxford Deanery, Oxford, UK*

### Summary

Interpleural blockade is effective in treating unilateral surgical and non-surgical pain from the chest and upper abdomen in both the acute and chronic settings. It has been shown to provide safe, high-quality analgesia after cholecystectomy, thoracotomy, renal and breast surgery, and for certain invasive radiological procedures of the renal and hepatobiliary systems. It has also been used successfully in the treatment of pain from multiple rib fractures, herpes zoster, complex regional pain syndromes, thoracic and abdominal cancer, and pancreatitis. The technique is simple to learn and has both few contra-indications and a low incidence of complications. In the second of two reviews, the authors cover the applications, complications, contra-indications and areas for future research.

*Correspondence to: Dr R. M. Dravid*

*E-mail: Ravi.Dravid@kgh.nhs.uk*

*Accepted: 14 January 2007*

The interpleural route for the administration of local anaesthetic agents is capable of providing effective analgesia for postoperative, acute and chronic pain originating within the distribution of intercostal nerves. Local anaesthetic solutions can be administered as single or intermittent boluses, or as continuous infusions via an interpleural catheter. It has been shown to provide safe, high quality analgesia after cholecystectomy, thoracotomy, renal surgery and breast surgery, and for some invasive radiological procedures of the renal and hepatobiliary system. It has also been used successfully in the treatment of pain from multiple rib fractures, herpes zoster, Complex Regional Pain Syndromes (CRPS), thoracic cancer, abdominal cancer and pancreatitis. The first part of this review focused on the history, anatomy, mechanism of action, technique and local anaesthetic dosage regimens for this block. In the second part, we consider the applications, complications, contra-indications and areas for future research.

### Indications for interpleural block

Interpleural blockade has been used with success in procedures listed in Table 1.

#### Gall bladder and liver

Interpleural block has been most extensively studied for postoperative analgesia in patients undergoing unilateral

subcostal and flank incisions, i.e. open cholecystectomy [1–11], renal surgery [1, 12–14] and unilateral breast surgery [1, 12, 15, 16]. The dosing regimens used have been dealt with in our first review [17]. Compared to open cholecystectomy, there are few data relating to its use in laparoscopic cholecystectomy. However, interpleural block may be useful when a laparoscopic procedure is converted to an open one because of technical difficulty, as the insertion of an epidural in an anaesthetised patient carries with it the risk of inadvertent neuraxial injury.

Laparoscopic cholecystectomy is less painful than an open procedure. Its feasibility as a day-case procedure has been established. Nevertheless, pain control and postoperative nausea and vomiting necessitating the use of opioids and anti-emetics are major impediments to recovery and early discharge [18–22]. Early pain after laparoscopic cholecystectomy is complex and includes pain components resulting from different mechanisms, such as trauma to the abdominal wall from instrumentation and removal of the gall bladder, abdominal distension from residual pneumoperitoneum and irritation of the peritoneum and diaphragm by blood or bile. Many methods of pain relief have been evaluated. Wills and Hunt [23] included 42 randomised controlled trials in their review, assessing interventions to decrease pain after the procedure. They concluded that nonsteroidal

**Table 1** Indications for interpleural block.

Head, neck and upper extremity	Thorax	Abdomen
Tumour invasion of the brachial plexus [68]	Unilateral breast surgery [1, 12, 15, 16]	Open cholecystectomy [1–11]
Pain of acute herpes zoster and post herpetic neuralgia [64–67]	Needle localisation and breast biopsy – sole anaesthetic [15]	Laparoscopic cholecystectomy [25, 26]
Chronic regional pain syndromes of the upper limb [36, 61, 63]	Thoracotomy [42, 43, 45, 48–51]	Renal surgery [1, 12–14]
Upper limb ischaemia [62]	Chest drain [108, 109]	Abdominal surgery (bilateral blocks) [55, 56]
	Cardiac surgery [53, 54]	Percutaneous hepatic and biliary drainage procedures [27–29]
	Thoracic sympathectomy [52]	Chronic pancreatic pain [75–79]
	Postoperative thoracic cancer pain [69]	Upper abdominal cancer pain [71, 73, 78]
	Chest wall and thoracic visceral pain [69]	Extracorporeal shock wave lithotripsy [12, 33]
	Chronic oesophageal cancer pain [71]	Percutaneous nephrostomy and nephrolithotomy [35]
	Benign chest wall pain [70, 110]	
	Multiple rib fractures and chest trauma [57, 59, 60, 82]	
	Pain of acute herpes zoster [64, 65]	
	Post-herpetic neuralgia [66, 67]	
	Pain of oesophageal perforation [72]	

anti-inflammatory drugs, intraperitoneal bupivacaine and local anaesthetic to the wounds may all decrease pain. Only one trial involving the use of interpleural bupivacaine was included, which showed a decrease in pain for the first 6 h. None of the studies has demonstrated a prolonged decrease in pain or improved functional outcome [23]. Bisgaard et al. [24], in their review of methods of pain relief for laparoscopic cholecystectomy, only made a very brief mention of interpleural block. They concluded that, although many methods produce a short-term benefit, this does not equate with earlier discharge or improved postoperative function. Schulte-Steinberg et al. [25], in a randomised, controlled trial, compared intraperitoneal and interpleural morphine and bupivacaine. They showed that intraperitoneal and interpleural morphine and intraperitoneal bupivacaine were unable to produce significant pain relief after laparoscopic cholecystectomy; only interpleural bupivacaine was effective.

One of the authors and his colleagues have successfully developed a care pathway for the management of day-case laparoscopic cholecystectomy incorporating interpleural block in the anaesthetic technique [26]. Induction and maintenance of general anaesthesia with a target-controlled infusion of alfentanil and propofol were followed by institution of the block with a 'continuous saline flow' technique. Pain was managed with intermittent bolus doses of bupivacaine 0.25% through the catheter. The effectiveness of the block and the absence of pneumothorax were confirmed by response to cold spray and a chest X-ray before interpleural catheter removal. The patients were discharged home according to

case criteria with regular oral analgesics. None of the patients needed systemic opioids or anti-emetics, there were no failed discharges or re-admissions for anaesthetic reasons, and the patients reported excellent oral intake and functional recovery with a very high satisfaction score on subsequent telephone follow-up.

#### **Percutaneous hepatobiliary drainage**

Two case series have confirmed the safety and efficacy with lack of haemodynamic and respiratory adverse effects of interpleural block for pain relief for percutaneous hepatobiliary drainage [27, 28]. In a double-blind, placebo controlled trial, Therasse et al. [29] performed biliary drainage after an interpleural block with bupivacaine 0.5% with adrenaline 30 ml. Fentanyl patient-controlled analgesia was available to both the block and the placebo groups. Although the block did not totally abolish the pain of the procedure, both pain intensity and opioid requirement were decreased in the interpleural group.

#### **Renal procedures**

Despite the large positive experience with cholecystectomy, the results from the few studies evaluating the block for pain relief after nephrectomy have been mixed. While Baude et al. [30] found interpleural analgesia to be effective, Murphy [31] reported inadequate analgesia in four of eight patients who had undergone nephrectomy. This was attributed to the presence of drainage tubes and a marked posterior extension of the scar. Other studies have reported good pain relief with a significant opioid sparing effect [14, 32]. Grief et al. [14] inserted interpleural catheters through the sixth intercostal space in the

mid-axillary line at the end of surgery with the patients in a supine position. The first bolus of bupivacaine 0.25% 20 ml was followed by similar doses every 6 h until the second postoperative day. The catheters were removed at 48 h. They reported excellent pain relief with significant prolongation of the time to first analgesic request and a decreased total postoperative opioid requirement. It is worth noting that pneumothorax in nephrectomy patients may also be due to damage to the pleura during surgery and that subsequent analgesia or lack of it may be influenced by the presence of a chest drain.

### Extracorporeal shock wave lithotripsy

Interpleural block has been successfully used for extracorporeal shock wave lithotripsy [33, 34]. Trivedi et al. described its use in four patients who were given bupivacaine 0.5% 30 ml interpleurally without the need for supplementary sedative or analgesics for percutaneous nephrostomy and subsequent nephrolithotomy [35].

### Breast procedures

Schlesinger et al. used the block as a sole technique for mammography during needle localisation and for subsequent breast biopsy. No supplementary analgesia was needed [15]. Higgins et al. have reported its use as a sole anaesthetic technique for mastectomy in a high-risk patient [16].

Reiestad and McIlvaine [36] have also reported unilateral block of the T1–T9 intercostal nerves, with complete skin anaesthesia sufficient to allow breast surgery. They recommend placing the patient in the lateral position with the affected side down and with a head-down tilt of 20° for 30 min after injection of the local anaesthetic.

### Thoracotomy

Whilst interpleural blockade is reproducibly effective after surgical flank incisions, the case for its use after thoracotomy is less clear; the evidence is somewhat conflicting [37–39]. Rosenberg et al. used the block in 14 consecutive patients who underwent exploratory thoracotomy, lobectomy and pneumonectomy, and found pain relief to be unsatisfactory [40]. Another study also found it unreliable [41], although Mann et al. found it useful [42]. Francois and colleagues [43], in a randomised, double-blind and placebo-controlled study, observed the effects of the interpleural administration of bupivacaine or lidocaine on pain and on morphine requirements after oesophagectomy and thoracotomy. They concluded that interpleural analgesia with bupivacaine after oesophagectomy decreased morphine consumption due to a reduction in thoracic pain but not in abdominal pain. The results after thoracotomy are therefore controversial.

Some reasons for the conflicting results include: loss of local anaesthetic through the unclamped chest drain, its dilution in pleural effusions, binding to blood proteins in bloody effusions and an uneven distribution in the pleural cavity where a part or whole lung is removed [43]. Up to 30% of the injected dose may be lost in the chest drain [2]. Another study noted that good pain relief from interpleural block was achieved in patients who underwent lateral and posterior thoracotomy, but not in those with anterior thoracotomy, or in patients in whom there was excessive bleeding into the pleural space [44]. Tartiere et al. [45] studied the effectiveness of interpleural block after thoraco-abdominal incision for oesophagectomy. The pain of the thoracotomy was decreased but the abdominal pain was unaltered. Thoracic epidural analgesia [46] or thoracic paravertebral blockade [47] are likely to be better alternatives in these situations. Richardson et al. [47], in a prospective, double-blind trial comparing interpleural with paravertebral block, found similar pain scores and patient-controlled morphine use but a greater preservation of lung function and fewer side-effects with paravertebral than with interpleural block. It is worth noting the advantage that interpleural and paravertebral catheters can be placed under direct vision at the time of thoracotomy by the surgeon [47]. Diaphragmatic irritation and scapular retraction may be other reasons why interpleural block alone may not be completely effective after a thoracotomy. It appears to be most useful in clinical settings such as the first thoracotomy in the healthy chest cavity or for the patient with a chest drain to treat spontaneous pneumothorax. However, studies in infants and children have reported good results after lateral thoracotomy [48–50]. McIlvaine et al. [49, 50] used continuous infusion of bupivacaine 0.25% with adrenaline at 0.5–1.0 ml.kg<sup>-1</sup>.h<sup>-1</sup> in children to achieve effective analgesia without the need for opioid supplementation. Giaufre et al. reported safe and effective analgesia in children with bupivacaine 0.1% infused at the rate of up to 1 ml.kg<sup>-1</sup>.h<sup>-1</sup> [51].

### Endoscopic thoracic sympathectomy

In a randomised, controlled trial, interpleural bupivacaine was associated with significantly reduced pain scores at rest and after coughing, and decreased morphine consumption compared to the control group [52].

### Cardiac surgery

Baxter et al. reported significantly lower postoperative pain scores when bilateral interpleural catheters had been placed during cardiac surgery [53]. Mehta et al. compared thoracic epidural analgesia and interpleural block in 50 patients undergoing minimally invasive direct coronary artery bypass (MIDCAB) surgery in a prospective

randomised trial [54]. The catheter was placed in the T4/T5 interspace in the epidural group or in the sixth intercostal space in the interpleural group. Visual analogue pain scores, supplementary analgesic use, haemodynamic and respiratory function and complications were recorded after bupivacaine boluses. They concluded that interpleural block is safe and effective, has a low complication rate and is especially useful after heparinisation. However, significant intercostal drainage could be a limiting factor [54].

### Bilateral blocks

Bilateral blocks have been described for managing postsurgical (laparotomy) [55, 56], bilateral rib fractures and chronic cancer pain [57]. These continue to be used by clinicians in their anaesthetic practice with success. One of the authors [26] has used sequential bilateral interpleural blocks in patients undergoing bilateral mastectomy. The first block is performed before surgery, and the second block before the start of the second mastectomy. Nitrous oxide is avoided, as the block supplements general anaesthesia when performed before surgery. The occurrence of a pneumothorax, its enlargement due to the use of nitrous oxide and the risk of local anaesthetic toxicity if larger doses are used are potential problems and, clearly, detailed studies are required to determine the efficacy and safety of a bilateral technique, as well as its effect on cardiopulmonary function.

### Rib fractures

There are many reports of the successful use of unilateral and bilateral interpleural blockade in patients with multiple rib fractures [57–60]. It provides comparable pain relief to that via the epidural route, although not all studies concur. However, due to its simplicity and because it can be performed with the patient in any position, it can be especially useful when a thoracic epidural is not feasible or is contra-indicated.

### Chronic pain

Whereas evidence for its use in acute postoperative pain emanates from trials, that for chronic pain conditions comes mostly from individual case reports or series. These also suggest its effects on the sympathetic system in the amelioration of chronic pain. It has been used to treat pain from CRPS [36, 61] and ischaemic conditions of the upper limb [62], acute herpes and postherpetic neuralgia of the head, neck and thorax [63–67], tumour involvement of the brachial plexus [68], pain in the pleura and chest wall from metastatic bronchogenic carcinoma [69], benign atypical chest pain [70], oesophageal cancer [71] and rupture pain [72], chronic pain in terminally ill patients with pancreatic, renal cell and breast cancers,

lymphomas [73], upper abdominal cancers and chronic benign and neoplastic pancreatic pain [74–79]. Czop et al. [61], in a prospective, randomised crossover study involving 10 patients, compared stellate ganglion blocks with interpleural block for CRPS of the upper extremity. Although five of the 10 patients undergoing interpleural block and six of the 10 undergoing stellate ganglion block reported at least a 50% decrease in their pain scores, they found that neither block was effective in producing a sympathetic denervation of the upper extremity when objective indices of vasomotor and sudomotor tone were measured. In their study, they used only 15 ml of bupivacaine, and it is not clear if they used appropriate positioning to facilitate the cephalad spread of the local anaesthetic during the interpleural block. Experience with the treatment of upper abdominal cancer pain has suggested that this might be an easier technique and a good alternative to the more difficult coeliac plexus block in selected cases, especially when appropriate positioning is difficult due to pain [78].

### Contra-indications and complications (Tables 2 and 3)

Abnormality or disruption of the anatomy of the space or underlying lung may cause difficulty in locating the interpleural space, thus increasing the risk of accidental

**Table 2** Contra-indications to interpleural blockade.

<i>Absolute</i>
Patient refusal
Allergy to local anaesthetic agent
Extensive infection at block or catheter insertion site
<i>Relative</i>
Emphysema
Bullous lung disease
Recent pulmonary infection or empyema
Pleural adhesions or pleurodesis
Haemothorax
Coagulopathy
Contralateral phrenic nerve paralysis

**Table 3** Complications of interpleural blockade.

Pneumothorax
Systemic local anaesthetic toxicity
Catheter misplacement
Horner's syndrome
Phrenic nerve paralysis
Infection
Pleural effusion – serous or bloodstained
Intrabronchial injection
Ipsilateral bronchospasm
Cholestasis
Administration error
Bronchopleural fistula
Direct myocardial depression

pneumothorax. The presence of a pleural effusion or blood in the pleural space may render the local anaesthetic less effective due to protein binding. Pleural inflammation may result in rapid systemic absorption of the local anaesthetic. It has been used in a patient with a coagulopathy in whom epidural analgesia was contraindicated [80].

The largest review of the side-effects and complications related to interpleural analgesia was published in 1990 [81]. We have been unable to find any similar articles published since this date. The two main complications of concern to both clinician and patient are pneumothorax and local anaesthetic toxicity. Pneumothorax may occur because of air entrainment while performing the procedure or as a result of damage to the lung parenchyma caused by the needle or catheter. A retrospective literature review found a 2% incidence of pneumothorax in 703 procedures. This included one tension pneumothorax, which followed the use of a loss-of-resistance technique to identify the space. Other reasons cited have been related to mechanical ventilation [4, 82], unexpected movement [83], needle type, a stiff catheter and a large amount catheter being inserted [84]. This can be avoided by giving careful consideration to the technique described in our first review, the use of a Tuohy-tipped needle, a soft, blunt catheter and the insertion of a shorter length.

It is likely that the true incidence of pneumothorax will never be known. It may be higher than that reported, as not all cases get reported, and small pneumothoraces may be undetectable symptomatically on clinical examination and even on plain chest radiography. Alternatively, it may be lower because of the adoption of safer techniques for identifying the interpleural space that prevent air entrainment. It is certainly the case that many anaesthetists familiar and experienced with the technique use it regularly without complications.

Of particular concern to the anaesthetist is the potential for any pneumothorax to expand when nitrous oxide is used as part of the anaesthetic technique. A high degree of vigilance should always be maintained at all times. Strömskag et al. feel that a routine X-ray is mandatory [81]. However, opinion is divided. Some advocate it only if there is a suspicion of a significant pneumothorax. One of the authors and his colleagues [26] recommend monitoring vital parameters and peripheral oxygen saturation in the recovery room, with routine observations on the ward, and reserves an X-ray only in the patients who are being treated as a day case.

Systemic toxicity from local anaesthetic agents is another major concern for the anaesthetist performing any regional anaesthetic technique. Its prevalence is reported as being 1.3% [81]. Plasma local anaesthetic concentrations during

interpleural administration are known to vary markedly. Signs and symptoms of central nervous system toxicity have been reported during interpleural blocks, but this is a rare occurrence. There have been no reports of cardiac toxicity of local anaesthetic drugs given by the interpleural route.

It is difficult to interpret the significance of plasma concentrations of local anaesthetic drugs after regional anaesthesia. Although the estimated threshold plasma concentration of bupivacaine that is associated with the onset of central nervous system toxicity is usually quoted at 2–4  $\mu\text{g}\cdot\text{ml}^{-1}$ , clinical toxicity is rarely seen even with concentrations reported in or above this range [85]. It may be that the rate of change in plasma concentration is more important in determining clinical toxicity than the absolute blood concentration [86, 87]. Many authors routinely use local anaesthetic solutions containing adrenaline, usually in a concentration of 1 : 200 000. The addition of adrenaline may help detect inadvertent intravascular injection (by producing an immediate rise in heart rate) and it may also delay and decrease the peak plasma concentration of local anaesthetics [44, 88, 89], although not all studies confirm this [11].

Accidental direct intravenous administration of bupivacaine has led to seizures at plasma levels of 2.3  $\mu\text{g}\cdot\text{ml}^{-1}$  and 3.0  $\mu\text{g}\cdot\text{ml}^{-1}$ . Both occurred as complications of epidural analgesia. Studies usually quote the peak plasma concentration and the time to reach this concentration. Both these indices show considerable interindividual variation [4, 90]. As might be expected, the peak plasma concentration increases with increasing dose of local anaesthetic agent [6]. Using high concentrations of local anaesthetic can decrease the time to peak concentration [91]. The plasma concentration will increase further when repeat boluses are given or a continuous infusion used [40]. Strömskag et al. measured arterial plasma concentrations in three groups of 10 patients each being given interpleural boluses of 20 ml of bupivacaine 0.25%, 0.375% and 0.5%, all with 1 : 200 000 adrenaline [6]. The mean (SD) peak plasma concentrations were 0.62 (0.25)  $\mu\text{g}\cdot\text{ml}^{-1}$ , 0.82 (0.4)  $\mu\text{g}\cdot\text{ml}^{-1}$  and 1.2 (0.44)  $\mu\text{g}\cdot\text{ml}^{-1}$ , respectively, all peak concentrations occurring approximately 15 min after injection. No side-effects were observed in any of these patients. Central nervous system toxicity after bolus interpleural injection of bupivacaine has been reported [55]. Symptoms of light-headedness, visual disturbance and eyelid twitching were reported in two of five patients who were given bupivacaine 0.75% 30 ml. Seizures did not occur despite plasma concentrations of 5.7  $\mu\text{g}\cdot\text{ml}^{-1}$  and 5.2  $\mu\text{g}\cdot\text{ml}^{-1}$ . Seizure activity after interpleural injection has been reported. Eleven study patients were given injections of bupivacaine 0.5% with adrenaline 1 : 100 000 30 ml via an interpleural catheter whilst still under general anaesthesia at the

conclusion of open cholecystectomy. One patient developed head and neck twitching within 1 min of injection, followed by delayed awakening. In this case, the measured plasma concentration was  $4.9 \mu\text{g}\cdot\text{ml}^{-1}$ . The patient underwent an uncomplicated recovery following this, and it was hypothesised that an inflamed pleural surface as a result of a recent chest infection may have accounted for the rapid absorption of the bupivacaine. The mean (SD) peak plasma concentration in the other 10 patients was  $2.07 (0.58) \mu\text{g}\cdot\text{ml}^{-1}$  [92]. Symptoms of agitation, tinnitus and tremor have been reported in a patient being given interpleural bupivacaine who developed a plasma bupivacaine concentration of  $3.86 \mu\text{g}\cdot\text{ml}^{-1}$  [85]. This patient had received three boluses of bupivacaine 0.5% 20 ml via an interpleural catheter over a 6-h period, followed by an infusion of bupivacaine 0.25% at  $10 \text{ ml}\cdot\text{h}^{-1}$ . The symptoms settled with discontinuation of the infusion. Kastrissios et al. studied eight cholecystectomy patients in whom a regimen of 6–8-hourly bolus doses of bupivacaine 0.5% with adrenaline 20 ml was used over a 52-h period. Although three had blood levels greater than those associated with the development of central nervous system toxicity, none of the patients actually developed clinical toxicity [93]. One of the reasons for the absence of clinical toxicity despite higher blood levels could be the fact that  $\alpha 1$ -acid-glycoprotein levels increase after surgery, producing enhanced binding and a decreased free fraction of bupivacaine [94]. There is one case report of central nervous system toxicity in a patient receiving continuous interpleural analgesia for pain relief after thoracotomy. This occurred during an actively running bupivacaine infusion when the surgeon clamped the chest drain without altering the infusion regimen [85].

In summary, it is clear from the available evidence that systemic toxicity is a potential risk, as is the case with other forms of regional anaesthesia. As Scott [87] suggests, development of adverse symptoms may be more dependent on the rate of increase than on the actual plasma bupivacaine concentration. It has been shown that effective analgesia can be safely achieved by limiting the total dose with lower concentration solutions, although at the cost of a decreased duration. This produces lower blood drug levels [6]. Bupivacaine in a concentration  $>0.5\%$  is not recommended [55]. Infusions have the potential advantage over bolus doses that they provide better analgesia and significantly lower blood concentrations.

Horner's syndrome may unintentionally occur as a result of blockade of the upper thoracic sympathetic ganglia with administration of local anaesthetic in the Trendelenburg position. It should be noted that, if interpleural block is being contemplated for analgesia after rib fractures in a patient with a concomitant head

injury, unilateral dilatation of the pupil associated with Horner's syndrome might confuse and complicate the management of the head injury. Interpleural analgesia could potentially block pain from a delayed splenic rupture, which should be considered when managing pain in a trauma victim [95].

Catheter misplacement may occur into subcutaneous tissue, blood vessels, or into lung parenchyma, which may cause pneumothorax [84]. Some authors confirm correct catheter placement with a contrast injection. This is sensible if the catheter is intended for use for several days. As with all invasive procedures, there is the potential for the introduction of infection, and meticulous aseptic technique should be routinely used. There are no data available in the literature about the incidence of infection from interpleural catheterisation. Where this complication is suspected, it would seem logical to treat it along the same lines as when treating infection from invasive lines or epidural catheters.

Lauder [96] has reported phrenic nerve paralysis following interpleural block for elective open cholecystectomy. The diagnosis was based on a raised hemidiaphragm on X-ray and failure to obtain improvement in the patient's lung function despite effective analgesia. It resolved completely after discontinuation of the block. It is suggested that the phrenic nerve could be blocked anywhere along its course from the thoracic inlet to the diaphragmatic surface. However, Aguilar et al. [97] argue that this complication is not often observed for two reasons. Firstly, the volumes used do not migrate to the cervical portion of the hemithorax where the phrenic nerve is in close relation to the pleura, and secondly, that it runs more internally in the inferior portion of the mediastinum and thus is less likely to be blocked by the local anaesthetic [97]. Diaphragmatic paralysis would compromise lung function and would predispose to basal atelectasis. Paralysis of both the phrenic nerves from a bilateral interpleural block can cause as much as a 50% decrease in vital capacity, depending on the position of the patient. The volume, concentration of the local anaesthetic and position of the patient after injection could contribute to this complication.

There is a possibility that cardiac function could be depressed if the local anaesthetic reached the myocardium directly because of a damaged or absent pericardium or as a result of blockade of the cardiac sympathetic nerves.

A case has been reported of accidental misadministration. A syringe-loaded local anaesthetic for intrapleural administration was not attached to a syringe driver but was left by the patient's side. The negative interpleural pressure resulting from the patient's spontaneous breathing produced a suction effect on the syringe and led to

the delivery of 40 ml of the local anaesthetic in 10 min before it was detected [98]. Ipsilateral bronchospasm [99], accidental intrabronchial injection [100], blood-stained pleural effusion [101] and cholestasis documented by clinical and laboratory findings [102] have also been reported.

### **Other analgesic drugs used in the interpleural space**

#### **Local anaesthetic agents**

Bupivacaine and lidocaine have both been extensively studied, the former being preferred for its longer duration of action. There are no large-scale studies at present of the use of ropivacaine or levobupivacaine, both of which would appear to be attractive agents because of their lower potential for cardiotoxicity. Ropivacaine has been used in one case as an alternative to bupivacaine to overcome problem of tachyphylaxis with long-term use [103].

#### **Opioids**

Morphine given into the interpleural space has been shown to be of no additional benefit over its systemic administration [25, 104]. Pethidine, which has both opioid and local anaesthetic effects, has not been studied in the interpleural space. Whether the addition of opioids to infusion regimens may have a local anaesthetic sparing effect has not been studied.

#### **Clonidine**

Clonidine, an alpha-2 adrenoceptor agonist, is known to have centrally mediated non-opiate antinociceptive properties. It has been shown to be a more potent analgesic than morphine in animals [105]. It is commonly used in anaesthetic practice to enhance epidural and intrathecal analgesia in conjunction with local anaesthetics. Canver et al. [106] reported excellent analgesia without side-effects with the use of interpleural clonidine alone in two patients in the first 48 h after open cholecystectomy. The first dose of 300 µg was effective within 30 min and was followed by subsequent 'on demand' 150-µg boluses.

#### **Phenol**

Phenol has been used to provide excellent analgesia in a patient with advanced cancer in whom life expectancy was expected to be > 3 months [71].

#### **Areas for future research**

More trials are needed to determine whether interpleural block improves overall quality of care, func-

tional outcomes and patient satisfaction, particularly in minimally invasive, short stay, ambulatory and fast-track surgery. Further work is needed with longer term catheter techniques, with safer alternatives to bupivacaine, usefulness of alpha-2 agonists, NMDA receptor agonists and steroids especially for the relief of chronic pain conditions. More studies are needed to look into its use either on its own or in combination with above additives in the prevention or treatment of post-surgical chronic pain syndromes (post thoracotomy neuralgia/post-mastectomy pain syndromes). Computer-aided three-dimensional animation [107] and bench models have been developed for teaching regional and other techniques, some of which are commercially available. It is a promising new tool to accelerate the learning of regional anaesthetic techniques. There is scope for such aids to be developed for teaching interpleural block to shorten the learning curve, improve safety and disseminate training.

#### **Conclusion**

The interpleural route for the administration of local anaesthetic agents is capable of providing effective analgesia for postoperative, acute and chronic pain originating within the distribution of intercostal nerves. Studies indicate that it also ameliorates acute and chronic sympathetic pain and that this technique can be used for long-term pain management. The block is simple and relatively easy to perform compared to techniques such as thoracic epidural catheter insertion, and requires little in the way of special equipment. In situations in which epidural analgesia is not feasible or is contra-indicated, interpleural analgesia can provide an excellent alternative. In addition, its success in relieving subdiaphragmatic chronic visceral pain makes it an attractive alternative to the more complex plexus blocks for pain management. Few anaesthetists use this technique on a regular basis. Therefore, it is not surprising that there is little training in the use of the technique. Today's need for ambulatory fast-track surgery and the increasing list of operations suitable for short-stay surgery pose a challenge to the anaesthetist. The high quality analgesia and opioid sparing, lack of motor blockade, cardio-respiratory stability, minimal side-effects and a low frequency of complications should make it an attractive alternative regional anaesthetic technique for such situations.

#### **Acknowledgement**

We gratefully acknowledge the suggestions and constructive criticism from Professor Henry McQuay in the preparation of this review.

## Addendum

Figures 1 and 2 from Interpleural block – part 1: reprinted from Acute Pain. *Mechanisms and Management*. Sinatra RS, Hord AH, Ginsberg B, Preble LM, eds. Mosby Year Book (1992), pp. 358–359. Copyright (1992), with permission from Elsevier.

Figure 3 from Interpleural block – part 1: adapted from *Neural Blockade in Clinical Anesthesia and Management of Pain*. Cousins MJ, Bridenbaugh PO, eds. Lippincott-Raven; 3rd Edition (1998), p. 473. Copyright (1998), with permission from Lippincott, Williams and Wilkins.

## References

- 1 Reiestad F, Strømskag KE. Interpleural catheter in the management of postoperative pain: a preliminary report. *Regional Anesthesia* 1986; **11**: 89–91.
- 2 Frenette L, Boudreault D, Guay J. Interpleural analgesia improves pulmonary function after cholecystectomy. *Canadian Journal of Anaesthesia* 1991; **38**: 71–4.
- 3 VadeBoncouer TR, Riegler FX, Gault RS, Weinberg GL. A randomized, double blind comparison of the effects of interpleural bupivacaine and saline on morphine requirements and pulmonary function after cholecystectomy. *Anesthesiology* 1989; **71**: 339–43.
- 4 Brismar B, Pettersson N, Tokics L, Strandberg A, Hedenstierna G. Postoperative analgesia with intrapleural administration of bupivacaine-adrenaline. *Acta Anaesthesiologica Scandinavica* 1987; **31**: 515–20.
- 5 Bruce DL, Gerken MV, Lyon GD. Post-cholecystectomy pain relief by intrapleural bupivacaine in patients with cystic fibrosis. *Anesthesia and Analgesia* 1987; **66**: 1187–9.
- 6 Strømskag KE, Reiestad F, Holmqvist EL. Intrapleural administration of 0.25%, 0.375%, and 0.5% bupivacaine with epinephrine after cholecystectomy. *Anesthesia and Analgesia* 1988; **67**: 430–4.
- 7 Laurito CE, Kirz LI, VadeBoncouer TR, et al. Continuous infusion of interpleural bupivacaine maintains effective analgesia after cholecystectomy. *Anesthesia and Analgesia* 1991; **72**: 516–21.
- 8 El-Naggar MA, Schaberg FJ, Phillips MR. Intrapleural regional analgesia for pain management in cholecystectomy. *Archives of Surgery* 1989; **124**: 568–70.
- 9 Frank ED, McKay W, Rocco A, Gallo JP. Interpleural bupivacaine for postoperative analgesia following cholecystectomy: a randomised prospective study. *Regional Anesthesia* 1990; **15**: 26–30.
- 10 Lee D, Boon P, Bagshaw and Kempthorne P. A randomised double-blind study of interpleural analgesia after cholecystectomy. *Anaesthesia* 1990; **46**: 1028–31.
- 11 Rademaker BM, Sih IL, Kalkman CJ, et al. Effects of interpleurally administered bupivacaine 0.5% on opioid analgesic requirements and endocrine response during and after cholecystectomy: a randomised double-blind controlled study. *Acta Anaesthesiologica Scandinavica* 1991; **35**: 108–12.
- 12 Kvalheim L, Reiestad F. Interpleural catheter in the management of postoperative pain. *Anesthesiology* 1984; **61**: A231.
- 13 van Kleef JW, Logeman A, Burm AG, et al. Continuous interpleural infusion of bupivacaine for postoperative analgesia after surgery with flank incisions: a double-blind comparison of 0.25% and 0.5% solutions. *Anesthesia and Analgesia* 1992; **75**: 268–74.
- 14 Greif R, Wasinger T, Reiter K, et al. Pleural Bupivacaine for pain treatment after nephrectomy. *Anesthesia and Analgesia* 1999; **89**: 440–3.
- 15 Schlesinger TM, Laurito CE, Baughman VL, et al. Interpleural bupivacaine for mammography during needle localization and breast biopsy. *Anesthesia and Analgesia* 1989; **68**: 394–5.
- 16 Higgins PC, Ravalia A. Interpleural anaesthesia for mastectomy. *Anaesthesia* 2005; **60**: 1150–1.
- 17 Dravid R M, Paul RE. Interpleural block: PART 1. *Anaesthesia* 2007; **62**: 1039–49.
- 18 Lillemoe KD, Lin JW, Talamini MA. Laparoscopic Cholecystectomy as a 'true' outpatient procedure. *Journal of Gastrointestinal Surgery* 1999; **3**: 44–9.
- 19 Ammori BJ, Davides D, Vezakis A, et al. Day-case laparoscopic cholecystectomy: a prospective evaluation of 6-year experience. *Journal of Hepato-Biliary-Pancreatic Surgery* 2003; **10**: 303–8.
- 20 Lau H, Brooks DC. Contemporary outcomes of ambulatory Laparoscopic Cholecystectomy in a major teaching hospital. *World Journal of Surgery* 2002; **26**: 1117–21.
- 21 Leeder PC, Matthews T, Krzeminska K, Dehn TCB. Routine day-case laparoscopic cholecystectomy. *British Journal of Surgery* 2004; **91**: 312–6.
- 22 Hession MC. Factors influencing successful discharge after outpatient laparoscopic cholecystectomy. *Journal of Peri-anesthesia Nursing* 1998; **13**: 11–5.
- 23 Wills VL, Hunt DR. Pain after laparoscopic cholecystectomy. *British Journal of Surgery* 2000; **87**: 273–84.
- 24 Bisgaard T, Kehlet H, Rosenberg J. Pain and convalescence after laparoscopic cholecystectomy. *European Journal of Surgery* 2001; **167**: 84–96.
- 25 Schulte-Steinberg H, Weninger E, Jokisch D, et al. Intraperitoneal versus interpleural morphine or bupivacaine for pain after laparoscopic cholecystectomy *Anesthesiology* 1995; **82**: 634–40.
- 26 Dravid RM, Mohroof R, Radhakrishnan L, Al-Hamali S. Interpleural block for day case laparoscopic cholecystectomy. *Journal of One-Day Surgery* 2006; **16** (Suppl. 1): A2.
- 27 Rosenblatt M, Robailno J, Bergman A, Shevde K. Pleural block: technique for regional anesthesia during percutaneous hepatobiliary drainage. *Radiology* 1989; **172**: 279–80.
- 28 Razzaq R, England RE, Martin DF. Technique for providing analgesia during percutaneous biliary interventional procedures. *Clinical Radiology* 2000; **55**: 131–5.
- 29 Therasse E, Choiniere M, Soulez G, et al. Percutaneous biliary drainage: clinical trial of analgesia with interpleural block. *Radiology* 1997; **205**: 663–8.



- 30 Baude C, Long D, Chabrol B, et al. Postoperative analgesia for nephrectomy. *Cahiers d'Anesthésiologie* 1991; **39**: 533–6.
- 31 Murphy DF. Intercostal nerve blockade for fractured ribs and postoperative analgesia: description of a new technique. *Regional Anesthesia* 1983; **8**: 151–3.
- 32 Kaukinen S, Kaukinen L, Kataja J, et al. Interpleural analgesia for postoperative pain relief in renal surgery patients. *Scandinavian Journal of Urology and Nephrology* 1994; **28**: 39–43.
- 33 Stromskag KE, Steen PA. Comparison of interpleural and epidural anesthesia for extracorporeal shock wave lithotripsy. *Anesthesia and Analgesia* 1988; **67**: 1181–3.
- 34 Reiestad F, McIlvaine WB. Interpleural anesthesia for extracorporeal shock wave lithotripsy. *Anesthesia and Analgesia* 1989; **69**: 551–2.
- 35 Trivedi NS, Robalino J, Shevde K. Interpleural block: a new technique for regional anaesthesia during percutaneous nephrostomy and nephrolithotomy. *Canadian Journal of Anaesthesia* 1990; **37**: 479–81.
- 36 Reiestad F, McIlvaine WB, Kvalheim L, Stokke T, Pettersen B. Intrapleural analgesia in treatment of upper extremity reflex sympathetic dystrophy. *Anesthesia and Analgesia* 1989; **69**: 671–3.
- 37 Covino BG. Interpleural regional analgesia. *Anesthesia and Analgesia* 1988; **67**: 427–9.
- 38 Silomon M, Claus T, Hanno H, et al. Interpleural analgesia does not influence post-thoracotomy pain. *Anesthesia and Analgesia* 2000; **91**: 44–50.
- 39 Murphy DF. Interpleural analgesia. *British Journal of Anaesthesia* 1993; **71**: 426–34.
- 40 Rosenberg PH, Scheinin BMA, Lepantalo MJA, Lindfors O. Continuous intrapleural infusion of bupivacaine for analgesia after thoracotomy. *Anesthesiology* 1987; **67**: 811–3.
- 41 Schneider RF, Villamena PC, Harvey J, et al. Lack of efficacy of intrapleural bupivacaine for postoperative analgesia following thoracotomy. *Chest* 1993; **103**: 414–6.
- 42 Mann U, Young GR, Williams JK, et al. Intrapleural bupivacaine in the control of post-thoracotomy pain. *Annals of Thoracic Surgery* 1992; **53**: 449–54.
- 43 Francois T, Blanloeil Y, Pillet F, et al. Effect of interpleural administration of bupivacaine or lidocaine on pain and morphine requirement after oesophagectomy with thoracotomy: a randomised, double-blind and controlled study. *Anesthesia and Analgesia* 1995; **80**: 718–23.
- 44 Kambam JR, Hammon J, Parris WC, Lupinetti FM. Intrapleural analgesia for post-thoracotomy pain and blood levels of bupivacaine following intrapleural injection. *Canadian Journal of Anaesthesia* 1989; **36**: 106–9.
- 45 Tartiere J, Samba D, Lefrancois C, et al. Intrapleural bupivacaine after thoraco-abdominal incision for oesophagectomy. *European Journal of Anaesthesiology* 1991; **8**: 145–9.
- 46 Riegler FX. Con: Unreliable benefit after thoracotomy: Epidural is a better choice. *Journal of Cardiothoracic and Vascular Anesthesia* 1996; **10**: 429–31.
- 47 Richardson J, Sabanathan S, Mearns AJ, Shah RD, Goulden C. A prospective, randomised comparison of interpleural and paravertebral analgesia in thoracic surgery. *British Journal of Anaesthesia* 1995; **75**: 405–8.
- 48 Semsroth M, Plattner O, Horcher E. Effective pain relief with continuous intrapleural bupivacaine after thoracotomy in infants and children. *Paediatric Anaesthesia* 1996; **6**: 303–10.
- 49 McIlvaine WB, Chang JH, Jones M. The effective use of intrapleural bupivacaine for analgesia after thoracic and subcostal incisions in children. *Journal of Paediatric Surgery* 1988; **23**: 1184–7.
- 50 McIlvaine WB, Knox RF, Fennessey PV, Goldstein M. Continuous infusion of bupivacaine via intrapleural catheter for analgesia after thoracotomy in children. *Anesthesiology* 1988; **69**: 261–4.
- 51 Giaufre E, Bruguerolle B, Rastello C, et al. New regimen for interpleural block in children. *Paediatric Anaesthesia* 1995; **5**: 125–8.
- 52 Lieou FJ, Lee SC, Ho ST, Wang JJ. Interpleural bupivacaine for pain relief after transthoracic endoscopic sympathectomy for primary hyperhidrosis. *Acta Anaesthesiologica Sinica* 1996; **34**: 21–5.
- 53 Baxter AD, Jennings FO, Harris RS, Flynn JF, Way J. Continuous intercostal blockade after cardiac surgery. *British Journal of Anaesthesia* 1987; **59**: 162–6.
- 54 Mehta Y, Swaminathan M, Mishra Y, et al. A comparative evaluation on intrapleural and thoracic epidural analgesia for postoperative pain relief after minimally invasive direct coronary artery bypass surgery. *Journal of Cardiothoracic and Vascular Anesthesia* 1998; **12**: 162–5.
- 55 El-Naggar MA, Benett B, Raad C, et al. Bilateral intrapleural regional anesthesia for postoperative pain control: a dose finding study. *Journal of Cardiothoracic and Vascular Anesthesia* 1989; **3**: 574–9.
- 56 Lee E, Ben-David B. Bilateral interpleural block for midline upper abdominal surgery. *Canadian Journal of Anaesthesia* 1991; **38**: 683–4.
- 57 Aguilar JL, Montero A, Vidal Lopez F, Llanazares JF. Bilateral interpleural injection of local anesthetics. *Regional Anesthesia* 1989; **14**: 93–4.
- 58 Wulf H, Jeckstrom W, Maier C, et al. Intrapleural catheter analgesia in patients with multiple rib fractures. *Anaesthetist* 1991; **40**: 19–24.
- 59 Graziotti P, Smith GB. Multiple fractured ribs and head injury – an indication for intercostal catheterisation and infusion of local anaesthetics. *Anaesthesia* 1988; **43**: 964–6.
- 60 Knottenbelt JD, James MF, Bloomfield M. Intrapleural bupivacaine analgesia in chest trauma: a randomized double-blind controlled trial. *Injury* 1991; **22**: 114–6.
- 61 Czap CL, Rauck RL, Koman LA, et al. Sympathetic denervation to the upper extremity in CRPS. Stellate ganglion block versus interpleural block. *Anesthesiology* 1997; **87**: 754A.
- 62 Perkins G. Interpleural anaesthesia in the management of upper limb ischaemia. A report of three cases. *Anaesthesia and Intensive Care* 1991; **19**: 575–8.
- 63 Reiestad F, Kvalheim L, McIlvaine WB. Pleural analgesia for the treatment of acute severe thoracic herpes zoster. *Regional Anesthesia* 1989; **14**: 244–6.

- 64 Thwaites BK, Powell DR. Interpleural block for acute combined cervical and thoracic herpes zoster. *Regional Anesthesia* 1995; **20**: 255–6.
- 65 Johnson LR, Rocco AG, Ferrante FM. Continuous subpleural-paravertebral block in acute thoracic herpes zoster. *Anesthesia and Analgesia* 1988; **67**: 1105–8.
- 66 Reiestad F, McIlvaine WB, Barnes M, et al. Interpleural analgesia in the treatment of severe thoracic post-herpetic neuralgia. *Regional Anesthesia* 1990; **15**: 113–7.
- 67 Sihota MK, Holmblad BR. Horner's syndrome after intrapleural anesthesia with bupivacaine for post-herpetic neuralgia. *Acta Anaesthesiologica Scandinavica* 1988; **32**: 593–4.
- 68 Dionne C. Tumour invasion of the brachial plexus: Management of pain with interpleural analgesia. *Canadian Journal of Anaesthesia* 1992; **39**: 520–1.
- 69 Fineman SP. Long-term post-thoracotomy cancer pain management with interpleural bupivacaine. *Anesthesia and Analgesia* 1989; **68**: 694–7.
- 70 Parkinson SK, Mueller JB, Rich TJ, Little WL. Unilateral Horner's syndrome associated with interpleural catheter injection of local anesthetic. *Anesthesia and Analgesia* 1989; **68**: 61–2.
- 71 Lema MJ, Myers DP, De Leon-Casasola O, et al. Pleural phenol therapy for the treatment of chronic oesophageal cancer pain. *Regional Anesthesia* 1992; **17**: 166–70.
- 72 Main A. Interpleural analgesia in the management of oesophageal perforation. *Regional Anesthesia* 1997; **22**: 185–7.
- 73 Myers DP, Lema MJ, de Leon-Casasola OA, et al. Interpleural analgesia for the treatment of severe cancer pain in terminally ill patients. *Journal of Pain Symptom Management* 1993; **8**: 505–10.
- 74 Ahlburg P, Noreng M, Molgaard J, Egebo K. Treatment of pancreatic pain with interpleural bupivacaine: an open trial. *Acta Anaesthesiologica Scandinavica* 1990; **34**: 156–7.
- 75 Durrani Z, Winnie AP, Ikuta P. Interpleural catheter analgesia for pancreatic pain. *Anesthesia and Analgesia* 1988; **67**: 479–81.
- 76 Ramajoli F, De Amici D. Is there a bilateral block of the thoracic sympathetic chain after unilateral intrapleural analgesia? *Anesthesia and Analgesia* 1998; **87**: 360–7.
- 77 Reiestad F, McIlvaine WB, Kvalheim L, et al. Successful treatment of chronic pancreatitis pain with interpleural analgesia. *Canadian Journal of Anaesthesia* 1989; **36**: 713–6.
- 78 El-Dawlatly A, al-Faqih SR. Interpleural catheter analgesia for chronic pain treatment – a case report. *Middle East Journal of Anesthesiology* 1994; **12**: 469–74.
- 79 Sihota MK, Holmblad BR, Ikuta PT, et al. Successful pain management of chronic pancreatitis with interpleural technique. *Regional Anesthesia* 1988; **13**: 33.
- 80 Sala-Blanch X, Izquierdo E, Molina MJ, Taura P. Can interpleural analgesia be used with safety in patients with haemostatic disturbances? *Regional Anesthesia* 1994; **19**: 151–2.
- 81 Strömskag KE, Minor BG, Steen PA. Side effects and complications related to interpleural analgesia: An update. *Acta Anaesthesiologica Scandinavica* 1990; **34**: 473–7.
- 82 Rocco A, Reiestad F, Gudman J. Intrapleural administration of local anaesthetics for pain relief in patients with multiple rib fractures: Preliminary report. *Regional Anesthesia* 1987; **12**: 10–4.
- 83 Ananthanarayan C, Kashtan H. Pneumothorax after interpleural block in a spontaneously breathing patient. *Anaesthesia* 1990; **45**: 342.
- 84 Gomez MN, Symreng T, Johnson B, Rossi NP, Chiang CK. Intrapleural bupivacaine for intraoperative analgesia – a dangerous technique. *Anesthesia and Analgesia* 1988; **67**: S78.
- 85 Kreitzer JM, Reuben SS. Central nervous system toxicity in a patient receiving continuous intrapleural bupivacaine. *Journal of Clinical Anesthesia* 1996; **8**: 666–8.
- 86 Tucker GT. Pharmacokinetics of local anaesthetics. *British Journal of Anaesthesia* 1986; **58**: 717–31.
- 87 Scott DB. Toxic effects of local anaesthetic agents on the central nervous system. *British Journal of Anaesthesia* 1986; **58**: 732–5.
- 88 Gin T, Chan K, Kan AF, et al. Effect of adrenaline on venous plasma concentrations of bupivacaine after interpleural administration. *British Journal of Anaesthesia* 1990; **64**: 662–6.
- 89 Aguilar JL, Montes M, Montero A, et al. Plasma bupivacaine levels after pleural block: the effect of epinephrine after unilateral or bilateral bupivacaine administration. *Regional Anesthesia* 1992; **17**: 99–101.
- 90 Blake DW, Bjorksten A, Dawson P, Hiscock R. Pharmacokinetics of bupivacaine enantiomers during interpleural infusion. *Anaesthesia and Intensive Care* 1994; **22**: 522–8.
- 91 Kuhlman G, Vigue B, Duranteau J, Orhant EE. Intrapleural lidocaine analgesia. Influence of volume and concentration. *Anesthesiology* 1989; **71**: A659.
- 92 Seltzer JL, Larjani GE, Goldberg ME, et al. Interpleural bupivacaine – a kinetic and dynamic evaluation. *Anesthesiology* 1987; **67**: 798–800.
- 93 Kastrissios H, Triggs EJ, Mogg GA, et al. Steady-state pharmacokinetics of interpleural bupivacaine in patients after cholecystectomy. *Anaesthesia and Intensive Care* 1990; **18**: 200–4.
- 94 Wulf H, Winckler K, Maier C, Heinzow B. Pharmacokinetics and protein binding of bupivacaine in postoperative epidural analgesia. *Acta Anaesthesiologica Scandinavica* 1988; **32**: 530–4.
- 95 Abraham ZA. Interpleural analgesia. In: Sinatra RS, Hord AH, Ginsberg B, Preble LM, eds. *Acute Pain. Mechanisms and Management*. St. Louis: Mosby Year Book, 1992: 326–39.
- 96 Lauder GR. Interpleural analgesia and phrenic nerve paralysis. *Anaesthesia* 1993; **48**: 315–6.
- 97 Aguilar JJ, Montero A, Lopez VF, Llamazares JF. Intrapleural analgesia and phrenic nerve palsy. *Regional Anesthesia* 1992; **17**: 45.
- 98 Milliet N, Studer W. Complication after interpleural analgesia. *Anesthesia and Analgesia* 1996; **83**: 890.

- 99 Shantha TR. Unilateral bronchospasm after interpleural analgesia. *Anesthesia and Analgesia* 1992; **74**: 291–3.
- 100 Dutta D, Hardy PA. Intra-bronchial injection, an unusual complication of interpleural analgesia. *British Journal of Anaesthesia* 1995; **74**: 98–9.
- 101 Khor KE, Josephson MA. Bloodstained pleural effusion complicating interpleural analgesia. *Acta Anaesthesiologica Scandinavica* 1995; **39**: 270–2.
- 102 Kopacz DJ, Thompson GE. Celiac and hypogastric plexus, intercostal, interpleural, and peripheral neural blockade of the thorax and abdomen. In: Cousins MJ, Bridenbaugh PO, eds. *Neural Blockade in Clinical Anesthesia and Management of Pain*, 3rd edn. Philadelphia: Lippincott-Raven, 1998: 472–5.
- 103 Strømskag KE, Kleiven S. Continuous intercostal and interpleural nerve blockades. *Techniques in Regional Anesthesia and Pain Management* 1998; **2**: 79–89.
- 104 Welte M, Haimer E, Groh J, et al. Effect of interpleural morphine on postoperative pain and pulmonary function after thoracotomy. *British Journal of Anaesthesia* 1992; **69**: 637–9.
- 105 Fielding S, Wilker J, Hynes M, Szewczak M. A comparison of clonidine with morphine for anti-nociceptive and anti-withdrawal actions. *Journal of Pharmacology and Experimental Therapeutics* 1978; **207**: 899–905.
- 106 Canver C, Pilli G. The use of intrapleural clonidine for postoperative pain control. *Journal of Cardiovascular Surgery* 1996; **37**: 183–5.
- 107 Lim MW, Burt G, Rutter SV. Use of three-dimensional animation for regional anaesthesia teaching: application to interscalene brachial plexus blockade. *British Journal of Anaesthesia* 2005; **94**: 372–7.
- 108 Reber A, Scheidegger D. An alternative technique for interpleural analgesia. *Anesthesiology* 1998; **88**: 553–4.
- 109 Engdahl O, Boe J, Sandstedt S. Intercostal bupivacaine for analgesia during chest drainage treatment for pneumothorax. A randomized double-blind study. *Acta Anaesthesiologica Scandinavica* 1993; **37**: 149–53.
- 110 Levine CB, Levin BH. Long-term interpleural analgesia using a subcutaneous implantable infusion system. *Canadian Journal of Anaesthesia* 1992; **39**: 408.