Anaesthesia, 2007, **62**, pages 1039–1049 doi:10.1111/j.1365-2044.2007.05183.x

REVIEW ARTICLE

Interpleural block – part 1

R. M. Dravid[1] and R. E. Paul[2]

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 nonsurgical 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 first of two reviews, the authors cover the history, taxonomy and anatomical considerations, the spread of local anaesthetic, and the mechanism of action, physiological, pharmacological and technical considerations in the performance of the block.

Correspondence to: Dr R. M. Dravid
E-mail: Ravi.Dravid@kgh.nhs.uk
Accepted: 14 January 2007

Interpleural blockade is the technique of injecting local anaesthetic into the thoracic cage between the parietal and visceral pleura to produce ipsilateral somatic block of multiple thoracic dermatomes. There is evidence that it also produces pain relief by spread of local anaesthetic bilaterally to block both the sympathetic chains and the splanchnic nerves. It is effective in treating unilateral surgical and non-surgical pain from the chest and upper abdomen in both the acute and chronic settings. Local anaesthetic solutions can be administered as single or intermittent boluses, or as continuous infusions via an indwelling interpleural catheter. 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 (CRPS), thoracic and abdominal cancer, and pancreatitis. The technique is simple to learn and has both few contra-indications and a low incidence of complications. Interpleural blockade has not been widely adopted by the anaesthetic community largely because of concerns about pneumothorax and local anaesthetic toxicity. However, recent improvements in technique that enhance its safety, and increased experience with this form of treatment, suggest that a revisit to this interesting and useful technique of regional anaesthesia would be of value. In the first of this two-part review, we discuss the history, taxonomy and anatomical considerations, the spread of local anaesthetic, and the mechanism of action, physiological, pharmacological and technical considerations in the performance of the block.

History

Interpleural injection was first described by Mandl in 1947 when he administered 6% phenol into the interpleural space of experimental animals without any evidence of pleural irritation or necrosis. Interest resurfaced in 1978, when Wallach used this space for therapy with tetracycline and lidocaine for malignant pleural effusions [2]. The concept of the injection of local anaesthetic into the interpleural space for the provision of pain relief was first presented by Kvalheim and Reiestad [3] in 1984, and was published in 1986 by Reiestad and Strømskag [4] as a means of treating pain after open cholecystectomy, kidney surgery and breast surgery.

Before this, interest had focused on the use of multiple intercostal nerve blocks for these indications. Nunn and Slavin showed in a cadaver study that local anaesthetic from a single injection around one intercostal nerve gained access to other intercostal nerves in adjacent spaces above and below the injection site. This occurred through both the intercostal and the subpleural spaces [5]. O'Kelly and Garry used this knowledge about the spread of local anaesthetic to provide continuous analgesia for pain relief after multiple rib fractures with a single intercostal catheter and intermittent drug administration [6]. This approach was also described in a series of patients undergoing gallbladder and kidney surgery [7, 8]. Kvalheim and Reiestad attempted to demonstrate fluid spread by injecting local anaesthetic and radiological contrast medium through a catheter placed in an intercostal space. They observed that, in addition to providing excellent analgesia, the radiological contrast medium spread over the lung surface, prompting them to conclude that the catheter was actually located interpleurally. The authors therefore decided to reproduce this analgesia by deliberately placing the catheter in the interpleural space. They thus exploited a technical mistake to achieve a positive result and developed a new regional anaesthetic technique [9].

Taxonomy

The original paper uses the term interpleural block, implying the injection of local anaesthetic solution into the potential space between the parietal and visceral layers of the pleura. Some authors prefer the term intrapleural because the pleura are one structure embryologically, and the solution is deposited within this structure [10]. Others feel that the latter term is unsatisfactory because it implies actual injection within or into the pleural layer itself [11]. Baumgarten suggested pleural block or pleural analgesia [12]. All these terms are used interchangeably. Interpleural is the more frequently used term in the literature and we have therefore used this term in this review.

Anatomical considerations

It is essential to review the literature relating both to the intercostal and interpleural space for a thorough understanding (Fig. 1). Recent studies suggest a greater variability in the anatomy of the intercostal space than that suggested in classic texts. Classically, the space has been described as having three muscle layers; intercostales externi, interni and intimi. Intercostalis intimi runs obliquely downwards and backwards, joining the internal surfaces of the adjacent ribs. Some fibres may bridge more than one intercostal space to be inserted into the second or third rib. Intercostales intimi separates the neurovascular bundle from the parietal pleura. The intercostal nerve is classically described as running under the shelter of the intercostal groove, and is situated below the intercostal vein and artery.

Nunn and Slavin [5] performed detailed studies in cadavers. At the sixth intercostal space, 7 cm from the posterior midline, the external intercostal muscle was of variable thickness but well developed and was bound internally by the posterior intercostal membrane, the sturdy, aponeurotic extension of the internal intercostal muscle. However, the innermost intercostal muscle, the intercostales intimus, was 'a flimsy structure composed of several fascicles through which injected India ink passes freely to reach the subpleural space'. The nerves, arteries and veins were consistently found in the tissue plane deep to the posterior intercostal membrane and superficial to the intercostales intimus muscle, with no fixed relationship to the ribs above or below. The intercostal nerves were found to run 'as three or four separate bundles with no single neural sheath' and with considerable variation in size and relationship to the associated intercostal arteries and veins. Hardy concurred with these findings. In 30 cadavers, the second to eleventh intercostal nerves were dissected and were found to occupy the classically described subcostal position in only 17% of cases [13].

In the embryo, the pleura is a layer of mesothelium into which each lung bud grows and expands. The original coelomic cavity is reduced to a slit-like space called the pleural cavity. The parietal layer lines the thoracic wall, the thoracic surface of the diaphragm and the lateral aspect of the mediastinum, and extends into the root of the neck to line the suprapleural membrane at the thoracic inlet. The visceral layer completely lines the outer surfaces of the lungs and extends into the depths of the interlobar fissures. The two layers become continuous with one another by means of a cuff of pleura that surrounds the structures entering and leaving the lung at the hilum. The two layers of pleura are separated by a distance of 10–20 μm. The space has a surface area of about 2000 cm^2 in a 70-kg man and contains 0.1–0.2 $ml.kg^{-1}$ of pleural fluid, permitting the two layers to move over each other with minimum friction. The parietal pleura is thinner than the visceral layer, and contains stomata of 2–12 μm diameter between its mesothelial cells, suggestive of a membrane capable of fluid transport [14]. The diffusion of local anaesthetic from the pleural space to the intercostal nerves is limited by uptake of drug by the visceral pleura. The rapidity and extent of absorption is unpredictable after pleural injury, disease or inflammation. The parietal pleura has the following nerve supply: the costal pleura is segmentally supplied by the intercostal nerves, the mediastinal pleura

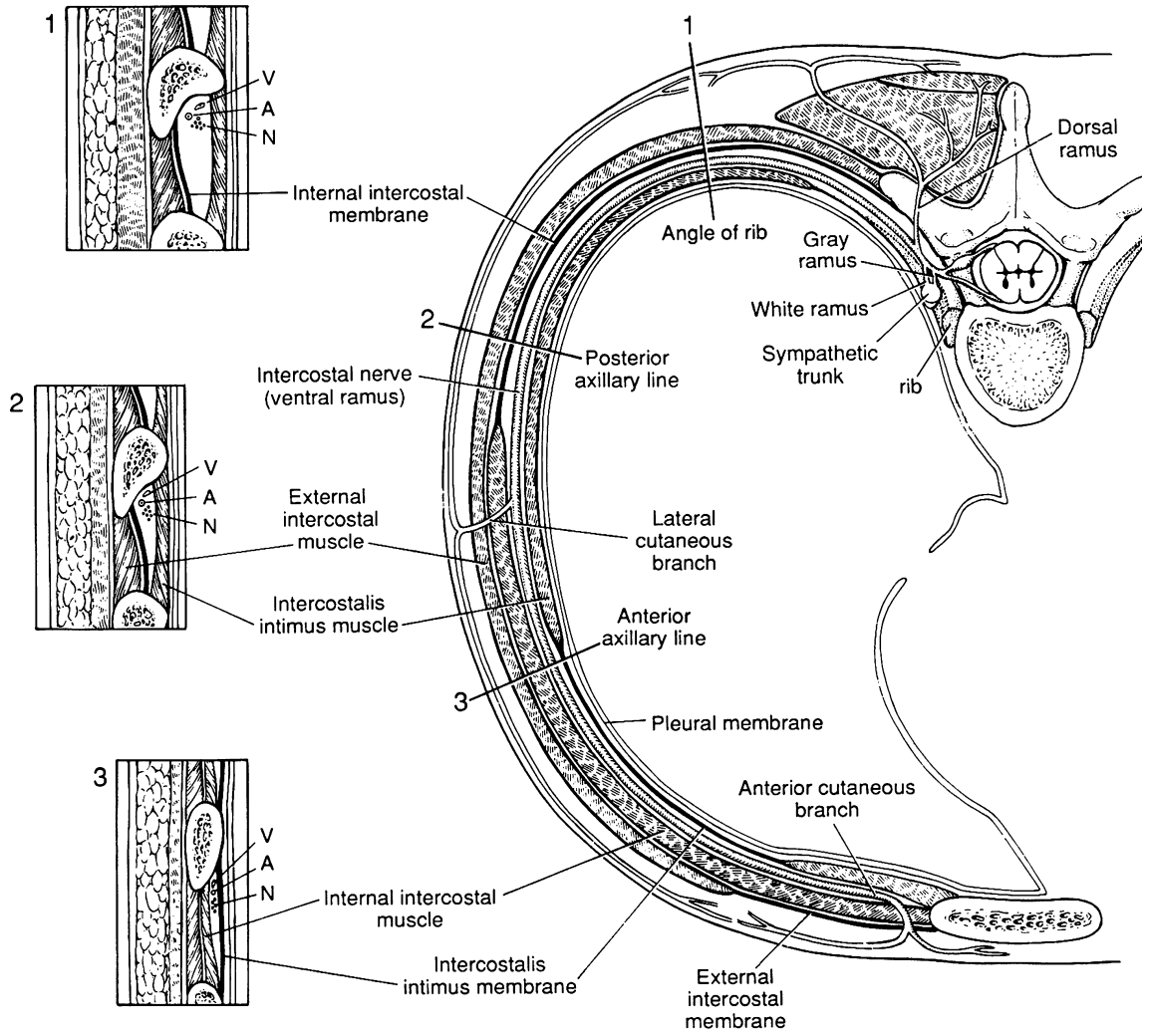

Figure 1 The anatomy of the intercostal space.

is supplied by the phrenic nerve and the diaphragmatic pleura is supplied over the domes by the phrenic nerve and around the periphery by the lower five intercostal nerves. The visceral pleura covering the lung receives an autonomic vasomotor supply but has no sensory innervation. Strømskag and Kleiven suggested that a volume of 3–5 ml of local anaesthetic would be confined only to the injected intercostal space but that the administration of a larger volume of 20 ml could extend subpleurally to up to five adjacent intercostal spaces [9] (Fig. 2).

In his study in cadavers, Murphy [15] demonstrated the spread of India ink from the injected intercostal space to adjacent intercostal spaces above and below. The spread was shown to occur medially to reach the paravertebral space in only 50% of the studies. In contrast, Mowbray et al. found that methylene blue injected through an intercostal catheter almost invariably spread to the paravertebral space and cited this as the reason that analgesia extends over several dermatomes [16]. Just how the fluid injected into the interpleural space reaches adjacent neural structures and how interpleural blockade can be used to treat pain arising from structures both above and below the diaphragm has been the subject of much interest (Fig. 3).

Cadaver studies have shown that interpleurally injected India ink diffuses through the parietal pleura to the subpleural space and backwards to multiple intercostal nerves [14]. Animal studies also support this spread [17, 18], the dye almost completely covering the chest wall, lung and diaphragm, and tending to pool in the interpleural paravertebral area (not the paravertebral space as used for the thoracic paravertebral block) which is dorsal to the parietal pleura and hence extra-pleural. Further evidence regarding the spread comes from a study

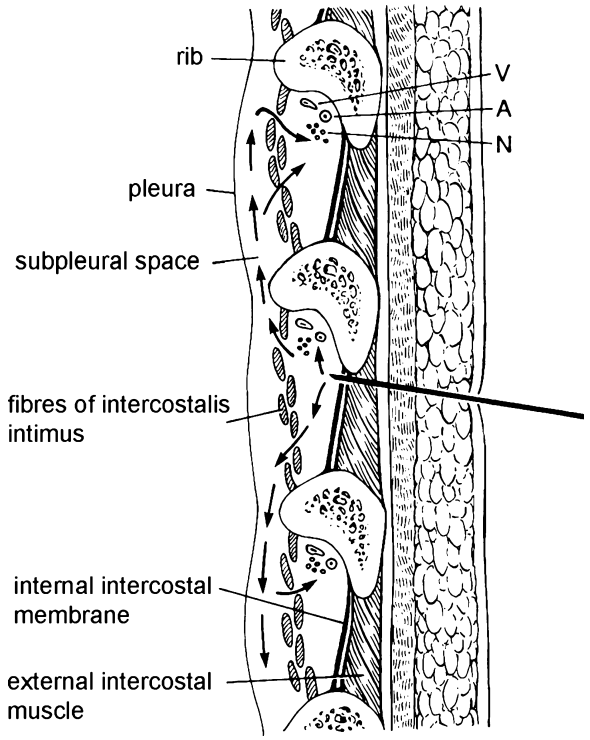

Figure 2 The paths taken by fluid injected into the intercostal space.

that used computerised tomography to investigate the behaviour of interpleural local anaesthetic injections in 21 subjects after open cholecystectomy [19]. Bupivacaine 0.375% 20 ml mixed with 10 ml of contrast medium was used for the injection. The study found that most of the fluid injected collects at the lowest point of the pleural cavity in a gravity-dependent manner, and so spread will vary with body position. In the supine position, the mean distribution in a cranio-caudal direction was from the T3 level to L1, and in the lateral position it was from T5 to L1. Although the paravertebral regions of the interpleural space were covered, there was no spread seen in any case to the epidural or paravertebral spaces.

However, in addition to intercostal nerve blockade, clinical evidence of analgesic effects suggest that other neural structures in close proximity can also be affected by interpleural block. Clinical studies reporting relief of sympathetically mediated pain point to autonomic blockade being produced by this block [20–22]. In the lateral position with the operative side up, the main fluid collection is against the mediastinum, supporting the suggestion that the technique can result in blockade of the thoracic sympathetic chain and the splanchnic nerves [19]. These structures are separated from the interpleural space by the parietal pleura alone. Where the standard supine and lateral positions are used, the uppermost part of the thoracic sympathetic chain is spared. The first thoracic sympathetic ganglion, from which the sympathetic fibres destined to the upper limbs (ganglia 1–4) and to the heart (ganglia 1–5) originate, is not blocked. This is supported by vasoconstriction seen in the arms and by the relative stability of blood pressure and heart rate. Vasoconstriction is also observed in the lower limbs, signifying that the blockade does not affect the lumbar sympathetic chain. It is suggested that this vasoconstriction above and below the level of block compensates for the vasodilation in the splanchnic area. This is mediated through the arterial

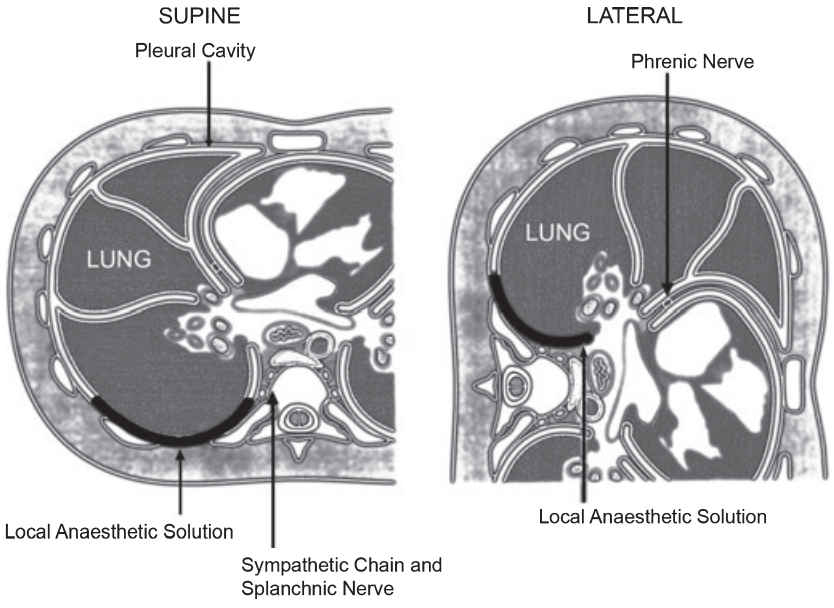

Figure 3 The effect of gravity on the spread of local anaesthetic solution injected into the intrapleural space.

baroreceptors in the aortic arch, as observed with an epidural block, with the difference that the integrity of the intervening spinal cord permits a vasoconstrictive response in lower limbs [19, 23]. Spread of local anaesthetic can be encouraged in a cephalad direction by using a 20° head-down position to achieve blockade of ipsilateral stellate and upper thoracic ganglia, and brachial plexus. This is discussed later in this review.

Based on a study using infrared telethermography, there is a suggestion that injection of local anaesthetic on one side, apart from causing an ipsilateral somatic block, can result in bilateral block of the thoracic sympathetic chains and the splanchnic nerves located between them and in front of the spinal column [24]. Ramajoli et al. [24] performed a unilateral block with bupivacaine in 15 patients suffering from benign or neoplastic pain of thoracic or abdominal origin. Catheters were placed on the same side as the thoracic or abdominal somatic pain and on the opposite side of maximally reported thoracic or abdominal visceral pain. Using infrared telethermography, they detected a uniform bilateral cutaneous temperature increase in the affected thoracic dermatomes and decreased temperatures in the upper and lower limbs in all the cases. The authors hypothesised that reflex vasoconstriction occurs in areas unaffected by the block in compensation for the region of sympathetic blockade. The exact mechanism of bilateral thoracic sympathetic block after unilateral injection is not known, although a greater negative mediastinal pressure may facilitate bilateral spread. The authors felt that this was the reason for a marked reduction in or disappearance of diffuse or unilateral visceral pain after the administration of local anaesthetic, regardless of the side of catheter placement.

In summary, it has been suggested that local anaesthetic solution diffuses outwards, producing a block of multiple intercostal nerves, the sympathetic chain of the head, neck and upper extremity, the brachial plexus, the splanchnic nerves, the phrenic nerves, the coeliac plexus and ganglia [23]. As the injected local anaesthetic diffuses out through both the layers of pleura, direct local effects on the diaphragm, lung, pericardium and peritoneum may contribute to some of the analgesic activity.

Effects on pulmonary function

The effect of interpleural analgesia on pulmonary function has been the focus of several studies, as blockade of intercostal nerves (and potentially the phrenic nerve) might be expected to affect respiratory muscle strength. Murphy demonstrated significant improvements in peak flow in patients with rib fractures and after cholecystectomy with continuous intercostal nerve blockade managed with intermittent boluses of bupivacaine [7, 8]. Other studies have reported improved respiratory function after interpleural block for postoperative pain [25–29]. Van Kleef et al. [29] compared bupivacaine 0.25% with adrenaline and 0.5% with adrenaline given as interpleural boluses followed by continuous infusions in patient undergoing surgery with a flank incision. They reported a significant improvement in forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC), and a decreased morphine requirement, which was similar with both local anaesthetic concentrations used. They went on to recommend the lower strength for these patients. Another study concluded that, although interpleural block did not significantly change lung function or inspiratory muscle strength after open cholecystectomy, it induced a slight decrease in abdominal wall muscle strength [30]. Oxorn et al. studied pulmonary function, comparing interpleural bupivacaine with intramuscular pethidine after open cholecystectomy [31]. Their findings are in direct contrast, showing intramuscular pethidine to be superior in terms of postoperative pulmonary mechanics. Ballantyne et al. showed that the block decreases the incidence of postoperative pulmonary complications, although not statistically significantly so, in a meta-analysis of postoperative analgesic techniques. They also concluded that surrogate measures of pulmonary function, i.e. FEV_1, FVC and peak expiratory flow rate (PEFR), could not be used to predict outcomes or complications [32]. Kastrissios et al. also reported early normalisation of bowel function and an early return to unaided mobilisation with interpleural block [26]. In summary, it would seem that interpleural block has no clinically significant adverse effect on respiratory muscle function, and is likely to be beneficial in the presence of painful conditions compromising pulmonary function. Although this block has been successfully used in patients with cystic fibrosis [33], in view of the above negative study and the possibility of phrenic nerve paralysis, however uncommon, a careful consideration must be given to its use, especially where a long-term or a bilateral block is being contemplated and in those with borderline respiratory function or with neuromuscular disease.

Technique

The first description of a technique for interpleural analgesia employed a 16-G Tuohy needle and a well-wetted and freely moving air-filled glass syringe. The block was performed at the end of surgery with the patient in the lateral position with the operated side uppermost. A site 10 cm from the posterior midline in the eighth intercostal space was chosen. Following skin puncture, the needle and syringe were advanced together

through the intercostal space towards and then through the parietal pleura. Puncture of this layer is often signified by a 'click'. Immediately upon entering the interpleural space the negative pressure therein would 'elegantly surge the plunger of the syringe forward'. The syringe was removed and a 5–6-cm length of an epidural-type catheter quickly inserted through the needle into the pleural space [3].

This could be described as a 'passive' loss of resistance technique or negative pressure technique. Some anaesthetists use the traditional 'loss of resistance' technique, where a gentle pressure is exerted on the plunger as the needle and air or fluid-filled syringe assembly is advanced through the intercostal space. A potential disadvantage is that a false loss of resistance can occur anywhere in the intercostal space, with the puncture of parietal pleura or when the needle is advanced too far into the lung parenchyma itself, and for this reason this should be strictly avoided [34].

The technique for identifying the interpleural space should rely on the identification of negative pressure within the space. Pleural pressures are negative throughout the normal respiratory cycle and hence key to successful identification of the space. In contrast to this, a study using epidural catheters for continuous intercostal and interpleural local anaesthetic blockade has shown the intercostal pressure to be positive during the expiratory phase, an important differentiating feature between the two blocks [35]. In an anaesthetised spontaneously breathing patient the needle advancements are undertaken in the expiratory phase, whereas in a paralysed and ventilated patient the needle is advanced at the end of exhalation with the ventilator disconnected. An awake patient should be advised to hold their breath at the end of exhalation and should be warned of the feeling of a sharp 'twinge' when the needle pierces the pleura.

The negative interpleural pressure has been identified with a passive suction of air-filled syringe [3], a fluid-filled syringe [36], deflation of a balloon [37], a falling column of fluid [38, 39], suction of a hanging drop from the hub of the needle [40], saline infusion [41], a continuous saline flow [42], or electronic devices that detect negative pressure [43], and is indicated by an unobstructed passage of the catheter. O'Leary et al. [1] suggested that electronic devices may prove useful adjuncts for identification of the space, especially in the obese and those with pleural disease, although presently there are no new data available to support this.

False endpoints remain a possibility with some of the techniques, and introduction of air into the pleural space is difficult to avoid if the Tuohy needle is open to air at any time, even for a short period, to enable connection of a syringe or to allow the passage of a catheter. As much as 20 ml of air may be entrained, causing air pockets, which may result in a patchy block [1]. Introducing air may also be hazardous if nitrous oxide is to be used as part the anaesthetic technique. Scott [41] used the 'saline infusion technique' to identify negative pressure in the interpleural space. This is a suitable technique for single bolus injections and also permits catheter placement through a catheter sheath adaptor. As a catheter sheath adapter is not routinely available, authors recommend the 'continuous saline flow' technique to avoid air entrainment during catheter placement. We perform the block in the lateral position approximately 8–10 cm from the dorsal midline. The needle insertion site is prepared and infiltrated with local anaesthetic if appropriate. A 500-ml bag of saline with an infusion set is positioned approximately 60 cm above the level of the patient and the infusion set is attached to the side port of a standard three-way connector ensuring sterility, and primed with the saline (Fig. 4). The other port is kept closed. The Tuohy needle is inserted through the skin and connective tissue until the rib is touched. The stylet is then removed and the three-way connector is attached to the hub of the Tuohy needle (Fig. 5).

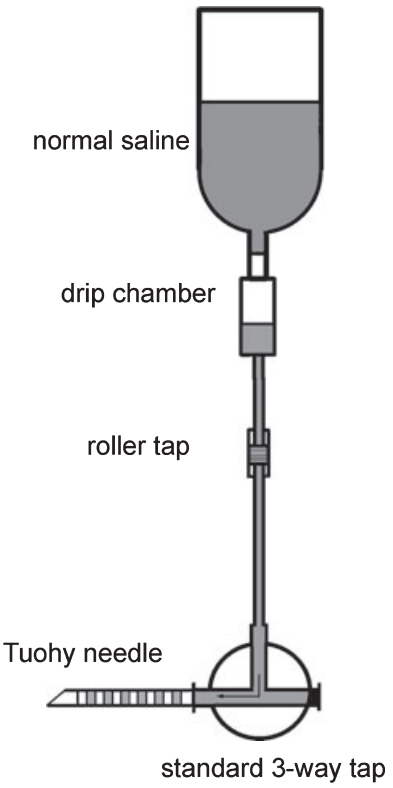

Figure 4 Arrangement of equipment for insertion of an intrapleural catheter.

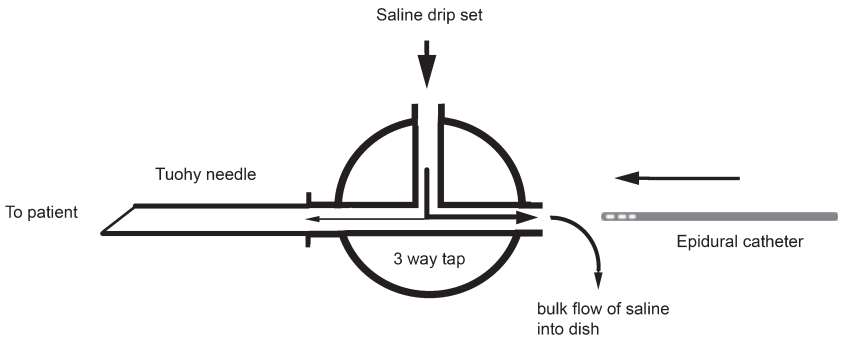

Figure 5 After insertion of the Tuohy needle, a catheter is passed through the open three-way tap and freely flowing saline.

The roller tap of the giving set is then fully opened. At this point, a few drops are usually seen in the drip chamber of the giving set, but free flow will not occur. Controlled ventilation is stopped and the breathing system is disconnected from the patient before the needle is advanced any further; if the patient is breathing spontaneously, all further movements of the needle are carried out in the expiratory phase. The anaesthetist then walks off the upper border of the rib, remembering to avoid angling the needle and accidentally entering the neurovascular bundle in the intercostal groove of the rib above. Further advance through the intercostal space is accompanied sometimes by a brisk flow of saline drops. This flow sometimes slows down just before the parietal pleura is punctured, which is associated with, and indicated by, a sudden and free flow of saline in the drip chamber due to the negative pressure in the space. We rely on this change in character of saline flow, which indicates negative pressure, rather than on a 'clicking' sometimes felt on puncturing the pleura. With the guiding hand still gripping the needle and firmly rested on the patient's torso, the connector is then opened to all three ports whereupon saline preferentially flows out towards the operator through the wide bore of the three-way connector rather than through the narrow bore needle into the chest (Fig. 4c).

The continuous flow of saline creates a pressure of at least 60 cmH_2O at the connector and prevents air entrainment. A standard epidural catheter is threaded through the jet of saline into the pleural cavity through the three-way connector and the needle. Approximately 5–10 cm of catheter is inserted into the interpleural space. The saline flow is continued until the needle is fully withdrawn from the chest [42].

Interpleural block can be performed with the patient flat or semirecumbent in either the supine or lateral position. Catheter insertion permits administration of repeat boluses or a continuous infusion regimen. Various approaches to the space have been used, which include the anterior axillary line [44], mid-axillary line [41, 45], the posterior axillary line [24], a site about 8–10 cm from the dorsal midline [42], and even anteriorly in the second intercostal space in the mid-clavicular line [24]. A site is chosen for needle insertion, ideally where the intercostal space and adjacent rib below are easily palpable. In general, the fourth to eighth intercostal spaces in the mid to anterior axillary line are used in the supine patient. Although not as convenient, the lateral position allows a more posterior needle insertion point, with the theoretical advantage of depositing the local anaesthetic into the paravertebral region of the interpleural space where the intercostal nerves and sympathetic chain are most superficial with regard to the parietal pleura, as discussed above. Strømskag et al. showed that collection in the paravertebral area occurs whether the patient is supine or lateral [19]. Iwama [44] performed the block with a 16-G Tuohy needle at the fourth intercostal space in the anterior axillary line and directed radio-opaque catheters either towards the apex or towards the base of the pleural space. The extent of the spread of the injected radioisotope and local anaesthetic was checked with a gamma camera and the extent of hypo-aesthesia to a cold stimulus. He recommended that the catheter should be inserted toward the apex of the pleural space and the local anaesthetic should be administered with the patient supine to obtain the best pain relief in the chest.

Interpleural block for postoperative analgesia can be performed after induction of anaesthesia. If performed after induction, it will decrease intra-operative anaesthetic and analgesic requirements, and haemodynamic responses to surgery [46]. The block can also be easily performed at the end of surgery, with the patient still anaesthetised and either mechanically ventilated or breathing spontaneously after reversal of the neuromuscular block. This provides good quality analgesia with opioid sparing and without the inherent risk of neuraxial injury to an anaesthetised patient, a concern with an epidural.

Interpleural catheters are most commonly placed percutaneously through the needle, although they may also been placed during thoracotomy by the surgeon.

Reber and Scheidegger have suggested inserting an epidural catheter for interpleural block via a chest tube under direct visual guidance [47].

The position of the patient can be optimised to facilitate local anaesthetic spread and block appropriate neural structures to achieve desired clinical effects. If blockade of the upper sympathetic ganglia is desired, as in the treatment of CRPS [20] or ischaemia affecting the upper limb [48], then the patient should be positioned with the affected side uppermost and with a 20° head-down tilt to encourage cephalad spread in the paravertebral area. This position should be maintained for 30 min after injection to give the local anaesthetic time to penetrate the tissues. Reiestad et al. [20] reported pain relief, lack of sweating, increased hand temperature and ipsilateral Horner's syndrome with this positioning. As O'Leary et al. suggests, this position, apart from unilaterally blocking cervical and superior thoracic segments of the sympathetic chain, would also cause partial blockade of the ipsilateral brachial plexus as demonstrated by hypo-aesthesia in C3–T1 dermatomes and motor weakness of shoulder, arm and forearm [1]. Diffusion of local anaesthetic to the ipsilateral brachial plexus contributes to relief of these head and neck and upper extremity pain syndromes. Although there is a theoretical risk of affecting cardiac sympathetic nerves by encouraging cephalad spread within the pleural space, this has not been reported and cardiovascular stability is well maintained. For surgical anaesthesia for unilateral breast tumour resection, the lateral position on the affected side and a head-down tilt maintained for about 30 min should produce unilateral block of the T1–T9 dermatomes with complete skin anaesthesia. For managing postoperative pain and chest trauma, the lateral position with a 20° head-up tilt and the affected side uppermost during injection over 5–6 min should achieve a blockade of both the sympathetic chain and intercostal nerves of the affected side. The patient is turned supine after injection [1]. In our experience, we use a posterior approach for catheter placement and perform injections with the patient supine while moving the patient into head-up and head-down positions to obtain a somatic block of the T1–T12 dermatomes, providing good pain relief for gall bladder, kidney and breast surgery, including axillary node clearance.

Consent for the procedure should be obtained to the published standard [49]. The block should be performed in an appropriate area which offers privacy, good lighting and ensures sterility, and with oxygen, monitoring and resuscitation drugs and equipment readily available [50]. A trained anaesthetic assistant should be present, and full aseptic precautions observed.

The focus of many studies has been the provision of safe dosing regimens, which provide a balance of good quality and prolonged pain relief with acceptable plasma local anaesthetic concentrations. Reiestad and Strømskag [4] administered a single bolus of bupivacaine 0.5% with adrenaline 20 ml via an interpleural catheter at the end of breast surgery, renal surgery and cholecystectomy for the management of postoperative pain. Of the 81 patients studied, 78 required no additional analgesic measures during the first 24 h after surgery. The duration of analgesia ranged from 6 to 27 h, with a mean duration of about 10 h. However, other studies have shown only 3–6 h of analgesia from each bolus despite the use of larger doses of local anaesthetic than were originally described [27, 28, 51]. Table 1 lists some published dosage regimens.

Table 1 Volumes and concentrations of bupivacaine reported for use intrapleural analgesia.

Volume	Concentration	References
Single injections		
10 ml	0.25%	61*
10 ml	0.5%	62
0.4 ml.kg^{-1}	0.5%	56*
20 ml	0.25%	24, 28*, 52*, 63*
20 ml	0.375%	19, 52*, 57*, 64
20 ml	0.5%	4, 24, 26*,27*, 30*, 31*, 46, 52*, 54*, 65*, 66, 67*, 68*
30 ml	0.25%	69
30 ml	0.5%	70, 71*, 72, 73*
Infusions		
0.125 ml.kg^{-1}.h^{-1}	0.25%	56*
5 ml.h^{-1}	0.25%	29*, 63
5–10 ml.h^{-1}	0.25%	9*
6 ml.h^{-1}	0.375%	64
5 ml.h^{-1}	0.5%	29*

*With adrenaline 1 : 200 000.

As for concentration, bupivacaine 0.25% 20 ml would appear to be as effective in relieving pain after open cholecystectomy as equal volumes of bupivacaine 0.375% and 0.5%, although decreasing the dose decreases the duration of analgesia [52]. The median time from the interpleural injection of 20 ml of bupivacaine with adrenaline 1 : 200 000 0.25%, 0.375% and 0.5% to the administration of supplementary analgesia was reported to be 4 h 20 min, 6 h 0 min and 7 h 45 min, respectively. Higher interpleural doses of bupivacaine with adrenaline 1 : 100 000 0.5% 30 ml have been used, with blood levels remaining in a safe range in all but one patient, who was deemed to have had inflamed pleura from recent pneumonia and who rapidly developed symptoms of central nervous system toxicity [51]. Similar volumes of bupivacaine 0.75% have been found to produce high plasma drug concentrations and are not recommended [53]. When the literature is assessed with regards to the volume of local anaesthetic administered into the inter-

pleural space, boluses from 8 to 40 ml have been used with good analgesic effects. When bupivacaine 0.5% 20 ml was compared to 40 ml of a 0.25% solution, little difference was seen in terms of onset time, extent and duration of analgesia [54]. It is suggested that bolus doses of 30 ml of bupivacaine 0.5% are safe and effective when administered no more frequently than every 6 h [55].

As an alternative to single or intermittent local anaesthetic boluses, indwelling catheters may be used for continuous infusions, which are safe, effective and less labour-intensive. This has been found to produce better postoperative analgesia and plasma levels well below toxic levels in some studies [56, 57], although not all studies are in agreement with this. Laurito et al. [56] used an infusion of bupivacaine 0.25% at a rate of 0.125 $ml.kg^{-1}.h^{-1}$ and found that it provided better analgesia and significantly lower plasma concentrations after open cholecystectomy when compared to 6-hourly boluses of 0.4 $ml.kg^{-1}$ of bupivacaine 0.5% with 1 : 200 000 adrenaline. Van Kleef et al. [57] compared infusion regimes of 5 $ml.h^{-1}$ of bupivacaine 0.25% and 0.5%, both with 1 : 200 000 adrenaline, started after a loading dose of 21 ml of the same solution in patients who underwent surgery with unilateral flank incisions. They reported comparable analgesic efficacies in both, but a lower bupivacaine plasma concentration in the group that received the lower strength solution [29]. Strømskag and Kleiven [9] favour infusion over intermittent boluses, and for adults recommends a loading bolus of bupivacaine 0.5% with 1 : 200 000 adrenaline 20 ml followed by infusion of bupivacaine 0.25% with adrenaline at a rate of 5–10 $ml.h^{-1}$. Whilst most experience comes from the use of this technique in adults, infusions are also used by some centres with good effect in infants and children for analgesia after thoracic surgery [58, 59]. With regards to duration of catheter placement, there are reports of interpleural catheter use for 10 days in patients with multiple rib fractures [60], for 130 days in patient with cancer [23] and for 9 months in a patient with chronic pancreatitis [9]. Local anaesthetic rotation, similar to opioid rotation, alternating bupivacaine and ropivacaine, has been used to overcome the problem of tachyphylaxis [9].

References

1 O'Leary KA, Yarussi AT, Myers DP. Interpleural catheters. Indications and techniques. In: Waldman SD, ed. *Interventional Pain Management*, 2nd edn. W. B. Saunders 2001: 409–14.

2 Wallach HW. Interpleural therapy with tetracycline and lidocaine for malignant pleural effusion. *Chest* 1978; **73**: 246.

3 Kvalheim L, Reiestad F. Interpleural catheter in the management of postoperative pain. *Anesthesiology* 1984; **61**: A231.

4 Reiestad F, Strømskag KE. Interpleural catheter in the management of postoperative pain: a preliminary report. *Regional Anesthesia* 1986; **11**: 89–91.

5 Nunn JF, Slavin G. Posterior intercostal nerve block for pain relief after cholecystectomy. Anatomical basis and efficacy. *British Journal of Anaesthesia* 1980; **52**: 253–60.

6 O'Kelly E, Garry B. Continuous pain relief for multiple fractured ribs. *British Journal of Anaesthesia* 1981; **53**: 989–91.

7 Murphy DF. Continuous intercostal nerve blockade for pain relief after cholecystectomy. *British Journal of Anaesthesia* 1983; **55**: 521–4.

8 Murphy DF. Intercostal nerve blockade for fractured ribs and postoperative analgesia: description of a new technique. *Regional Anesthesia* 1983; **8**: 151–3.

9 Strømskag KE, Kleiven S. Continuous intercostal and interpleural nerve blockades. *Techniques in Regional Anesthesia and Pain Management* 1998; **2**: 79–89.

10 Miguel R, Smith R. Intrapleural not interpleural analgesia. *Regional Anesthesia* 1991; **16**: 299.

11 Armitage EN. *Thorax, Abdomen and Perineum*. In: Nimmo WS, Rowbotham DJ, Smith G, eds. *Anaesthesia*, 2nd edn., Oxford: Blackwell Scientific, 1994: 1510–2.

12 Baumgarten RK. Intrapleural, interpleural or or pleural block? Simpler may be better. *Regional Anesthesia* 1992; **17**: 116.

13 Hardy PA. Anatomical variation in the position of the proximal intercostal nerve. *British Journal of Anaesthesia* 1988; **61**: 338–9.

14 McKenzie AG, Mathe S. Interpleural local anaesthesia. anatomical basis for mechanism of action. *British Journal of Anaesthesia* 1996; **76**: 297–9.

15 Murphy DF. Continuous intercostal nerve blockade: An anatomic study to elucidate its mode of action. *British Journal of Anaesthesia* 1984; **56**: 627–30.

16 Mowbray A, Wong KKS, Murray JM. Intercostal catheterisation: An alternative approach to the paravertebral space. *Anaesthesia* 1987; **42**: 958–61.

17 Reigler FX, Pelligrino DA, VadeBoncouer TR. An animal model of intrapleural analgesia. *Anesthesiology* 1988; **69**: A365.

18 Riegler FX, VadeBoncouer TR, Pelligrino DA. Interpleural anesthetics in the dog: Differential somatic neural blockade. *Anesthesiology* 1989; **71**: 744–50.

19 Strømskag KE, Hauge O, Steen PA. Distribution of local anesthetics injected into the interpleural space, studied by computerized tomography. *Acta Anaesthesiologica Scandinavica* 1990; **34**: 323–6.

20 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.

21 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.

22 Durrani Z, Winnie AP, Ikuta P. Interpleural catheter analgesia for pancreatic pain. *Anesthesia and Analgesia* 1988; **67**: 479–81.

23 McIlvaine WB. Intrapleural anesthesia is useful for thoracic analgesia. *Journal of Cardiothoracic and Vascular Anesthesia* 1996; **10**: 425–8.

24 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.
25 Frenette L, Boudreault D, Guay J. Interpleural analgesia improves pulmonary function after cholecystectomy. *Canadian Journal of Anaesthesia* 1991; **38**: 71–4.
26 Kastrissios H, Mogg GAG, Triggs EJ, Higbie JW. Interpleural bupivacaine infusion compared with intravenous pethidine infusion after cholecystectomy. *Anaesthesia and Intensive Care* 1991; **19**: 539–45.
27 VadeBoncouer TR, Riegler FX, Gautt 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.
28 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.
29 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.
30 Gallart L, Gea J, Aguar C, et al. Effects of interpleural bupivacaine on respiratory muscle strength and pulmonary function. *Anesthesiology* 1995; **83**: 48–55.
31 Oxorn DC, Whatley GS. Post-cholecystectomy pulmonary function following interpleural bupivacaine and intramuscular pethidine. *Anaesthesia and Intensive Care* 1989; **17**: 440–3.
32 Ballantyne JC, Carr DB, deFerranti S, et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomised, controlled trails. *Anesthesia and Analgesia* 1998; **86**: 598–612.
33 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.
34 Kopacz DJ, Thompson GE. Celiac and hypogastric plexus, intecostal, 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.
35 Kawamata M, Omote K, Namiki A, Miyabe M. Measurement of intercostal and pleural pressures by epidural catheter. *Anaesthesia* 1994; **49**: 208–10.
36 Weston S, Clark I. Intrapleural catheter placement. *Anaesthesia and Intensive Care* 1990; **18**: 140.
37 McDonald PF. The use of a collapsing balloon to identify the interpleural space. *Anaesthesia and Intensive Care* 1992; **20**: 393–4.
38 Ben-David B, Lee E. The falling column: a new technique for interpleural catheter placement. *Anesthesia and Analgesia* 1990; **71**: 212.
39 Lee E, Ben-David B. Identification of the interpleural space. *British Journal of Anaesthesia* 1991; **67**: 130.
40 Squier RC, Morrow JS, Roman R. Hanging drop technique for intrapleural analgesia. *Anesthesiology* 1989; **70**: 882.
41 Scott PV. Interpleural regional analgesia: Detection of the interpleural space by saline infusion. *British Journal of Anaesthesia* 1991; **66**: 131–3.
42 Nalwaya P, Dravid R. 'Continuous saline flow technique' prevents air entrainment during intrapleural block. *Anaesthesia* 2003; **58**: 92–3.
43 Gomar C, De Andres J, Caltrava P, et al. An electronic device (Episensor) for detection of the interpleural space. *Regional Anesthesia* 1991; **16**: 112–5.
44 Iwama H. Catheter location and patient position affect spread of interpleural regional analgesia. *Anesthesiology* 1993; **79**: 1153–4.
45 Baxter AD, Jennings FO, Harris RS, Flynn JF, Way J. Continuous intercostal blockade after cardiac surgery. *British Journal of Anaesthesia* 1987; **59**: 162–6.
46 Abdulatif M, Al-Ghamdi A, Adu Gyamfi Y, et al. Can preemptive interpleural block reduce perioperative anesthetic and analgesic requirements? *Regional Anesthesia* 1995; **20**: 296–302.
47 Reber A, Scheidegger D. An alternative technique for interpleural analgesia. *Anesthesiology*; 1998; **88**: 553–4.
48 Perkins G. Interpleural anaesthesia in the management of upper limb ischaemia. A report of three cases. *Anaesthesia and Intensive Care* 1991; **19**: 575–8.
49 Association of Anaesthetists of Great Britain and Ireland. *Consent for anaesthesia*, January. London: AAGBI, 2006.
50 Association of Anaesthetists of Great Britain and Ireland. *Recommendations for Standards of Monitoring during Anaesthesia and Recovery*, December. London: AAGBI, 2000.
51 Seltzer JL, Larijani GE, Goldberg ME, et al. Interpleural bupivacaine-a kinetic and dynamic evaluation. *Anesthesiology* 1987; **67**: 798–800.
52 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.
53 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.
54 Strømskag KE, Minor BG, Lindeberg A. Comparison of 40 milliliters of 0.25% intrapleural bupivacaine with epinephrine with 20 milliliters of 0.5% intrapleural bupivacaine with epinephrine after cholecystectomy. *Anesthesia and Analgesia* 1991; **73**: 397–400.
55 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.
56 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.
57 Aguilar JL, Montes A, Montero A, Vidal F, Llamazares JF, Pastor C. Continuous pleural infusion of bupivacaine offers

better postoperative pain relief than does bolus administration. *Regional Anesthesia* 1992; **17**: 12–4.
58 Giaufre E, Bruguerolle B, Rastello C, et al. New regimen for interpleural block in children. *Paediatric Anaesthesia* 1995; **5**: 125–8.
59 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.
60 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.
61 Tartiere J, Samba D, Lefrancois C, et al. Intrapleural bupivacaine after thoraco-abdominal incision for oesophagectomy. *European Journal of Anaesthesiology* 1991; **8**: 145–9.
62 Lieou FJ, Lee SC, Ho ST, Wang JJ. Interpleural bupivacaine for pain relief after transthoracic endoscopic sympathectomy for primary hyperhydrosis. *Acta Anaesthesiologica Sinica* 1996; **34**: 21–5.
63 Higgins PC, Ravalia A. Interpleural anaesthesia for mastectomy. *Anaesthesia* 2005; **60**: 1150–1.
64 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.
65 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.
66 Silomon M, Claus T, Hanno H, et al. Interpleural analgesia does not influence post-thoracotomy pain. *Anesthesia and Analgesia* 2000; **91**: 44–50.
67 Reiestad F, Kvalheim L, McIlvaine WB. Pleural analgesia for the treatment of acute severe thoracic herpes zoster. *Regional Anesthesia* 1989; **14**: 244–6.
68 Engdahl O, Boe J, Sandstedt S. Interpleural bupivacaine for analgesia during chest drainage treatment for pneumothorax. A randomized double-blind study. *Acta Anaesthesiologica Scandinavica* 1993; **37**: 149–53.
69 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.
70 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.
71 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.
72 Sihota MK, Holmblad BR. Horner's syndrome after intrapleural anesthesia with bupivacaine for post-herpetic neuralgia. *Acta Anaesthesiologica Scandinavica* 1988; **32**: 593–4.
73 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.

Anaesthesia, 2007, **62**, pages 1143–1153 doi:10.1111/j.1365-2044.2007.05181.x

REVIEW ARTICLE

Interpleural block – part 2

R. M. Dravid[1] and R. E. Paul[2]

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]	
	Postoperative thoracic cancer pain [69]	Chronic pancreatic pain [75–79]
	Chest wall and thoracic visceral pain [69]	Upper abdominal cancer pain [71, 73, 78]
	Chronic oesophageal cancer pain [71]	Extracorporeal shock wave lithotripsy [12, 33]
	Benign chest wall pain [70, 110]	Percutaneous nephrostomy and nephrolithotomy [35]
	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 $ml.kg^{-1}.h^{-1}$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 $ml.kg^{-1}.h^{-1}$[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.

Absolute
Patient refusal
Allergy to local anaesthetic agent
Extensive infection at block or catheter insertion site
Relative
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 contra-indicated [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. Strømskag 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 $mg.ml^{-1}$, 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 $\mu g.ml^{-1}$ and 3.0 $\mu g.ml^{-1}$. 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]. Strømskag 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) $\mu g.ml^{-1}$, 0.82 (0.4) $\mu g.ml^{-1}$ and 1.2 (0.44) $\mu g.ml^{-1}$, 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 $\mu g.ml^{-1}$ and 5.2 $\mu g.ml^{-1}$. 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 $\mu g.ml^{-1}$. 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) $\mu g.ml^{-1}$ [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 $\mu g.ml^{-1}$ [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 $ml.h^{-1}$. 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 α1-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 adrenoreceptor 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, functional 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, Gautt 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 Perianesthesia 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, Radhakrishanan 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, Mcllvaine 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 Mcllvaine 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 Mcllvaine 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 hyperhydrosis. *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, Llaxnazares 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 Czop 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 Strømskag 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, Larijani 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. Intrabronchial 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, intecostal, 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. Interpleural 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.